A SYSTEMATIC REVIEW OF THE GLOBAL TRENDS IN DENTAL FLUOROSIS FROM 1980 TO 2000

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A minithesis submitted in partial fulfilment of the requirements for the degree of MChD in the Department of Community Dentistry, University of the Western Cape.

PRETORIA 2003

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Key Words:

concentration

dose-response

fluoridation

fluoride

fluorosis

indices

part per million

risk

systematic review

trends

ABSTRACT

A SYSTEMATIC REVIEW OF THE GLOBAL TRENDS IN DENTAL FLUOROSIS FROM 1980 TO 2000

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This minithesis presents a systematic review of dental literature with the objective to investigate trends in dental fluorosis during the period 1980 to 2000. A Medline search was carried out for peer-reviewed scientific dental literature published in English from 1 January 1980 to 31 December 2000. From the publications retrieved 54 satisfied the inclusion criteria. The data on fluorosis prevalence were examined in three categories: 0 to $\leq$ 0.3 ppm F, > 0.3 to $\leq$ 0.7 ppm F and 0.7 to $\leq$ 1.4 ppm F. Since there was no significant difference in fluorosis between 1980 to1989 and 1990 to 2000 the whole period was regarded as one entity.

The dose response with increasing concentration of fluoride in water was consistent with the scientific literature. The percentage prevalences of fluorosis for the three fluoride categories were 16.7, 27.4 and 32.2, respectively. There was an increasing trend in dental fluorosis, although not statistically significant, in both fluoridated and non-fluoridated areas over time. The increase in fluoridated areas was 2-fold and that in non-fluoridated areas 16-fold which was consistent with the scientific literature, the prevalence of fluorosis more so in non-fluoridated areas. The fluorosis was mostly in the very mild to mild categories but more moderate and severe fluorosis was observed in all three categories when the data were pooled. Fluorosis has increased in the period from 1980 to 2000. There is a shift from very mild to mild to moderate and severe categories. This calls for further investigation, particularly to look for statistical significance and the role of confounding variables.

DECLARATION

I declare that A Systematic Review of the Trends in Fluorosis Globally from 1980 to 2000 is my own work, that it has not been submitted before for any examination in any other university, and that all sources I have used or quoted have been indicated and acknowledged by complete reference.

ABDULLA KHAN June 2003

SIGNED.....

Acknowledgements

I am grateful to Professor M H Moola, Dean, Oral Health Centre, University of the Western Cape, for encouraging me to enrol for the MChD-Community Dentistry course and persisting that I complete the course. His many reminders, messages and granting me permission to be supervised by Professor P Cleaton-Jones, Professor of Experimental Odontology, Director, MRC/University of the Witwatersrand, Dental Research Institute is evidence that he was committed to see that I completed this dissertation as an important part of the programme. For this I will always be indebted to him.

I would like to put on record my indebtedness to Professor P Cleaton-Jones for accepting to supervise me on behalf of the University of the Western Cape. He provided me the attention, guidance, encouragement and support when I most needed it. He accommodated me at my every request to see him and spent much of his valuable time taking me through my project. Without this support the completion of this dissertation would not have been possible.

I would like to thank Professor N Myburgh for his encouragement always whenever I consulted him regarding my work. He has always supported me in my work positively.

Professor.R Lalloo was always accessible to me with prompt replies to all my queries. He always provided me with ideas when I was short of them so that I could make progress towards the completion of my work.

I cannot forget Professor T S Gugushe, Dean, Dental Faculty, Medunsa and Professor J Kroon who worked out a schedule for me to complete my work during the normal working hours of the faculty.

The written words cannot fully express my gratitude to all involved in taking me through this journey. My loving wife and my four children were with me through this journey all the way. We all say from deep down in our hearts may God bless you all.

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CHAPTER ONE

CHAPTER 1: Introduction and Review of literature

1.1. Introduction

The available evidence on dental fluorosis indicates that there is a temporal sequence between exposure to fluoride during the period of tooth development (0-7 years of life) and dental fluorosis (Ismail and Messer 1996, Osuji et al 1988). There is some evidence that a dose-response relation exists between the ingestion of fluoride and the occurrence of fluorosis (Kalsbeek et al 1992). Since Dean's studies (Dean et al 1941) the potential of fluoride exposure has increased substantially. Dean's data were collected around 1940 in populations whose only sources of fluoride were food and water(Evans and Darvell). Much has changed since then and the use of other systemic (tablets, drops, salt, milk) and topical (toothpaste, rinses, gel, varnishes) fluoride measures in caries prevention has introduced a large number of additional fluoride sources (Leverett 1986). Dietary habits have changed extensively in the last 50 years among children. For example, children now consume more soft drinks than water (Ferjerskov et al 1996).

There is no doubt that the increased awareness and knowledge about dental fluorosis by both lay people and health professionals are causing concern; global trends need to be monitored since many researchers are reporting that fluorosis is increasing in both fluoridated and non-fluoridated communities. The current statements of the dental profession in support of fluoridation do not appear to take into account changes since the 1940's (Gray 1987), so a systematic review of published fluorosis on a global scale is timely.

1.2. Review of current literature on fluorosis

Approximately 317 million people in 39 countries benefit from artificially fluoridated water (CRD Report No.18, 2000). An additional 40 million benefit from water supplies which are naturally fluoridated. Community water fluoridation schemes have been in existence in the United States for over 50 years and are employed in 39 countries throughout the world including Spain, Switzerland, Australia, the United Kingdom, Israel, Singapore and New Zealand, Vietnam and 39 cities in South Korea (CRD Report No.18, 2000). South Africa has enacted mandatory legislation to fluoridate water although this is not yet implemented (Department of Health 2000).

The United States is now 65 per cent fluoridated and will soon reach at least 70 percent when California's water fluoridation law is implemented (CRD Report No. 18, 2000). In recent years many researchers have claimed that the prevalence of fluorosis is increasing in North America (Szpunar and Burt 1987, Rozier 1999). Jackson et al (2002) reported that there has been an increase in the prevalence of mild to moderate fluorosis. In addition to this, the difference in prevalence between optimally and negligibly fluoridated communities has narrowed considerably.

Dental fluorosis, a hypoplasia or hypo-mineralisation of the tooth enamel or dentine, ranges in intensity from barely noticeable whitish striations to confluent pitting and staining produced by chronic ingestion of excessive amounts of fluoride during the period when teeth are developing. Dental fluorosis is the undesirable effect of fluoride ingestion and it is, therefore, questioned and debated (Ferjerskov et al 1996).

The major determinant of the prevalence and severity of dental fluorosis is the concentration of fluoride in water consumed by infants and children during the first five years of life, tending to affect permanent teeth more than primary teeth (Horowitz 1986). The risk of fluorosis is negligible if the exposure of fluoride occurs after the age of six yearsas majority of the teeth are mineralised (Burt 1992). Dental fluorosis is a dose response effect due to fluoride ingestion. The original studies by Dean showed that at a level of one part per million fluoride (1 mg per day equivalent) the prevalence of fluorosis in a population was 10-12 per cent (Dean et al 1942). In contrast to the common belief, there is no longer a threshold value below which dental fluorosis may not occur (Ferjerskov et al 1990).

The introduction of fluoride delivery methods other than water fluoridation has increased the prevalence of fluorosis in communities. A review on the trends in the prevalence of dental fluorosis in North America showed that in fluoridated areas the fluorosis was twice as high as in the original studies (Clark 1994). Since the 1980's there has been a growing concern regarding dental fluorosis due to the increased consumption of fluoride from a number of sources (Driscoll et al 1986, Szpunar and Burt 1988). There are also reports that fluorosis in optimally fluoridated communities has ranged from 13 percent in Ontario to about 46 and 50 percent in Illinois and Michigan (Leverett 1986, Szpunar and Burt 1987, Kumar et al 1989, Burt 1992). Estimates in the 1940s put the appropriate exposure of fluoride at 1 to 1.5 mg per day which is the equivalent of 0.05 mg fluoride / kilogram body weight. Current estimates put the optimal exposure at 0.05 to 0.07 mg per kilogram body weight per day (Burt 1992, Levy 2000) based on Dean's concentration of 1 part per million in water.

A vast amount of research has been carried out on fluoride over the past fifty years. However, there are still important areas that need further investigation. The prevalence of dental caries is reducing in fluoridated as well as non-fluoridated communities, especially in developed countries (Horowitz 1991). The current decision regarding the optimal concentration of fluoride in water does not take this into consideration (Gray 1987). There is concern that the profession is using the same expressions of effectiveness and providing new communities with information based on Dean's research when adopting fluoridation. This is being questioned since issues regarding fluoride have not remained the same beyond the 1940s (Gray 1987). The reasons for this concern is that the other sources of fluoride introduced beyond this period complicate the calculation of the optimal concentration of fluoride to balance desired dental caries prevention with risks of dental fluorosis (Levy et al 1995). Since fluorides have played a very great part in the reduction of caries, many other sources have appeared, particularly fluoride toothpaste, fluoride supplements, topical fluoride solutions and rinses (Gray 1987). In addition to these other sources such as beverages, infant formulae and condiments such as magadi used in Tanzania for traditional cooking have been cited as background fluoride that add to the flourosis (Akpata 2001).

1.2.1. What has changed?

- Dean's 1 part per million as the optimal concentration in water needs a rethink with the advent of other modes of fluoride delivery. Prior to 1940 water and food were the main source of fluoride. Since then the introduction of other sources of fluoride has led to the increase in other potential sources of fluoride (Szpunar and Burt 1987).

- The topical effect of fluoride is now being regarded as more important than the systemic effect (Clarkson and Mc Loughlin 2000, Koch et al 1996). The evidence based review on fluoride gel concluded that either professionally or self applied, gels are associated with substantial reduction in caries increment (Marihno et al 2002).
- Most toothpastes are now fluoridated and are widely used. Osuji et al (1988) found that the odds ratio of developing fluorosis were greater among children who started brushing before the age of two years.
- In Established Market Economies where caries seen is mostly in the pits and fissures are not considered preventible by fluoride but by fissure sealants (Burt and Ekland 1999).
- Fluoride rinses, gel applications and varnishes, that have since been marketed extensively, pose a risk of fluorosis for school children (Levy et al 1995).
- There is a a smaller difference between caries experience in fluoridated and non-fluoridated areas reflecting the widespread diffusion of fluoride from foods and drinks processed in fluoridated areas (Heller et al 1997). The diffusion effect, also known as the"halo" effect is the effect of water fluoridation on caries in non-fluoridated communities benefiting those consuming products processed in fluoridated areas (Horowitz 2000).
- Infant formulas are being processed with fluoridated water (Clarkson and McLoughlin 2000).
- Prescribing patterns of fluoride supplements by dentists, pediatricians and physicians are not being monitored. Gift et al (1984) found that some physicians

prescribed supplements for those children already on optimally fluoridated community water systems.

- In addition to this, recent studies indicate that the prevalence and intensity of mild and moderate dental fluorosis have increased due to sources of fluoride in the environment other than in water (Leverett 1986, 1991).

1.2.2. The post-eruptive mode of action of fluoride

The debate on whether the topical effect is more important than the systemic effect of fluoride has become an important issue for both fluoridated and negligibly fluoridated areas as researchers report on the increase of fluorosis globally (Silverstone et al 1981, Featherstone 1999). Evidence is being provided that the topical effect is more important than the systemic effect but is by no means conclusive.

Since fluorosis is caused by pre-eruptive consumption of fluoride, it is not surprising that the cariostatic effect of fluoride was thought to be due to the incorporation of fluoride into enamel (Featherstone 1999, Limeback 1999, Groeneveld et al 1990). The current view of some researchers is that the main mode of action of fluoride in reducing dental caries is post-eruptive because it promotes re-mineralisation and prevents de-mineralisation of dental enamel during the caries process (Chow 1990, Koulourides 1990, Silverstone et al 1981). Featherstone (1999) believes that there is now overwhelming evidence that the primary caries prevention mechanisms are post eruptive through topical effects for both children and adults. Various fluoride products particularly toothpaste provide frequent sources of fluoride ions for this reparative process. The consumption of water provides an initial source of topical fluoride when ingested and delivers fluoride

to the oral cavity through saliva(Featherstone 1999). Salivary fluoride concentrations are functionally sufficient to facilitate re-mineralisation. The understanding of the post-eruptive effect of fluoride is that frequent exposure to low concentration of fluoride in the oral cavity is the most important factor in its use in the prevention and control of dental caries (Clarkson et al 2000, Levy 1994). The concentration of fluoride in the oral cavity is due to direct contact with fluoride ions and secretions from the salivary glands (Whitford et al 1987).

The addition of small amounts of fluoride to the oral environment through the ingestion of water has apparently been able to control dental caries progression by about 50 per cent (Thylstrup and Fejerskov1996). If fluoride is added to the oral environment from the very beginning of tooth eruption, it is obvious that caries reduction becomes greater than if fluoride is added later during the lifetime of the same tooth. Some important observations published early on in the "fluoride story" have not been fully appreciated. Thus, Russel (1949) found that children moving out of fluoridated areas experienced increase in caries incidence. In addition, it was apparent that teeth which had not been formed without exposure to systemic fluoride certainly experienced a reduced caries rate after eruption when exposed to very low concentrations of fluoride in the oral cavity (Koch et al 1996).

Brunelle and Carlos (1990) reported that the National Survey data from the United States showed that on average there was only a 17 per cent difference in dental caries experience between artificially fluoridated and non-fluoridated areas. Gillcrist et al (2001) are of the view that this reduction in caries experience has made it difficult to

establish statistically significant reductions in caries due to water fluoridation alone and partly attribute it to topical sources. In Denmark it was apparent that the difference in the caries experience between the naturally fluoridated and low fluoride areas had virtually disappeared within a period of ten years (Thylstrup et al 1982). Could it be assumed that this difference between the flouridated and low fluoride areas was due to the topical effect of fluoride?

According to Koch et al (1996) it was thought to be necessary to incorporate fluoride into the forming enamel in order to achieve caries reducing effect. It was acceptable to experience a slight amount of fluorosis than to experience painful carious cavities. They say that this argument no longer holds true as it is possible to achieve this through a topical fluoride therapy for those at any age who are in need. It is relevant today to turn to other measures whose risk of inducing dental fluorosis is negligible (Koch et al 1996). Koch et al (1996) do not accept that dental fluorosis should be regarded as a necessary side effect in the use of fluoride in the prevention of dental caries. The predominant cariostatic effect of fluoride derives from its topical effect on the local dissolution process (Koch et al 1996). Denmark has a 90 per cent reduction in caries by using only topical fluoride with no increase in fluorosis (Koch et al 1996).

It is well known from Dean's studies that artificially fluoridated water (0.7 to 1.2 parts per million) will result in a prevalence of about 10 per cent fluorosis (Dean et al 1942). Bearing the dose-response curves in mind, it is obvious that any additional fluoride ingested in fluoridated areas will inevitably add to the increase in prevalence and severity of dental fluorosis such as has been seen in North America (Szpunar and Burt 1992).

DePaola (1991) supports the view that systemic fluoride acts in two ways. Fluoride leads to the conversion of hydroxyapatite to a fluoridated state which makes it less soluble in acid. He also believes that systemic fluoride may enhance the morphology of the tooth so that they have more rounded cusps, shallow inclines and more favourable fissural approximations making them more resistant to dental caries. He goes on to argue that if most or all the benefit of fluoride stems from local effects, water fluoridation may be unnecessary and could be replaced by delivery systems that operate mainly post-eruptively. Groenveld et al (1990) believes that fluoride has an important pre-eruptive effect on caries experience in all permanent teeth. The maximum DMFS reduction in a fluoridated area at age 15 attributed about half to the pre-eruptive and half to the post-eruptive effect of fluoride. The greater part of reduction in caries in pits and fissures is derived from the pre-eruptive phase whilst in the smooth surfaces the post-eruptive phase is more significant. Most caries is in pit and fissure, therefore, the pre-eruptive exposure is critical to reducing the caries burden

Featherstone (1999) in his summary and conclusion emphasised that the anti-caries effects of fluoride are primarily topical for children and adults, the systemic benefits of fluoride are minimal and therapeutic levels of fluoride can be achieved from drinking water and topically applied fluoride products. Before the most documented preventive measure in public health history is discarded, there should be a valid rationale as the literature implies the need for both the topical as well as the systemic mode of fluoride use.

1.2.3. Sources of Fluoride and risk of fluorosis.

The main sources of fluoride in the Established Market Economies are drinking water, fluoridated salt, foods and beverages, baby cereals and formulas, fluoride supplements, toothpaste, rinses, and topical fluoride (Levy et al1995). . In addition to this, fluoride in water has a "diffusion" or "halo" effect because drinks and food manufactured in fluoridated areas may be available throughout an entire population including those in non-fluoridated areas (Clarkson and Mc Loughlin 2000). Recent increases in fluorosis are attributed to these additional sources of fluoride and many of these sources are regarded as risk factors for fluorosis especially during the critical period of tooth development (Riordan 1993, Evans 1991, Milsom and Mitropoulos 1990, Osuji et al 1988). Another source of fluoride is the community based milk fluoridation scheme which was first established in 1988 in Bulgaria. This led to the introduction of similar projects in Russia, the United Kingdom, the Peoples Republic of China, Chile and more recently in Peru and Thailand (WHO 2001).

