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Information Paper – Water fluoridation: dental and other human health outcomes

WORKING TO BUILD A HEALTHY AUSTRALIA

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Plain language summary

Take-home message

This Information Paper explores the potential link between water fluoridation and human health based on the findings of the 2016 National Health and Medical Research Council's (NHMRC) Evidence Evaluation.[a]

The 2016 NHMRC Evidence Evaluation shows that water fluoridation helps to reduce tooth decay in children and adults. There is no reliable evidence that water fluoridation at current Australian levels causes health problems.

NHMRC found consistent evidence of an association between water fluoridation and dental fluorosis. In Australia, however, most dental fluorosis is very mild or mild, does not affect the function of teeth and is not of aesthetic concern to those who have it. Dental fluorosis is a change in the appearance of teeth that most commonly appears as white lines or areas on tooth surfaces. It is caused by a high intake of fluoride from one or more sources during the time when teeth are developing. During the time period between the 1990s and 2014, when the extent of fluoridation in Australia has expanded, dental fluorosis has declined from about 40% of children showing any dental fluorosis to 16.8%.

Why is this work important?

Tooth decay is one of the most common health problems in Australia. It can cause pain, difficulty eating and sleeping, and may make people feel unhappy about their appearance.

Water fluoridation can help to prevent tooth decay in people of all ages. It is of particular benefit to communities of low socio-economic status. Tooth decay is more common among people from lower socio-economic backgrounds i.e. those with lower income and education levels. People from a lower socio-economic background and those living in regional and remote areas may also have limited access to dental services and/or they may face other barriers to seeking treatment for tooth decay, such as the costs of dental treatment.

Fluoride occurs naturally in all Australian water supplies, but in most places the levels are too low to help prevent or reduce tooth decay. Therefore, Australian water suppliers adjust the amount of fluoride to a level that can help prevent tooth decay. This process is called community water fluoridation and has been happening across Australia for many decades.

Australian water suppliers add fluoride under strict controls that are typically set out in legislation or Codes of Practice. The fluoride chemicals recommended for use in the NHMRC *Australian Drinking Water Guidelines*[b] are controlled by state and territory legislation and regulations, and local regulations. In Australia, the chemicals used for water fluoridation are subject to safety and quality control measures and are regularly monitored.

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a The Clinical Trials Centre, University of Sydney, conducted an independent evidence evaluation of all of the relevant scientific research on water fluoridation. The findings of this comprehensive independent evidence evaluation are presented in the 2016 NHMRC Evidence Evaluation Report and Technical Report at https://www.nhmrc.gov.au/health-topics/health-effects-water-fluoridation.

b The NHMRC *Australian Drinking Water Guidelines* (ADWG) available at: https://www.nhmrc.gov.au/guidelines-publications/eh52

In some regions in Australia there are already sufficient levels of fluoride naturally occurring in the groundwater to help reduce tooth decay. Their water suppliers do not need to add fluoride to the water supply.

What is NHMRC's role in water fluoridation?

NHMRC develops health advice for the Australian community, health professionals and governments. NHMRC has publicly supported community water fluoridation as a population health measure since 1952, and regularly reviews the scientific evidence on this topic.

In 2014, NHMRC commenced a new evidence evaluation on the health effects of fluoride in drinking water to ensure that the body of evidence that underpins its advice (issued as a public statement) is up to date and relevant for the Australian community. The findings of the comprehensive evaluation have been published in the 2016 NHMRC Evidence Evaluation and are summarised in this Information Paper.[c] The NHMRC Fluoride Reference Group – a committee of health, dental and other experts, such as those with expertise in epidemiology, ethics and water management - guided this work.[d]

Who will be interested in this Information Paper?

Many different people will be interested in knowing about the effects of water fluoridation including:

- government decision makers
- those involved in dental and public health policy, as well as those monitoring water quality
- dentists, oral health therapists, and dental hygienists
- community members.

What questions did the evidence evaluation answer?

- What is the effect on tooth decay of drinking water with fluoride in it?
- What is the effect on dental fluorosis of drinking water with fluoride in it?
- Are there any other health effects (benefits and/or harms) from drinking water with fluoride in it?

Which studies were included in the evidence evaluation?

The 2016 NHMRC Evidence Evaluation looked at previous reviews on the health effects of water fluoridation (2000 McDonagh[e] and 2007 NHMRC review). It then updated these by identifying and assessing new studies published between 2006 and 2015. The 2016 NHMRC Evidence Evaluation focussed on the effects of water fluoridation on tooth decay, dental fluorosis and general health. The following studies were considered:

- the 2015 Cochrane review[f] of water fluoridation, tooth decay and dental fluorosis

c Additional products may be developed to support these documents such as an updated Public Statement and nationally consistent Questions and Answers resource.

d Details of the Fluoride Reference Group are contained within the Administration Report available on the NHMRC website at: https://www.nhmrc.gov.au/health-topics/health-effects-water-fluoridation.

e McDonagh M, Whiting P, Bradley M. et al. 2000, *A Systematic Review of Public Water Fluoridation*, available at: http://www.nhs.uk/conditions/fluoride/documents/crdreport18.pdf

f 2015 Cochrane review: Water fluoridation for the prevention of dental caries, available at: http://www.cochrane.org/CD010856/ORAL_water-fluoridation-prevent-tooth-decay

- additional studies from 2006-2015 on tooth decay that are relevant to Australia
- studies from 2006-2014 reporting on any health effects (other than tooth decay or dental fluorosis).

These studies all compared:

- a group of people who drank fluoridated water with a group who drank non-fluoridated water; or
- two groups of people who drank water with different levels of fluoride.

Studies that compare these different groups of people are important because they help to show whether any differences in the reported health outcomes can be due to different levels of fluoride in drinking water.

Research studies vary in quality and this affects how much confidence we can have in the findings. Apart from water fluoridation, different factors such as age, income and diet can also impact on the health of people in the groups being studied. These factors can affect the results of the study and are called confounding factors (or confounders).

There is more confidence in study findings when:

- the study includes a large number of people
- there are many studies showing the same results
- the studies have taken into account confounding factors
- the effect is biologically plausible.[g]

More emphasis is placed on study findings which are relevant to Australia. The relevant studies were from countries that have a similar level of fluoride in drinking water, similar dental services and access to dental care, or similar socio-economic factors like income and education levels.

The quality of the evidence from the research studies was assessed using an internationally established system (GRADE[h]). GRADE was also used to determine the strength of the conclusions presented in the Information Paper.

This Information Paper:

1. describes how the 2016 NHMRC Evidence Evaluation was performed
2. presents the findings on tooth decay, dental fluorosis and other possible health outcomes. These findings are discussed in the 'Description of the Evidence' section in each chapter. Each description of evidence includes:
    a. conclusions from the two existing reviews (2000 McDonagh review and the 2007 NHMRC review)
    b. evidence on tooth decay and dental fluorosis from the 2015 review conducted by the Cochrane Collaboration (referred to as the 2015 Cochrane review)
    c. new evidence from this 2016 NHMRC Evidence Evaluation
3. presents the findings of any other research on the dental and other human health outcomes relevant to water fluoridation in Australia provided outside of the 2016 NHMRC Evidence Evaluation. These findings are discussed in the 'Additional considerations' sections
4. makes conclusions based on all of these reviews.

g Existing medical and biological knowledge supports this effect being possible.

h *Grading of Recommendations Assessment, Development and Evaluation* (GRADE), available at: http://www.gradeworkinggroup.org/

What does the 2016 NHMRC Evidence Evaluation tell us?

