

# Effect of combined caries-preventive methods: a systematic review of controlled clinical trials

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The aim of this systematic review was to evaluate the caries-preventive effect of combined caries-preventive methods, defined as two or more different interventions in combination, each expected to prevent dental caries. The Medline database was searched for articles published in the period January 1966 to June 2003. Twenty-four controlled studies met the inclusion criteria, and their value as evidence was assessed according to predetermined criteria. The level of evidence for the overall conclusion regarding each method was graded according to the protocol of the Swedish Council on Technology Assessment in Health Care. The scientific evidence for the combination of treatments involving fluoride that had a preventive effect on caries in children and adolescents was graded as moderate. However, for elderly patients the scientific evidence for the caries-preventive effect of different combinations of treatments was found to be incomplete. No conclusion could be drawn regarding the evidence for combinations of treatments being effective for groups at high caries risk, as the results from the identified clinical studies were conflicting. □ *Caries risk; dental caries; intervention programs; prevention*

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The prevalence of dental caries has decreased considerably among children and young adults in most industrialized countries during recent decades. However, it is still a common disease even in young children (1), and in many developing countries the general trend is that dental caries prevalence is increasing (2).

Intervention programs using a combination of various methods for caries prevention, aimed at both children and adolescents, have been initiated in many industrialized countries. Examples of these programs are plentiful, e.g. child health centers offering special information sessions for parents where dental staff provide information about tooth-brushing, good dietary habits, and use of fluoride; dental nurses receiving special training in order to educate and instruct children and parents about oral hygiene, and to give local fluoride treatment, for example rinsing with fluoride or topical application of fluoride. Effective and controlled ways of removing bacterial plaque from tooth surfaces using professional tooth cleaning by dental staff or supervised tooth-brushing have also been important components in promoting oral health. Strategies such as fissure sealants or topical application of chlorhexidine have sometimes been used in combination with other caries-

preventive methods. However, to our knowledge, no systematic evaluation has been published of the available evidence for preventing caries using combinations of interventions.

The aim of the present systematic literature review was to evaluate the scientific evidence for the effect of combinations of methods used for caries control. The review is one in a series of systematic reviews of methods for caries prevention carried out by the Swedish Council on Technology Assessment in Health Care (3).

## Methods

### *Search strategies for identification of studies*

The Medline database was searched from 1966 to November 2001, and subsequently updated in June 2003, in cooperation with an information specialist at the Swedish Council on Technology Assessment in Health Care. Primary search strategy included the MeSH terms 'dental caries', 'clinical trial', 'oral hygiene', 'health promotion', and 'patient education'.

Table 1. Excluded studies and the main reason for their exclusion

Reason	Reference no.
Large attrition rate	(29–33)
Later results available	(34, 35)
Risk assessment	(36)

### Inclusion of studies

The studies that were included had to have been investigations of the caries-preventive effect of a combination of caries-preventive methods, i.e. two or more different interventions in combination, each expected to prevent caries to some degree. The control treatment had to be standard care, no treatment, or use of a placebo to replace active components. Some studies compared the test treatment to standard care, defined as oral hygiene instructions, fluoridated toothpaste for unsupervised use or fluoride rinsing every second week. Studies comparing different combinations of interventions without the use of one of the above-mentioned control groups were excluded. All studies had to be prospective. The follow-up period had to be at least 2 years—with the exception of studies on primary teeth—and primary endpoint was caries increment in the primary ( $\Delta dmfs/t$ ) or permanent ( $\Delta DMFS/T$ ) dentition.

Animal studies and experimental studies were excluded, as were abstracts, letters, short communications, and textbooks. Articles published in languages other than English, Swedish, Danish, Norwegian, Spanish, French, Italian, or German were excluded.

The preliminary search resulted in retrieval of 229 scientific articles which were evaluated for inclusion by two of the authors of this review. If it was not clear from the

Table 3. Definition of evidence level for conclusions

Evidence level	Definition
1 Strong evidence	At least 2 studies assessed grade A
2 Moderate evidence	One grade A study and at least 2 grade B studies
3 Limited evidence	At least 2 studies graded B
4 Incomplete evidence	Fewer than 2 studies graded B

abstract whether the article met the inclusion criteria, it was ordered in full text. A total of 104 papers were thus selected and subsequently ordered in full text. The reference lists of the retrieved articles were hand-searched for additional relevant studies that might not have appeared through the database search. An additional 31 articles—the result of the hand search—were ordered in full text. Thirty-two studies fulfilled the final criteria for inclusion, and, of these, 8 were excluded from the final assessment process for specific reasons (listed in Table 1).

