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Fluoride toothpastes and fluoride mouthrinses for home use

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Corresponding author: Andrew Rugg-Gunn Morven, Boughmore Road Sidmouth, Devon EX10 8SH UK <i>andrew@rugg-gunn.net</i> Tel.: + 44 1395578746	purchased by the individual. By the 1960s, research indicated that fluoride could be successfully incorporated into toothpastes and clini- cal trials demonstrated their effectiveness. By the end of the 1970s, almost all toothpastes contained fluoride. The widespread use of fluo- ride-containing toothpastes is thought to be the main reason for much improved oral health in many countries. Of the many fluoride com- pounds investigated, sodium fluoride, with a compatible abrasive, is the most popular, although amine fluorides are used widely in Europe. The situation is similar for mouthrinses. Concentrations of fluoride (E) commonly found are 1500 ppm (1500 ug E/g) for toothpastes and
Received: 15 April 2013 Accepted: 13 May 2013	225 ppm (225 μ g F/ml) for mouthrinse. Several systematic reviews have concluded that fluoride-containing toothpastes and mouthrinses are effective, and that there is added benefit from their use with other fluoride delivery methods such as water fluoridation. Guidelines for the appropriate use of fluoride toothpastes and mouthrinses are avail- able in many countries. Conclusion. Fluoride toothpastes and mouth-
Copyright © 2013 by	rinses have been developed and extensive testing has demonstrated
Academy of Sciences and Arts	that they are effective and their use should be encouraged.
of Bosnia and Herzegovina.	
E-mail for permission to publish:	Key words: Toothpaste, Mouthrinse, Fluoride, Dental caries preven-
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Introduction

An oft-quoted observation is that increasing consumption of sugar has been responsible for the rise in dental caries experienced by much of the world, while the fall in dental caries observed in many countries has been due to the use of fluoride. This epidemic of dental decay and its partial cure was discussed more fully in an earlier article in this issue of the Journal (1). In the UK, the first

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signs of improving dental health became evident in the late 1970s (2, 3). Surveys in other countries recorded similar improvements, and a conference was convened in Boston, USA in 1982, to explore possible reasons for this unexpected occurrence (4). The summary of the report included the following: "All 16 speakers agreed that the prevalence of dental caries has declined substantially in several countries represented in areas both with and without organised preventive programmes or fluoridation. Most agreed that fluoride in toothpastes, rinses and community water supplies provides the best single association and that there were many factors, including unknowns, which might be involved." Further data were collected and a second conference and report (5), under the auspices of the WHO and World Dental Federation, concluded that "the most probable reasons for the decrease in dental caries in children in the developed countries were considered to be associated with: (i) the widespread exposure to fluoridated water and/or fluoride supplements, especially the regular use of fluoride toothpaste The factors common to all countries with a substantial reduction in caries was fluoride, either as fluoridated water or toothpaste." Evidence accumulating over the past twenty years confirms the above views.

Table 1 Estimate of the number of people throughout the world using various types of fluoride therapy in 1990 and 2000. Numbers in millions (27).

Tune of fluoride thereasy	Period (years)	
Type of huonde therapy	1990	2000
Water fluoridation (n)	210	300
School fluoridation (n)	0.2	0
Fluoridated salt (n)	4	97
Fluoridated milk (n)	0.1	0.2
Drops/tablets (n)	20	15
Mouthrinses (n)	20	100
Clinical topicals (n)	20	30
Toothpastes (n)	450	1500

Although there are several ways of delivering fluoride (1), the number of people using each type of fluoride therapy differs considerably (Table 1).

It can be seen that fluoride toothpastes are by far the most important way of providing fluoride worldwide. This has been recognised by WHO for many years (6), not least by the World Health Assembly 2007 which urged Member States to "... consider ... the provision of affordable fluoride toothpaste". Previous articles in this issue of the Journal have considered fluoride in water, salt, and milk; this article will provide a brief commentary review (7) of the development, effectiveness and use of fluoride-containing toothpastes and mouthrinses. These products are used almost exclusively in the home, in comparison with fluoride in water, salt or milk, which are suitable for community preventive programmes. Details of the very many clinical trials will not be given in this review and the reader is referred to a textbook (8) and the numerous reviews of the Cochrane Collaboration, mentioned below, for further information. By tradition, the common way of expressing fluoride concentration in toothpastes and mouthrinses (and other vehicles such as water) is 'parts per million' or 'ppm': this is equivalent to $\mu g/g$ (µgF/g toothpaste) or mg/kg for toothpaste, and approximately mg/l for mouthrinse.

