

York Review

Fluoridation of drinking water: a systematic review of its efficacy and safety.

1. Introduction

The debate regarding whether or not fluoride should be added to drinking water with the aim of reducing dental decay has existed since the early part of this century. At the beginning of the 20th century researchers in the USA noticed an association between the occurrence of mottled teeth and a reduction of dental decay in children. Following investigations showed that mottled enamel (fluorosis) was caused by naturally occurring fluoride in drinking water. The discovery that fluoride was responsible for the observed effects on tooth enamel soon led to suggestions that its presence was also responsible for conferring protection against caries. Studies in other countries, including the UK, soon followed which appeared to confirm the association between fluoride water content and caries reduction. In light of this evidence major public health programmes around the world were initiated to raise fluoride levels in drinking water where it was considered deficient (fluoridation). Historically 1ppm has been taken as the optimal fluoride level in drinking water, above this concentration the risk of fluorosis is considered to outweigh the benefits of dental protection. Concerns have been raised that the efficacy of water fluoridation has not been proven and that artificially fluoridating water may not be safe. Suggested side effects of fluoridation include dental and skeletal fluorosis, kidney disease, genetic mutations, birth defects and cancer.

The first fluoridation of public water supplies started in 1945 in Grand Rapids, Michigan USA and was quickly followed by similar programmes at other sites across the USA. Fluoridation was first introduced to the UK as part of an experimental programme in 1955 before being adopted at other sites around the country in the 1960s. However, in the UK fluoridation has not been widely adopted. At present about 10% of the UK population, which mostly reside in either the West Midlands or Newcastle-upon-Tyne, receive artificially fluoridated water.

In most countries in the developed world there has been a dramatic decline in the prevalence of dental caries in the last 30 years. In countries where fluoridation is widespread, for example the USA and Australia, fluoridation is frequently cited as the reason for this improvement. However, a similar reduction in caries has also been observed in other countries, such as the UK, where

fluoridation is less wide spread. Here the reduction has been attributed to the use of fluoridated toothpaste, educational programmes and an awareness of the need for a healthy lifestyle. However, in these countries it has been suggested that in fluoridated areas the caries rates have fallen further than those in the non-fluoridated regions suggesting that water fluoridation provides benefits in addition to the regular use of fluoridated toothpaste.

Legislation was introduced in 1985 in England and Wales that leaves the water industry in the position of deciding whether to agree to local Health Authority requests for new fluoridation schemes. In the white paper "Our Healthier Nation" the government acknowledged concerns regarding the safety and efficacy of fluoridation and proposed to commission this review to evaluate the scientific evidence. If this review confirms that there are benefits to dental health from fluoridation and that there are no significant risks then the government intends to change the 1985 legislation by introducing a legal obligation on water companies to fluoridate where there is strong local support for doing so.

1.1 Understanding the literature

A variety of study designs can be used to assess the effectiveness of a population based intervention. There are several levels of epidemiological study which range from simple descriptive studies (e.g. cross-sectional), to studies of correlation at the population level (e.g. ecological studies), to studies of individual based associations (e.g. case-control & cohort studies) and to the most conclusive types of studies which provide experimental confirmation of an empirical relationship (e.g. randomised controlled trials):

1.11 Cross sectional studies

These are used to investigate the prevalence of a defined condition. Data is collected in a planned way from a defined population. The aim of such studies is to describe individuals in the

population at a particular point in time in terms of their personal attributes and their history of exposure to suspected causal agents. These data are then investigated in relation to the presence or absence of the disease under investigation or its severity with a view to developing or testing hypotheses. These studies are relatively simple to conduct, take only a short time and are relatively cheap. However, these studies are often difficult to interpret, as it is not possible to assess whether the outcome followed the exposure or the exposure resulted from the outcome.

1.12 Ecological studies

Such studies provide a relatively simple and inexpensive method of looking at disease occurrence, especially with regard to an environmental exposure determined by geography. The average exposure of the population is plotted against the rate of the outcome for that population to investigate any possible association between the two. These studies are considered to provide weak evidence because of concern about compatibility of information from different areas, data is often unavailable on many risk factors and because of uncertainties in extrapolating results of analyses at population level to the individual.