### Evaluation of papers and levels of evidence

The 2 examiners read the 24 papers independently. The external and internal validity of each study, i.e. their value as evidence, was assessed and the studies were graded with a score of A (high value as evidence), B (moderate value as evidence), or C (limited value as evidence) according to predetermined criteria (Table 2). If the examiner evaluations differed, the paper was discussed with the other members of the review group until consensus was reached. Only studies with high or moderate value as evidence were then used for assessing the scientific evidence for each method, according to the protocol of the Swedish Council on Technology Assessment in Health Care (Table 3).

Table 2. Criteria for grading the papers. For grade A, all criteria had to be fulfilled. Papers were rated grade B or C when at least one of the criteria was met

Grade A	Grade B	Grade C
RCT, randomization described and by subject; $\geq 3$ -year duration	RCT, duration between 2 and 3 years	RCT, randomization unclear or not described; CCT; duration between 2 and 3 years
Study group representative, inclusion criteria described	Large CCT	Small, single-blind study
Double-blind or independent operators	Double- or single-blind	Attrition rate $>10\%$ per year, not explained
Attrition rate $<10\%$ per year and explained	Attrition rate $<$ or $\approx 10\%$ per year, not explained	Methods for caries diagnosis not fully described, several examiners, non-calibrated
Methods for clinical caries diagnosis defined, (clinical/radiographs/fiber optic transillumination) with reliability tests, calibrated examiners	Methods for caries diagnosis not completely described or validated	Baseline values omitted
Baseline values presented	Minor bias or confounders evident or likely	Major bias or confounders evident or likely
Apparent bias or confounders taken into account		

RCT = randomized controlled trial, CCT = controlled clinical trial.

Table 4. Studies on prevention programs

First author, year	Design	Intervention test	Intervention control	No. of subjects	Age (years)	Drop-outs (%)	Follow-up (years)	Effect % caries reduction	Value as evidence
Maltz, 2003 (15)	CCT	Individual prevention program 2x/yr, OH instr, TB F gel	No intervention	201	5-6	28	2	54%	C
Ekstrand, 2000 (8)	CCT	OH instr, TB F TP, PTC +F, fissure sealant (comb) Individual intervals	No intervention	290	3, 6, 11	2 ind	2.5	43% (3 yrs), 89% (6 yrs) 51% (11 yrs)	B
Arrow, 1998 (5)	CCT	PTC +F, OH instr Individual intervals	Standard care	404	6	17	2	NS	B
Axelsson, 1994 (4)	RCT	OH instr, F TP, motivation, control every 3rd month	C 1 OH instr, F TB, C 2 F TP	222	12-13	16	3	50% reduction approx. compared to C 1, C 2	A
Lalloo, 1994 (14)	CCT	Supervised TB, F TP every schoolday, fissure sealant	No intervention	ca 407	4-5	48	7	68%	C
Stephen, 1990 (17)	CCT	F rinsing 2x/month F tabl 1x/d,	C 1 F tabl 1x/d, C 2 F rinsing 12x/yr	192	4.5-5	38	6	NS	C
Klimek, 1985 (10)	CCT	OH instr, supervised TB and flossing 5x/yr, F varnish 2x/yr, F TP	No intervention	282	12-13	22	2	46%	B
Pettersson, 1985 (11)	CCT	OH instr, F TP 2x/d, F tabl 2x/d, F varnish 2x/yr comb with placebo products	No intervention	376	3	5	2	NS	B
Zickert, 1982 (12)	RCT	OH instr, PTC, F rinsing, F tabl in comb with placebo products every month or 3rd month	No intervention	290	13-14	10	2	40-46% for F-containing programs	B
Melsen, 1980 (16)	CCT	OH instr, F rinsing 2x/month	F rinsing 2x/month	164	11-13	MD	2	NS	C
Bagramian, 1978 (6)	RCT	OH instr, dietary advice, F gel 2x/yr, fissure sealant	OH instr, dietary advice	1200	6, 11	23	3	67% (6 yrs, molars) 58% (11 yrs)	B
Hamp, 1978 (9)	CCT	OH instr, PTC +F, F rinsing every 3rd week	F rinsing 2x/month	406	10-11	32	3	51%	B
Fischman, 1977 (13)	CCT	F appl 1x/yr, fissure sealant, OH instr (comb)	No intervention	1504	11	MD	3	13-15%	C
Downer, 1976 (7)	CCT	Supervised TB, F TP daily, PTC +F 3x/yr	Placebo	551	11-12	12	3	31%	B