Epidemiological studies in North America have shown that the prevalence of fluorosis has increased since the 1930s and 1940s (Heifetz et al 1988, Szpunar and Burt 1988, Szpunar and Burt 1987). Kuthy and McTigue (1987) found that only 6.2 per cent of physicians who prescribed fluoride supplements adhered to the minimum protocol by inquiring about the fluoride of the child's drinking water, having water analysed and continuing fluoride till at least the age of 10. According to Leverett (1986) the increase in the prevalence of fluorosis in fluoridated as well as non-fluoridated areas may be largely due to the ingestion of dietary fluoride supplements and fluoride toothpaste. Fluoride supplements and tooth brushing have at least an additive effect on the risk of

developing dental fluorosis in children who brush their teeth with fluoridated dentrifices (Ismail and Bandekar 1999). Uncontrolled and unrestricted fluoride intake is a major concern during the period from birth to the age of seven. When considering exposure to fluoride it is most important to take into account the various sources of available fluoride. The mechanisms that cause dental fluorosis are dynamic and not fully understood. Studies exploring methods of reducing the unintentional ingestion of fluoride or minimising its effect from the multiple sources of fluorides are necessary (Leverett 1991). Prudent public health practice calls for the investigation of variables other than mean annual temperature that may influence fluoride intake. Factors which contributes to excessive fluoride ingestion should be identified in order to provide optimal fluoride benefits whilst protecting individuals from excessive intake (Yoder et al 1998).

1.2.4. Water Fluoridation -A Political issue in light of increasing dental fluorosis.

Water fluoridation's continued success in the United States and elsewhere is difficult (Horowitz 1990). Not only does organised resistance to fluoridation continue, but economic and political factors may impede its future. In the United States it has become a political issue. Fluoridation must compete with other issues that usually have greater priority (Horowitz 1990). Among the concerns may be the increase in the prevalence of fluorosis and the equalisation of dental caries prevalence in fluoridated and non-fluoridated communities.

The resistance to water fluoridation may be related to topical effect of fluoride which is now being regarded as more important than the systemic effect. The other fact may be that some researchers have shown that the discontinuation of fluoridation of water has not resulted in the increased incidence of dental caries. For example in Kuopio, Finland

no increase in caries in primary teeth were observed in the three year period since the discontinuation of water fluoridation (Seppa et al 2000). In Chemitz, Germany, caries in children and adolescents decreased between 1991 and 1995 in spite of the discontinuation of water fluoridation (Kunzel et al 1997). The opposite may also be true, therefore, more evidence is required.

It is well documented that water fluoridation is more effective in preventing smooth surface dental caries than fissure caries (Murray and Rugg-Gunn 1992). The National Oral Health Survey (Van Wyk 1989) showed that more than 90 per cent of the dental caries seen in urban children between the ages of 6 and 15 years were fissure caries on occlusal surfaces of molars and premolars. Occlusal surfaces are least protected by fluorides and this strengthens the case for the use of sealants over fluoride (Burt and Eklund 1999).

Pendrys (2000) has elaborated on the benefits and risk of using fluoride to prevent or control dental caries in Established Market Economies. He defined the limit of effectiveness as the balance between maximising fluoride's caries-preventive effect and avoiding unwanted side effects such as dental fluorosis. He summed up the problem faced by the Established Market Economies as "a tale of two prevalences"- that is, the historic decline in the prevalence of dental caries and the recent increase in the prevalence of dental fluorosis.

1.3. History of water fluoridation

The discovery of the dental benefits of fluorides came about almost by accident as a result of the search for the cause of dental mottling (dental fluorosis). Endemic stained teeth have been described by observers of various communities in Europe and North America since the late 19th Century (Koch et al 1996).

The first scientific investigation of the cause of stained teeth was carried out by Dr Frederick McKay in 1901(Jones and Lennon1997). It was believed that the condition was characterised by brown or yellow staining of enamel often accompanied by pitting. Public water supplies were implicated in the etiology based on evidence provided by two small communities which successfully eliminated changing their water supplies.

Dr H. Trendly Dean, of the United States Public Health Services National Institute of Dental Research, was given the mission to " resolve the relation of water borne fluoride to endemic fluorosis." His work not only established the relation between water fluoride levels and dental fluorosis but more importantly between fluorides and the prevalence of dental caries.

In order to quantitatively record the degrees of severity of mottled enamel an index which classified fluoride mottling into six grades was developed (Dean et al 1942). The index provided Dean with the tool necessary for epidemiological surveys. In the early 1940's Dean and colleagues published the now classical 21 cities study which clearly demonstrated an inverse relationship between fluoride concentration in public water supplies and the prevalence of dental caries in children aged between 12 -14 years of age

(Dean et al 1941, 1942). The most important finding was the strikingly low rates of dental caries prevalence associated with the use of domestic water supplies whose fluoride content was about 1 part per million, a concentration which under the conditions prevailing in the localities studied produced only the sporadic instances of the mildest forms of dental fluorosis of no practical aesthetic significance. It was extrapolated from this that 1 part per million of fluoride in water was associated with significantly lower levels of dental caries and an acceptable prevalence of the mildest form of fluorosis. Dean's work led to the hypothesis that the adjustment of fluoride levels in public drinking water might also confer the benefits of caries reduction seen in naturally fluoridated areas. The United States Public Health Services approved the study based on the knowledge of the health of generations of populations drinking water with naturally occurring fluoride at 1 part per million or more.

Grand Rapids, in Michigan, became the first community in the world to fluoridate its drinking water artificially. The cities of Muskegon (Michigan) which was non-fluoridated and Aurora (Illinois) which had about 1.2 parts per million naturally occurring fluoride, served as controls. The first dental data were published in 1950 and the results were so impressive that in the United Kingdom, Anglesey County Council agreed to ask the government for a grant to introduce water fluoridation.

In the 1940s, '50s and early '60s dental caries was rife among Americans, particularly among children causing widespread affliction and pain (Horowitz 2000). The mean baseline DMFS in 1958, of rural school children aged 12 in Northern Pennsylvania was

13.51. A series of surveys carried out in the 1970s and 1980s showed that dental caries had declined steadily during that period. This change was attributed to the growth in the use of fluoride as an important factor in this phenomena (Horowitz 2000).

Since 1945, when community water fluoridation was first implemented in the United States, not only has the procedure grown to cover more than half of the United States population but the development and the use of other fluoride methods have expanded greatly (Horowitz 1992).

1.4. Systematic Reviews

It is more than a quarter of a century since Gene Glass coined the term "meta-analysis" to refer to the quantitative synthesis of the results of primary studies (Glass 1976). In this thesis the term Systematic Review is used in preference to Meta-Analysis on the advice of the South African Cochrane Centre (Personal Communication 2002) which regards Meta-Analysis as a specific tool within the Systematic Review. Another view is that a qualitative systematic review summarises the primary investigations without statistical pooling. A quantitative systemic review is synonymous with meta-analysis (Petticrew 2001).

The systematic literature review is a method of locating, appraising, and synthesising evidence. The value of regularly updated systematic reviews of the assessment of the effectiveness of healthcare interventions are dramatically illustrated by Antman and colleagues (Antman et al 1992), who showed that review articles failed to mention advances in treatment identified by an updated systematic review.

Single experiments or studies do not provide sufficiently definitive answers upon which to base policy. This situation is made more difficult due to the proliferation of studies that address common research questions. These studies use disparate definitions, variables, procedures and sampling methods resulting in conclusions that are open to bias and error (Detsky et al 1992). This leads to an enormous waste of effort in research with conflicting results to guide policy nowhere but to call for more research which is costly. Literature reviews are notorious for depending on subjective judgements, preferences and biases of reviews and conflicting interpretation of evidence (Wolf 1983).

Answers to important health questions can be obtained from overviews of randomised clinical trials. The least formal type of overview is a literature review which compiles evidence from individual studies and qualitatively weighs the trends and outcomes to reach an informed judgement about the relative utility of certain therapeutic interventions. More systematic and quantitative overviews employ a statistical pooling technique, known as a systematic review, to aggregate findings of individual studies (Johnson 1993).

Even if one were to read all available information on a particular subject, the quality of information varies, much of it may be conflicting, and it may not answer the question under consideration. In reality, decisions have to be made, regardless of whether there is convincing, scientifically reliable and valid information available to answer the question posed. Systematic reviews can aid this process by maximising the usefulness

of available data and providing a structure for interpreting the information. Systematic assessments of literature can provide meaningful answers to important policy questions (White and Antczack-Bouckoms 1995).

Systematic Reviews in which the results of individual studies are statistically combined, are valuable instruments to resolve conflicts when reports of primary studies disagree, to increase the likelihood of detecting small but clinically important effects, and to generate new hypotheses and avoid unnecessary research (Gerbarg and Horowitz 1988).

Generally a Systematic Review is a statistical procedure for combining analytical results from a collection of studies for the purpose of obtaining an overall estimate of treatment effect. Such formal systematic overviews are becoming increasingly popular in medical literature and have been undertaken successfully in a variety of therapeutic areas, most notably in the cardiovascular and oncology fields to help guide clinicians in their selection of therapies.

Formal methods for systematically reviewing published research and synthesising data may help to address issues that traditional reviews cannot address. A systematic review can enable one to accumulate results from prior research and review and combine these results in a way that identify similarities and differences among the studies (White and Antczack-Bouckoms 1995).

1.4.1. Myths and Misconceptions of Systematic Reviews

1.4.1.1. Systematic reviews are the same as ordinary reviews, only bigger.

Systematic reviews are not simply bigger, they are quantitatively different. The aim is not to be simply comprehensive but to answer specific questions, to reduce bias in the selection and inclusion of studies, to appraise quality of studies and to summarise them objectively (Petticrew 2001).

1.4.1.2. Systematic reviews include only randomised controlled trials.

There is no reason why systematic reviews of study designs other than randomised controlled trials cannot be carried out . Systematic reviews of non-randomised clinical trials are common, and qualitative studies, for example, can be included in systematic reviews (Petticrew et al 1999).

1.4.1.3 Systematic reviews require the adoption of a biomedical model of health.

This common myth holds that systematic reviews adopt a biomedical model that is of relevance to medicine and that they should not be applied to other domains. Systematic reviews are efficient techniques for hypotheses testing, for summarising the results for existing studies, and for assessing consistency among previous studies; these are not unique to medicine (Petticrew 2001).

1.4.1.4. Systematic reviews are of no relevance to the real world.

Systematic reviews have been portrayed as being obsessed solely with disease outcomes and randomised controlled clinical trials carried out within health care systems. However, they have also been widely used to examine an array of contemporary and often contentious "real world" issues such as prevention of vandalism, crime deterrence, domestic violence, child abuse and other social issues (Petticrew 2001).

1.4.1.5. Systematic reviews necessarily involve statistical synthesis.

Some reviews summarise the primary studies by narratively describing their methods and results. Others take a statistical approach (meta-analysis) by converting data from each study into a common measurement scale and combining the studies statistically (Delgado-Rodriguez 2001). The above myth assumes that such reviews can only be done this way.

1.4.1.6. Systematic reviews have to done by experts.

Although expert practitioners are often involved in systematic reviews, most systematic reviewers are not expert practitioners (Petticrew 2001).

1.4.1.7. Systematic reviews can be done without experienced information / library support.

Systematic reviews can indeed be carried out without proper information or library support, though researchers not typically experienced in information retrieval and their searches are likely to be less sensitive, less specific and slower than those done by information professionals. Improvements in information technology has facilitated this (Petticrew 2001).

1.4.1.8 Systematic reviews are a substitute for doing good quality individual studies.

They do not always provide definitive answers and are not intended to be a substitute for primary research. Rather, they often identify the need for additional primary studies as they are often an efficient method of identifying where research is currently lacking. Systematic reviews can help identify future research needs (Wortman and Yeaton 1987). They also prevent unnecessary new primary studies (Petticrew 2001).

1.4.2. Systematic Reviews affect three groups of people:

1.4.2.1 The community- whether the benefits of interventions outweigh the risks of any procedure.

1.4.2.2. The practitioner- assessments are necessary to determine the value of learning new procedures, investing in new equipment and hiring new personnel.

1.4.2.3 The administrator- from the administrator's point of view evaluations can provide answers to questions about the use of limited resources to support competing programmes (White and Antczak-Bouckoms 1995).

1.4.3. The Main Objectives of Systematic Reviews

Systematic reviews are more advantageous than traditional reviews of a body of evidence which may suffer from bias in selecting articles and lack of objectivity. The main objectives of systematic reviews are to obtain information about treatment effects that cannot be obtained from any of the studies alone. If considered separately, any single study may be either too small to detect moderate treatment effects or too limited in scope to provide unequivocal or generalisable conclusions that allow extrapolations to other patient populations. Combining results across studies can often strengthen the evidence about treatment efficacy (Johnson 1993). Systematic reviews in which results of individual studies are combined statistically are valuable instruments to resolve conflicts when reports of primary studies disagree or increase the likelihood of detecting small but clinically important effects, generate new hypothesis and avoid redundant research. Systematic reviews can be misused easily producing inaccurate, biassed and / or

misleading effectiveness of medical interventions. Researchers must be aware of the limitations and risks of systematic reviews and strive to reduce the amount of bias (Jadad and McQuay 1996).

The difference between traditional reviews and systematic reviews is that in reviews no explicit criteria are applied leaving recommendations open to bias whereas in systematic reviews more explicit and quantitative methods of synthesising data are applied (Detsky et al 1992).

Systematic Reviews have been helpful:

- to answer particular research questions
- in the review of previous studies for planning further clinical trials
- as a means of providing required data for decisions, analysis and analysis of costs (Detsky et al 1992).

In systematic reviews the study and not the patient becomes the unit of analysis. The constructing of tables enumerating the characteristics of studies selected can shed light on controversies. By depicting the results from multiple studies in a single figure one may be able to demonstrate trends that are not evident by individualised components of a study. A primary benefit of the quantitative summarisation is that the data set develops adequate statistical power from a group of studies which have a sample size too small for detecting clinically significant differences (White and Antczack-Bouckoms 1995).

1.4.4. Advantages of systematic reviews

- They can help to identify present and future research needs (Wortman and Yeaton 1987).
- Systematic reviews can help clarify contradictions in the literature (White and Antczak-Bouckom 1995)
- Systematic reviews provide a gain in statistical power (Dickersin and Berlin 1992).
- Combining data from a number of smaller clinical trials is an attractive economic alternative (White and Antczak-Bouckom 1995)

1.4.5. Limitations of systematic reviews

- Systematic reviews cannot enhance data usefulness from poorly conducted studies (Dickersin and Berlin 1992).
- The difficulty in identifying relevant research, varying quality of studies, concern about combining certain studies result in publication bias (Dickersin and Berlin 1992).
- Identification of relevant research does not guarantee that data from studies can be combined.
- Publication bias from research not published limits findings (White, Antczack-Bouckoms 1995).
- Single studies on many occasions could be more relevant to a particular patient or particular setting. Data available at certain institutions based on patient records, for example, are often more informative than using therapeutic effect size from a systematic review (Riegalman et al 1996).

- Problems associated with combining results from individual experiments may differ considerably from each other.
- Scepticism about combining results from poorly designed and poorly conducted studies.
- Sophisticated results will not improve poor data but could lead to unwarranted comfort with ones conclusions.
- Poor quality studies inadequately blinded generates a biased estimate and if combined with high quality studies will materially affect the results of systematic reviews and have reduced precision and added variability (Detsky et al 1992).

1.4.6. Basic methods applied to improve quality in systematic reviews:

- Randomisation
- Use publications of full length articles
- Blinded outcome to reduce bias
- A data driven method that weights the individual and aggregate effect size rather than arbitrary scores.
- Electronic searches must be supplemented by hand searches of key journals and querying experts (Detsky et al 1992).

1.5. Fluorosis and its measurement

1.5.1. General problems in diagnosing fluorosis

Non-carious lesions of enamel may present in a variety of forms ranging from small diffuse white opacities to large hypoplastic areas completely devoid of enamel. Any

disturbance, whether local or systemic, that affects the sensitive ameloblasts can result in a disruption in the cycle of matrix formation and maturation (King and Brook 1984). According to Chellappah et al (1990) ninety-seven potential causes of enamel mineralisation defects have been described. Although fluoride is frequently implicated as a systemic aetiologic agent, it is just one of several dozen which could give rise to generalised defects. The possibility exists that opacities may be erroneously classified as fluorotic when they may be of idiopathic origin. Although there is no unanimity about the intra-oral distribution of dental fluorosis there is consensus that contra-lateral teeth exhibit similar severity of fluorosis (Manji et al 1986). The reason for this is that dental fluorosis is a developmental disturbance of systemic nature, therefore, there is always a certain symmetry in the degree to which homologous teeth are affected (Fejerskov et al 1988). Various indices have been used in surveys to measure the presence and severity of enamel fluorosis. Other systems record all defects in enamel based on a premise that the aetiology for the conditions should not be presumed. If all defects are recorded, a retrospective attempt to reconstruct which of the opacities are fluoride induced is inappropriate (Horowitz 1986). Dental fluorosis has a characteristic appearance, yet the classification of individual teeth present difficulties. Dean's classification of normal and moderate fluorosis are determined by criteria that are reasonably objectively defined but an acute judgement is required to interpret the signs of fluorosis between these limits. The diagnosis of questionable, very mild and mild are difficult and variable. Teeth could be judged as mild on one occasion and very mild on another occasion and vice versa.