1.13 Case-control studies

A population with the outcome of interest (cases) is selected and compared with another group in which the outcome is absent (controls), differences in exposures between the groups are assumed to be responsible for the occurrence of the disease. One of the advantages of this design is that multiple exposures can be examined for one particular outcome. This type of study design has many methodological weaknesses and is particularly susceptible to bias. The most important methodological issues relate to the way in which the cases and controls are selected and the comparability of the exposure data obtained; controls should be a representative sample of the population from which the cases were drawn. As data is collected retrospectively it is difficult to demonstrate whether or not an observed correlation is causal.

1.14 Cohort, or follow-up, studies

Individuals are recruited into the study and are allocated to one of two or more study groups depending on whether they have or have not been exposed to the agent under investigation. The selected study groups are followed-up for a period of time that may extend to many years in order to measure the frequency of occurrence of the outcome of interest in those exposed compared to those not exposed. The group which is not subjected to the exposure of interest must be drawn from a population that is similar to the exposed group in all respects other than the exposure under investigation. Cohort studies have the advantage that the exposure and confounding factors are measured before the outcome of interest has developed and so are unbiased in terms of disease development, time-order relationships are known as subjects are

classified by risk factors before the outcome becomes manifest, and multiple outcomes can be examined for one exposure. Potential weaknesses of this type of design include loss to follow-up, changes in subject characteristics, and surveillance bias where one population is observed in more detail than the other.

1.15 Randomised control trials

These are designed to measure the efficacy and safety of particular types of health care interventions, by randomly assigning people to one of two or more treatment groups and, where possible, blinding them and the investigators to the treatment that they are receiving. The outcome of interest is then compared between the treatment groups. Such studies are designed to minimise the possibility of an association due to confounding and remove many sources of bias present in other study designs. However, such studies are not infallible and there are areas of methodological concern: selection bias (bias in the way subjects are assigned to experimental groups), issues relating to reproducibility of results, bias introduced by co-interventions and bias in assessing the outcomes.

1.16 Systematic reviews

This study aims to provide a systematic review of all the available evidence in order to assess the efficacy and safety of water fluoridation. Systematic reviews locate, appraise and synthesise evidence from scientific studies in order to provide informative empirical answers to scientific research questions. They are therefore valuable sources of information for decision makers. In addition, by identifying what we know and don't know, they are an invaluable first step before carrying out new primary research. Systematic reviews differ from other types of review in that they adhere to a strict scientific design in order to make them more comprehensive, to minimise the chance of bias, and so ensure their reliability. Rather than reflecting the views of the authors or being based on only a (possibly biased) selection of the published literature, they contain a comprehensive summary of the available evidence.

The study of water fluoridation poses problems for the use of the more conclusive study designs such as randomised controlled trials. Water fluoridation tends to affect population groups and it is thus difficult to randomly assign individuals to receive either fluoridated or non-fluoridated water, the fact that whole populations are either exposed or not exposed also poses a problem for cohort and case-control studies. Comparing exposures and outcomes between different population groups may cause problems as the two populations may differ with respect to other exposures and so a causal relationship between the observed exposure and outcomes cannot be assumed. Most people know whether or not a water supply is fluoridated and so blinding would not be possible leading to bias in many investigations. Water fluoridation is also a difficult subject on which to ensure the neutrality of the investigators. Some possible side effects of

water fluoridation may take many years to develop and so unless a study is specifically designed to investigate the relationship of these outcomes to fluoridation the relationship may go undetected. An assessment of the effectiveness of fluoridation to prevent caries is difficult because there are potentially a number of factors that may influence caries protection other than fluoride in water and these have changed over time. These factors include the introduction of fluoridated toothpaste, mouth rinses and improved dental hygiene in general. Traditional reviews of the literature tend to ignore the variable quality of studies and are therefore unlikely to present an objective view. The explicit methods used in this systematic review will limit bias through the use of specific inclusion criteria, and a formal assessment of the quality of the studies reviewed. The use of meta-analysis will increase power and precision of estimates of treatment effects and exposure risks.