A/B/C = high/moderate/limited value as evidence, approx = approximal surfaces, C 1, 2 = control group 1, 2, CCT = clinical controlled trial, comb = combination of interventions in different test groups, F = fluoride, MD = missing data, NS = no statistically significant difference, OH = oral hygiene, PTC = professional tooth cleaning, PTC +F = professional tooth cleaning with fluoride paste, RCT = randomized controlled trial, TB = tooth brushing, TP = toothpaste, perm = permanent dentition.

Table 5. Elderly patients

First author, year	Design	Intervention test	Intervention control	No. of subjects	Age (years)	Drop-outs %	Follow-up (years)	Effect % caries reduction	Value as evidence
Powell, 1999 (20)	RCT	Info, CHX rinsing 1x/week, varnish 2x/yr, SRP 2x/yr (comb)	Standard care	297	≥60	32	3	NS	C
Fure, 1998 (18)	RCT	OH instr, F TP 3x/d or F tabl 2x/d or F rinsing 2x/d	OH instruction	176	≥60	7	2	17-65% for F-containing programs	B
Mojon, 1998 (19)	CCT	Info to personnel, F TP, PTC ≥ 2x/yr	No intervention	116	≥65	32	1.5	55% secondary caries 16% root caries	C

A/B/C = high/moderate/limited value as evidence, CCT = clinical controlled trial, CHX = chlorhexidine, comb = combination of interventions in different test groups, F = fluoride, NS = no statistically significant difference, OH = oral hygiene, PTC = professional tooth cleaning, RCT = randomized controlled trial, SRP = scaling and root planning, TP = toothpaste.

## Results

### *Combined prevention methods for children and adolescents*

Of the 14 studies included concerning treatment for children and adolescents, 1 was graded as high-value evidence (4), 8 were assessed as moderate-value evidence (5-12), and 5 as limited-value evidence (13-17) (Table 4).

Seven studies of high-value or moderate-value evidence showed a statistically significant beneficial effect on caries increment. Combined prevention methods described by Axelsson et al. (4), Bagramian et al. (6), Ekstrand et al. (8), Hamp et al. (9), and Klimek et al. (10) used fluoride products along with either hygiene instructions or supervised brushing and were more effective in preventing caries than control treatment. Studies by Downer et al. (7) and Zickert et al. (12) also found the combination of professional tooth-cleaning with fluoride containing products and supervised daily tooth-brushing or oral hygiene instructions to be superior in preventing caries compared to the same treatment with placebo products. The studies by Fischman et al. (13), Laloo & Solanki (14), and Maltz et al. (15) supported these results, although these were graded as limited-value evidence.

Contrary to these results, Petersson et al. (11) showed no changes in treatment effect on 3-year-old children between different combinations of fluoridated and placebo products, tablets, toothpaste, and varnish. No additional effect of a combination of professional tooth-cleaning with fluoridated toothpaste and oral hygiene instructions for preschool children was found by Arrow (5), compared to what was described as standard care. The children in the control group were selectively treated with fissure sealants, and the study was conducted in an area with artificially fluoridated water.

Two of the identified studies compared a combination of fluoride rinsing and oral hygiene instructions or daily intake of fluoride tablets, respectively, with only fluoride-rinsing (16, 17). Melsen & Agerbaek (16) found no difference between a combination of fluoride-rinsing twice per month and oral hygiene instructions compared to only fluoride-rinsing in 11-year-old schoolchildren. There was no information on the drop-out rate, so the value as evidence for this study was limited. A similar study by Stephen et al. (17) showed no difference in caries increment between two groups rinsing with fluoride when the test group was also given fluoride tablets daily. The drop-out rate was high (38%), and the study was graded as limited-value evidence.

### *Combined prevention methods for elderly patients*

There are only a few studies regarding combinations of caries-preventive interventions for aging and elderly patients. Three studies were identified concerning this group of patients, one with moderate-value evidence (18) and two with limited-value evidence (19, 20) (Table 5).