In addition to this, there are variations in reporting fluorosis which are partially due to different measurement instruments. More than three indices in use have different

graduations and criteria. At least one classification involves drying of teeth, a feature that reveals more fluorosis than those indices that do not require drying teeth. Comparisons of findings of wet and dry indices should be qualified to verify over estimations (Chau and King 1989). Granath et al (1985) emphasised that teeth must be exposed to prolonged drying to ensure correct diagnosis and also apply relevant criteria for the differential diagnosis of disturbances of other origin. Fluoride has long been recognised as one of the causes of imperfect enamel development, unfortunately, the characteristics of dental fluorosis are not unique making it more difficult to diagnosis. It is frequently claimed that opacities of non-fluoride origin may be indistinguishable from early signs of dental fluorosis (Cutress et al 1985). Positive identification of fluorosis is dependent on the presence of enamel opacities of a certain type, a distinctive between-teeth distribution and a history of fluoride ingestion during the period of tooth development (Burt and Ekland 1999, Fejerskov et al 1988).

1.5.2. Methods used to verify fluorosis defects

There is consensus that contra-lateral teeth exhibit similar severity of fluorosis. To a certain extent there is also consensus regarding the similarity in distribution of flourotic enamel among corresponding tooth type in the mandible and maxilla (Fejerskov et al 1988). The occurrence of diffuse opacities has been used as the discriminating factor between fluoride and non-fluoride opacities (Suckling and Pearce 1984). The criteria used by the various researchers together with the history of fluoride exposure and experience will make the diagnosis of fluoride induced opacities less difficult.

1.5.3. Indices used to categorise dental fluorosis.

Since the 1940s various indices have been proposed for the measurement of enamel defects, including fluorosis. These indices may be conveniently divided into two main groups: specific fluorosis indices and descriptive indices encompassing all types of defects. The fluorosis indices are designed to measure defects of enamel due only to excessive fluoride ingestion, usually described as enamel mottling or fluorosis (Clarkson and O' Mullane 1989).

The following indices will be presented from a review of literature:

- ☐ Dean's Index (including the Community Fluorosis Index)
- ☐ Tooth Surface Index of fluorosis
- ☐ Thylstrup and Fejerskov Index
- ☐ The Developmental Defects of Enamel Index (DDE)
- ☐ Flourosis Risk Index

1.5.3.1. The Dean's Index (Dean et al 1934) (Appendix A)

When it was discovered that fluoride concentration of drinking water was correlated to dental fluorosis Dean (1934) conducted a series of surveys to elucidate the relation. To do this he developed this classification system in 1934 for the assessment and severity of dental fluorosis (Dean 1934). This is the most widely used index in the fluorosis group which is still widely used in epidemiological studies worldwide and it value is in its importance when making comparisons between the various studies past and present (Clarkson and O' Mullane 1989).

Dean et al (1942) in his report suggested that a community fluorosis index or CFI be calculated for a geographic location based on the mean of all scores for all individuals

examined. The CFI between 0.4 and 0.6 are regarded as borderline whereas those that are above the score of 0.6 are considered a public health concern as this score progresses to 4.0.

The Dean's index, however, has the following shortcomings (Horowitz 1986):

- ☐ the index gives a single score to a tooth rather than separate scores to each tooth surface.
- ☐ traditionally an individual is classified according to the tooth which is the second most severely affected by fluorosis. The teeth with most fluorosis may be second molars or other teeth located posteriorly in the mouth which have less cosmetic importance.
- ☐ scores for individuals and community may be misleading if all individuals categorised as "Questionable" could have a CFI (0.5), a borderline public health problem which overstates the situation.
- ☐ the "questionable" category is difficult to define.
- ☐ the distinctions between some of the other diagnostic categories are also unclear, imprecise or lack sensitivity.
- ☐ the scores are not easily reproducible as the criteria are subjective.
- ☐ it is statistically difficult to analyse as a quantitative measure as the scores are qualitative.

1.5.3.2. Tooth Surface Index of Fluorosis (Horowitz et al 1984). (Appendix B)

In an attempt to reduce some of the shortcomings of Dean's Index, a new Index, the Tooth Surface Index of Fluorosis (TSIF) was developed. With the TSIF, a separate score is given to each unrestored tooth surface. Two scores are assigned to anterior (from the

labial and lingual aspects) and three to posterior teeth (from the buccal, lingual and occlusal aspects). The TSIF contains no "questionable" category. Fluorosis diagnosed in categories 1, 2 and 3 may be confined to a single area of enamel or may occur irregularly over an entire surface. An examiner determines the extent of affected enamel by estimating the amount of fluorosis as a fraction of total visible enamel surface. The TSIF permits a distinction between discrete pitting and more advanced confluent pitting and between staining alone and staining in conjunction with pitting.

The Tooth Surface Index of Fluorosis is useful in determining fluorosis of tooth surfaces of special cosmetic significance. It has proven itself to be more sensitive than Dean's Index which did not show a dose response relation between water fluoride levels of 2 or 3 times the optimum whereas the TSIF had a distinct relationship (Driscoll et al 1983).

The advantages of the TSIF are that it is more sensitive than the Dean's Index for the mildest forms of fluorosis and ascribes a score to each tooth surface whereas the Dean's Index applies to the two worst teeth in the mouth.

1.5.3.3. The Thylstrup-Fejerskov Index (TF) (Thylstrup and Fejerskov 1978). (Appendix C)

This index has a stronger biologic basis than Dean's more or less arbitrary index, because the index scores were developed by relating them to histologic features of affected enamel. Since it requires that teeth be dried before an examination, the TF index is the most sensitive of the existing indices. It requires the assessment of only one surface per tooth because fluorosis affects all tooth surfaces equally. It can be used on selected teeth or the whole dentition.

One frequent criticism of the TF Index is that it may be complicated for practical use in the field. The entire spectrum of the TF scores is unlikely to be applied in any given area and usually a range of 5-6 categories will be sufficient. The range of scores available in the TF scores makes it a versatile classification system enabling it to be used to measure the effects of fluoride exposure in population exhibiting the mildest to the most severe forms of dental fluorosis. The TF index has the benefit of being clear, precise and sensitive for the measurement of dental fluorosis under most circumstances (Fejerskov et al 1988).

1.5.3.4. The Developmental Defects of Enamel Index (DDE Index) (Ainamo and Cutress 1982). (Appendix D)

The Commission on Oral Health, Research and Epidemiology established a Working Group in 1977 to develop a system of classification of developmental defects of enamel suitable as an international epidemiological index. For the purpose of this section the most important objective was that classifications based on aetiological considerations are premature because only a few defects can be assigned an aetiology (Ainamo and Cutress 1982). The DDE Index is comprehensive and suitable for full mouth and as well as adaptable for partial mouth recording. To this end the DDE Index was modified into two forms viz; one for general purpose epidemiological studies and one for simple screening surveys .

Since diffuse opacities are regarded to be fluoride induced it would be possible to extract fluorosis data from the modified general purpose as well as the modified screening index although information on severity will not be available.

The main drawbacks of the DDE Index:

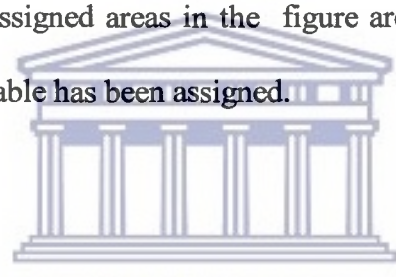
- ☐ The DDE Index gives information on a wide range of defects, their distribution and location. This has caused difficulties in presenting the results in a meaningful fashion, on interpretation and making comparisons (Clarkson and O' Mullane 1989).
- ☐ The severity of the defects cannot be recorded with the DDE Index (Clarkson and O' Mullane 1992).
- ☐ The large amount of data generated requires numerous complicated tables to present results.
- ☐ It lacks sensitivity and specificity and is recommended for screening purposes.

1.5.3.5. Fluorosis Risk Index (Pendrys 1990). (Appendix E)

In the past, scoring methods for enamel fluorosis were developed, with waterborne fluoride being the primary agent of interest, and were designed to measure the prevalence of fluorosis severity based on the concentration of fluoride in drinking water (Pendrys 1990). Non-water-borne routes of fluoride exposure usually are age related. For example, the form (drops and tablets) and the dosage of fluoride supplements vary considerably with age. This age-relatedness of non-water-borne sources of fluoride is important, since the formation of the dentition is also age related, with different teeth beginning their formation at different ages and at different rates (Pendrys 1990). Thus given the knowledge of the histopathology of enamel fluorosis, the degree to which a particular enamel site is at risk of fluorosis as a result to a particular fluoride source is dependent on the age of development of the enamel site and the likelihood of exposure to a fluoride source at that specific age. There are a number of indices and the need for another index should be evaluated on whether there is a need for it. The rationale for the Fluorosis Risk

Index is in its use for analytical epidemiologic studies which permits the identification of association between age-specific exposures to fluoride sources and dental fluorosis (Pendrys 1990).

In this index the enamel surface zones that begin formation (with commencement of the secretory phase) during the first year of life (birth to first birthday) were designated as classification I enamel surface zones. Enamel surface zones that begin formation between the third and sixth year of life (between 2nd and 6th birthday) were designated as classification II enamel surface zones. Based on these decisions, an age-related scoring map was developed for enamel surfaces of the permanent dentition. Classification I is indicated as darkly shaded in the figure. The lightly shaded areas are designated as classification II. The unassigned areas in the figure are shown as clear for which a classification of questionable has been assigned.



1.5.4. Future surveys.

The many indices that have been developed to assist researchers better identify fluorosis raises the issue on the comparability of results. For this reason future surveys of dental fluorosis should be designed to facilitate the comparison of new data with the historic information, without sacrificing the more objective and finite diagnosis of fluorosis that may be possible today, using recently developed indices such as the Thylstrup and Fejerskov Index and the Tooth Surface Index of Fluorosis (Szpunar and Burt 1987).

1.5.5. Concluding thoughts.

Fluorosis and its measurements have been described with reference to the many indices used for this purpose. In the mass of literature these indices have provided the data to document the trend in fluorosis globally for the purpose of this systematic review.

1.6. Objectives of the study

1.6.1. To conduct a systematic review of available literature on trends in fluorosis since 1980 when the first concerns on the increase in fluorosis was reported in fluoridated and non-fluoridated communities.

1.6.2. To determine the prevalence of fluorosis at fluoride levels ≤.0.3 ppm, > 0.3 ppm to ≤ 0.7 pmm and > 0.7 ppm to ≤ 1.4 ppm.

CHAPTER TWO

CHAPTER 2: MATERIALS AND METHOD

2.1 Search for Literature.

A Medline literature search was carried out using PubMed supplemented by hand search using references obtained from articles found in the initial search. The key words for the search were fluoride, fluoridation, dental fluorosis, topical fluorides, systemic fluoride and dental caries. The search was restricted to peer-reviewed journals.

2.2. Inclusion criteria.

- Only published primary articles in peer-reviewed journals.
- Age range of the sample from 0 to19 years of age. School children were included if the sample was a convenient sample.
- Subjects in the research were lifelong residents or had lived in the area for at least seven years of their life where the research was carried out.
- Fluoride in water ranging from ≤0.3 parts per million, > 0 .3 - ≤ 0.7 parts per million and 0.7 - ≤1.4 parts per million.
- Study sample was random or convenience but did not include hospital and clinic samples.
- Sample size had to be specified.
- Article published from 1980 to 2000 inclusive

2.3. Data Collection

Data were entered on a special data abstraction form (Appendix F) developed for the review indicating variables as follows: Study Group, country, sample, index, examination

year, age, fluoride intake period, percentage distribution of fluorosis scores. The data were categorised according to the fluorosis index used.

For the Developmental Dental Defects of Enamel Index diffuse opacities were regarded as induced by fluorosis and other opacities were regarded as score "none" for the purposes of this systematic review. Diffuse opacities as indicated (Cutress et al 1986) were regarded as fluorosis, Russell's criteria that fluorotic defects occur symmetrically was applied when collecting data on fluorosis. A history of exposure to fluoride was used to provide additional evidence that opacities were fluoride-induced.

The overall fluorosis prevalence was determined proportionally based on the total number of individuals with fluorosis from each publication in relation to the total number of individuals examined in all publications. A weighted sample was not possible due the heterogeneity of the studies.

2.4. Limitations of study.

Limitations of the study were that the studies did not use the same approaches, used different indices, and many researchers who regarded opacities as fluoride induced may have been due to other causes.

2.5. Data Management

The individual publications were obtained and the references in each were examined for further publications, these were found by hand search. Once the data had been extracted from the publications the analysis was carried out by a statistician, Mr Maupi

Letsoalo, of the Medical Research Council's Institute of Biostatistics in Pretoria. The statistical software used was Strata, Version 7, Texas, United States of America, date of manufacture 2000.

2.6. Types of Statistical Tests Applied

2.6.1. Independent samples t-test

The purpose of the t-test in relation to this systematic review was to determine if a significant difference existed in the prevalence of fluorosis between the decades 1980-1989 and 1990-2000.

It is used when there are two experimental conditions and different subjects were assigned to each condition. It requires that the population distribution are normal but, is robust against departures from this assumption. When comparing two means, the validity of the t-test also depends on the equality of the two sample/population standard deviations, which (in many situations) is reasonable to assume this equality. The null hypothesis of the significance test is that the two populations/sample means are statistically not different. In essence the t-test is calculated from the following equation:

$$t = \frac{O - E}{se}, \text{ where}$$

O = observed difference between sample means

E = Expected difference between population means (when the null hypothesis is true)

se = estimate of the standard error of the difference between the two samples.

2.6.2. ANOVA.

The ANOVA analysis was carried out to determine if there was a significant difference in the proportions of fluorosis from none to severe when the different indices were used in the publications included for the systematic review.

Sets of data comprising more than two groups (assumed to be normally distributed) are common, and their analysis often involves the comparisons of the means of the component subgroups. Conceivably it would be possible to do this using a series of t-tests, which is theoretically unsound, since carrying out a large number of significance tests is likely to lead to spurious significance results. An approach, ANOVA (which is robust), is used instead. One-way ANOVA is appropriate when subgroups to be compared are defined by just one factor. A factor is chosen for inclusion on ANOVA either because it is desired to compare it's different levels or because it represents a source of variation that it is vital to take into account. The variance of all observations is determined/calculated, and in one-way ANOVA, this sum of squares is partitioned into:

1. The sum of squares due to differences between the group means.
2. The sum of squares due to differences between the observations within each group, and this is called residual sum of squares.

In the statistical analysis the fluorosis indices were used as continuous variables and the three fluoride concentrations (≤ 0.3, > 0.3 -≤ 0.7, and > 0.7-1.4 ppm) groups as categorical variables. Because the fluorosis indices have more than one or two categories, a one- way analysis of variance (ANOVA) was carried out. For the categorical variables

a Chi-square test was carried out together with Cramer's V to test the strength of the association between the variables. The tests were carried out at the 95% confidence level so $P < 0.05$ was considered to be statistically significant. With regards to the data abstracted from the various indices used, a P-value for Cramer's V test was carried out to find out if there were significant differences in the distribution of scores of the different indices. A Bonferroni test was carried out to determine if there was a significant difference between the means of the proportions of the prevalence.

Scattergrams were plotted with proportions of fluorosis on the Y axis and the year of publication on the x-axis; for each scattergram a linear regression line was attached.

CHAPTER THREEE

CHAPTER 3: RESULTS

Fifty-seven publications reporting the prevalence and severity of fluorosis met the inclusion criteria for this systematic review details of which are listed in Appendix F. The data extracted from the publications on an abstraction form were categorized into 0 - ≤ 0.3 ppm (non-fluoridated), > 0.3 - ≤ 0.7 ppm (intermediate) and > 0.7 – ≤1.4 ppm (fluoridated). Multiple references were made to most publications to extract the three categories of data sets. The indices used in the publications were not uniform. In the non-fluoridated category the Dean Index was used in 12 publications, the Tooth Surface Index of fluorosis was used in 13 publications, the Thylstrup Fejerskov Index was used in 9 publications, 12 publications used the Developmental Defects of Enamel Index and the Fluorosis Risk Index was used in one publication. In the intermediate category 4 publications used the Dean Index, 2 publications used the Thylstrup Fejerskov Index and 3 publications used the Developmental Defects of Enamel Index. In the fluoridated category 14 publications used the Dean Index, 8 publications used the Tooth Surface Index of Fluorosis, 6 publications used the Thylstrup Fejerskov Index, 8 publications used the Developmental Defects of Enamel Index and 1 used the Fluorosis Risk Index. Except for the Developmental Defects of Enamel Index and the Fluorosis risk index all the indices provided scores for severity of fluorosis ranging from none to severe. These were regarded as continuous variables. The prevalence of fluorosis increased as the concentration of fluoride increased from non-fluoridated to fluoridated with non-fluoridated areas having 16.7 percent fluorosis, areas with intermediate concentration of fluoride having 27.4 percent fluorosis, and the fluoridated areas having 32.2 percent fluorosis. Table 3.1 provides the data on the maximum, minimum and the mean percentage fluorosis for the three fluoride concentration categories.