Tooth decay

Over sixty years of research shows that water fluoridation helps to prevent tooth decay by protecting against damage and helping with the repair of teeth.

All of the studies in previous reviews and in the 2016 NHMRC Evidence Evaluation found that water fluoridation reduces tooth decay by 26-44% in children, teenagers and adults.

Dental fluorosis

Dental fluorosis is a change in the appearance of teeth that most commonly appears as white lines or areas on tooth surfaces. Dental fluorosis is caused by a high intake of fluoride from one or more sources during the time when teeth are developing. Sources include food, fluoride supplements (now unavailable for purchase in Australia), drinking water and toothpaste.

Australian studies indicate that at current water fluoridation levels, dental fluorosis has declined. Most cases of dental fluorosis in Australia are very mild or mild, not readily visible and have no effect on the function of teeth. In Australia very mild or mild dental fluorosis is not of aesthetic concern to those affected. Moderate dental fluorosis is very uncommon and severe dental fluorosis is rare in Australia.

International studies show that fluoride in drinking water is linked to the amount and severity of dental fluorosis. Water fluoride levels in the countries of these studies are up to five times greater than the current Australian water fluoridation levels. This difference makes these results less relevant to Australia.

Other health outcomes

NHMRC searched for all evidence reporting any human health outcomes of water fluoridation.

The 2016 NHMRC Evidence Evaluation found no reliable evidence of an association between water fluoridation at current Australian levels and other human health outcomes.[i]

Most of the evidence on humans is from areas with higher levels of fluoride than current Australian levels. Confidence in some of the evidence is affected by several issues including the small number of studies, the study designs, the low quality of studies and the lack of control for possible confounding factors such as a lack of consideration of: fluoride from other sources; socio-economic status; and iodine exposure.

Conclusion

The evidence shows that water fluoridation at current Australian levels reduces the occurrence and severity of tooth decay. Water fluoridation at current Australian levels is associated with dental fluorosis. In Australia, however, most dental fluorosis is very mild or mild, does not affect the function of teeth and is not of aesthetic concern to those who have it.

i The studies reported on cancer (all incidences, osteosarcoma, Ewing sarcoma), Downs syndrome, cognitive function and IQ, mortality, muscle and skeletal effects (hip fracture, skeletal fluorosis), chronic kidney disease, heart disease and high blood pressure, kidney stones, low birth weight, muscle and skeletal effects (musculoskeletal pain, osteoporosis, skeletal fluorosis, hip fracture), thyroid function, and self-reported health outcomes (gastric discomfort, headache, insomnia).

There is evidence that water fluoridation at current Australian levels is not associated with cognitive dysfunction, lowered IQ, cancer, hip fracture and Down syndrome. There is no reliable evidence of an association between water fluoridation at current Australian levels and other human health outcomes.

Introduction

Purpose of this document

This Information Paper provides Australians with a summary of evidence on the dental and other human health outcomes of the addition of fluoride to drinking water. It is based on the findings of the comprehensive 2016 NHMRC Evidence Evaluation[1] and the input of the NHMRC Fluoride Reference Group. It also includes consideration of the ethics of water fluoridation.

Fluoride

Fluoride is a natural part of the earth's crust. Fluoride occurs naturally in minerals, and is found in rocks, soil, natural water sources, plants and animals. Fluoride is found in all natural waters but the amount varies depending on the region and original source of water. In Australia, the amount of naturally occurring fluoride in water is mostly very low (<0.1 mg/L), with the exception of central Australian water well supplies.[2, 3] Naturally occurring fluoride levels are higher in water found in parts of the United States of America (USA), South America, Africa, the Middle East, China and the Indian subcontinent. In these areas, levels of fluoride greater than 3 mg/L are common[4-9] and can also be considerably higher.[5, 10, 11]

Fluoride can form compounds with other chemicals, including for example sodium fluoride or calcium fluoride.[12] Fluoride compounds such as sodium fluoride are added to the drinking water supply for the purpose of water fluoridation. Fluoride compounds have entirely different properties than fluorine gas.[12, 13]

After fluoridated water is consumed, fluoride is rapidly absorbed by the gut and distributed throughout the body via the circulatory system. Some fluoride is taken up by bones and teeth while some is distributed into the salivary glands. About two thirds of the fluoride consumed quickly leaves the body in the urine.[14]

Fluoride helps prevent tooth decay by protecting against damage and helping with repair.

Tooth decay is very common in Australia. Five out of ten children and nine out of ten Australian adults have had some decay in their teeth.[15] This makes it the most common health problem in Australia.[16] The consequences of tooth decay include infection, pain and difficulties chewing. Concerns about the appearance of the teeth, absence from work or school, costly dental treatment and hospitalisation for treatment of complications also add to the burden of the disease.[17]
The number of affected tooth surfaces usually increases over a person's lifespan.

Water fluoridation in Australia

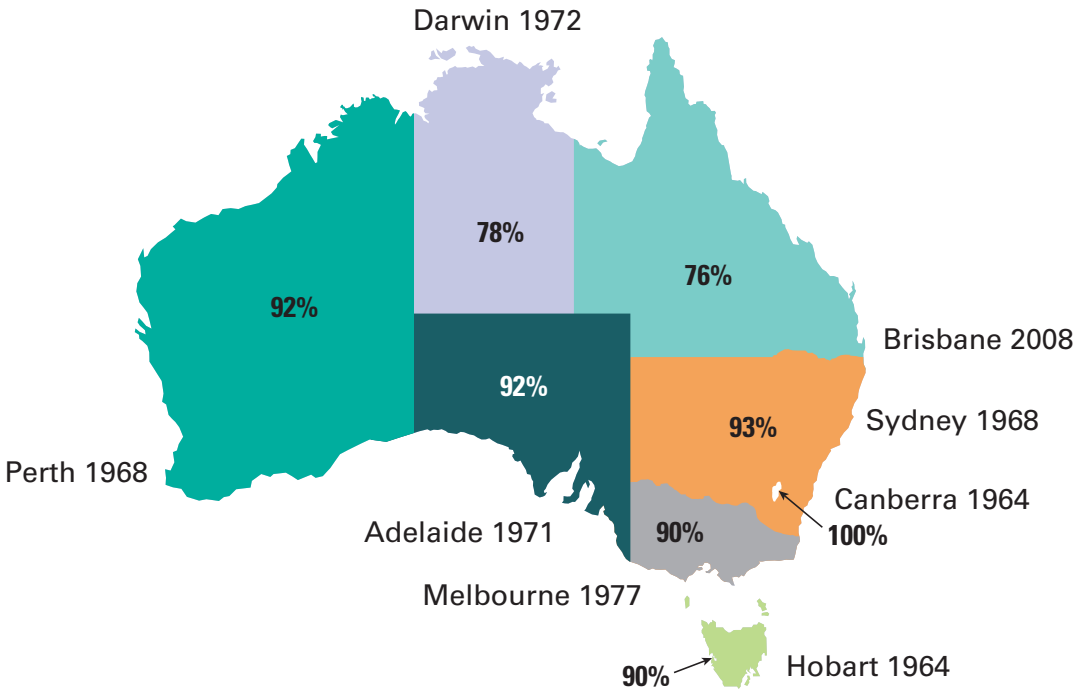
The intentional addition of a precise amount of fluoride to the water supply is a public health measure that aims to benefit dental health. Fluoride was first added to the water supply in Australia over 60-years-ago. Beaconsfield, Tasmania,[18] was the first community to receive fluoridated drinking water in 1953, followed by Yass, New South Wales (NSW), in 1956.[19]

Australia mostly has very low levels of naturally occurring fluoride. In regions where levels of naturally occurring fluoride fall within Australia's recommended range, water suppliers do not add fluoride to the water supply.