The aim of this article is to give a narrative account of the history and development of these products, and recommendations for their use.

History of the development of fluoride-containing toothpastes and mouthrinses

Toothpastes

The remarkable caries-inhibiting effect of fluoride had become clear by the early 1940s and this knowledge led to the introduction of water fluoridation in 1945 and publication of the first trial of a fluoride-containing toothpaste, also in 1945 (9). Formulating an effective fluoride toothpaste is not easy and it took 25 to 30 years before they were widely available. In 1970, less than 5% of toothpastes sold in the UK contained fluoride; by 1976, over 90% contained fluoride. Issues dominating early research were: the incompatibility of abrasives included in toothpastes, different fluoride compounds, effective concentrations, and stability of fluoride compounds in toothpastes during storage. Fluoride compounds that have been tested for caries-inhibitory properties when incorporated into toothpastes include: sodium fluoride, acidulated phosphate fluoride, stannous fluoride, sodium monofluorophosphate, and amine fluoride.

Sodium fluoride (NaF) is the simplest fluoride compound and is very soluble in water. It was added to water in the first water fluoridation scheme and was the first fluoride compound to be added to toothpaste. The first trial, lasting two years, found no preventive effect (9). The abrasive in the toothpaste was calcium carbonate, which was the abrasive usually used at that time. Three more trials of sodium fluoride, using the same or different abrasives, were published up to 1961, all reporting a lack of caries prevention. In 1961, Ericsson, in Sweden, concluded from laboratory research (10) that sodium bicarbonate would be a suitable compatible abrasive, and a subsequent trial in Sweden demonstrated the effectiveness of this formulation (11). A few years later, another Swedish trial showed a toothpaste containing sodium fluoride with an inorganic (acrylic bead) abrasive to be very effective a 40 to 48% reduction in caries development during the three year trial (12). The formulation was expensive, though. Subsequently, almost all toothpastes containing sodium fluoride included a silica abrasive, and these toothpastes were shown to be effective.

Early laboratory experiments showed that more fluoride was incorporated into enamel when the fluoride-containing solution was acidified. The most promising compound was 'acidulated phosphate fluoride' (APF). Four trials of toothpastes containing APF were published between 1966 and 1972, but the results were mixed and this line of research was not pursued. It should be noted, however, that APF has been the compound of choice in fluoride-containing gels used for topical application in clinics.

Following the initial negative results with sodium fluoride, attention turned to other readily soluble fluoride compounds. Laboratory experiments showed that stannous fluoride could be suitable, and the results of a one year trial of a toothpaste containing stannous fluoride with a calcium pyrophosphate abrasive were published in 1955, showing a substantial caries-preventive effect (13). This was marketed with the name 'Crest' in the USA in the same year. Subsequently, some 40 clinical trials of toothpastes containing stannous fluoride have been published, almost all using the same pyrophosphate abrasive system, although effectiveness was less than that reported in the first 1 year results. There were, however, two problems. First, was the poor stability of stannous fluoride, which tended to hydrolyse to ineffective stannic fluoride; and, second, that use of stannous fluoride toothpastes resulted in teeth accumulating some dark stain. After nearly 30 years, the manufacturers of 'Crest' changed to a sodium fluoride, silica abrasive formulation.

Another compound showing promise in laboratory and animal experiments was sodium monofluorophosphate (MFP). The first clinical trial of a toothpaste containing MFP (with an insoluble metaphosphate abrasive) was published in 1963 (14). This two-year trial demonstrated the clinical effectiveness of this formulation, as has been the case in over 30 subsequent trials testing MFP with a variety of abrasives including chalk, alumina and silica. The way MFP exerts its effect has been debated for nearly 50 years; some research supports the view that the main effect is by direct incorporation of MFP into the apatite lattice, while other research emphasises the importance of enzymatic hydrolysis of MFP within dental plaque.