Table 3.1. Percentage prevalence rates by fluoride concentration category

Category Fl ppm	Datasets % (n)	Mean %	S D	Min %	Max %
0 - ≤ 0.3	49	16.7	17.9	0	78
≤ 0.3 - ≤ 0.7	9	27.4	32.2	2.4	93.7
> 0.7 – 1.4	37	32.2	23.5	6.3	87.6

Measure of association between categorical variables.

All the statistical calculations are provided in Appendix G. The cross tabulation of the categorical variables are performed with chi-square test being employed to test for the significance of association between variables. However, it does not say anything about how strong the association might be. The Cramers V is used to measure the strength of association between the two categorical variables. The significance of P-value of Chi-square (P-value < 0.05) implies that the null hypothesis between the two categorical variables are independent is not accepted and accepts the hypothesis that they are in some way related.

The distribution of the severity of fluorosis for each category is indicated on the abstraction form with weighted percentages for the different indexes. As indices used in the publications selected for this systematic review were not uniform, a test for a significance was carried out for any difference in percentage fluorosis assessed for any given index. The different indices showed a P-value > 0.05 in the percentage fluorosis reported by applying the one-way ANOVA analysis the results of which are shown in Table 3.2.

Table 3.2. Summary of results of one-way ANOVA analysis.

Analysis-variables	F	P
No fluorosis vs fluorosis index	0.88	0.4797
Fluorosis prevalence vs fluorosis index	1.08	0.3703
No fluorosis vs distribution of scores	2.40	0.0967
Fluorosis prevalence vs distribution of scores *	5.57	0.0053
Questionable fluorosis vs distribution of scores **	4.71	0.0173
Very mild fluorosis vs distribution of scores	0.37	0.6917
Mild fluorosis vs distribution of scores	0.70	0.5005
Moderate fluorosis vs distribution of scores	1.35	0.2690
Severe fluorosis vs distribution of scores	0.94	0.3985
Fluorosis index vs questionable score distribution	1.75	0.1917
Fluorosis index vs very mild score distribution	18.5	0.1663
Fluorosis index vs mild score distribution	1.98	0.1474
Fluorosis index vs moderate score distribution ***	3.09	0.0545
Fluorosis index vs severe score distribution	1.78	0.1794

* There is a significant difference between the proportions of severity (P-value < 0.05). In particular, the means intermediate and fluoridated categories (i.e >0.3 -≤ 0.7 and > 0.7-≥1.4 ppm) from the means of no fluorosis (0-≤ 0.3 ppm) with P-value of 0.041 and 0.020 respectively. The test for variance used was the Bonferroni test.

** As the Dean Index is the only index having a "questionable" score these results have not been elaborated on. *** Not regarded as significant as P-value > 0.05

Table 3.3. Distribution of fluoride categories by fluorosis index.

Index	0-≤ 0.3 ppm		> 0.3- ≤ 0,7 ppm		> 0.7 –1.4 ppm		Total	
	n	%	n	%	n	%	n	%
Dean's	13	(41.9)	4	(12.9)	14	(45.2)	31	(100)
TSIF	13	(61.9)	0	(0.0)	8	(38.1)	21	(100)
TFI	9	(52.9)	2	(11.6)	6	(15.3)	17	(100)
DDE	13	(41.9)	3	(13.0)	8	(34.8)	23	(100)
FRI	3	(61.9)	0	(0.0)	1	(33.3)	3	(100)

n=number of studies

Table 3.3 shows the indices used in the 46 publications satisfying the inclusion criteria. There was no significant difference in the distribution of the scores levels with respect to index level (P-value > 0.05). The association between index and distribution of scores is not as strong as the P-value of Cramer's V which is greater

than 0.05. This means that the fluorosis data of all indexes could be pooled and the trends could be observed. Table 3.4 shows the distribution of scores for decades 1980 to 1989 and 1990 to 2000.

Table 3.4. Percentage prevalence of fluorosis by decade and fluorosis index.

Index	1980-1989	%	1990-2000	%	1980-2000	%
Dean's	22	(70.9)	9	(29.0)	31	(100)
TSIF	8	(38.1)	13	(61.9)	21	(100)
TFI	7	(41.2)	10	(58.8)	17	(100)
Total	37	(53.6)	32	(46.4)	69	(100)

* figures outside the brackets are the number of studies. All data from 46 publications.

There was no significant difference in the trends between the decades 1980 to 1989 and 1990 to 2000 as the t-test had a P-value > 0.05 for all three categories of fluoride concentrations. The conclusion from this is that the results from 1980-2000 may be treated as a single entity and be the main thrust of the report. The scattergrams, therefore, were combined for the period 1980-2000. Each scattergram (Figures 3.1-3.11) has the same structure with percent prevalence on the Y-axis and the year of publication on the X-axis. Trends are indicated by the linear regression lines. Only Dean's index has been presented in figures 3.1 –3.7 because of the low number of studies in the other indices. However, all the indices are presented in figures 3.8-3.11.

Table 3.5. Independent t-test: Trends for each continuous variable.

Analysis-variables	P-value
Questionable code vs trends	0.3813
Very mild code vs trends	0.0985
Mild code vs trends	0.2879
Moderate code vs trends	0.2013
Severe code vs trends	0.3324

Table 3.5 explains the trends in the two decades for each proportion of fluorosis from questionable to severe fluorosis. The proportions compared for the decades 1980-189 and 1990-2000 did not show any significant difference.

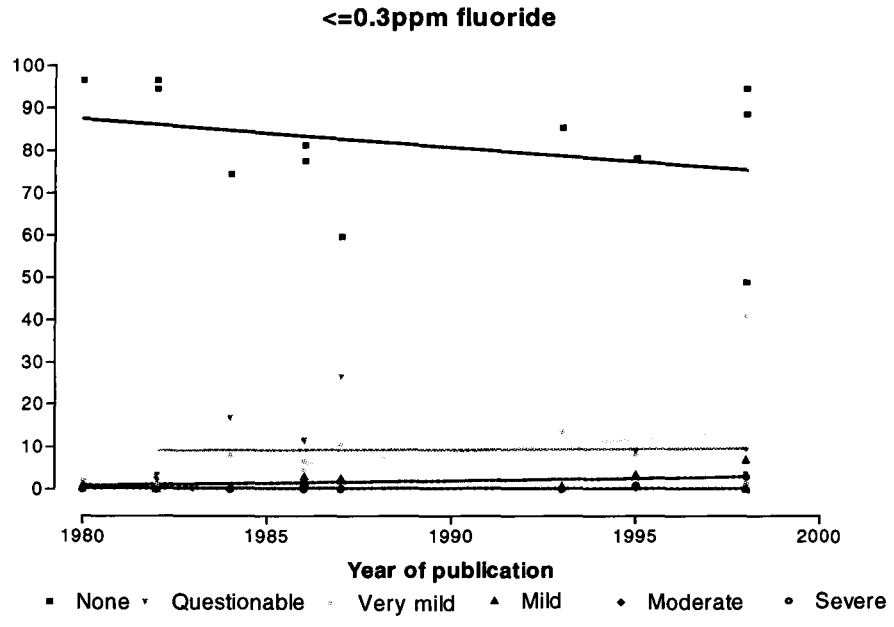


Figure 3.1.Scattergram for percentage prevalence of the Dean's Index in the non-fluoridated category.

Figure 3.1. Scattergram for percent prevalence for the Dean's Index in the non-fluoridated category.

This scattergram shows the scatter for the Dean's Index from none to severe fluorosis in the non-fluoridated category from 12 studies. Linear regression analysis showed no statistically significant trends. What is interesting, however, is the downward trend of "no fluorosis". In the analysis of variance in scoring for all indices there was no significant difference. Table 3.2 shows that the P-values were greater than 0.05. Although the rising trend in the fluoridated area is not statistically significant, it should be used for comparisons in future reviews to monitor this trend.

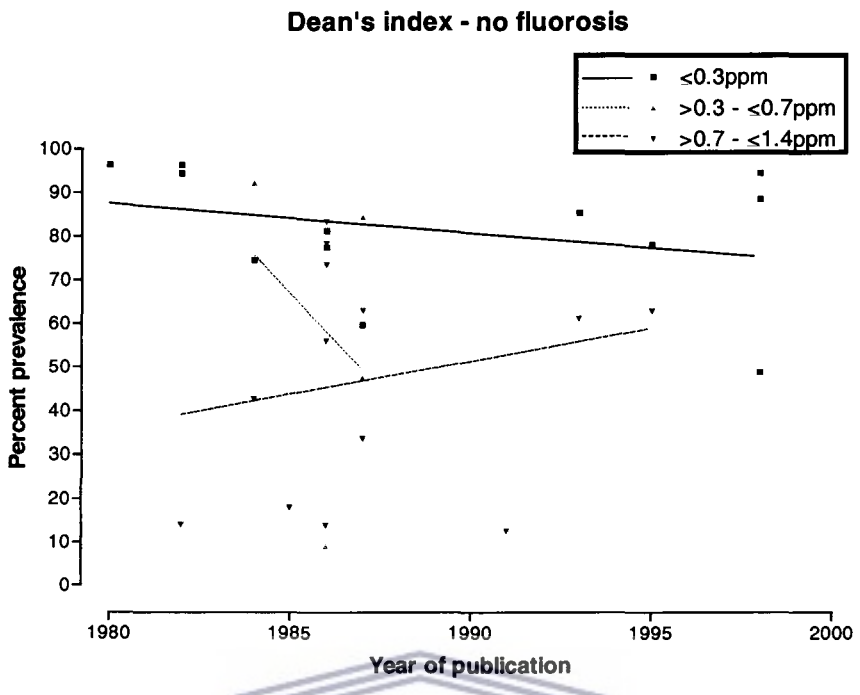


Figure 3.2. Scattergram for no fluorosis for percent prevalence for the three fluoride concentration categories.

Figure 3.2. Scattergram for no fluorosis – Dean's Index for the three fluoride concentration categories.

In figure 3.2 the scattergram shows values and linear regression lines for no fluorosis in the three fluoride concentration categories. None of the trends differed significantly from zero. The small number of values in the intermediate category is responsible for the steep downward trend. Because of the small number of values no importance is attached to this nor in subsequent scattergrams. In contrast, the declining prevalence in the non-fluoridated category and the rising prevalence in the fluoridated category are of concern.

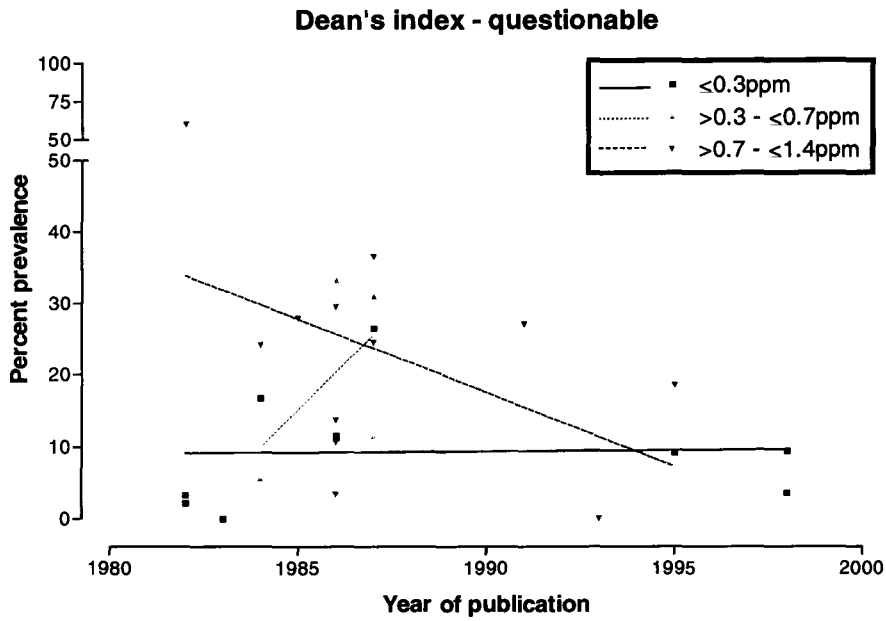


Figure 3.3. Scattergram for questionable fluorosis for the three fluoride concentration categories.

Figure 3.3. Scatter plots Dean's Index – Questionable.

An apparently confusing picture is shown for the questionable score (Figure 3.3). However while there is no change in the non-fluoridated category, the decreasing prevalence in the fluoridated category may be explained by rising trends in more severe scores shown in Figures 3.4-3.7. None of the trends differed significantly from zero.

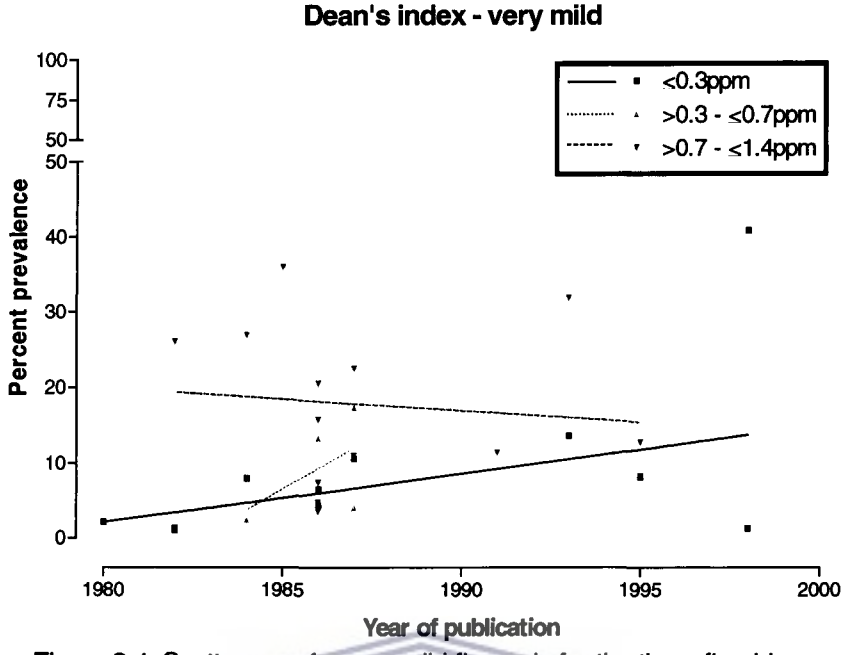


Figure 3.4. Scattergram for very mild fluorosis for the three fluoride concentration categories.

Figure 3.4. Scattergram for Dean's Index – Very mild fluorosis for the three fluoride concentration categories.

The trends in very mild fluorosis (Figure 3.4) are similar to those for the questionable fluorosis (Figure 3.3) with a rise in the non-fluoridated category. None of the trends differed significantly from zero. The outlier in the non-fluoridated category is considered in the calculation of the linear regression but the statistician was of the view that one or two outliers would have an insignificant effect on the trend.

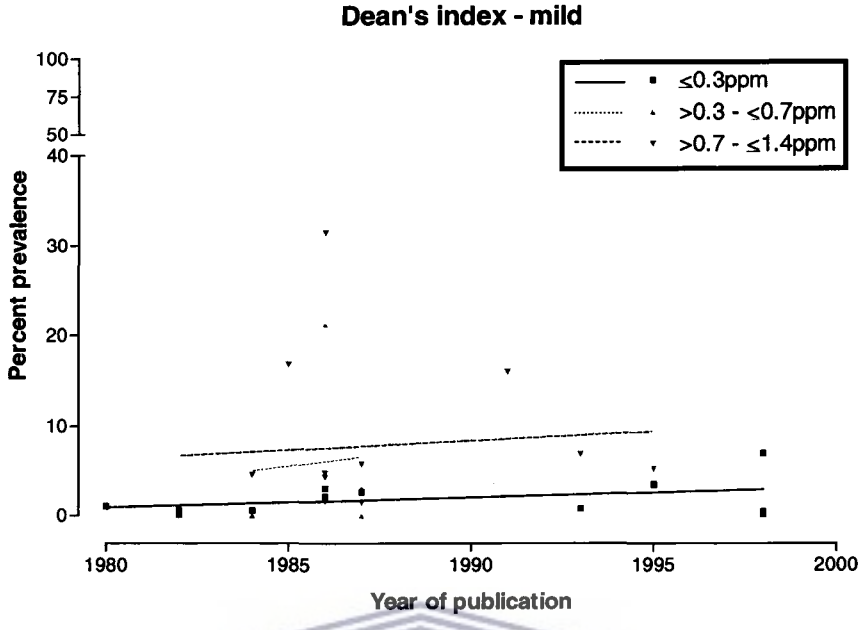


Figure 3.5. Scattergram for mild fluorosis for the three fluoride concentration categories.

Figure 3.5. Scattergram for Dean's Index – mild fluorosis for the three fluoride concentrations.

In the mild fluorosis score (Figure 3.5) there was little change over the 20 year study period.