Fure et al. (18) found that home-care programs

Table 6. Risk patients

First author, year	Design	Intervention test	Intervention control	No. of subjects	Age (years)	Drop-outs %	Follow-up (years)	Effect % caries reduction	Value as evidence
Zimmer, 2001 (24)	CCT	PTC +F varnish 4x/yr, OH instr	OH instr	419	9-10	24	2	NS (D3)	B
Hausen, 2000 (22)	RCT	OH instr, F toothpaste daily, F varnish 2x/yr, dietary advice, CHX gel, Xyl gum, fissure sealant	Same as test group without CHX gel	760	12	23	3	NS	B
Seppä, 1991 (26)	RCT	Intensive preventive treatment by ordinary dentist	Ordinary treatment for risk patients	513	13	9	2	NS	C
Rask, 1988 (25)	RCT	Dietary advice, F treatment, CHX gel	OH instr, F varnish dietary advice	124	50-60	21	5	89% (1 yr)	C
Gisselsson, 1983 (21)	CCT	PTC +F and F rinsing 1x/week	F rinsing 1x/week	74 at end	10-11	15	2	NS (5 yr)	B
Kerebel, 1985 (23)	CCT	Daily supervised TB	No intervention	244	7-8	19	3	68% 60% (perm)	B
Zickert, 1982 (27)	CCT	F tooth paste, PTC +F-gel 5x/yr CHX gel, fissure sealant	No intervention	101	13-14	10	3	81% (highest ms score)	C

A/B/C = high/moderate/limited value as evidence, CCT = clinical controlled trial, CHX = chlorhexidine, D3 = established carious lesions, F = fluoride, ms = mutans streptococci, NS = no statistically significant difference, perm = permanent dentition, PTC +F = professional tooth cleaning with fluoride paste, RCT = randomized controlled trial, SRP = scaling and root planing, Xyl gum = xylitol chewing gum.

including fluoride toothpaste, tablets or rinsing, reduced caries increment on coronal and root surfaces compared to oral hygiene instructions alone. On the contrary, Powell et al. (20) observed no difference in caries increment in patients over 60 years of age who participated in prevention programs compared to ordinary treatment. The programs used different combinations of topical application of fluoride varnish, chlorhexidine rinsing, and education as well as scaling and root planing.

Mojon et al. (19) found that if information about caries-preventive measures was given to the personnel, fewer secondary and root caries lesions developed in aging patients living in an assisted-living facility. The information was combined with professional tooth-cleaning with fluoridated toothpaste. However, confounding dental treatment performed during the study and a high drop-out rate weakened the evidence for the investigated combinations of treatments.

*Combined prevention methods for risk patients*

Combined interventions for preventing caries in patients with high numbers of mutans streptococci or with previous carious lesions have not been extensively studied. Seven studies were identified for this systematic review, 4 with moderate-value evidence (21-24) and 3 with limited-value evidence (25-27) (Table 6).

In a Swedish study by Gisselsson et al. (21), a regular supply of fluoride and professional tooth-cleaning had a restraining effect on the development of caries in 10 to 12-year-old risk patients. These findings were supported by Kerebel et al. (23) in a study of French children with poor oral hygiene.

The combination of regular treatment with chlorhexidine gel in a gel-tray and fissure sealing for children with high numbers of mutans streptococci was shown by Zickert et al. (27) to have a better effect than standard preventive care. In a follow-up study 2 years after discontinuation of the special preventive program, however, caries activity was shown to be similar in the control and test groups (28). For older risk patients, 50-60 years, Rask et al. (25) found a short-term additional beneficial effect on caries increment for chlorhexidine gel, used in combination with dietary advice and fluoride treatment. However, after 5 years, no significant difference could be detected between the groups.

In a similar study by Hausen et al. (22), no additional effect of chlorhexidine in gel-trays in combination with fluoride treatment, dietary advice, xylitol chewing-gum, and fissure sealants was shown. Neither did professional tooth-cleaning combined with the application of fluoride varnish and oral hygiene information have a better effect in preventing caries than hygiene instructions alone in a study by Zimmer et al. (24). In addition, the results of an intensified prevention strategy on risk patients were no better than those obtained with ordinary prevention methods in a study by Seppä et al. (26).