NHMRC supports Australian states and territories fluoridating their drinking water supplies. The addition of fluoride to the water supply is controlled by laws and government policies within each Australian state and territory, as listed in Appendix D. All Australian states and territories have access to fluoridated drinking water. All Australian states and territories provide fluoridated drinking water, however coverage in each jurisdiction varies (see Figure 1 below).

Historically, Queensland has had much lower rates of water fluoridation than other states and territories. In 2008 the Queensland Government mandated the addition of fluoride to its water supplies. This legislation was amended in 2012, transferring the decision about adding fluoride to water from state level to local council level. The coverage of water fluoridation in Queensland has decreased by nearly ten percent since this time.[20]

Figure 1 Percentage of population with access to fluoridated water as at February 2017[i] and dates of introduction of water fluoridation to Australian capital cities[ii] (Sources:[i] Confirmed with state and territory government health departments;[ii] based on reference 3)



Why NHMRC conducted this work

NHMRC is responsible for ensuring that Australians receive the best available, evidence based advice on health and on preventing, diagnosing and treating disease.

In 2007 NHMRC published *A Systematic Review of the Efficacy and Safety of Fluoridation*.[3] Based on this work, NHMRC issued a *Public Statement: The Efficacy and Safety of Fluoridation 2007*[10] which recommends that water be fluoridated in the target range of 0.6 to 1.1 mg/L, depending on climate, to balance reduction of dental caries and occurrence of dental fluorosis. It is recognised, however, that therapeutic protection against dental caries can be derived from concentrations of 0.5 mg/L and above.[21]

Since the 2007 NHMRC review[3], new research has been published that examines the relationship between fluoride levels in drinking water and possible impacts on health. Some community members have also expressed concerns about the potential health problems from drinking water that is fluoridated at current Australian levels.

Therefore, in 2014-15, NHMRC decided to investigate recent research on the dental and other human health outcomes of water fluoridation. The findings of this comprehensive 2016 NHMRC Evidence Evaluation were released in 2016 and are summarised in this Information Paper.

A summary of the relevant government policy advice on these issues and other matters related to fluoride, such as fluoride intake from food and drinks, is provided at Appendix E.

Overview of the NHMRC process

Oversight by the Fluoride Reference Group

In May 2014, NHMRC established the Fluoride Reference Group. The Fluoride Reference Group's role was to guide a review of the evidence on the possible dental and other human health outcomes of water fluoridation in humans and to develop this Information Paper.

The Fluoride Reference Group members have expertise in public health, oral health, epidemiology, child health, toxicology, cancer, bone biology, neurodevelopment, Aboriginal and Torres Strait Islander health, water management and health ethics. The Fluoride Reference Group included a member of the *NHMRC Water Quality Advisory Committee*, which advises on the NHMRC's *Australian Drinking Water Guidelines 2011*, and another member with expertise in urban water and water resources management. Information on the membership and terms of reference of the Fluoride Reference Group is included in Appendix A.

The Fluoride Reference Group:

- guided the search for relevant studies on the dental effects and any other human health outcomes of water fluoridation and the review of this evidence
- reviewed and commented on drafts of the 2016 NHMRC Evidence Evaluation
- provided scientific advice on the meaning of some of the research studies, based on members' knowledge and expertise
- helped to find additional material that was relevant in the Australian context
- considered the results of the 2016 NHMRC Evidence Evaluation along with other factors including:
    1. whether there were any benefits or harms
    2. the likely values and preferences of the community
    3. the effects of water fluoridation on disadvantaged Australians
    4. the costs of tooth decay versus water fluoridation
    5. other ethical considerations raised by water fluoridation
- guided the development of the Information Paper
- guided the identification of key issues to be considered by the Council and CEO of NHMRC.

The Fluoride Reference Group considered comments received during public consultation on the draft Information Paper in finalising this work.

2016 NHMRC Evidence Evaluation

In examining the possible health outcomes of water fluoridation in humans, NHMRC contracted the Clinical Trials Centre, University of Sydney, to conduct an independent evidence evaluation of all of the relevant scientific research on water fluoridation. The Clinical Trials Centre used internationally recognised systematic review methods to perform the evidence evaluation to the highest possible standard. This approach provided the most rigorous way for finding out the dental and other human health outcomes of adding fluoride in water.

The findings of this comprehensive independent evidence evaluation are presented in the Evidence Evaluation Report[1] and Technical Report[22], which were released by NHMRC in 2016. This work is referred to in this document as the 2016 NHMRC Evidence Evaluation.

Quality assurance processes

NHMRC takes care to ensure that its health advice is of the highest possible quality. Some of the steps taken to ensure the quality of the advice include:

- all Fluoride Reference Group members were required to make a public declaration of their interests and NHMRC managed any perceived or real conflicts of interest that were identified
- the methodology of the 2016 NHMRC Evidence Evaluation was reviewed by an independent body
- public consultation on the Information Paper
- further revisions of the Information Paper by the Fluoride Reference Group and other experts to take account of public comments.

These processes are summarised in Figure 2. More details on the processes used to ensure the quality of the 2016 NHMRC Evidence Evaluation and development of the Information Paper is in Appendix B.