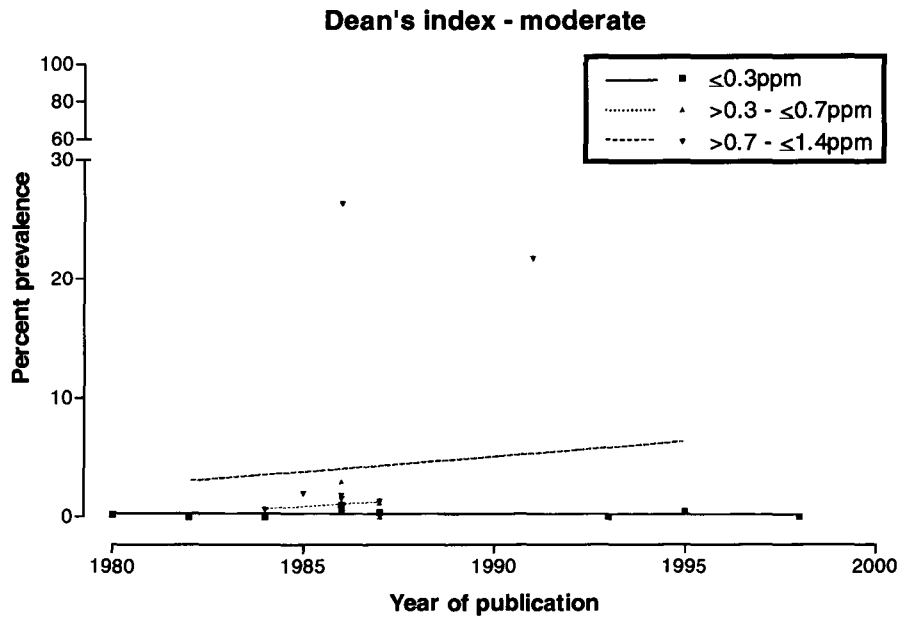


Figure 3.6. Scattergram for moderate fluorosisfor the three fluoride concentration categories.

Figure 3.6. Scatter plots Dean's Index – moderate fluorosis.

There were few scores in the fluoridated category so the increasing, although non-significant trend (Figure 3.6) should be considered with caution.

The prevalence of fluorosis in non-fluoridated areas for moderate fluorosis globally shows no trend as indicated by the linear regression.

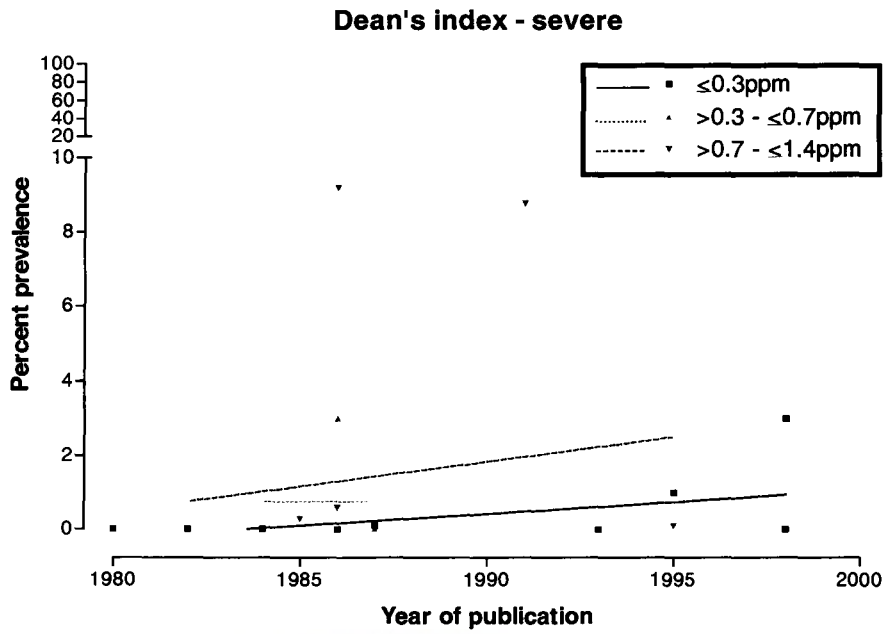


Figure 3.7. Scattergram for severe fluorosis for the threefluoride concentration categories.

Figure 3.7. Scatter plots- Dean's Index –Severe fluorosis.

In both non-fluoridated and fluoridated categories there were slight rises in prevalence trend (Figure 3.7). These trends did not differ significantly from zero.

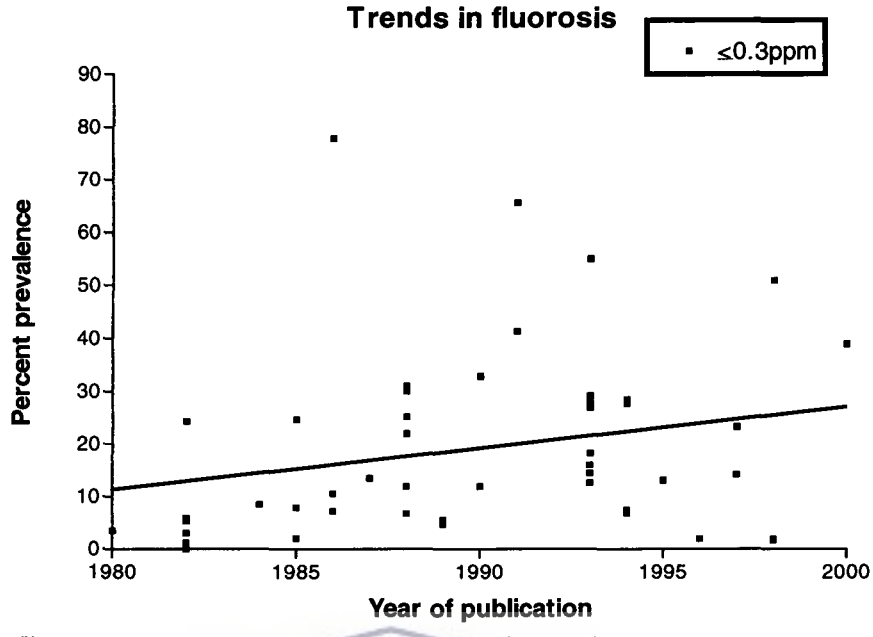
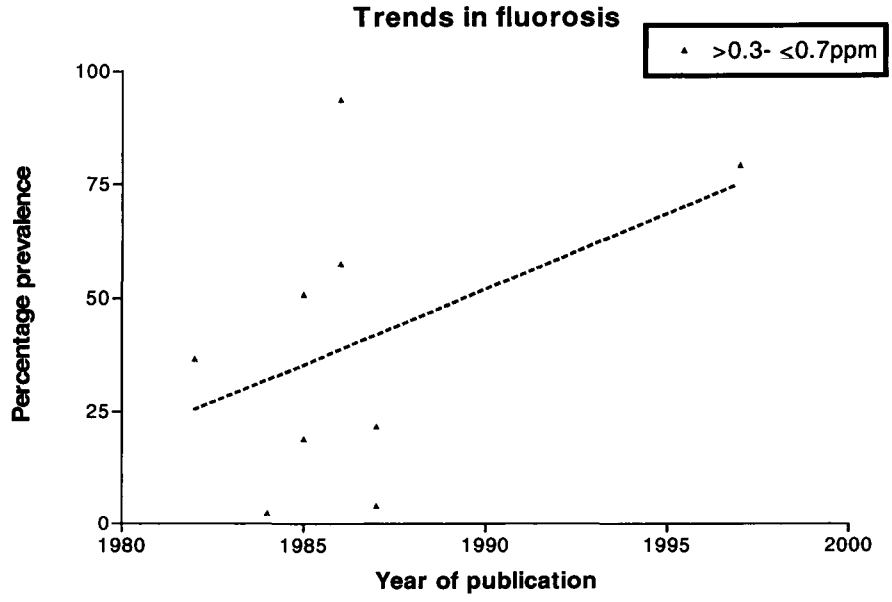


Figure 3.8. Percentage prevalence of fluorosis of any severity in thenon-fluoridated category.

Figure 3.8. Percentage prevalence of fluorosis of any severity in non-fluoridated category for all indices.

Figure 3.8 shows the trend in fluorosis in the non-fluoridated category using all fluorosis indices combined. There is a rising trend which does not differ significantly from zero although it is approaching significance (P=0.0998)



3.9. Percentage prevalence of fluorosis of any severity in the intermediate category.

Figure 3.9. Percentage prevalence of fluorosis of any severity in the intermediate category for all indices.

Figure 3.9 shows a fitted linear regression line for the intermediate concentration of fluoride. Not many publications were available in this category. Although the linear regression line showed a steeper slope than the non-fluoridated category the deviation from 0 was not significant.(P=0.2442). Due to insufficient data in this category more research is required in this category. According to the statistician the outliers make an insignificant contribution to the trend.

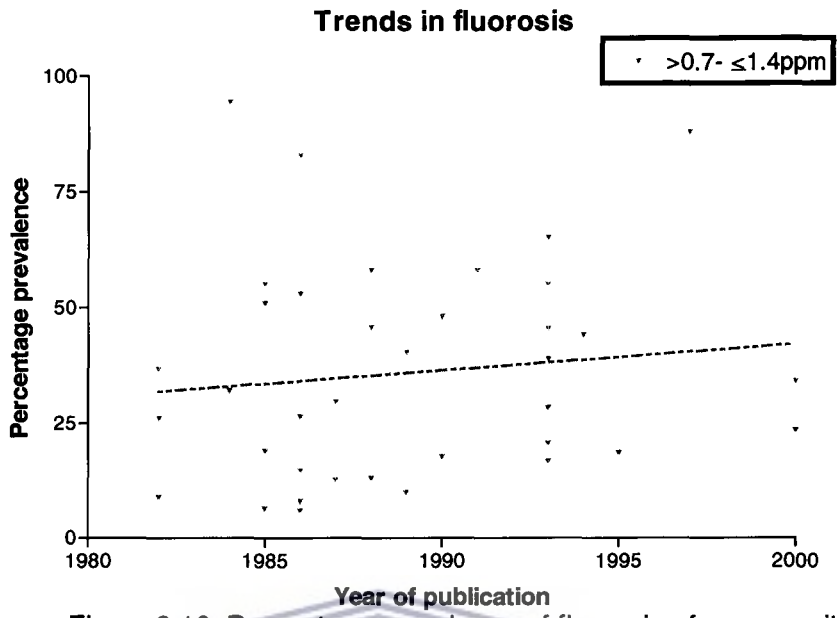
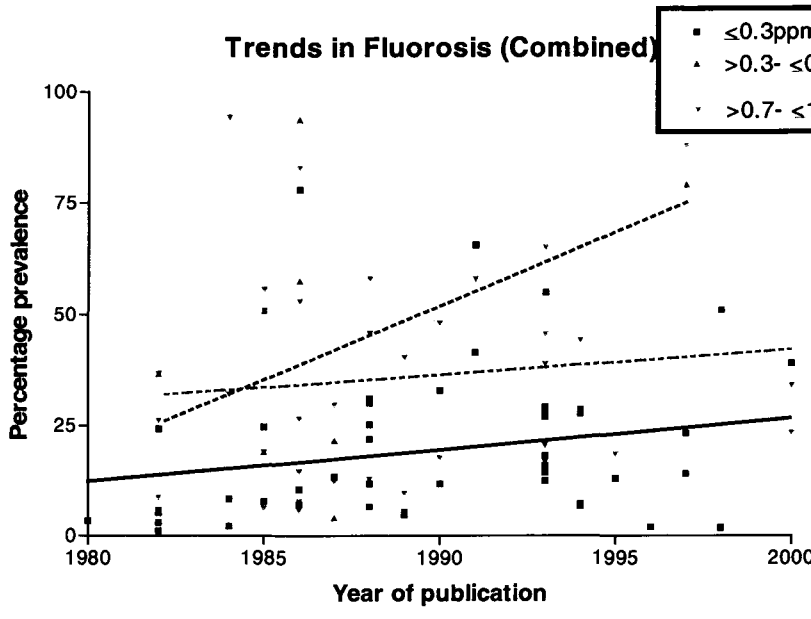


Figure 3.10. Percentage prevalence of fluorosis of any severity in the fluoridated category.

Figure 3.10. Percentage prevalence of fluorosis of any severity in the fluoridated category for all indices.

Figure 3.10 shows a fitted linear regression line for the fluoridated category with an upward slope with no significant deviation from 0 (P= 0.4910).



3.11. Percentage prevalence of fluorosis of any severity in the three fluoride categories.

Figure 3.11. Percentage prevalence of fluorosis of any severity in all three fluoride concentration categories for all indices.

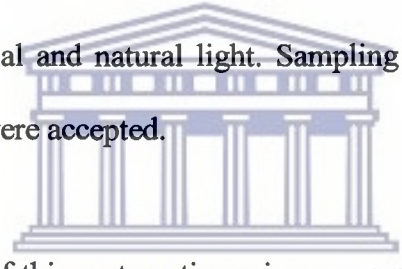
The percentage prevalence of fluorosis trends in all the fluoride concentration categories are shown together in Figure 3.11. They are rising but are not statistically significant in all three categories, the steepest of which is in the intermediate category that has the lowest number of publications. A dose–response is evident between the non-fluoridated and the fluoridated categories.

CHAPTER FOUR

CHAPTER 4: DISCUSSION.

4.1. General remarks

Before the implications of these results can be discussed some general remarks on the shortcomings of this systematic review are necessary. As stated by Szpunar and Burt (1987) when studies use different indices the percentage prevalence of fluorosis may be the only means of comparison. Based on this the data from the various studies were pooled after it was confirmed that there were no significant differences in the mean scores of fluorosis when different indices were applied but the criteria in their application in the studies were not taken into consideration. In many studies the examiners were not blinded and could have introduced some bias in the study. In some studies teeth were dried whilst in other studies they were not dried which could have been responsible for the differences in the prevalence in fluorosis. Studies differed in the use of artificial and natural light. Sampling techniques whether they were random or convenient were accepted.



Comparison of the findings of this systematic review were made with other scientific publications including Dean's historical data. Dean in his studies included only Caucasian children and relied on them for the fluoride history. Recent studies have involved parents in eliciting fluoride histories. Parents could have over, or under, represented information provided but they are probably a more reliable source. Although examiner standardization was reportedly done, measures of examiner agreement were not published. Even when the same index was used, examiners may have applied the criteria differently. These shortcomings do not invalidate comparisons but suggest that the changes in fluorosis rates may be partially due to

different criteria applied (Szpunar and Burt 1987). Therefore, the prevalence of fluorosis in this systematic review must be viewed with these limitations in mind.

This systematic review, however, has many strengths to balance its weaknesses. The pooling of data from single studies with increased sample size enabled conclusions that were more meaningful. An important strength of this systematic review is that it has summarised and integrated data from a wide variety of publications. Finally, it has highlighted areas that may need further investigation.

4.2. Trends in fluorosis

There was no statistically significant trend in the prevalence of dental fluorosis due to the wide variation in the mean fluorosis scores, however, the dose response was consistent with reports in scientific literature with increase in the fluorosis prevalence as the concentration of fluoride increased. The mean fluorosis prevalence for the non-fluoridated areas was 16.7 percent, for the intermediate areas it was 27.4 percent and for the fluoridated areas it was 32. 2 percent.

The wide variation in mean fluorosis scores seen from community to community showed a range 0 to 78 percent, 2.4 to 93.7 percent and 6.3 to 94.1 for the non-fluoridated, intermediate and fluoridated areas, respectively.

Dean demonstrated that in ten communities with negligible to 0.3 ppm fluoride in drinking water, the dental fluorosis was 2.2 percent or less with a mean of 0.9 percent (Dean et al 1941). Comparison of the mean prevalence of fluorosis in this systematic review with Dean's finding shows a 16-fold increase in prevalence. Pendrys and

Stamm (1990) in their narrative review of dental fluorosis in areas with negligible fluoride estimated that the prevalence increased from 1 percent in the 1940's to 10 percent during the 1980's. During Dean's time the exposure to fluoride was through water and diet but recently communities have been exposed to a wider variety of ingestible fluorides. Some non-fluoridated communities may have been exposed to more fluoride than others, thus the wide variation in the mean prevalence of fluorosis from community to community.

Communities exposed to the intermediate concentration of fluoride showed a mean prevalence of fluorosis of 27.4 percent, with a range from 2.4 to 93.7 percent. The intermediate category had only nine publications making them too few to come to a conclusion. Nevertheless, because mean fluorosis prevalence for this category was 27.4 percent further investigation is warranted.

In the fluoridated areas the mean fluorosis prevalence was 32.1 percent. Dean's studies in four communities with 0.9 to 1.2 ppm fluoride in drinking water, dental fluorosis reported a range between 12.2 and 33.3 percent with a mean prevalence of 16.0 percent (Dean et al 1941). The severity of fluorosis observed by Dean in all those communities was in the very mild and mild range that was not regarded as a public health concern (Pendrys and Stamm 1990). The increase shown by the current systematic review in fluoridated areas is a two-fold increase from what was observed by Dean. Szpunar and Burt (1987) estimated an increase in fluorosis in optimally fluoridated areas was 16 percent in the 1940's to 23 percent during the 1980's.

The systematic review has highlighted the larger increase of dental fluorosis prevalence in the non-fluoridated areas than in the fluoridated. This finding is consistent with the scientific studies published by Leverett (1986) as well as by Pendrys and Stamm (1990).