## Discussion

Many studies investigating the effect of combined caries-preventive methods were undertaken when the caries situation was different from what it is today in most Western countries. Even though there are groups of patients with a caries situation similar to that in the 1960s, the contemporary social and environmental factors are different, and the prevention strategies that worked well 20 or 30 years ago may not have the same effect today. This makes it difficult to evaluate the relevance of the results, and the level of evidence for older studies.

Research in the field of population-based prophylactic interventions for caries prevention presents many difficulties. The complexity of, for example, managing large patient materials for several years and calibrating co-workers for diagnostics, treatment procedures, and data collection is challenging. Clinical research thus seldom produces strong evidence and definite answers to all clinical questions, and clinicians must learn to live with uncertainty in regard to many interventions. It is also important to realize that even if the clinical evidence for a treatment method is weak or lacking, the method is not necessarily ineffective and not to be used. Nevertheless, the best possible evidence on what method or combination of methods for preventing caries is the safest, most efficient, and most cost-effective in the long term is needed. It is also important to extend our knowledge of how to treat risk groups, for example, persons with high caries activity, elderly patients in institutions, and diseased and disabled people.

In conclusion, this systematic review provides moderate scientific evidence that combinations of treatments involving fluoride have a preventive effect on caries in children and adolescents (Evidence level 2; see Table 2). However, for elderly patients the scientific evidence for the caries-preventive effect regarding combinations of treatments was found to be incomplete (Evidence level 4; see Table 2). No conclusion can be drawn regarding the evidence for combinations of treatments being effective for groups at high caries risk, as the results from the identified clinical studies are conflicting.

## References

- Stecksén-Blicks C, Sunnegårdh K, Borssén E. Caries experience and background factors in 4-year-old children: time trends 1967–2002. *Caries Res* 2004;38:149.
- Nithila A, Bourgeois D, Barmes DE, Murtomaa H. WHO Global Oral Data Bank, 1986–96: an overview of oral health surveys at 12 years of age. *Bull World Health Organ* 1998;76:237–44.
- SBU-rapport2002. p. 161 Att förebygga karies. En systematisk litteraturoversikt.
- Axelsson P, Buischi YA, Barbosa MF, Karlsson R, Prado MC. The effect of a new oral hygiene training program on approximal caries in 12–15-year-old Brazilian children: results after three years. *Adv Dent Res* 1994;8:278–84.
- Arrow P. Oral hygiene in the control of occlusal caries. *Community Dent Oral Epidemiol* 1998;26:324–30.
- Bagramian RA, Graves RC, Srivastava S. A combined approach to preventing dental caries in schoolchildren: caries reductions after 3 years. *Community Dent Oral Epidemiol* 1978;6:166–71.
- Downer MC, Holloway PJ, Davies TG. Clinical testing of a topical fluoride caries preventive programme. *Br Dent J* 1976;141:242–7.
- Ekstrand KR, Kuzmina IN, Kuzmina E, Christiansen ME. Two-and-a-half-year outcome of caries-preventive programs offered to groups of children in the Solntsevsky district of Moscow. *Caries Res* 2000;34:8–19.
- Hamp SE, Lindhe J, Fornell J, Johansson LA, Karlsson R. Effect of a field program based on systematic plaque control on caries and gingivitis in schoolchildren after 3 years. *Community Dent Oral Epidemiol* 1978;6:17–23.
- Klimek J, Prinz H, Hellwig E, Ahrens G. Effect of a preventive program based on professional toothcleaning and fluoride application on caries and gingivitis. *Community Dent Oral Epidemiol* 1985;13:295–8.
- Pettersson LG, Koch G, Rasmusson CG, Stanke H. Effect on caries of different fluoride prophylactic programs in preschool children. A two-year clinical study. *Swed Dent J* 1985;9:97–104.
- Zickert I, Lindvall AM, Axelsson P. Effect on caries and gingivitis of a preventive program based on oral hygiene measures and fluoride application. *Community Dent Oral Epidemiol* 1982;10:289–95.
- Fischman SL, English JA, Albino JE, Bissell GD, Greenberg JS, Juliano DB, et al. A comprehensive caries control program—design and evaluation of the clinical trial. *J Dent Res* 1977;56 Spec No:C99–103.
- Laloo R, Solanki GS. An evaluation of a school-based comprehensive public oral health care programme. *Community Dent Health* 1994;11:152–5.
- Maltz M, Barbachan e Silva B, Carvalho DQ, Volkweis A. Results after two years of non-operative treatment of occlusal surface in children with high caries prevalence. *Braz Dent J* 2003;14:48–54.
- Melsen B, Agerbaek N. Effect of an instructional motivation program on oral health in Danish adolescents after 1 and 2 years. *Community Dent Oral Epidemiol* 1980;8:72–8.
- Stephen KW, Kay EJ, Tullis JI. Combined fluoride therapies. A 6-year double-blind school-based preventive dentistry study in Inverness, Scotland. *Community Dent Oral Epidemiol* 1990;18:244–8.
- Fure S, Gahnberg L, Birkhed D. A comparison of four home-care fluoride programs on the caries incidence in the elderly. *Gerodontology* 1998;15:51–60.
- Mojon P, Rentsch A, Budtz-Jørgensen E, Baehni PC. Effects of an oral health program on selected clinical parameters and salivary bacteria in a long-term care facility. *Eur J Oral Sci* 1998;106:827–34.
- Powell LV, Persson RE, Kiyak HA, Hujuel PP. Caries prevention in a community-dwelling older population. *Caries Res* 1999;33:333–9.
- Gisselsson H, Björn AL, Birkhed D. Immediate and prolonged effect of individual preventive measures in caries and gingivitis susceptible children. *Swed Dent J* 1983;7:13–21.
- Hausen H, Kärkkäinen S, Seppä L. Application of the high-risk strategy to control dental caries. *Community Dent Oral Epidemiol* 2000;28:26–34.
- Kerebel LM, Le Cabellec MT, Daculsi G, Kerebel B. Report on caries reduction in French schoolchildren 3 years after the introduction of a preventive program. *Community Dent Oral Epidemiol* 1985;13:201–4.
- Zimmer S, Bizhang M, Seemann R, Witzke S, Roulet JF. The effect of a preventive program, including the application of low-concentration fluoride varnish, on caries control in high-risk children. *Clin Oral Invest* 2001;5:40–4.
- Rask PI, Emilson CG, Krasse B, Sundberg H. Effect of