The protection of enamel from acid dissolution by aliphatic monoamines in laboratory experiments led Swiss researchers, certainly by 1960 (15, 16), to test the hypothesis that the detergent action of these organic compounds could be combined with the action of fluoride to give increased protection from acid attack. These organic compounds were superior to more widely used inorganic compounds in laboratory experiments. It was also suggested that amine fluoride compounds had a strong affinity for enamel and had a direct anti-enzymatic effect on microbial activity within plaque. An impressively long trial in Switzerland (17) demonstrated the effectiveness of an amine fluoride toothpaste. Subsequent trials in Germany, USA and Hungary (18) confirmed the caries-preventive effect. At the end of the 1980s, amine fluoride was combined with stannous fluoride; several studies providing evidence of an increased effect of this compound on dental plaque and enamel fluoride accumulation (18, 19).

Mouthrinses

As with most of the early investigations into fluoride and caries, the first trials of fluoride mouthrinses were carried out in the USA. Since then, results of clinical trials have been reported in at least 14 countries. The first publication of a clinical trial appeared in 1946 (20) – a year after publication of the results of the first trial of a fluoride-containing toothpaste (*vide supra*) – and the second trial in 1948. Both trials were of short duration (12 mo) and did not demonstrate effectiveness; perhaps, also, because the rinse was acidified to pH 4.5. At that time dental caries experience was very high in Sweden and a number of Swedish researchers took investigations into fluoride mouthrinses a stage further: they saw the potential for fluoride mouthrinsing by children in school to be an alternative to water fluoridation since this was unlikely to happen in Sweden. These Swedish trials, lasting two or three years resulted in substantial reductions in dental caries (11). Supervised school-based mouthrinsing programmes became popular in Sweden and some other countries and were credited with a substantial improvement in the oral health of Swedish children.

As with water fluoridation, toothpastes and topically applied solutions, sodium fluoride was the compound of choice in the early mouthrinse trials. In 1972, the first of many trials was published, testing a mouthrinse containing acidulated phosphate fluoride (APF). This followed the pattern of research on fluoride compounds in toothpaste: mouthrinses containing stannous fluoride were tested (first publication in 1973), a trial of a mouthrinse containing amine fluoride was published in 1979, and a trial of a mouthrinse containing ammonium fluoride was published in 1977 - all demonstrated effectiveness in caries prevention. The possibility of enhancing the effectiveness of NaFcontaining mouthrinses by the addition of ions such as Al, Mn, Fe, Mg, Zr and K was studied by Swedish researchers for over 20 years. Although some of the results suggested that effectiveness may be increased by the presence of various combinations of the above ions, their superiority to simple NaF mouthrinses was not established.

Effectiveness and recommendations for use of fluoride-containing toothpastes

A very large number of clinical trials of toothpastes containing compounds men-

tioned above have been published during the past 65 years. These have usually lasted for three years and have involved several hundred subjects. They have been, therefore, expensive, and it is testament to the manufacturers of these toothpastes that they have been prepared to invest heavily to improve their products. This has been highly successful, with the four major global manufacturers working ethically together, with the result that oral health has improved very significantly in most of the world. There have been scientific disagreements between manufacturers, for example over the degree of clinical effectiveness of stannous fluoride toothpastes, but these have been rare. Four aspects of the effectiveness and use of fluoride-containing toothpastes will now be considered.

Type of fluoride compound

The incompatibility of sodium fluoride with commonly used, and cheap, abrasives, led to the development of toothpastes containing other fluoride compounds. Stannous fluoride had drawbacks of stability and staining (vide supra) and was abandoned: despite manufacturer's claims, stannous fluoride was never shown to be superior to sodium fluoride or sodium monofluorophosphate (MFP). Presently, results of trials indicate that the clinical effectiveness of toothpastes containing sodium fluoride, MFP, and amine fluoride are similar. In some trials, toothpastes contained both NaF and MFP, but any clinical advantage was small. Additions aimed at increasing effectiveness of toothpastes, such as calcium glycerophosphate, have been tested but, again, any additional benefit was small. During the past twenty years, toothpastes which reduce 'tartar' (dental calculus), reduce gum inflammation (gingivitis), reduce dentine sensitivity, and whiten teeth have been developed. It has been important to show that these additions did not reduce the caries-preventing role of fluoride – it would appear that caries prevention has not been compromised. It should be noted that toothpastes containing stannous fluoride are available, marketed mainly for their protection against plaque, gingivitis and tooth sensitivity.