2. Objective of this review

Many studies and reviews are available on fluoridation, but no systematic review has been undertaken. The aim of this systematic review is to assess the evidence on the positive and negative effects of population wide drinking water fluoridation strategies to prevent caries. To achieve this aim four objectives have been identified:

1. Assessment of the effects of fluoridation of public water supplies in preventing caries (is a causal relationship likely?).
2. If fluoridation is shown to have beneficial effects, what is the effect over and above that offered by the use of alternative interventions and strategies (i.e. fluoridated toothpaste, educational programmes, and increased self awareness of health issues?).
3. Determination of whether fluoridation results in a reduction of caries across social groups and between geographical locations.
4. Assessment of the negative health effects of fluoridation.

5. Comparison of the effects of natural and artificial fluoridation to investigate any possible differences

3. Assessment of the scope of the systematic review

A preliminary literature search was undertaken to provide information on available reviews of fluoridation and feel for the potential size of the literature about the safety, efficacy and cost-effectiveness of fluoride supplementation in drinking water.

The terms in the preliminary strategy were identified through discussion and by browsing the Medline and Embase thesauri (MeSH and Emtree respectively). The preliminary literature search process was carried out in four stages:

- Initial WWW browse
- Rapid appraisal of the review literature
- Medline search using a quality filter strategy to identify the scope of the systematic reviews and meta-analyses literature (date range covered 1966 - 03/1999).
- Medline and Embase searches using a quality filter strategy to identify primary studies including any randomised controlled trials. The Medline search covered the date range 1966 - 05/1999. The Embase search covered the date range 1980 – 05/1999

The Medline and Embase databases were both searched using WinSpis/ SilverPlatter software. Full details of the search strategies, databases searched and the results of the searches are given in **Appendix A**.

The titles and abstracts of the bibliographic records retrieved were downloaded and imported into Endnote reference management software to remove duplicate records. After deduplication, the Endnote library of 394 references was scanned by the authors for relevance and relevant papers were ordered. A number of papers were rejected upon reading as being irrelevant.

The preliminary search has revealed the potential size of the final literature search, and on the basis of the searches it is expected that after searching a wider range of databases, 400 documents will need to be obtained and assessed for inclusion in the review. Given the average cost of document acquisition for CRD to be £4, the document acquisition costs are expected to be £1600.

The full review search will develop the preliminary search strategies and will involve searching a wide range of medical, political and environmental/scientific databases to identify primary studies. Databases to be searched will include the following:

- Medline
- Embase
- Ntis
- Biosis
- Current Contents Search (Science Citation Index and Social Science Citation Index)
- Healthstar
- HSRProj
- TOXLINE
- Chemical Abstracts
- CAB Health
- Food Science and Technology Abstracts
- JICST- E Plus
- Pascal

- EI Compendex
- Enviroline
- Aqualine
- PAIS
- SIGLE
- Conference Papers Index
- Water Resources Abstracts
- Agricola
- Waternet
- Pure Water Association
- British Fluoridation Society

The cost of searching a range of databases, based on preliminary searches, and obtaining abstracts for assessment, will be approximately £1750.

4. Inclusion criteria

The following methodological issues will be considered when assessing studies for inclusion:

- ii selection,
- ii confounding,
- ii measurement.

The degree to which each study satisfies these methodological issues will be graded into three levels of evidence:

Level A: Highest quality of evidence, minimal risk of bias.

1. Prospective (planned) studies that started at either initiation or discontinuation of water fluoridation and have a follow up of at least two years for positive effects and at least 5 years for negative effects
2. Studies address at least three possible confounding factors and make corrections in the analysis where appropriate
3. Studies with the lowest bias where primary outcomes were blinded to examiners for fluoridation status of participants.

Level B: Evidence of moderate quality, moderate risk of bias.

1. Studies that started less than one year after fluoridation was initiated or discontinued and had a prospective follow up of outcomes
2. Studies that measured and made corrections for less than three but at least one confounding factor
3. Studies that failed where primary outcomes were not blinded to examiners for fluoridation status, but made other provisions to prevent measurement bias

Level C: Lowest quality of evidence, high risk of bias.