Public consultation

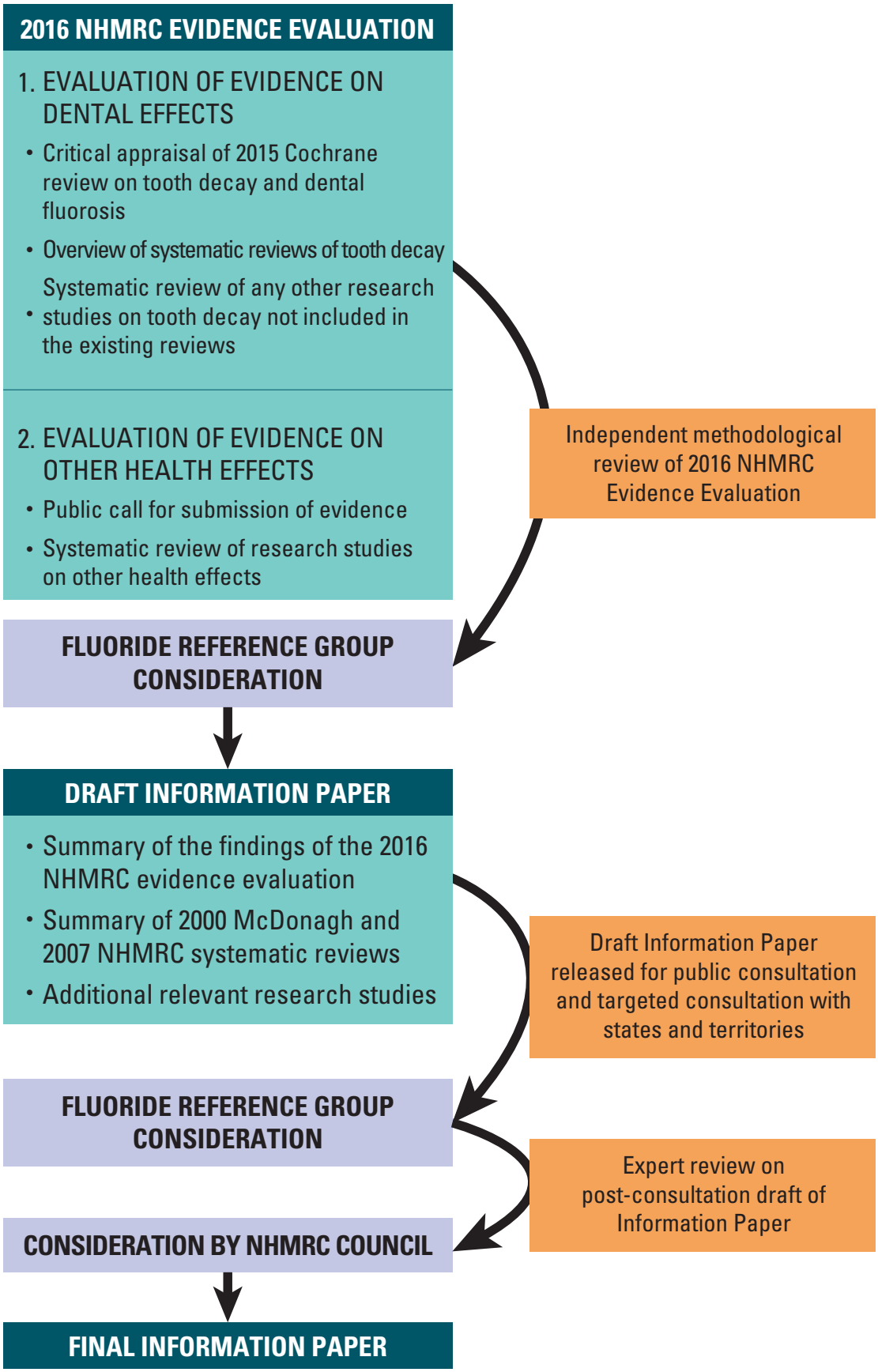
Public consultation aimed to provide the Australian public with the opportunity to participate in how NHMRC develops health advice, and to ensure that the Information Paper was informed by all relevant and recent literature. A draft was released for public consultation from 14 September to 13 October 2016, and NHMRC encouraged the submission of additional evidence not already considered in the 2016 NHMRC Evidence Evaluation.

Thirty complete submissions were received including 923 references, which were considered by the Fluoride Reference Group. This feedback informed their advice to revise the draft Information Paper.

Independent expert review

Six Australian expert reviewers provided comments on the post consultation draft of the Information Paper. The aim of this independent expert review was to check that the Fluoride Reference Group had appropriately interpreted the evidence and considered comments from public consultation. The expert reviewers were also asked to comment on the appropriateness of the Information Paper for the target audiences, and to provide any extra evidence that they thought should have been considered. Five expert review reports (one report was co-authored by two reviewers) were received. These reports informed further revisions.

Figure 2 Overview of the 2016 NHMRC Evidence Evaluation and quality assurance processes in the development of the *NHMRC Information Paper*



Evaluating the evidence

The 2016 NHMRC Evidence Evaluation[1] was designed to update the previous systematic review conducted by NHMRC in 2007.[3] Similarly, the 2007 NHMRC review updated an earlier 2000 review from the United Kingdom (UK) (referred to as the 2000 McDonagh review)[22] by identifying new studies published since the 2000 report. Given this history, the findings for dental and other human health outcomes from the two previous reviews are presented first in the section 'Findings of the 2016 NHMRC Evidence Evaluation' of the Information Paper, followed by the results of the 2016 NHMRC Evidence Evaluation.

The 2016 NHMRC Evidence Evaluation involved several complex steps:

- a critical appraisal of a review published in 2015 by the Cochrane Collaboration, a global evidence-synthesis network (see www.cochrane.org), evaluating the effects of water fluoridation on tooth decay and dental fluorosis[24]
- a review of other reviews of water fluoridation and tooth decay published after 2007
- a systematic review of research studies published since October 2006 that were not already included in the existing reviews on tooth decay and water fluoridation
- a systematic review of research studies published since October 2007 on any other human health outcomes of water fluoridation.

As well as reporting on the findings of the 2000 McDonagh review, 2007 NHMRC review, and the 2016 NHMRC Evidence Evaluation, this Information Paper includes information from other studies ('additional considerations') which were considered by the Fluoride Reference Group as being important for making decisions about water fluoridation in Australia (See Figure 3). These additional studies were provided by Fluoride Reference Group members, or through the two NHMRC public consultations.

Identification of the evidence

The 2016 NHMRC Evidence Evaluation identified relevant studies using standardised methods. A comprehensive search followed pre-approved review protocols and search strategies. These methods are described in detail in the 2016 NHMRC Evidence Evaluation Report[1] and Technical Report.[22]

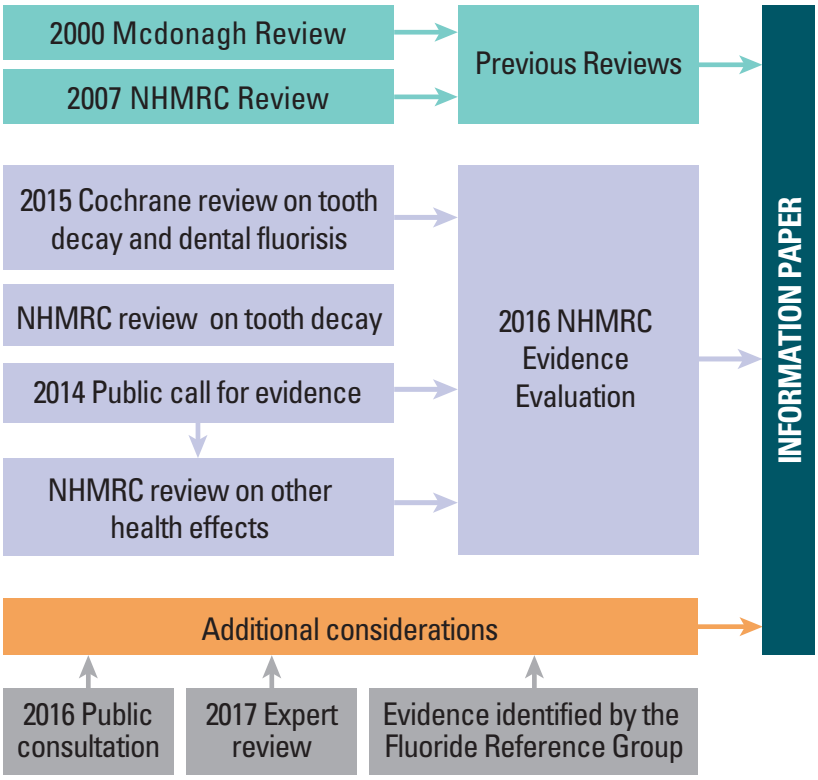
Scientific literature that might be relevant for the 2016 NHMRC Evidence Evaluation was identified by:

- searching electronic databases for published reviews which followed a systematic approach to evaluate research studies on tooth decay
- searching electronic databases for research studies on tooth decay, other dental effects and/or human health outcomes of water fluoridation
- searching for research studies in national and international government, health and water authority websites and the *Fluoride Action Network* website
- checking the reference lists of relevant systematic reviews and studies included in the report.