A Cochrane Collaboration review of the effectiveness of fluoride toothpastes in preventing dental caries (21) gave the prevented fraction, pooled from over 42,000 children in the 70 studies included, as 24% (95% confidence interval of 21 to 28%). The conundrum that this reduction is substantially lower than the decline in caries recorded in many countries will be discussed below. Almost all of the above trials involved permanent teeth: a recent systematic review (22) identified eight trials involving primary teeth and reported caries reductions similar to those recorded for permanent teeth. The ability of fluoride-containing toothpastes to prevent caries in the roots (dentine and cementum) of teeth has been tested in a number of trials and with several compounds, with encouraging results (23).

Concentration of fluoride in toothpastes

There is a dose response for fluoride in many vehicles, including toothpaste. The prevented fractions for various fluoride concentrations in toothpastes, taken from a recent Cochrane review (24) are given in Table 2.

The higher the concentration of fluoride, the greater the effect. There has been considerable discussion about the effectiveness of toothpastes containing less than 1000 ppm. For toothpastes containing about 500 ppm, it can be seen that the 95% confidence interval includes zero, indicating that the prevented fraction (15.4%) is not statistically significantly different from zero at the 5% level of significance. One argument is that such toothpastes cannot be recommended as effective. The counter argument is that Table 2 Clinical effectiveness of fluoride-containing toothpastes. Prevented fraction (PF), compared with a fluoride-free placebo toothpaste, for toothpastes containing various concentrations of fluoride, obtained by network meta-analysis. Data for caries increment, measured by the D(M)FS index (24)

Fluoride concentration (ppm)	Prevented fraction (%; 5% confidence interval)
250	9.1 (-3.6, 22.0)
440-550	15.4 (-1.9, 32.5)
1000-1250	23.0 (19.3, 26.6)
1450-1500	29.3 (21.2, 37.5)
1700-2200	33.7 (16.5, 50.8)
2400-2800	35.5 (27.2, 43.6)

there is such a clear dose-response for six concentrations from zero to 2800 ppm, that it is disingenuous to conclude that concentrations around 500 ppm are ineffective. Added to that, while there were 54 trials comparing 1000 ppm with 0 ppm (placebo), there were only two comparisons of 500 ppm toothpastes with a 0 ppm placebo: it is very unlikely that any more trials will be undertaken with a 0 ppm placebo, since it would now be ethically unacceptable to withhold benefits of fluoride-containing toothpastes from subjects for at least two years. Thus, the issue is difficult to resolve and opinion on the role of 500 ppm toothpastes is fairly evenly split across the world.

Frequency of brushing, amount of toothpaste, and method of rinsing after brushing

This information is frequently obtained from subjects during clinical trials by questionnaire. Frequency of brushing information has been available for most trials and metaanalyses have indicated that brushing twice a day is more effective than brushing once a day – the prevented fraction is increased by 14% (95% CI 6 to 22%) moving from once to twice a day (21). However, it should be noted that the trials were not set up to investigate this aspect of toothbrushing. There is little clinical data on the variable 'amount of toothpaste', although opinion is that amount is much less important than fluoride concentration and brushing frequency. There is some evidence that the degree of rinsing the mouth after brushing affects the effectiveness of the fluoride toothpaste (25, 26). Rinsing thoroughly (with water from a cup) reduces effectiveness compared with less thorough rinsing with water from the hand.

Recommendations regarding the use of fluoride-containing toothpastes

The first recommendation is that everyone should use a fluoride-containing toothpaste. A comment was made in 2001 (27) that if all dentate people in the UK brushed their teeth twice a day, the amount of toothpaste used would be twice the current amount. Hypersensitivity to fluoride is exceedingly rare: cases reported were generally due to hypersensitivity to other components. Sensitivity to flavouring or preserving agents in toothpastes is reasonably common. The debate about what concentration is appropriate was mentioned above.