The current review of studies published since the 1980s provides a mixed picture because some investigations are consistent with Dean's studies while others suggest that fluorosis has continued to increase. A range of prevalences from very low to very high was found. It was also observed that for the similar concentrations of fluoride in drinking water the fluorosis prevalences in many areas were different. The wide variations in the prevalence of fluorosis implies exposure to fluoride from sources other than water. This needs to be taken into consideration when optimal concentration is to be determined in future.

Although most studies report very mild to mild categories of fluorosis, moderate to severe categories of fluorosis are beginning to appear. Fejerskov et al (1996) believe that there exists no "critical " value for the fluoride intake below which fluorosis will not manifest.

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Driscoll et al (1986) in their study of fluorosis failed to find support for the hypothesis that there was an increase in dental fluorosis in negligible and optimally fluoridated areas because of consumption of fluoride from all sources. The prevalence of fluorosis was in the very mild and mild categories. The presence of eight children with moderate to severe fluorosis could have been a sign of the shift of fluorosis to more

severe forms. This systematic review found that at least 15 studies had a moderate category of fluorosis and ten studies had a severe category of fluorosis. Although the percentages in these categories were very low two studies suggest otherwise. One in Connecticut (Pendrys 2000) found 50 percent of the total fluorosis prevalence (39 percent) was in the moderate category; in the other in Kenya (Manji et al 1986b) 24.4 percent of the fluorosis prevalence was in the severe category.

Osuji et al (1988) found that the prevalence of fluorosis in children 8, 9 and 10 years old was 13 percent with most children exhibiting scores of 1 or 2 of the Thylstrup and Fejerskov index indicating that their results were consistent with those of Dean et al (1942) and with that of Driscoll et al (1983). Their study found a lower prevalence than Leverett (1986) who reported that 20 percent of 12 and 13 year old children in Rochester, New York had fluorosis. Compared with Dean's studies in 1942, for children of comparable age in communities with essentially the same water fluoride levels, the prevalence of dental fluorosis in Leverett's study (1986) was 3.5 times higher in non-fluoridated communities and two times higher in fluoridated communities.

The systematic review has confirmed that there is an increase in fluorosis, mostly in the very mild and mild categories with a number of studies observing very low percentage fluorosis in moderate and severe categories that necessitates monitoring. In this review the non-fluoridated areas had 15 publications with moderate fluorosis and 10 with severe fluorosis. In the intermediate category there were 4 publications with moderate fluorosis and 3 with severe fluorosis. Fluoridated areas had 20 publications with moderate fluorosis and 12 publications with severe fluorosis. There seems to be a

shift from very mild and mild fluorosis to moderate and to a certain extent severe fluorosis.

One of the concerns expressed by many researchers is that unlike in the 1940s, there is now exposure to many more sources of fluorides. The main sources of fluoride, currently, are drinking water, fluoridated salt, food, beverages, baby cereals and formulas, toothpaste, rinses, and topical fluoride. In addition to water, communities may be exposed to the diffusion or halo effect from drinks and food manufactured in fluoridated areas (Clarkson and McLoughlin 2000). These sources have been implicated in the increase in fluorosis (Leverett 1986). Ismail and Bandekar (1999) found that fluoride supplements and tooth brushing have an additive effect on the risk of developing dental fluorosis in children who brush their teeth with fluoridated dentrifice. Water consumption as predicted by the mean annual air temperature can no longer be the sole determinant of optimal fluoride concentration in water taking into consideration the change in fluoride exposure from 1940 to the present time. Total exposure must be taken into account if fluorosis is to be controlled, especially when communities are to implement water fluoridation. Epidemiologic studies that have explored the relation of increased fluorosis to the various causative factors have pinpointed the improper prescribing of dietary fluoride supplements as most likely factor in this increase (Horowitz 1992). It is encouraging that other researchers have followed up on suggestions by Manji et al (1986a) to investigate the influence of fluoride and altitude which would be of value in any modifications necessary under these conditions. Yoder et al (1998) identified altitude as a risk factor for fluorosis in spite of negligible water fluoride concentration and their studies concurred with other investigators such as Mabelya et al (1992) who reported disproportionately severe

fluorosis in residents of high altitude in developing countries. Altitude could be regarded as a confounding variable

4.3. Conclusion

This systematic review concurs with Szpunar and Burt (1987) who highlighted the need for continued study and monitoring of dental fluorosis in fluoridated and non-fluoridated communities, given the multitude of fluoride sources available today. Fluorosis has increased in fluoridated as well as in non-fluoridated communities, more so in non-fluoridated communities although it was not statistically significant. There was a wide variation in the prevalence of fluorosis with communities with similar concentration of fluoride showing different prevalences. In spite of all the information at our disposal dental fluorosis is not yet regarded as a public health problem. Where fluorosis is disproportionately high there are specific problems in those communities such the misuse of and mis-prescription of dietary fluoride supplements, re-constitution of infant food and formulas in fluoridated water, altitude and traditional cooking methods such as the use of magadi in Tanzania. Nevertheless some general precautions will be in order for both fluoridated and non-fluoridated as well those communities contemplating the adjustment of the fluoride concentration in water.

The major recommendations are that:

- The fluoride content of foods and beverages, particularly infant formulas and water used in their reconstitution, should continue to be monitored closely in an effort to limit the excessive intake of fluoride.
- Ingestion of fluoride from dentrifices by young children should be controlled and the use of only small quantities should be emphasized.

- Dietary fluoride supplements should not be prescribed for children who consume fluoridated drinking water. Dentists, pediatricians, other medical practitioners and parents must be educated on this issue (Horowitz 2000).
- Dietary fluoride supplements should be considered a targeted preventive regimen only for those children at higher risk for dental caries and with low levels of ingested fluoride from other sources (Levy et al 1995)
- Dental public health authorities must work with toothpaste manufacturers, professional organizations and regulatory agencies to facilitate the approval and marketing of pediatric fluoride toothpaste (Horowitz 1992).
- There must be a concerted effort in providing revised information on all aspects of fluoride on a regular basis and encourage collaboration between all practitioners and community members on the issue of fluorosis.
- When decisions are to be made on the optimal concentration of fluoride in water the use of all fluoride and consumption must be taken into consideration. Air temperature is no longer sufficient to determine the optimal concentration of fluoride in water. Dean's definition of optimal no longer pertains and that attempts must be made to maintain the lowest level capable of producing the desired therapeutic effect (Leverett 1991). The Department of Health (2000) has recommended a range from 0.05-0.07 parts per million.
- Investigations in the knowledge of dental and other professionals of the use and abuse of fluoride.
- Provision of advice to parents of young children regarding the early use of toothpaste and fluoride supplements to reduce the impact of fluorosis in both fluoridated and non-fluoridated communities.

- The manufacturers of bottled water should provide appropriate labeling stating the fluoride content and mechanisms to monitor this should be instituted.

The recommendations have been mentioned repeatedly by many well-known researchers but perhaps they have not been given much attention as the profession has become too much the crusaders for fluorides. Horowitz (1991) expressed the idea that mild fluorosis is generally interpreted by investigators as having minimal cosmetic importance but it may be considered an aesthetic problem by individuals concerned. Dental researchers, who are supporters of water fluoridation and other fluoride distribution mechanisms are considered to lack objectivity (Riordan 1993). There is much information on a scientific basis for the dental profession to maintain the reputation fluoride has earned as a population strategy in caries prevention.

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APPENDICES

Appendix A. Criteria for Dean's Classification (Dean et al 1942)

Classification	Criteria
Normal (0)	The enamel represents the usual translucent semi-vitriform type of structure. The surface is smooth, glossy and usually of a pale creamy white colour.
Questionable (0.05)	The enamel discloses slight aberration from the normal translucency of enamel ranging from a few white flecks to occasional white spots. The classification is used in those instances where a definite diagnosis of the mildest form of fluorosis is not warranted and a classification of "normal" not justified.
Very mild (1)	Small, opaque paper white areas scattered irregularly over the tooth but not involving as much as approximately 25 per cent of the tooth surface. Frequently included in this classification are the teeth showing no more than about 1-2 mm of white opacity at the tip of the summit of the cusps of the bicuspids or second molars.
Mild (2)	The white opaque areas in the enamel of the teeth are more extensive, but do not involve as much as 50 per cent of the tooth.
Moderate (3)	All enamel surfaces of the teeth are affected and surfaces subject to attrition show wear. Brown stain is frequently a disfiguring feature.
Severe (4)	All enamel surfaces are affected and hypoplasia is so marked that the general form of the tooth may be affected. The major diagnostic sign of this classification is discrete or confluent pitting. Brown stains are widespread and teeth often present a corroded like appearance.

Public Health Significance of the Community Fluorosis Index scores, as defined by Dean (1946).

Range of scores for CFI	Public Health Significance
0.0-0.4	Negative
0.4-0.6	Borderline
0.6-1.0	Slight
1.0-2.0	Medium
2.0-3.0	Marked

Appendix B. The Tooth Surface Index of Fluorosis and descriptive criteria (Horowitz et al 1984)

Numerical score	Descriptive criteria
0	Enamel shows no evidence of fluorosis
1	Enamel shows definite evidence of fluorosis, namely areas with parchment- white colour that total less than one third of the visible enamel surface. The category includes fluorosis confined only to incisal edges of anterior teeth and cusp tips of posterior teeth (snow capping)
2	Parchment-white fluorosis totals at least one third of visible surface, but less than two thirds.
3	Parchment-white fluorosis totals at least two thirds of the visible surface.
4	Enamel shows staining in conjunction with any of the preceding levels of fluorosis. Staining is defined as an area of definite discolouration that may range from very light to dark brown.
5	Discrete pitting of the enamel exists, unaccompanied by evidence of staining of intact enamel. A pit is defined as a definite physical defect in the enamel surface with a rough floor that is surrounded by a wall of intact enamel. The pitted area is usually stained or differs in colour from the surrounding enamel.
6.	Both discrete pitting and staining of the intact enamel exist.
7.	Confluent pitting of the enamel surface exist. Large areas of enamel may be missing and the anatomy of the tooth may be altered. Dark-brown stain is usually present.

Appendix C. Clinical criteria and scoring for the Thylstrup-Fejerskov Fluorosis Index (Thylstrup and Fejerskov 1978)

0 Normal translucency of enamel remains after prolonged air drying.

1 Narrow white lines located corresponding to the perikymata.

2 Smooth surfaces: More pronounced lines of opacity which follow the perikymata. Occasionally the confluence of adjacent lines

Occlusal surfaces:Scattered areas of opacity < 2 mm in diameter and pronounced opacity of cuspal ridges.

3 Smooth surfaces: Merging and irregular cloudy areas of opacity. Accentuated drawing of perikymata often visible between opacities

Occlusal surfaces: Confluent areas of marked opacity. Worn areas appear almost normal but usually circumscribed by a rim of opaque enamel

4 Smooth surfaces: The entire surface exhibits marked opacity or appears chalky white. Parts of surface exposed to attrition appear less affected.

Occlusal surfaces: The entire surface exhibits marked opacity. Attrition is often pronounced shortly after eruption.

5 Smooth and Occlusal surfaces: Entire surface displays marked opacity with focal loss of outermost enamel (pits) < 2 mm in diameter.

6 Smooth surfaces: Pits are regularly arranged in horizontal bands < 2 mm in vertical extension.

Occlusal surfaces: Confluent areas < 3 mm in diameter exhibit loss of enamel. Marked attrition.

7 Smooth surfaces: Loss of outer most enamel in irregular areas involving < ½ of entire surface

Occlusal surfaces: Changes in the morphology caused by merging pits and marked attrition.

8 Smooth and Occlusal surfaces: Loss of outermost enamel involving > ½ of surface.

9 Smooth and Occlusal surfaces: Loss of main part of enamel with change in anatomic appearance of surface. Cervical rim of almost unaffected enamel is often noted.

Appendix D. The DDE Index for use in general purpose epidemiological studies (Ainamo and Cutress 1982)

Normal	0
Demarcated opacities:	
white / cream	1
yellow / brown	2
Diffuse opacities	
Diffuse - lines	3
Diffuse - patchy	4
Diffuse - Confluent	5
Confluent / patchy + staining+ loss of enamel	6
Hypoplasia:	
Pits	7
Missing Enamel	8
Any other defect	9
Extent of Defect	
Normal	0
< 1/3	1
at least 1/3 < 2/3	2
at least 2/3	3

Table 5.8 Modified DDE Index for use in screening surveys (Clarkson and O' Mullane 1989)

	CODE
Normal	0
Demarcated opacity	1
Diffuse opacity	2
Hypoplasia	3
Other defects	4

Appendix E. Fluorosis Risk Index scoring criteria

Each visible surface zone will be scored according to the following criteria:

Negative finding:

Score = 0

A surface zone will receive a score 0 when there is absolutely no indication of fluorosis being present. There must be complete absence of any white spots or striations, and tooth surface colouration must appear normal.

Questionable finding

Score = 1

Any surface zone that is questionable as to whether there is fluorosis present (i.e. white spots, striations, or fluorotic defects cover 50 percent or less of the surface zone) should be scored as 1

Score = 7

Any surface that has an opacity that appears to be a non-fluoride should be scored as 7
Positive findings

Score = 2

A smooth surface zone will be diagnosed as being positive for enamel fluorosis if greater than 50 percent of the zone displays parchment-white striations typical of enamel fluorosis. Incisal edges and occlusal tables will be scored as positive for enamel fluorosis if greater than 50 percent of that surface is marked by snow-capping typical of enamel fluorosis.

Score = 3

A surface zone will be diagnosed as positive for severe fluorosis if greater than 50 percent of the zone displays pitting, staining, and deformity, indicative of severe fluorosis.

Surface zone excluded:

Score = 9

A surface zone is categorised as excluded (i.e. not adequately visible for diagnosis to be made) when any of the following conditions exist:

(1) Incomplete eruption:

Rule 1: If a tooth is in proximal contact but the occlusal surface is not parallel with existing

occlusion, the occlusal two thirds of the tooth is scored, but the cervical one-third is recorded as excluded.

Rule 2: If a tooth is erupted, but not yet in contact, the incisal/occlusal edge is scored, but all other surfaces are recorded as excluded.

(2) Orthodontic appliance and bands:

Rule 1: If there is an orthodontic band present on a tooth only the occlusal table or the incisal edge should be scored.

Rule 2: If greater than 50 percent of the surface zones are banded, the subject should be excluded from the examination.

(3) Surfaces crowned or restored.

Rule: Surface zones that are replaced by either a crown or restoration covering greater than 50 percent of the surface zone should be recorded as excluded.

(4) Gross plaque and debris:

Rule: Any subject with gross deposits of plaque or debris on greater than 50 percent of the surface zones should be excluded from examination