In July 2014, NHMRC called for public submissions of relevant published studies (published between 1 October 2006 and 22 August 2014) to be evaluated as part of the systematic review of other human health outcomes.

From 14 September to 13 October 2016, NHMRC called for public comments on the draft Information Paper and invited the submission of additional evidence[j] that met specified inclusion criteria. 923 references were received by NHMRC during this public consultation. These were assessed against the criteria outlined in the section 'Evidence submitted during the 2016 public consultation'.

Figure 3 Evidence sources that contributed to the Information Paper



Selection of the evidence

Evidence on water fluoridation and tooth decay

The 2016 NHMRC Evidence Evaluation captured evidence from a critical appraisal of a systematic review of tooth decay and dental fluorosis published by the Cochrane collaboration in 2015.[24]

The 2015 Cochrane review included studies on tooth decay. These studies compared the introduction or cessation of water fluoridation in a new community over a period of time with a community without water fluoridation over the same period of time. Therefore, many relevant observational studies and recent studies conducted in Australia and other similar countries with longstanding water fluoridation programs were not considered. An additional search was conducted in November 2015 to identify these studies that are relevant to Australia, and are important for decision making.

The 2016 NHMRC Evidence Evaluation of tooth decay included scientific literature that was either:

- a published review which followed a systematic approach to examine the effect of water fluoridation on tooth decay; or

j Evidence not already considered in the 2014 public call for evidence and/or 2016 NHMRC Evidence Evaluation.

- a research study not included in a published review which:
    1. reported on tooth decay
    2. studied water fluoridation
    3. compared a group with fluoridated water and a group without fluoridated water[k]
    4. included confounders in its analysis
    5. was the most recent publication if it was based on information from a regular survey.

The systematic literature searches described above included evidence on water fluoridation and tooth decay published between 1 October 2006 and 12 November 2015 (the date that the searches were conducted).

Three existing reviews (Figure 6, Appendix C) and 25 research studies (Figure 7, Appendix C) were identified in this component of the 2016 NHMRC Evidence Evaluation.

Evidence on water fluoridation and dental fluorosis

The 2016 NHMRC Evidence Evaluation, which included the critical appraisal of the 2015 Cochrane review, formed the basis of NHMRC's consideration of the effects of fluoridation on dental fluorosis. The 2015 Cochrane review had broad inclusion criteria for studies on dental fluorosis. All study designs were included in this component of the review, as long as the study compared two communities with different levels of fluoride in drinking water (natural or added) and looked at the occurrence of dental fluorosis in these communities. The range of fluoride levels in the included studies exceeded current Australian levels.

Evidence on other human health outcomes of water fluoridation

The 2016 NHMRC Evidence Evaluation of other human health outcomes included research studies which:

- reported on any human health outcomes (other than tooth decay or dental fluorosis) in humans; and
- studied fluoride in drinking water.

These studies all compared:

- a group of people who drank fluoridated water with a group who drank non-fluoridated water[l]; or
- two groups of people drinking water with different levels of fluoride.

This systematic literature search included evidence on water fluoridation and other human health outcomes published between 1 October 2006 and 14 October 2014 (the date that the search was conducted).

A total of 41 studies were identified on other human health outcomes in this component of the 2016 NHMRC Evidence Evaluation (Figure 8, Appendix C).

k In the 2016 NHMRC Evidence Evaluation the intervention of interest was drinking water with a fluoride level between 0.4mg/L to 1.5mg/L. This covers current Australian levels. The lower level of 0.4mg/L was chosen for consistency with the 2015 Cochrane review and the upper level of 1.5mg/L for consistency with the maximum acceptable level recommended in the Australian Drinking Water Guidelines.

l In the 2016 NHMRC Evidence Evaluation the intervention of interest was drinking water with a fluoride level between 0.4mg/L to 1.5mg/L. This covers current Australian levels. The lower level of 0.4mg/L was chosen for consistency with the 2015 Cochrane review and the upper level of 1.5mg/L for consistency with the maximum acceptable level recommended in the Australian Drinking Water Guidelines. Studies are more applicable to Australia when the fluoride levels are between 0.6mg/L to 1.1mg/L, and less applicable when it exceeds 1.5mg/L.

General selection criteria

The 2016 NHMRC Evidence Evaluation included only studies where the full text was available, published in English and reported results in a form that could be used in the review (for example, the results for an outcome had to be reported for both fluoride levels being compared).

Non-systematic reviews (including narrative reviews), personal opinions, medical records, raw data, letters, editorials, laboratory studies, and technical reports were not included in the 2016 NHMRC Evidence Evaluation, Public Call for Evidence or public consultation processes. These types of reports can raise the possibility of health outcomes from water fluoridation. However, only high quality research that compares different levels of fluoride in water can show whether the reported health problems are associated with drinking water with fluoride in it.

Animal studies were excluded from the 2016 NHMRC Evidence Evaluation and also from this Information Paper, because the focus is on health outcomes in humans only, and there is evidence on humans with which to work. Animal studies might suggest mechanisms to explain how fluoride could affect health, but the applicability of these studies to human health is uncertain due to biological differences between species.[25]

Additional considerations identified by the Fluoride Reference Group

The Fluoride Reference Group recognised that the Information Paper should focus on evidence that is highly relevant to Australia. Based on their expertise and knowledge of current literature in the field, the Fluoride Reference Group knew of some evidence about Australian water fluoridation that was not identified or was excluded from the 2016 NHMRC Evidence Evaluation due to its rigorous systematic review processes. Where this evidence was considered important for decision making, despite not being included in the 2016 NHMRC Evidence Evaluation, the Fluoride Reference Group included this evidence under the 'additional considerations' sections throughout the Information Paper. This step was taken to distinguish between the evidence that was formally assessed in the 2016 NHMRC Evidence Evaluation and the evidence subsequently identified and accepted by the Fluoride Reference Group.

Additional considerations raised by Fluoride Reference Group members included:

- the effect of water fluoridation on oral health inequalities
- the effect of water fluoridation on rates of hospital admissions for the treatment of tooth decay
- current perceptions of dental fluorosis in Australia.