1. Studies of other designs (prospective or retrospective, concurrent or historical control) that meet other inclusion criteria
2. Studies that failed to account for confounding factors
3. Studies that did not prevent measurement bias

Evidence rated below level B will not be considered in the evaluation of efficacy. However, it is plausible that this may restrict an assessment of the evidence for objective 2, if insufficient data

is available then the best level of evidence which is relevant to this objective (from any study design) will be included. In the assessment of safety all levels of evidence will be considered

In studies investigating all four of the study objectives the groups exposed or not exposed to fluoride and whose outcomes are to be compared will almost certainly differ in respect to factors other than fluoride exposure itself. Some of these differences may be related to the outcomes under investigation (level of tooth decay, skeletal fluorosis, fractures etc) and so will act to confound any observed relationship and thus should be controlled for in the analysis. Confounding factors are likely to include: age, gender, ethnicity, other sources of fluoridation and social class. Factors likely to modify the effect of fluoride on the outcomes under investigation such as the level of tooth decay in the population before the introduction of fluoridation should also be considered.

This review will be limited to studies investigating the effect of water fluoridation on human populations. An effect seen in animal studies resulting from fluoride exposure does not necessarily infer that there will be a similar effect in human populations. There are several examples in the literature where animal studies have suggested a causal relationship between an exposure and effect which have not been confirmed in trials in human populations.

4.1 Assessment of the effects of fluoridation of public water supplies in preventing caries

Participants:

1. Populations receiving fluoridated water (either naturally or artificially)
2. Populations receiving non fluoridated water

Intervention:

A defined fluoride -concentration present in drinking water, either controlled or naturally occurring

Outcomes:

Number of decayed, missing or filled teeth (DMFT, dmft, deft) and/or number of decayed, missing or filled surfaces (DMFS, dmfs), or percentage of caries free teeth or caries free subjects in those receiving fluoridated compared to non-fluoridated water

Study designs:

Prospective studies comparing two populations, one receiving fluoridated the other non-fluoridated water

4.2 If fluoridation is shown to have beneficial effects, what is the effect over and above that offered by the use of alternative interventions and strategies

Participants:

1. Populations receiving fluoridated water (either naturally or artificially) who receive fluoride from other artificially supplemented sources (e.g. food, toothpaste, fluoride tablets, bottled drinks)
2. Populations receiving non fluoridated water who receive fluoride from other artificially supplemented sources

Intervention:

Fluoride at any concentration present in drinking water

Outcomes:

Number of decayed, missing or filled teeth (DMFT, dmft, deft) and/or number of decayed, missing or filled surfaces (DMFS, dmfs), or percentage of caries free teeth or caries free subjects in the four different participant groups

Study designs:

Prospective studies comparing the four populations outlined above, to investigate the differences in levels of tooth decay between the populations

4.3 Determination of whether fluoridation results in a reduction of caries across social groups and between geographical locations bringing equity

Participants:

1. Populations receiving fluoridated water (either naturally or artificially), from different social groups and geographic locations
2. Populations receiving non fluoridated water, from different social groups and geographic locations

Intervention:

Fluoride at any concentration present in drinking water, either controlled or naturally occurring

Outcomes:

Number of decayed, missing or filled teeth (DMFT, dmft, deft) and/or number of decayed, missing or filled surfaces (DMFS, dmfs), or percentage of caries free teeth or caries free subjects in those receiving fluoridated compared to non-fluoridated water compared between different social groups and geographic locations within the two participant groups

Study designs:

Prospective studies comparing two populations, one receiving fluoridated the other non-fluoridated water, across different social groups and geographic locations

4.4 Assessment of the negative health effects of fluoridation

Participants:

1. **Groups** receiving fluoridated water (either naturally or artificially)
2. **Groups** receiving non fluoridated water

Intervention:

A defined fluoride -concentration present in drinking water, either controlled or naturally occurring

Outcomes:

Dental fluorosis, skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality and any other adverse effects reported in the literature compared between those receiving fluoridated compared to non-fluoridated water

Study designs:

1. Prospective study design which follows up 2 or more exposure groups with different levels of exposure to fluoride and continues for several years to allow comparison of possible adverse effects in the different groups
2. Retrospective study design comparing risks of adverse effects in two or more exposure groups

3. Retrospective design comparing odds of exposure to differing levels of fluoride in groups of people experiencing adverse effects which may be linked to water fluoridation compared to those without the condition under study
4. Geographical study comparing average exposure of the population to fluoride with the rate of the adverse effect for several populations to look for a relationship between the two

4.5 Comparison of the effects of natural and artificial fluoridation to investigate any possible differences

Participants:

1. Populations receiving artificially fluoridated water
2. Populations receiving naturally fluoridated water
3. Populations receiving non-fluoridated water

Intervention:

Fluoride at any concentration from a naturally and an artificially fluoridated water source

Outcomes:

Positive effects: Number of decayed, missing or filled teeth (DMFT, dmft, deft) and/or number of decayed, missing or filled surfaces (DMFS, dmfs), or percentage of caries free teeth or caries free subjects in those receiving artificially fluoridated compared to naturally fluoridated and non-fluoridated water

Negative effects: Dental fluorosis, skeletal fluorosis, hip fractures, cancer, congenital malformations, mortality and any other adverse effects reported in the literature compared between those receiving artificially fluoridated compared to naturally fluoridated and non-fluoridated water

Study designs:

1. Prospective study design which follows up 2 or more exposure groups, at least one of which receives artificially fluoridated and another receives naturally fluoridated water, with different levels of exposure to fluoride and continues for several years to allow comparison of possible adverse effects in the different groups

2. Retrospective study design comparing risks of adverse effects in two or more exposure groups, at least one of which receives artificially fluoridated and another receives naturally fluoridated water.
3. Retrospective design comparing odds of exposure to differing levels of fluoride, at least one of which receives artificially fluoridated and another receives naturally fluoridated water, in groups of people experiencing adverse effects which may be linked to water fluoridation compared to those without the condition under study
4. Geographical study comparing average exposure of the population to fluoride with the rate of the adverse effect for several populations to look for a relationship between the two

5. Quality assessment tools

The evidence grading system described in the inclusion criteria will provide a level of quality assessment, however it is anticipated that a range of study designs will contribute to the evidence suggesting that further quality assessment will be necessary. The quality of each trial will be assessed using an existing quality assessment tool where appropriated (as described in CRD report no.4, NHS Centre for Reviews and Dissemination) and the results will be used to explore the validity of the outcome data. The different inclusion criteria for studies of efficacy and safety will necessitate the use of different quality assessment tools. Quantitative analysis by a scoring system may be used to define threshold values which will allow sensitivity analysis to be performed on the overall outcome data.

Quality assessment will be an important part of the review process since the intervention is community wide which makes studies inherently more difficult to perform and interpret, than an assessment of a single intervention administered to individual patients. The effect is increased influence of confounding factors and studies should account for this both in the allocation of communities and in the analysis. Other problems associated with internal validity will be that random allocation of communities is difficult considering that whether to fluoridate or not will be a political decision and blinding is not possible since people, at least in theory, know if their water is fluoridated. In addition randomising at cluster level needs special consideration in the analysis of those studies in which it is used. In our experience few studies use the appropriate analysis methods which account for cluster effects, suggesting that this will be an important issue to consider in the quality assessment.

6. Search strategy

The search strategy will be a refined version of that used in the scoping search for studies [see **Appendix A**]. In addition to the electronic searches hand searching of *Index Medicus* and *Excerpta Medica* will be undertaken using the headings of fluoridation, fluoride, water, teeth and caries to find relevant studies published between 1945 and 1965. A further sample of studies published before 1945 will be retrieved from *Index Medicus* and *Excerpta Medica*, to establish if further searching is required. The bibliographies of retrieved articles will be searched for additional studies and experts in the field will be approached to identify any missed articles. Searches will not be restricted by language, country of origin, or date.