Toxicity issues must be considered when making recommendations and these revolve around two issues. First, what concentration is appropriate for use by the general public? And, second, what concentration is appropriate for young children whose teeth are still forming and who could be at risk of developing dental fluorosis? The first question has been answered, certainly in Europe, as there is a ceiling of 1500 ppm for fluoridecontaining toothpastes sold 'over the counter'. Toothpastes containing more than this concentration have to be prescribed. This is so in many other countries too. The second question is more difficult. There is no EU recommendation. The UK Department of Health said in 2009, for children up to 3 years: "Use only a smear of toothpaste containing no less than 1000 ppm fluoride" (28). The European Academy of Paediatric Dentistry is more flexible, saying in 2009: "A children's toothpaste with a lower concentration of fluoride may be indicated although the evidence for a caries-preventive effect of formulas with less than 500 ppmF is insufficient" (29). A recent report of a trial in Brazil made the interesting comment that "The anticaries effect of the low-F dentrifice [500 ppm] was similar to the conventional F dentrifice [1100 ppm] when used by caries-inactive children. However, in children with active caries lesions the low-F dentrifice was less effective than the 1100-ugF/g dentrifice in controlling the progression of lesions" (30). This rather reinforces evidence from Australia that there is little penalty of a rise in caries experience, or reduced caries prevention, in recommending use of 500 ppm toothpastes rather than 1000 ppm toothpastes for use by young children (31). Thus, some flexibility in advice may be needed. Toothpastes containing around 500 ppm are on sale and recommended in many areas of the world.

Toothbrushing for children under 7 years should be supervised by an adult, to ensure adequate brushing and prevent unnecessary swallowing of toothpaste. Children up to 3 years of age should have only a smear of toothpaste placed on their toothbrush; children aged 3 to 6 years should use no more than a small pea-sized amount of paste. Thorough rinsing after brushing should be avoided; spitting out excess toothpaste is usually sufficient. Brushing is recommended last thing at night and at least one other occasion during the day.

Effectiveness and recommendations for use of fluoride-containing mouthrinses

There has been less research into fluoride mouthrinses than with fluoride toothpastes. The reasons are likely to be, first, that mouthrinses are easier to formulate and, second, the habit of mouthrinsing at home is much less established than toothbrushing. The market is smaller, although its popularity has increased over the past 20 years. Some issues will now be considered.

Type of fluoride compound, concentration of fluoride and frequency of rinsing

Results of trials indicate that rinses containing acidulated phosphate fluoride, stannous fluoride or ammonium fluoride were not as effective as sodium fluoride rinses at neutral pH. It is also easier to formulate a pleasanttasting rinse with sodium fluoride. The one trial comparing an amine fluoride rinse with a sodium fluoride rinse showed them to be of equal effectiveness; however, the combination of amine fluoride and stannous fluoride seems to be superior (18). The vast majority of rinses sold now contain sodium fluoride at neutral pH, although the amine fluoride / stannous fluoride formulation has a big market share in Europe.

Concentrations of fluoride in mouthrinses tested have varied between 45 ppm and 3000 ppm. However, unlike toothpastes which are used daily, mouthrinsing may be done daily, once, twice or three times a week, every two weeks, or 3 or 4 times a year. Mouthrinses with higher concentrations of fluoride are usually for infrequent use. Frequency as low as 3 or 4 times a year would not now be recommended. In the textbook mentioned above (8), cross-tabulations were made to examine prevented fractions in relation to fluoride concentration and rinsing frequency. The authors concluded: "... there was only a moderate trend towards increasing effectiveness with increasing fluoride concentration especially within the most popular range 200 to 1000 ppm F." In addition: "In conclusion, rinsing frequency would appear to be important and the concentration of fluoride slightly less important than frequency. Rinsing once a week or more is likely to be more effective than less frequent rinsing." The most common quantity of rinse dispensed is 10ml; with a rinsing duration of one to two minutes. The rinse is then expectorated.

Recommendations regarding the use of fluoride-containing mouthrinses

Almost all the fluoride mouthrinses now on sale contain around 225 ppm F – this is usually on the label as '0.05% sodium fluoride' -- although there are other compounds in mouthrinses (*vide supra*). These are recommended for rinsing once a day, for 1 to 2 minutes, before spitting out. Advice is to avoid eating or drinking for 15 minutes after rinsing, and to rinse at a different time to toothbrushing. This is to increase the frequency of exposure of dental plaque to fluoride: a trial testing the use of a fluoride mouthrinse straight after brushing with a fluoride toothpaste recorded no added benefit over brushing alone (32).