Studies were included as 'additional considerations' if they:

- were based on scientific research (i.e. report on data that had been systematically collected and analysed)
- were relevant to water fluoridation and human health
- had publicly available findings, published in English, either as a full text article in a peer-reviewed journal or as an abstract from international conference proceedings.

Evidence submitted during the 2016 public consultation

Additional evidence submitted during public consultation was assessed for consideration using the same criteria as for the formally assessed evidence. Studies were considered if they:

- were based on scientific research (i.e. report on data that had been systematically collected and analysed)

- were relevant to water fluoridation and human health
- had publicly available findings, published in English, either as a full text article in a peer-reviewed journal or as an abstract from international conference proceedings[m]
- were published after 1 October 2006
- compared at least two groups with exposure to different levels of fluoride in drinking water
- had not exclusively selected participants only on the basis of reported health outcomes (for example case reports).

Studies that had already been considered in the 2016 NHMRC Evidence Evaluation, or provided during the 2014 call for published studies, were not re-considered. Animal studies and non-scientific papers were not included for the reasons explained in the 'General selection criteria' above.

A total of 23 references met the criteria for consideration, eight of which were included in the Information Paper. Inclusion of these eight references was based on the Fluoride Reference Group's assessment that the evidence was relevant to Australia and was important for decision making.

Relevant evidence submitted during public consultation contributed to the 'Additional considerations', and 'Ethical considerations' sections of the Information Paper, or Appendix G 'Resource use and cost-effectiveness. The relevant submitted evidence could add to the Evidence Statement but could not be used to alter them because this additional evidence was not formally assessed during the 2016 NHMRC Evidence Evaluation.

Critical appraisal of the evidence

Critical appraisal is a process to assess the quality (strengths and weaknesses) of published research. High quality research has more valid results than poor quality research. The more valid the results, the more useful they are in answering the review questions.[26]

There are several aspects to the critical appraisal of individual research studies. The two most important questions are:

- Is the study design able to answer the research question?
- What are the key methodological features of the study design?

Specific features that are important in critically appraising research on the association between water fluoridation and health outcomes include:

- the way in which participants were selected
- how information about the participants' exposure to water fluoridation and health outcomes was collected
- whether the study took account of possible confounding factors
- whether the study took account of likely alternative explanations for any association between water fluoridation and human health outcomes
- the suitability of the statistical methods used
- the interpretation of the findings
- how applicable the study was to the Australian context
- any conflicts of interest of the authors.[27]

m Unpublished papers or abstracts from international conference proceedings were only considered if they fulfilled the other criteria listed and the Fluoride Reference Group were satisfied that they contained enough information to assess whether the evidence was relevant to Australia and important for decision making.

Each existing review was assessed by the evidence reviewers using an established valid checklist [the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool.[28] The individual studies making up each review were not assessed for quality – any quality assessment made by the review authors was accepted by the evidence reviewers.

Each individual study was assessed by the evidence reviewers against an agreed checklist.[29-31] Each study was then rated as:

- high quality – the majority of criteria in the relevant checklist were met, indicating that there is little or no risk of bias in the study's results
- acceptable quality – most criteria in the relevant checklist were met, however there were some flaws in the study with an associated risk of bias in the study's results
- low quality – either most criteria in the relevant checklist were not met, or there were significant flaws relating to key aspects of the study design, meaning there is a high risk of bias in the study's results.

It should be emphasised that these ratings relate to the quality of the individual studies. The quality rating for each individual study contributed to the overall quality of the body of evidence (i.e. the group of studies about the same health outcome), which was assessed in a subsequent process (see the section 'The GRADE approach to assess the evidence on dental and other human health outcomes and reach a conclusion about the intervention of water fluoridation').

Study design

All of the studies included in the 2016 NHMRC Evidence Evaluation were observational studies. This means that the study investigators measured the dental and other human health outcomes in groups of participants supplied with fluoridated water and compared those findings to participants with either non-fluoridated water supplies or water supplies containing different levels of fluoride. However, in these studies it is possible that associations between water fluoridation and dental and other human health outcomes may be biased due to other factors ('confounding factors' or 'confounders'). Bias is less likely to occur in studies where participants are randomly allocated to different levels of fluoride. For this reason, many observational studies are assessed as low quality (they have less valid results) than research studies where the participants are randomly assigned to different groups.

Studies included in the 2016 NHMRC Evidence Evaluation were one of the following:

- Ecological studies – these studies measure exposure to water fluoridation at a population level and the health outcome is either measured at a population level or individual level.[32] Given ecological studies do not involve randomisation, it is more difficult to account for other factors that may affect the dental and other human health outcomes in question. These studies are generally unable to show whether a health outcome occurred (or changed in severity) before, during or after the exposure to fluoride. In the case of water fluoridation, the outcome is measured many years after water fluoridation was introduced. Despite this limitation, ecological studies remain convenient and appropriate to include given that water fluoridation is a population-wide exposure.
- Cross-sectional studies – in these studies, dental and other human health outcomes in communities with differing levels of fluoride in water supplies were compared at a single point in time.[27] These studies are also generally unable to show whether a health outcome occurred (or changed in severity) before, during or after the exposure to fluoride but are still appropriate for water fluoridation for the reasons stated above.

- Prospective cohort studies – these studies follow the same group (cohort) of participants over a period of time and measure dental and other human health outcomes in the cohort with fluoridated water supplies and those in the cohort with non-fluoridated water supplies.[27] These studies help to determine how likely it is that an exposure causes particular health outcomes as they can show that the health outcome occurred during or after the exposure.

Sample size

There were varying numbers of participants in the studies included in the 2016 NHMRC Evidence Evaluation. Studies with larger numbers of participants provide greater certainty that the observed association between water fluoridation and a health outcome is not due to chance. Larger studies have greater power to detect an effect if one is present, while studies with small sample size may not accurately detect effects. Larger numbers are particularly important if fluoridation is likely to have only a small effect on health, or when a health outcome is rare in the study population.

Bias

In research studies, there are a number of reasons why the results may not be accurate or valid. These are called biases. Bias can come from poorly designed studies, or from problems in the collection, analysis, reporting, publication or review of study data. Bias can lead to invalid results.[27] Where bias was of concern in any of the included studies, this has been noted in this Information Paper and the 2016 NHMRC Evidence Evaluation.

One source of bias occurs if only some of the people who are asked to be part of a study agree to participate in it. This can cause bias if the people who participate are different in relevant ways (such as their health status) compared to those who do not participate. Many of the included studies did not include this information.

Some studies used self-reporting to measure the dental or other human health outcome (for example, how many headaches the participants had in the past). This may introduce bias as people do not tend to recall health details accurately. More importantly, if people already have a view about the dental or other human health outcomes of fluoride and are aware of the purpose of the study, they may more readily recall having more headaches than the group with non-fluoridated water. This can lead to an invalid finding about an association between fluoride and headaches. This type of bias can be avoided if participants and researchers do not know which participants have been exposed to fluoridated water (this is called 'blinding'). The studies included in the 2016 NHMRC Evidence Evaluation were mostly not blinded and this may be unavoidable in studies of water fluoridation. This lack of blinding is common in observational studies and contributes to them being considered to be lower quality.