7. Methods

7.1 Selection of studies for inclusion

Two reviewers will independently select the studies to be included. Initially studies will be selected for relevance by assessing study abstracts and / or titles downloaded from the databases described in appendix 1. Retrieved studies from either the initial screening or identified through hand searching will be reviewed and the inclusion criteria applied. Disagreements at each stage will be resolved by discussion between reviewers, where disagreements persist a third party will be consulted.

7.2 Data extraction

Data extraction will be undertaken independently by two reviewers, at least one of whom will be based in York, into pre-designed and piloted data extraction tables. The tables will include headings for: authors, date, country of study, year, study design, population characteristics, use of co-interventions (e.g. toothpaste), assessment of bias (see inclusion criteria), fluoride concentration, outcomes for efficacy and safety, geographical area of the population, socio-economic factors, and additional comments.

Complete data extraction tables will be compared between reviewers and discrepancies resolved by referral to the original studies, if necessary arbitration will be by a third reviewer.

7.21 Study quality assessment

Two reviewers will independently assess the studies for quality. Discrepancies will be resolved through discussion or, when agreement cannot be reached, by consultation with a third party.

7.3 Data Analysis

Data analysis will be performed according to the main objectives of the review. For positive and negative effects, the data will firstly be described qualitatively. The homogeneity / heterogeneity in terms of populations, interventions and outcomes studied will be assessed in a qualitative manner, using the judgement of the reviewers. Quantitative data in the form of DMFS/DMFT counts, relative risks or odds ratios, will be entered into the Review Manager software package (Cochrane Collaboration) and possibilities for further analysis will be explored. Forest plots will be created and formal statistical tests of heterogeneity will be performed.

Where judged appropriate (no heterogeneity) statistical pooling (meta-analysis) will be performed using fixed effects models as the main analysis. Where appropriate data are available, we will use weighted mean differences (preferred above standardised mean differences) to summarise continuous data, and relative risks (preferred above odds ratios) for discrete data. To

test the sensitivity of the fixed effects analysis we will also analyse the data by a random effects model.

Where statistical pooling is judged inappropriate (heterogeneity present: threshold P-value < 0.05, or qualitative assessment indicating heterogeneity), reasons for heterogeneity will be investigated and explanations provided.

For continuous data (e.g. DMFTs) standard deviations will be required for meta-analysis. It is likely that some studies will fail to report the standard deviation in which case it will be derived from the total number of individuals, mean of the outcome data and discrete p-values (e.g. $p=0.023$, rather than $p<0.05$) using appropriate formulas. If this is not possible, the study will not be eligible for statistical pooling.

For all efficacy and safety analyses, subgroups of studies performed before and after the availability of fluoridated toothpaste will be considered separately. The effect of modification variables such as age, social class, ethnicity and other related intermediates will be explored.

The separate analyses for efficacy and safety will be integrated descriptively and compared with appropriate cost effectiveness data where available; e.g. water fluoridation prevents x% caries at y% of dental mottling at z costs. In such a description there can be multiple outcomes for both efficacy and safety. The report will not provide a value judgement of these descriptions. However, it will provide a value judgement of the strength (or weakness) of the evidence for the separate components in the discussion section. This value judgement will be motivated by referral to the tables of the quality assessment of the included studies, so readers will be able to check how judgements were derived and consider the strength of the reviews conclusions (validity) with regard to the evidence.

A sensitivity analysis will be conducted to assess the degree to which the results are affected by the inclusion of studies with different degrees of adjustment for confounding.

8. Advisory panel

An advisory panel will be recruited to help refine the review questions, identify relevant literature, and referee the draft report. The panel will include those involved in the debate of fluoridation whom are known to be proponents or opponents, and individuals whom are considered neutral. It is envisaged that the expert panel will provide opinions from scientific, political and consumer perspectives. Members of the advisor panel and other experts in relevant areas will also be contacted to help identify further information and theoretical perspectives relevant to the review.

9. Publication bias

Evidence of publication bias regarding efficacy and safety will be evaluated by funnel plots. Studies published as an abstract but not appearing as a full journal article will be used as an indicator of publication bias. It may be difficult to detect publication bias as most studies, especially those with retrospective study designs, will show some selection bias.

10. Suggested time scale

The review will begin at the point of funding.