Appendix F

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
1	Segreto et al	Texas, USA	326	DEANS	1984	7-18	Lifetime	74.6 (243)	16.87 (55)	7.96 (26)	.60 (2)	0.0 (0.0)	0.0 (0.0)		8.56 (28)
2	EL-Nadeef, Honkala	Bauchi, Kandap, Nigeria	213	DEANS	1998	12-15	Lifetime	49 (104)		41 (87)	7 (15)	0.0 (0.0)	3 (6)		51 (109)
3	Driscoll et al	Illinois and Iowa, USA	316	DEANS	1980	8-16	Lifetime	96.5 (305)		2.2 (70)	1.1 (3)	.2 (6)	0.0 (0.0)		3.5 (11)
4	Driscoll et al	Illinois, USA	807	DEANS	1982	8-16	Lifetime	96.5 (779)	2.2 (18)	1.1 (9)	.2 (2)	0.0 (0.0)	0.0 (0.0)		1.3 (10)
5	Leverett	NewYork State, USA	934	DEANS	1981-1982	7-17	Mixed	94.53 (883)	3.32 (30)	1.384 (12)	0.642 (5)	0.0 (0.0)	0.0 (0.0)		5.34 (5)
6	Jackson et al	Cornersville, Indiana. U.S.A.	124	DEANS	1993	7-14	Lifetime	85.5 (106)	0.0 (0.0)	13.7 (17)	0.8 (1)	0.0 (0.0)	0.0 (0.0)		14.5 (18)
7	Kumar, Swango	Newburgh and Kingston, New York State, USA	848	DEANS	1986	7-14	Lifetime	77.69 (659)	11.66 (99)	6.63 (55)	3.06 (26)	1.03 (9)	0.0 (0.0)		10.72 (91)
8	Kumar, Swango	Newburgh and Kingston, New York State, USA	1057	DEANS	1995	7-14	Lifetime	78.3 (828)	9.27 (98)	8.23 (87)	3.5 (37)	0.47 (5)	0.9 (9)		13.1 (138)
9	Kumar et al	Kingston, New York State, USA	425	DEANS	1986	7-14	Lifetime	81.43 (346)	11.29 (48)	4.47 (19)	2.11 (9)	0.7 (3)	0		7.29 (31)
10	Heller et al	National Survey U.S. Schools USA	6,239	DEANS	1986-87	7-17	Lifetime	59.8 (3731)	26.6 (1660)	10.7 (668)	2.4 (150)	0.4 (24)	0.1 (6)		13.5 (842)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
11	Tsutsui et al	Japan	412	DEANS	1998 (0-.2)	10-12	Lifetime	94.7 (390)	3.6 (15)	1.4 (6)	0.2 (1)	0.0 (0.0)	0.0 (0.0)		1.7 (7)
12		Japan	209	DEANS	1998 (.2-.4)	10-12	Lifetime	88.7 (185)	9.4 (20)	1.4 (3)	0.5 (1)	0.0 (0.0)	0.0 (0.0)		1.9 (4)
13	Ismail et al	Truro, Nova Scotia, Canada	41	TSIF	1991	6 +	1st 6 years	58.5 (24)		41.5 (17)					41.5 (17)
14	Driscoll et Al	Illoinois, USA	80 7	TSIF	1982	8-16	Lifetime	94.1 (759)		5.4 (44)	0.5 (4)	0.0 (0.0)	0.0 (0.0)		5.9 (47)
15	Ismail et al	Sherbrooke, Quebec, Canada	251	TSIF	1988	11-17	Lifetime -public	68.9 (173)							31.1 (79)
16	Ismail et al	Sherbrooke, Quebec, Canada	248	TSIF	1988	11-17	Lifetime-private	69.9 (173)							30.1 (75)
17	Selwitz et al	Nebraska, USA	235	TSIF	1990	8-16	Lifetime	87.94 (206)		10.72 (24)	1.965 (4)	1.18 (2)	.044 (1)		12.054 (28)
18	Spunzar & Burt	Comparisons of studies in USA	1103	TSIF	1986	6-12	Lifetime	87.8 (968)		12 .2 (134)	0.0 (0.0)				12.2 (134)
19	Woolfolk et al	Michigan, USA	412	TSIF	1887/18 8	9-13	Lifetime	93.1 (384)		6.1 (25)	0.6 (2)	0.2 (1)	0.0 (0.0)		6.8 (28)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
20	Clark et al	Vernon, Canada	510	TSIF	1993	SC	Lifetime	45 (229)		48 (245)	5 (25)	<1 (5)	<1 (5) 5=<1 (5) 6&7=0		55 (285)
21	Skotowski	Univ of Iowa, USA	157	TSIF	1991	8-17	Lifetime (clinic)	34.4 (54)		42.7 (67)	12.7 (20)	3.8 (6)	4.5 (7)	0.6 1.3 (1) (2))	65.6 (102)
22	Brothwell and Limeback	Wellington-Dufferin-Guelph, Ontario. Canada	752	TSIF	1996-1997	7-8	Lifetime (1st 6 years)	76.7 (577)		18.4 (138)	3.5 (26)	0.9 (7)	0.5 (4)		23.3 (175)
23	Jackson et al	Cornersville, Indiana. U.S.A.	126	TSIF	1993	7-14	Lifetime	81.8 (103)		15.1 (19)	3.2 (4)	0.0 (0)	0 (0)	0 (0)	18.3 (23)
24	S.Vignar-ajan	Antigua, West Indies	154	TSIF	1988-1989	12-14	Lifetime	95.2 (147)		3.9 (6)	0.5 (1)	0.4 (1)	0.0 (0)	0.0 (0)	4.8 (8)
25	Ismail et al	Truro, Nova Scotia, Canada	116	TSIF	1993	SC	Lifetime	87.4 (102)		10.3 (12)	2.3 (3)				12.6 (15)
26	Cortes et al	Maceio, Brazil	160	TFI	1994	6-12	Lifetime	92.5 (148)		12(7.5) 1-2					7.5 (12)
27	Heintze & Bastos	Itapolis, Brazil	115	TFI	1995-1996	5-19	0-3 years	97.95 (112)		0.86 (1)	1.23 (2)	0.0 (0)	0.86 (1)		2.05 (4)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
28	Wentzel and Thylstrup	Ry, Denmark	116	TFI	1982	12-15 (F)	Lifetime	97 (112)		2.98 (3)	0.02 (0)	0.0 (0)	0.0 (0)	0.0 (0)	3.00 (4)
29	Barsden et al	Horderland, Norway	105	TFI	1997	5-18	Lifetime	85.7 (90)		12.3 (13)	1.9 (2)	0.0 (0)	0.0 (0)		14.2 (15)
30	Wiktors-son et al	Encoping, Sweden	236	TFI	1982	Adult	Lifetime	100 (236)		0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
31	Spencer & Slade	Southern Australia	?	TFI	1992-1993	10-17	Lifetime	70.7		28.0	0.6	0.6	0		29.2
32	Riordan & Banks	Bunbury, Australia,	321	TFI	1990	12	Lifetime	67 (227)		25.5 (81.8)	6.9 (22)	0.6 (2)	0.0 (0)		33 (106)
33	Nganga & Valder haug	Nairobi, Kenya	513	TFI	1993	6-15	Lifetime	84 (431)		14 (72)		2 (10)			16 (82)
34	Manji Baelum, Ferjeskov Germet	Machakos District, Kenya	317	TFI	1986	11-15	Lifetime	22 (70)			53.6 (170)		24.4 (77)		78 (247)
35	Milsom & Mitro poulos	Nortwich, Cheshire, UK	131	DDE	1988	8	Lifetime	78 (102)							22 (29)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
36	Angelillo et al	Naples, Italy	215	DDE	1989	11-13	Lifetime	94.4 (203)							5.6 (15)
37	Dummer, Kingdon	South Wales, UK	579	DDE	1985	11-12	Lifetime	97.1 (562)							2.09 (17)
38	Downer & Blinkhorn	London, UK	653	DDE	1993	12	Lifetime	69.5 (454)							27.7 (199)
39	Downer & Blinkhorn	Edinburgh, UK	289	DDE	1993	12	Lifetime	59.1 (171)							28.6 (118)
40	Downer & Blinkhorn	Glasgow, UK	435	DDE	1993	12	Lifetime	72.6 (316)							26.9 (119)
41	Downer	North London, UK	939	DDE	1994	12	Lifetime	72.3 (679)							27.7 (260)
42	Downer	Edinburgh, UK	489	DDE	1994	12	Lifetime	71.4 (358)							28.6 (140)
43	Downer	Glasgow	599	DDE	1994	12	Lifetime	93.1 (558)							6.9 (41)
44	Liefde & Herbison	Hawkes Bay New Zealand	237	DDE	1982	9	Lifetime	75.66 (179)							24.34 (58)
45	Liefde & Herbison	Hawkes Bay New Zealand	263	DDE	1985	9	Lifetime	75.27 (198)							24.73 (65)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores Nonfluoridated ≤ 0.3 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
46	Cutress et al	Frankton & Rodney New Zealand	700	DDE	1985	9	Lifetime	92 (644)							8.00 (56)
47	Pendrys	Connecticut, USA	429	FRI	2000	10-14	Lifetime	61 (261)			19.5 (84)	19.5 (84)			39 (168)
48	Pendry & Katz	Connecticut and Massachusetts, USA	1242	FRI	1988	11-14	Lifetime	74.8 (929)							25.2 (313)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores > 0.3 -≤ 0 .7 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
1	Tsutsui et al	Japan	119	DEANS	1987	10-12	Lifetime	84.4 (100)	11.5 (14)	4.1 (5.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)		4.1 (5.0)
2	Segreto et al	San Antonio, Texas, USA	126	DEANS	1984	14-18	Lifetime	92.1 (116)	5.6 (7)	2.4 (3)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)		2.4 (3)
3	Heller et al	National Survey, USA	1793	DEANS	1986-1987	7-17	Lifetime	47.4 (850)	31 (556)	17.3 (310)	3.1 (56)	1.2 (22)	0.0 (0.0)		21.6 (387)
4	Grobler et al	Nourivier South Africa	33	DEANS	1986	12-13	Lifetime	9.1 (3)	33.3 .(11)	30.3 (10)	21.2 (7)	3 (1)	3 (1)		57.5 (19)
5	Bardsen et al	Western Norway	113	TFI	1997	5-18	Lifetime	21 (24)		30 (34)	30 (34)	10 (11)	1 , 6 (1) (7)	1, 2 (1) (2)	79 (89)
6	Manji, Baelum, Fejerskov & Germet	Region B, Machakos, Kenya	160	TFI	1986	11-15	Lifetime	6.2 (11)				60.6 (97)	33.1 (53)		93.7 (150)
7	Cutress et al	Auckland, New Zealand	1063	DDE	1985	9	Lifetime	81 (861)							19 (202)
8	Liefde & Hobison	Hawkes Bay, New Zealand	260	DDE	1985	9	Lifetime	49.24 (128)							50.76 (132)
9	" "	" "	191	DDE	1982	9	Lifetime	63.36 (121)							36.64 (70)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores > 0.7 ppm- - 1.4 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
1	Bagram ian	Singapore	1739	DEANS	1986	9-16	Lifetime	13.9 (242)	3.4 (59)	15.7 (273)	31.5 (548)	26.3 (457)	9.2 (160)		82.6 (1436)
2	Evans & Stamm	Hong Kong	1062	DEANS	1985	7-12	Lifetime	17.89 (190)	27.87 (286)	36.06 (383)	16.85 (179)	1.97 (21)	0.28 (3)		55.16 (567)
3	Tsutsui et al	Japan	192	DEANS	1987	10-12	Lifetime	63 (121)	24.5 (47)	11 (21)	1.5 (3)	(0.0)	0.0		12.5 (24)
4	Kumar, et al	Newburgh, New York State, USA	608	DEANS	1986	7-14	Lifetime	83.4 (507)	10.69 (65)	3.61 (22)	1.64 (10)	0.65 (4)	0		5.92 (36)
5	Villa et al	San Felipe, Chile	134	DEANS	1986	-10	Lifetime								52.9 (71)
6	Lewis et al	Kwandabele, South Africa	262	DEANS	1991	6-18	Lifetime	12.59 (33)	27.09 (71)	11.45 (30)	16.03 (42)	21.75 (57)	8.77 (23)		58.01 (152)
7	Kumar & Swango	Newburgh New York State, USA	459	DEANS	1986	7-14	Lifetime	78.4 (360)	13.7 (63)	4.8 (22)	2.2 (10)	0.9 (4)	0		7.9 (36)
8	Kumar & Swango	Newburgh New York State, USA	847	DEANS	1995	7-14	Lifetime	62.9 (533)	18.5 (157)	12.8 (108)	5.3 (45)	0.4 (3)	0.1 (1)		18.6 (157)
9	Wentzel and Thylstrup	Neastved, Denmark	50	DEANS	1982	12 & 15	Lifetime	14 ((7)	60 (30)	26 (13)	0.0 (0.0)	0.0 0.0	0.0 (0.0)		26 (13)
10	Jackson et al	Brownsburg, Indiana, USA	116	DEANS	1993	11-17	Lifetime	61.2 (71)	0.0 (0.0)	31.9 (37)	6.9 (8)	0.0 (0.0)	0.0 (0.0)		38.8 (45)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores > 0.7 ppm- - 1.4 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
11	Driscoll et al	Iowa, USA	336	DEANS	1986	8-16	Lifetime	56.0 (188)	29.5 (99)	7.4 (25)	4.8 (16)	1.8 (6)	0.6 (2)		14.6 (49)
12	Segreto et al	Texas, USA	887	DEANS	1984	8-14	Lifetime	42.6 (378)	24.2 (215)	26.8 (238)	4.62 (41)	0.57 (5)	0.0 (0.0)		32.01 (284)
13	Heller et al	National Survey, USA	6708	DEANS	1986-1987	7-17	Lifetime	33.6 (2261)	36.5 (2456)	22.5 1514	5.8 (390)	1.3 (87)	0.0 (0.0)		29.6 (1991)
14	Leverett	New York State, USA	729	DEANS	1986	12-17	Mixed	73.5 (536)		20.5 (150)	4.38 (32)	1.5 (11)	0.0 (0.0)		26.38 (192)
15	Clark et al	Kelowna, Canada	621	TSIF	1993	SC	Lifetime	35 (217)		55 (341)	7 (43)	3,4,5,6= <1	7=0		65 (408)
16	Ismail et al	Kentville, Nova Scotia, Canada	103	TSIF	1993	SC	Lifetime	71.6 (74)		23.4 (24)	5.0 (6)				28.4 (13)
17	Leake et al	Toronto, Canada	5285	TSIF	1999-2000	7-13	Lifetime	76.2 (4028)		10.61 (561)	7.48 (422)	4.21 (233)	1.00 (53)		23.3 (1232)
18	Clark et al	Vernon, Canada	510	TSIF	1993	SC	Lifetime	45 (229)		48 (244)	5 (25)	<1 (4)	<1 (4)	<1 (4)	55 (281)
19	Ismail al	Trois-Rivieres, Quebec, Canada	222	TSIF	1988	11-17	1st 6 years of life Public	54.4 (121)							45.6 (101)
20	" "	" "	215	TSIF	1988	11-17	1st 6 years of life Private	42 (90)							58 (125)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores > 0.7 ppm- - 1.4 ppm (Number of individuals in brackets)							
								None 0	Question-able	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
21	Jackson et al	Brownsburg, Indiana, USA	117	TSIF	1993	11-17	Lifetime	54.7 (64)		34.2 (40)	9.4 (11)	0.9 (1)	0.9 (1)	0.0 (0)	45.4 (53)
22	Selwitz et al	Kewanee Nebraska, USA	260	TSIF	1990	8-16	Lifetime	82.69 (215)		13.84 (36)	2.69 (7)	1.15 (3)	0.0 (0.0)	0.0 (0.0)	17.69 (46)
23	Riordan & Banks	Perth Metro, Australia	338	TFI	1989	12	Lifetime (0-4)	59.8 (202)		29.0 (98)	8.9 (30)	2..4 (8)	0.0	0.0	40.3 (136)
24	Cortes et al	Vitoria, Brazil	200	TFI	1994	6-12	Lifetime	48 (96)		47.5 (95) (1-2)		4.5 (9) (3-4)	0.5 (10) (≥5)		57 (114)
25	Wiktor -sson et al	Uppsala, Sweden	237	TFI	1982	Adult	Lifetime	91.2 (237)		8.1 (21)	0.7 (2)	0.0	0.0	0.0	8.8 (23)
26	Akpata et al	Hail Region Saudi Arabia	2355	TFI	1993	12-15	Lifetime	4.79 (113)			173 (1-2)		309 (3-4)		20.46 (482)
27	Osuji et al	East York, Toronto, Canada	633	TFI	1988	7-10	Lifetime	87 (551)		9.95 (63)	2.21 (14)	0.63 (4)	1		12.9 (82)
28	Akpata et al	Hail, Saudi Arabia	719	TFI	1997	12-15	Lifetime	12.37 (89)		18.91 (136) (1-2)	30.59 (220) (3-4)	22.67 163 (5-6)	15.43 (111) (7-9)		87.62 (630)
29	Cutress et al	Auckland Mtro,Rodney & Frankton, New Zealand	837	DDE	1985	9	Lifetime	81 (678)							19 (159)

	Study group	Country	Sample	Index	Exam year	Age	Fluoride intake period	% distribution of scores > 0.7 ppm- - 1.4 ppm (Number of individuals in brackets)							
								None 0	Questionable	Very mild 1	Mild 2	Mode Rate 3	Severe 4	5	%prev
30	de Liefde & Herbison	Auckland , New Zealand	191	DDE	1982	9	Lifetime	63.36 (121)							36.64 (70)
31	de Liefde & Herbison	Auckland, New Zealand	260	DDE	1985	9	Lifetime	49.24 (128)							50.76 (132)
32	Angelillo et al	Naples, Italy	216	DDE	1989	11-13	Lifetime	90.3 (195)							9.7 (21)
33	Downer et al	Dublin, Ireland	551	DDE	1993	12	Lifetime	83.3 (459)							16.7 (92)
34	Dummer et al	South Wales, UK	759	DDE	1985	11-12	Lifetime	93.7 (711)							6.3 (48)
35	King and Brook	Hong Kong	202	DDE	1984	20.4	Lifetime	5.9 (12)							94.1 (190)
36	Milsom & Mitro-poulos	Nantwich Cheshire, UK	91	DDE	1990	8	Lifetime	52(47)							48 (44)
37	Pendrys	Connecticut, USA	234	FRI	2000	10-14	Lifetime	66 (156)			19.5 (39)	19.5 (39)			34 (78)

Appendix G

Dr Khan
29 Aug 2002

Part1 (all variables)

```
. for var  nonecode   prevcode: oneway X  index, bonf


->  oneway nonecode index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      31960.5179       4   7990.12947      0.88     0.4797
 Within groups      799561.327      88   9085.92417
------------------------------------------------------------------------
    Total           831521.844      92   9038.28092

Bartlett's test for equal variances:  chi2(4) = 141.3916  Prob>chi2 = 0.000


->  oneway prevcode index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      2345.61295       4   586.403238      1.08     0.3703
 Within groups      44942.2123      83   541.472437
------------------------------------------------------------------------
    Total           47287.8252      87   543.538221

Bartlett's test for equal variances:  chi2(4) =  10.2768  Prob>chi2 = 0.036

. for var  nonecode   prevcode: oneway X  distscor, bonf

[redacted].

->  oneway nonecode distscor, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      42071.9582       2   21035.9791      2.40     0.0967
 Within groups      789449.886      90    8771.6654
------------------------------------------------------------------------
    Total           831521.844      92   9038.28092

Bartlett's test for equal variances:  chi2(2) =  73.5268  Prob>chi2 = 0.000

[redacted]
```

```
-> oneway prevcode distscor, bonf

                        Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups       5476.10096      2   2738.05048      5.57  [redacted]
 Within groups       41811.7243     85   491.902639
------------------------------------------------------------------------
    Total            47287.8252     87   543.538221

Bartlett's test for equal variances:  chi2(2) =   6.1264  Prob>chi2 = 0.047

       Comparison of Proportions: Prevelence by Distribution of scores
                                  (Bonferroni)
Row Mean-|
Col Mean |   (0.0 ; 0   (0.3 ; 0
---------+----------------------
(0.3 ; 0 |      20.38
         |   [redacted]
         |
(0.7 ; 1 |      14.04      -6.34
         |   [redacted]     1.000
```