Confounding

A study may suggest an association between drinking water with fluoride in it and a health outcome. It is important to determine whether this association is actually due to water fluoridation, or to another factor linked to both the exposure and the outcome. These are called confounding factors.[27] Confounding factors can lead to invalid results by showing an association when in reality there is none or, vice versa, no association even if one exists.

For example, a child's measured intelligence is likely to be higher if the child's parents are well educated. Therefore, in a fluoridation study, if people living in an area with low levels of fluoride in their drinking water were, on average, better educated than those living in an area with high fluoride levels, then the children's IQ would be higher in the areas with lower fluoride levels. This association may not be related to fluoride in the water supply. In this example, education is the confounding factor.

Fluoride from other sources, such as fluoridated toothpaste or some types of food, can confound the association between fluoride in water and dental and other human health outcomes. This is difficult to assess without good measurement of exposure to other sources of fluoride. Many of the included studies did not report on other sources of fluoride.

It can be very difficult for researchers to identify and account for all of the potential confounding factors in studies. In many of the studies included in the 2016 NHMRC Evidence Evaluation, potential confounding variables were not consistently measured or taken into account when analysing the data. This reduces the validity of these studies.

Applicability

The aim of the 2016 NHMRC Evidence Evaluation is to inform decisions about water fluoridation in Australia. Studies that took place in Australia, or in countries with similar conditions to Australia, are considered highly applicable. These results can be generalised to Australia and are therefore very relevant to making decisions about water fluoridation in Australia.[27]

However, some of the studies considered by the Fluoride Reference Group were conducted in countries that were very different to Australia, making their results less relevant. For example, some studies were performed in areas where the water had significantly higher levels of naturally occurring fluoride than current Australian levels. Other studies were less relevant because they were conducted in countries that had different dental care systems and social structures than Australia.

Consistency

Several studies are usually required in order to confidently say that fluoridation may cause any health outcome. If an association in one study is consistently found in other studies, then it is more likely that a cause-and-effect relationship exists. However, when study results are not consistent, it is more likely that any association in a single study is due to chance, bias, or confounding.

This is important to bear in mind when examining the effect of water fluoridation. There is a large body of studies which show a consistent effect for the outcomes of tooth decay and dental fluorosis. For the other human health outcomes, there are frequently only a small number of studies with less consistent findings.

Further details about critical appraisal can be found in the 2016 NHMRC Evidence Evaluation[1] and the Technical Report.[22]

The GRADE approach to assess the evidence on dental and other human health outcomes and reach a conclusion about the intervention of water fluoridation

Judgements about the quality of evidence in research studies and the health advice based on those judgements should be as transparent and explicit as possible. To help with this process, NHMRC uses *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) which is an internationally recognised system for rating the quality of evidence and strength of recommendations in healthcare. GRADE is designed to be an explicit, comprehensive, transparent, and pragmatic way of making decisions.[33]

The Fluoride Reference Group followed three steps in applying the GRADE process:

Assessing the quality of the evidence by outcome

Under the GRADE framework, the quality of evidence is assessed across studies for each dental or other human health outcome. Research results are assigned a quality rating based on an assessment of how valid the findings are and how much confidence we can have in them.

The confidence in the evidence is classified as follows:

- high – we are very confident in the results
- moderate – we are moderately confident in the results
- low – we have limited confidence in the results
- very low – we are not confident in the results

As discussed in the section 'Critical appraisal of the evidence', there are many ways in which research may produce invalid results. Because of these risks, GRADE - which was designed to assess evidence for clinical practice interventions - classifies observational studies as low level evidence. GRADE has limitations though, when applied to public health interventions like water fluoridation, where the only evidence available is often from observational studies sourced from monitoring existent programs. These are viewed by GRADE as low or very low quality, differing from randomised study designs (more commonplace in individualised clinical practice interventions) which are assessed as being of higher quality. For large-scale population level interventions like water fluoridation, which has effects over lifetime exposure, evidence from randomised controlled trials is rarely available due to them being impractical to conduct.

In making pragmatic decisions about water fluoridation in Australia, rather than relying on study design alone or existing criteria/tools for appraising evidence on public health interventions, the Fluoride Reference Group recognised that the evidence needed to be considered based on a broader assessment of multiple factors (see 'Making a decision about water fluoridation').

In the 2016 NHMRC Evidence Evaluation, observational study designs which were less prone to bias (e.g. prospective cohort studies) were initially rated as moderate rather than low quality. This approach was adopted based on a proposal for using GRADE in public health as described by Harder et al (2015).[34] In addition, if there is an 'overall pattern of evidence across settings or study design' that suggests consistency and lessens any plausible threats to validity, the quality of that evidence may be able to be upgraded.[34] These innovations to using GRADE for public health are being considered by NHMRC and the international Grade Working Group.[34]

From the initial GRADE rating, the quality of the evidence can be upgraded or downgraded based on various factors that influence confidence in the results. Observational studies are first assessed as being of low or moderate quality because of their inherent higher risk of bias compared to randomised controlled trials (which are first assessed as high quality in the GRADE approach). The GRADE approach notes that it is not possible to upgrade observational studies if they have already been downgraded e.g. for risk of bias. For this reason, observational studies on water fluoridation are unlikely to be assessed as high or moderate quality under the GRADE framework even though they may be the most available and appropriate study design for this question.

The GRADE assessments of the quality of the evidence for each health outcome are identified and presented in the 2016 NHMRC Evidence Evaluation.[1] The Fluoride Reference Group confirmed each of the GRADE assessments and considered the overall quality rating in interpreting the body of evidence on each health outcome.

Developing Evidence Statements

Evidence Statements were developed by the Fluoride Reference Group to provide a summary of all the relevant studies on the effects of water fluoridation for each dental and other human health outcome.

The Evidence Statements in the Information Paper take into consideration all of the evidence captured in the 2000 McDonagh review, the 2007 NHMRC review and the 2016 NHMRC Evidence Evaluation (see Figure 3). The Evidence Statements also take into account the additional material brought forward by the Fluoride Reference Group that was considered to be important for making decisions about water fluoridation in Australia. The evidence source is described in each Evidence Statement.

Some of the important factors considered by the Fluoride Reference Group when developing the Evidence Statements were:

- level of confidence that the findings reported by each individual study were valid
- the consistency of the findings from the body of evidence
- any limitations of the body of evidence which, for some outcomes, included the small number of studies, the poor methodological quality of many of the studies and the rarity of particular health outcomes
- the applicability of the body of evidence to the Australian context.

The Fluoride Reference Group adopted consistent language in the Evidence Statements to reflect these factors. The Evidence Statements generally fit within one of the following categories:

- *Consistent evidence of an association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and consistently did show an association between water fluoridation and the dental or other human health outcome.
- *The evidence shows no association*– this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.
- *Limited evidence of an association* – this wording was used when the Fluoride Reference Group had limited confidence that the body of evidence showed an association between water fluoridation at current Australian levels and the dental or other human health outcome
- *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

The Office of NHMRC conducted a quality assurance process to ensure that the evidence was summarised consistently across all of the outcomes and reflected the overall quality ratings from the GRADE assessment.