July: Protocol discussed at advisory panel meeting; literature searching initiated; retrieval of identified articles.

August: Protocol revised and finalised; literature search completed; data extraction forms developed.

September: Data extraction forms piloted and data extraction initiated.

October: Identification and retrieval of studies completed.

November: Data extraction completed.

December: Data synthesis.

January: Data synthesis completed.

February: Report production.

We propose to adopt a staggered approach to reviewing the literature with most of the early work being conducted on the assessment of efficacy. If in preliminary analyses efficacy is not established then an assessment of safety will be considered inappropriate and the review concluded.

11. Appendix A

11.1 The literature search process for the fluoridation review

1. Initial WWW browse. This was not intended to be a systematic examination of web-based information resources on the topic, but the main dental websites were visited [**Appendix, 11.2**for a list of websites and URLs visited]. As a result of the preliminary web search 41 reports and journal references were identified and obtained.

1. A rapid appraisal of the literature was carried out in order to identify the scope and scale of existing review literature surrounding this topic. The rapid appraisal search process involves searching a checklist of the following resources [**Appendix, 11.3** for the rapid appraisal checklist and the results)] in order to gauge the amount of literature surrounding this topic. Scoping searches were also carried out on the DataStar and Dialog services in order to identify other databases for inclusion for future searching.

1. The next level of searching involved an initial literature search of the Medline database. The date period covered was 1966 – 03/1999, and foreign language papers were not excluded. This level of searching focussed on retrieval of systematic reviews and meta-analyses only; therefore the literature search used a quality filter component to identify such material. The filter strategy was included to identify systematic reviews, overviews and meta-analysis literature, and to exclude editorials, case studies and other irrelevant publication types.

Full details of the search strategy are given in **Appendix, 11.4**.

I. The final stage of searching involved the retrieval of primary studies looking at the fluoridation. Medline and Embase were both searched using a strategy designed to retrieve primary studies including cohort studies, clinical trials, RCTs, longitudinal studies, prospective studies etc. The Medline search covered the date range 1966 - 05/1999. The Embase search covered the date range 1980 – 05/1999 (due to technical difficulties, the 07/1999 – 12/1999 section of Embase was omitted from the search). Full details of the strategies used are given in **Appendix 11.5**.

The primary studies strategy retrieved the following number of records:

	Medline	Embase
1966-05/1999	295	
1980-05/1999*		107
Total	295	107

Overall Total = 402

Total after deduplication = 394

*The Embase search excluded the section 07/1999-12/1999, due to technical reasons.

11.2 WWW Resources searched

- American Dietetic Association

<http://www.eatright.org/fluoride.html>

- British Dental Association

<http://www.dba-dentistry.org.uk>

- British Fluoridation Society

<http://www.derweb.ac.uk/bfs/>

- International Society for Fluoride Research

<http://www.fluoride-journal.com/>

- OMNI (Organising Medical Networked Information)

<http://www.omni.ac.uk>

- National Institute of Dental and Craniofacial Research

<http://www.nidr.nih.gov/news/index.htm>

- World Health Organization

<http://www.who.org>

- Fluoride Issues

<http://www.sonic.net/~kryptox/fluoride.htm>

- Dangers of fluoridated water

<http://www.nofluoride.com/>

· Preventive Dental Health Association

<http://emporium.turnpike.net/P/PDHA/health.htm>

11.3 Rapid appraisal checklist and results

Completed and ongoing reviews	
Cochrane Library: Cochrane Database of Systematic Reviews	1 protocol
Cochrane Library: DARE	6
National Research Register	0
SHPIC Reports	0
SIGN Guidelines	0
Agency for Health Care Policy and Research (AHCPR)	Not available
Guide to Clinical Preventive Guidelines	Not available
Development and Evaluation (DEC) Reports	0
INAHTA Published Reports	0
INAHTA Ongoing Reviews	0
National Co-ordinating Centre for Health Technology Assessment	0
Indexes to clinical effectiveness sources including reviews, appraisal of reviews, and evidence-based guidelines	
TRiP (Turning Research into Practice)	2
SCHARR-Lock's Guide to the Evidence	0
IDEA Topic List	0