- preventive measures in 50–60-year-olds with a high risk of dental caries. *Scand J Dent Res* 1988;96:500–4.
26. Seppä L, Hausen H, Pöllänen L, Kärkkäinen S, Helasharju K. Effect of intensified caries prevention on approximal caries in adolescents with high caries risk. *Caries Res* 1991;25:392–5.
  27. Zickert I, Emilson CG, Krasse B. Effect of caries preventive measures in children highly infected with the bacterium *Streptococcus mutans*. *Arch Oral Biol* 1982;27:861–8.
  28. Zickert I, Emilson CG, Krasse B. Microbial conditions and caries increment 2 years after discontinuation of controlled antimicrobial measures in Swedish teenagers. *Community Dent Oral Epidemiol* 1987;15:241–4.
  29. Bagramian RA. A 5-year school-based comprehensive preventive program in Michigan, U.S.A. *Community Dent Oral Epidemiol* 1982;10:234–7.
  30. Croft LK. The effectiveness of the toothkeeper program after six years. *Tex Dent J* 1980;98:6–8.
  31. Klein SP, Bohannon HM, Bell RM, Disney JA, Foch CB, Graves RC. The cost and effectiveness of school-based preventive dental care. *Am J Public Health* 1985;75:382–91.
  32. Louw AJ, Carstens IL, Hartshorne JE, Blignaut RJ. Effectiveness of two school-based caries preventive programmes. *J Dent Assoc S Afr* 1995;50:43–9.
  33. McKee DP, Faine RC, Murphy RF. The effectiveness of a dental health education program in a nonfluoridated community. *J Public Health Dent* 1977;37:290–9.
  34. Axelsson P, Lindhe J. Effect of fluoride on gingivitis and dental caries in a preventive program based on plaque control. *Community Dent Oral Epidemiol* 1975;3:156–60.
  35. Bagramian RA, Graves RC, Bhat M. A combined approach to preventing dental caries in schoolchildren: caries reductions after one year. *J Am Dent Assoc* 1976;93:1014–9.
  36. Mattila ML, Paunio P, Rautava P, Ojanlatva A, Sillanpää M. Changes in dental health and dental health habits from 3 to 5 years of age. *J Public Health Dent* 1998;58:270–4.

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