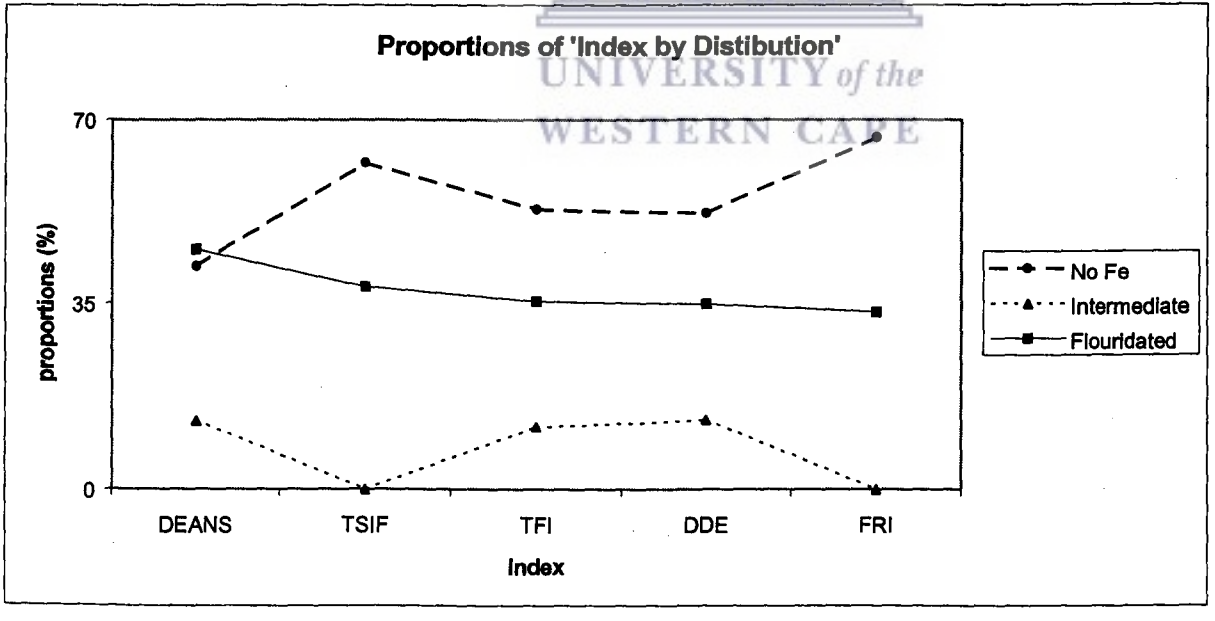
The model shows that there's a significant difference between the means of 'proportions of the prevalence' [redacted]. In particular, means of 'Intermediate' and 'Fluoridated' differ significantly with the mean of 'No Fe' with p-values of 0.041 and 0.020 respectively.

```
. tab  index distscor,row col chi2 V
```

Index	Distribution of scores (0.0 ; 0.	(0.3 ; 0.	(0.7 ; 1.	Total
DEANS	13	4	14	31
	41.94	12.90	45.16	100.00
	26.53	44.44	37.84	32.63
TSIF	13	0	8	21
	61.90	0.00	38.10	100.00
	26.53	0.00	21.62	22.11
TFI	9	2	6	17
	52.94	11.76	35.29	100.00
	18.37	22.22	16.22	17.89
DDE	12	3	8	23
	52.17	13.04	34.78	100.00
	24.49	33.33	21.62	24.21
FRI	2	0	1	3
	66.67	0.00	33.33	100.00
	4.08	0.00	2.70	3.16
Total	49	9	37	95
	51.58	9.47	38.95	100.00
	100.00	100.00	100.00	100.00

Pearson chi2(8) = 4.6915 [redacted]
Cramer's V = [redacted]

There's no significant difference in the 'distribution of scores' levels with respect to 'Index' level [redacted]. The association between 'Index' and 'Distribution of scores' is not strong as p-value for Cramer's V is more than [redacted].



Part2[Index 3 and 4 Omitted]

```
. for var quescode vmildcod mildcode modecode sevecode: oneway X  distscor, bonf

->  oneway quescode distscor, bonf

                        Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      1596.77981      2   798.389905      4.71     [redacted]
 Within groups      4747.66838     28   169.559585
------------------------------------------------------------------------
    Total           6344.44819     30   211.481606

Bartlett's test for equal variances:  chi2(2) =   4.9050  Prob>chi2 = 0.086

        Comparison of Question-proportion by Distribution of scores
                                (Bonferroni)
Row Mean-|
Col Mean |   (0.0 ; 0   (0.3 ; 0
---------+----------------------
(0.3 ; 0 |       11.0
         |      0.476
         |
(0.7 ; 1 |       15.6         4.6
         |     [redacted]     1.000
```

```
->  oneway vmildcod distscor, bonf

                    Analysis of Variance
    Source              SS         df      MS             F      Prob > F
------------------------------------------------------------------------
Between groups      157.407065       2   78.7035323       0.37      0.6917
 Within groups      12094.1302      57   212.177723
------------------------------------------------------------------------
    Total           12251.5373      59   207.653174

Bartlett's test for equal variances:  chi2(2) =   0.3389  Prob>chi2 = 0.844


->  oneway mildcode distscor, bonf

                    Analysis of Variance
    Source              SS         df      MS             F      Prob > F
------------------------------------------------------------------------
Between groups      7.7078e+15       2   3.8539e+15       0.70      0.5005
 Within groups      3.0242e+17      55   5.4985e+15
------------------------------------------------------------------------
    Total           3.1013e+17      57   5.4408e+15

Bartlett's test for equal variances:  chi2(2) = 941.5693  Prob>chi2 = 0.000


                    Analysis of Variance
    Source              SS         df      MS             F      Prob > F
------------------------------------------------------------------------
Between groups      2.3898e+18       2   1.1949e+18       1.35      0.2690
 Within groups      4.3414e+19      49   8.8599e+17
------------------------------------------------------------------------
    Total           4.5803e+19      51   8.9811e+17

Bartlett's test for equal variances:  chi2(2) = 1185.0809  Prob>chi2 = 0.000

->  oneway sevecode distscor, bonf

                    Analysis of Variance
    Source              SS         df      MS             F      Prob > F
------------------------------------------------------------------------
Between groups      1.2132e+16       2   6.0662e+15       0.94      0.3985
 Within groups      2.9724e+17      46   6.4618e+15
------------------------------------------------------------------------
    Total           3.0937e+17      48   6.4453e+15

Bartlett's test for equal variances:  chi2(2) = 927.7095  Prob>chi2 = 0.000

. for var quescode vmildcod mildcode modecode sevecode: oneway X  index, bonf
```

```
-> oneway quescode index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      706.137245       2   353.068622      1.75     0.1917
 Within groups      5638.31094      28   201.368248
------------------------------------------------------------------------
    Total           6344.44819      30   211.481606

Bartlett's test for equal variances:  chi2(1) =   0.1501  Prob>chi2 = 0.698

note: Bartlett's test performed on cells with positive variance:
      1 single-observation cells not used

-> oneway vmildcod index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups       747.50056       2    373.75028      1.85     0.1663
 Within groups      11504.0367      57   201.825206
------------------------------------------------------------------------
    Total           12251.5373      59   207.653174

Bartlett's test for equal variances:  chi2(2) =   5.5710  Prob>chi2 = 0.062

-> oneway mildcode index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      2.0856e+16       2   1.0428e+16      1.98     0.1474
 Within groups      2.8927e+17      55   5.2595e+15
------------------------------------------------------------------------
    Total           3.1013e+17      57   5.4408e+15

Bartlett's test for equal variances:  chi2(2) = 1383.0881  Prob>chi2 = 0.000

-> oneway modecode index, bonf

                    Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      5.1286e+18       2   2.5643e+18      3.09     0.0545
 Within groups      4.0675e+19      49   8.3010e+17
------------------------------------------------------------------------
    Total           4.5803e+19      51   8.9811e+17

Bartlett's test for equal variances:  chi2(2) = 1434.5039  Prob>chi2 = 0.000
```

```
->  oneway sevecode index, bonf

                        Analysis of Variance
    Source              SS         df      MS            F      Prob > F
------------------------------------------------------------------------
Between groups      2.2266e+16      2   1.1133e+16      1.78      0.1794
 Within groups      2.8711e+17     46   6.2415e+15
------------------------------------------------------------------------
    Total           3.0937e+17     48   6.4453e+15

Bartlett's test for equal variances:  chi2(2) = 1201.6585  Prob>chi2 = 0.000
```

```
. for var quescode vmildcod mildcode modecode sevecode:ttest X ,by ( trends)

->  ttest quescode ,by ( trends)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
    80's |      20    20.60405    3.203058    14.32451    13.89998    27.30813
    90's |      11    15.73423    4.550231    15.09141    5.595685    25.87278
---------+--------------------------------------------------------------------
combined |      31    18.87605    2.611893    14.54241    13.54186    24.21025
---------+--------------------------------------------------------------------
    diff |            4.869822    5.478092               -6.334134    16.07378
------------------------------------------------------------------------------
Degrees of freedom: 29

                    Ho: mean(80's) - mean(90's) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
       t =   0.8890                 t =   0.8890                 t =   0.8890
   P < t =   0.8093             P > |t| =   0.3813             P > t =   0.1907

->  ttest vmildcod ,by ( trends)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
    80's |      30    13.00947    2.267084    12.41733    8.372766    17.64618
    90's |      30    19.19849    2.877871    15.76275    13.31258     25.0844
---------+--------------------------------------------------------------------
combined |      60    16.10398    1.860346    14.41018    12.38144    19.82653
---------+--------------------------------------------------------------------
    diff |           -6.189017    3.663579               -13.52247    1.144433
------------------------------------------------------------------------------
Degrees of freedom: 58

                    Ho: mean(80's) - mean(90's) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
       t =  -1.6893                 t =  -1.6893                 t =  -1.6893
   P < t =   0.0483             P > |t| =   0.0965             P > t =   0.9517
```

```
-> ttest mildcode ,by ( trends)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
    80's |      31    5.574042    2.025312    11.27646    1.437803    9.710281
    90's |      27    2.08e+07    2.08e+07    1.08e+08   -2.20e+07    6.36e+07
---------+--------------------------------------------------------------------
combined |      58     9685421     9685415    7.38e+07    -9709288    2.91e+07
---------+--------------------------------------------------------------------
    diff |           -2.08e+07    1.94e+07               -5.97e+07    1.80e+07
------------------------------------------------------------------------------
Degrees of freedom: 56

                 Ho: mean(80's) - mean(90's) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
       t =  -1.0729                 t =  -1.0729                 t =  -1.0729
   P < t =   0.1440           P > |t| =   0.2879           P > t =   0.8560

-> ttest modecode ,by ( trends)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
    80's |      27    3.903645    2.382294    12.37876   -.9932302     8.80052
    90's |      25    3.38e+08    2.72e+08    1.36e+09   -2.23e+08    8.99e+08
---------+--------------------------------------------------------------------
combined |      52    1.63e+08    1.31e+08    9.48e+08   -1.01e+08    4.27e+08
---------+--------------------------------------------------------------------
    diff |           -3.38e+08    2.61e+08               -8.63e+08    1.87e+08
------------------------------------------------------------------------------
Degrees of freedom: 50

                 Ho: mean(80's) - mean(90's) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
       t =  -1.2948                 t =  -1.2948                 t =  -1.2948
   P < t =   0.1007           P > |t| =   0.2013           P > t =   0.8993
```

```
->  ttest sevecode ,by ( trends)

Two-sample t test with equal variances

------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
    80's |      24    2.942504    1.688494    8.271899   -.5504122    6.435421
    90's |      25    2.25e+07    2.25e+07    1.12e+08   -2.39e+07    6.89e+07
---------+--------------------------------------------------------------------
combined |      49    1.15e+07    1.15e+07    8.03e+07   -1.16e+07    3.45e+07
---------+--------------------------------------------------------------------
    diff |           -2.25e+07    2.30e+07               -6.87e+07    2.37e+07
------------------------------------------------------------------------------
Degrees of freedom: 47

                 Ho: mean(80's) - mean(90's) = diff = 0

     Ha: diff < 0                 Ha: diff ~= 0                 Ha: diff > 0
       t =  -0.9794                 t =  -0.9794                 t =  -0.9794
   P < t =   0.1662             P > |t| =   0.3324             P > t =   0.8338
```

```
. tab   index distscor,col row V chi2

           |      Distribution of scores
     Index | (0.0 ; 0.  (0.3 ; 0.  (0.7 ; 1. |     Total
-----------+---------------------------------+----------
     DEANS |        13          4         14 |        31
           |     41.94      12.90      45.16 |    100.00
           |     37.14      66.67      50.00 |     44.93
-----------+---------------------------------+----------
      TSIF |        13          0          8 |        21
           |     61.90       0.00      38.10 |    100.00
           |     37.14       0.00      28.57 |     30.43
-----------+---------------------------------+----------
       TFI |         9          2          6 |        17
           |     52.94      11.76      35.29 |    100.00
           |     25.71      33.33      21.43 |     24.64
-----------+---------------------------------+----------
     Total |        35          6         28 |        69
           |     50.72       8.70      40.58 |    100.00
           |    100.00     100.00     100.00 |    100.00

         Pearson chi2(4) =   3.9568   Pr = 0.412
              Cramer's V =   0.1693
```

```
. tab   index  trends,col row V exact

           |        Trends
     Index |      80's       90's |     Total
-----------+----------------------+----------
     DEANS |        22          9 |        31
           |     70.97      29.03 |    100.00
           |     59.46      28.13 |     44.93
-----------+----------------------+----------
      TSIF |         8         13 |        21
           |     38.10      61.90 |    100.00
           |     21.62      40.63 |     30.43
-----------+----------------------+----------
       TFI |         7         10 |        17
           |     41.18      58.82 |    100.00
           |     18.92      31.25 |     24.64
-----------+----------------------+----------
     Total |        37         32 |        69
           |     53.62      46.38 |    100.00
           |    100.00     100.00 |    100.00

           Cramer's V =   0.3150
         Fisher's exact =                 0.036
```

```
. tab    distscor  trends,col row V exact
```

Distribution of scores	Trends 80's	90's	Total
(0.0 ; 0.3]: Non Fe	16	19	35
	45.71	54.29	100.00
	43.24	59.38	50.72
(0.3 ; 0.7]: Interme	5	1	6
	83.33	16.67	100.00
	13.51	3.13	8.70
(0.7 ; 1.4]: Flourid	16	12	28
	57.14	42.86	100.00
	43.24	37.50	40.58
Total	37	32	69
	53.62	46.38	100.00
	100.00	100.00	100.00

```
           Cramer's V =   0.2136
      Fisher's exact =                 0.226
```

```
. tab index

      Index |      Freq.     Percent        Cum.
------------+-----------------------------------
      DEANS |         31       44.93       44.93
       TSIF |         21       30.43       75.36
        TFI |         17       24.64      100.00
------------+-----------------------------------
      Total |         69      100.00
```

. tab distscor

Distribution of scores	Freq.	Percent	Cum.
(0.0 ; 0.3]: Non Fe	35	50.72	50.72
(0.3 ; 0.7]: Intermediate	6	8.70	59.42
(0.7 ; 1.4]: Flouridated	28	40.58	100.00
Total	69	100.00	

```
. tab trends

     Trends |      Freq.     Percent        Cum.
------------+-----------------------------------
       80's |         37       53.62       53.62
       90's |         32       46.38      100.00
------------+-----------------------------------
      Total |         69      100.00
```

All Variables

```
. for var distscor index trends: tab X

->  tab distscor
```

Distribution of scores	Freq.	Percent	Cum.
(0.0 ; 0.3]: Non Fe	49	51.58	51.58
(0.3 ; 0.7]: Intermediate	9	9.47	61.05
(0.7 ; 1.4]: Flouridated	37	38.95	100.00
Total	95	100.00	

```
->  tab index

      Index |      Freq.     Percent        Cum.
------------+-----------------------------------
      DEANS |         31       32.63       32.63
       TSIF |         21       22.11       54.74
        TFI |         17       17.89       72.63
        DDE |         23       24.21       96.84
        FRI |          3        3.16      100.00
------------+-----------------------------------
      Total |         95      100.00
```

```
-> tab trends

     Trends |      Freq.     Percent        Cum.
------------+-----------------------------------
       80's |         53       55.79       55.79
       90's |         42       44.21      100.00
------------+-----------------------------------
      Total |         95      100.00
```