The toxicity of fluoride mouthrinses should be considered, since 10ml of a 225 ppm mouthrinse contains 2.25 mg F Young children swallowing this quantity daily would create an unacceptable risk to forming teeth. Because of this potential risk, the use of fluoride mouthrinses is not recommended (in the UK, at least) by children younger than 8 years. Alcohol has traditionally been included as a solvent for flavouring and other ingredients: during the last 15 years, health professionals have urged that alcohol be removed, with widespread success. While everyone (with teeth) is advised to brush their teeth with a fluoride-containing toothpaste (toothbrushing has benefits other than caries prevention), such a blanket recommendation is not made for fluoride mouthrinses. They can be prescribed or recommended by dental professionals, or they may be purchased because the user likes the idea of using a rinse.

The role of fluoride toothpastes and mouthrinses in the prevention of dental caries

There is no magic bullet for preventing or curing dental caries. An earlier article in this issue of the Journal (1) discussed approaches to preventing caries development and noted that those of greatest practical importance are diet, fluoride and fissure sealing. This article (1) also divided ways of delivering fluoride into Automatic, Home care, and Professional care, with toothpastes and mouthrinses grouped under Home care (Table 4 in reference 1). The above approaches are not alternatives but they should be selected to provide the most appropriate -- including considerations of cost and availability -- combinations at a national level, community level and the level of the individual. It is beyond the scope of this article to consider these preventive strategies in detail, but some comments will be made which relate to the current use of fluoridecontaining toothpastes and mouthrinses.

First, diet: use of an effective fluoride toothpaste and mouthrinse is not an excuse for ignoring control of sugar intake – both diet control and fluoride are important. Second, there is substantial evidence that fluoride toothpastes and mouthrinses are effective in areas where the water supply contains an optimum concentration of fluoride (about 0.8 to 1.0 ppm in Europe) (21, 33) - there is added benefit. This applies to other ways of delivering fluoride, too. For example, there is added benefit from using a fluoride-containing toothpaste and a fluoride-containing mouthrinse (34), although the timing of their use should be considered (vide supra). Professional application of topical fluorides in the form of varnish, solution or gel will bring benefit in addition to the benefit from regular use of a fluoride toothpaste (34). It has already been stated that evervone should brush their teeth with a fluoride-containing toothpaste, but the decision whether to also use a fluoride mouthrinse or attend a dental professional to receive a topical application of fluoride will depend, primarily, on perception of risk of dental caries development and cost of the mouthrinse or topical application of fluoride. That is a personal decision made, it is likely, with the aid of professional advice.

One of the conundrums, yet unravelled, is why the decline in caries severity recorded in many countries is so much greater than the relatively modest 24% given as the prevented fraction for fluoride toothpastes in general by a Cochrane review (21). Do the results of 3 year trials underestimate the effect of lifelong use of fluoride toothpastes? Has the use of other fluoride therapies increased the benefit? Are we now better at controlling our sugar intake? These are questions which we leave to be answered by others. It should be recognised that caries prevalence has not declined in every country; in some, it has increased (6, 35). We need a better understanding of the factors operating in these countries. To give just one example, it is known that in some countries, so called 'fluoride toothpastes' made locally do not contain fluoride or contain fluoride in an inactive form.

While water fluoridation or the addition of fluoride to salt or milk (see previous articles in this issue of the Journal) are equitable community measures - in that they reduce social inequalities - it has to be accepted that home care products, i.e. toothpastes and mouthrinses, increase social inequalities, since the more affluent can afford to buy them while the less affluent may struggle to do so. It is likely that the widespread use of fluoride toothpastes has increased inequalities in oral health both within countries and between countries. That is definitely not to infer that they are 'bad' but, rather, that specific programmes are needed to ensure that well-formulated, effective toothpastes are available for all. This approach has been strongly supported by WHO (35, 36) in their drive for 'affordable fluoride toothpastes'. There are several examples of successful demonstration programmes of supervised toothbrushing (with fluoride toothpaste) and distribution of toothpaste and brushes to those in greatest need (36-38). On a national scale, to give just one example, all Thai schoolchildren brush their teeth with a fluoride-containing toothpaste every day in school. Although there are inherent advantages for total oral care of toothbrushing over mouthrinsing, mouthrinse programmes are cheaper than brushing programmes and thus favoured in some community programmes (39, 40). There is no doubt that the development, marketing and use of fluoride-containing toothpastes have been a great success story in improving the oral health of thousands of millions of people throughout the world. This would not have occurred without the close collaboration between industry, dental researchers and the dental profession in general - each should be proud of their contribution. The task now is to ensure universal benefit.

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