Making a decision about water fluoridation

When making clinical or public health decisions, the GRADE framework helps to determine the strength of a recommendation for a particular intervention or course of action. These decisions are influenced in the two phases of the GRADE Framework. Firstly, by the quality of the evidence on the possible dental and other human health outcomes of the intervention, as described in the previous section. Secondly, the decisions are influenced by considering the overall balance of possible desirable and undesirable consequences of the intervention. The authors of the 2016 NHMRC Evidence Evaluation guided the first phase, while a 'guideline development panel' or expert committee, known as the Fluoride Reference Group, guided the second phase.

In its 2007 Public Statement, NHMRC recommends that fluoride should be added to drinking water within the range of 0.6 to 1.1 mg/L, depending on climate, to balance reduction of tooth decay and occurrence of dental fluorosis. The purpose of the 2016 NHMRC Evidence Evaluation was to update the body of evidence underpinning the 2007 Public Statement and to assess the relevance of any new evidence to Australian conditions.

The steps involved in making a decision about water fluoridation were:

1. 2016 NHMRC Evidence Evaluation authors reached conclusions about the quality of the evidence on the dental and other human health outcomes associated with fluoridated water, and suggested a draft Evidence Statement.
2. The Fluoride Reference Group considered the 2016 NHMRC Evidence Evaluation and finalised the Evidence Statements about the association between water fluoridation and dental and other human health outcomes (which reflects the quality, quantity, consistency and applicability of the evidence for each dental or other human health outcome).
3. The Fluoride Reference Group then addressed the second phase of the GRADE framework, by focussing its attention on the **intervention** of water fluoridation. It discussed the overall balance of possible desirable and undesirable consequences of the intervention of water fluoridation, based on its knowledge of the health and dental outcomes summarised in the Evidence Statements.

For the purposes of this Information Paper, the GRADE framework was used to develop the overall conclusion about the potential association between water fluoridation at current Australian levels and dental and other human health outcomes.

In the assessment of water fluoridation in the second GRADE phase (evidence to overall conclusion), the Fluoride Reference Group explicitly considered the overall balance of possible desirable and undesirable consequences which covers:

- the overall confidence in the estimates of any effect for critical outcomes[n], specifically tooth decay and dental fluorosis
- balance of benefits and any potential or possible harms
- community values and preferences
- impact on health equality
- acceptability of fluoridation to key stakeholders
- costs and resource implications
- feasibility.

n The Fluoride Reference Group agreed on the importance of outcomes before the evaluation of the evidence began. Tooth decay and dental fluorosis were considered critical for decision making, and all other health outcomes important but not critical for decision making.

All of these issues were discussed and the factors that influenced the Fluoride Reference Group's decisions were documented. This process resulted in the development of an overall conclusion in this Information Paper on the effectiveness and safety of water fluoridation at current Australian levels.

Following public consultation and finalising this Information Paper, the Council of NHMRC considered updating the NHMRC Public Statement.

Findings of the 2016 NHMRC Evidence Evaluation

Water fluoridation and dental effects

Summary

Tooth decay

There is consistent evidence[o] that water fluoridation at current Australian levels is associated with decreased occurrence and severity of tooth decay.

- Recent reviews found that there was a mean/median decrease in tooth decay measured by the dmft/s[p] or DMFT/S[q] in children and adolescents between 26 and 44%.
- A further recent review found that there was a decrease in tooth decay measured by the DMFT in adults of 27%.
- Additional primary studies identified in the NHMRC review between 2012 and 2015 found decreases in tooth decay measured by dmft/s or DMFT/S similar to the above.

Inequalities

While the findings are inconsistent across the previous reviews and the 2016 NHMRC Evidence Evaluation, there is some limited evidence[r] suggesting that water fluoridation reduces inequalities in tooth decay across socio-economic groups.

Hospital visits

A small number of published and unpublished Australian and international studies suggest that the rate of hospital admissions for dental treatment is lower in areas with water fluoridation.

Tooth loss

There is no reliable evidence of an association[s] to reach a conclusion about any association between water fluoridation at current Australian levels and tooth loss.

Delayed eruption and tooth wear

The 2016 NHMRC Evidence Evaluation indicates that at current Australian levels, water fluoridation is not associated[t] with delayed eruption of adult teeth or tooth wear.

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o *Consistent evidence of an association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and consistently did show an association between water fluoridation and the dental or other human health outcome.

p Number of decayed, missing and filled deciduous teeth / tooth surfaces

q Number of decayed, missing and filled permanent teeth / tooth surfaces

r Limited evidence of an association – this wording was used when the Fluoride Reference Group had limited confidence that the body of evidence showed an association between water fluoridation and the dental or other human health outcome.

s *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

t *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.

Tooth decay

Introduction

Tooth decay is the breakdown of the outer layers of teeth. It is one of the most common health problems in Australia. Tooth decay causes people concern and can lead to pain, infection and tooth loss. These symptoms can lead to a reduction in the overall wellbeing and quality of life by affecting people's ability to eat, sleep and socialise. Untreated tooth decay can result in avoidable hospitalisation.[35, 36-39]

Treating tooth decay is costly. The financial impact on individuals is greater than for other health problems as most dental treatments are not covered by Medicare. A number of schemes financing some aspects of dental services, mostly for means tested eligible children and adolescents, have been implemented during the last decade, but each has had a limited period of operation. While states and territories provide public oral health services for school-aged children and adults with a concession card, the eligibility criteria, co-payments, level of dental services and waiting periods vary across jurisdictions.[40]

Teeth are constantly undergoing repair as they are damaged by acids produced by bacteria in the mouth. Diet affects the amount of acid damage, with sugar consumption increasing the risk of damage. Fluoride both reduces the damage and helps with repair. Tooth brushing with toothpaste containing fluoride and eating a healthy diet are measures that an individual can do to help prevent tooth decay. The fluoridation of drinking water is another measure to reduce tooth decay. It differs from tooth brushing and diet in that water fluoridation can help prevent tooth decay for large numbers of people even where individuals do not change their behaviour. It also provides a regular source of fluoride to teeth over the course of the day which may contribute to dental benefits.

Tooth decay is measured in studies by counting the number of teeth a person has which are decayed, missing (due to decay) and filled (as this is a sign of treated decay) and adding them together. They are written as 'dmft' for deciduous/primary (baby) teeth and 'DMFT' for permanent (adult) teeth. Some studies count the number of tooth surfaces which are decayed, missing or filled rather than the number of teeth, this measure is written as 'dmfs' for deciduous teeth and 'DMFS' for permanent teeth. Occasionally, the 'missing' component is not measured and this is written as 'dft', 'DFT', 'dfs' or 'DFS', depending on whether deciduous or permanent teeth or surfaces are being measured. Another measure of tooth decay is the percentage of people (often children) who have no decay, or alternatively, the percentage with decay.

Description of evidence

Reviews

The 2000 McDonagh review included 26 studies in which water fluoridation was commenced or ceased during the study period in one group and there was a second group with no change in water fluoridation.[23] Sixteen analyses used DMFT or dmft as a measure of tooth decay. Of these analyses, 15 showed significantly less decayed, missing and filled teeth after fluoridation compared to the non-fluoridated area. Thirty analyses[u] measured the percentage of children with no tooth decay. Of these analyses, 19 found significantly more children with no tooth decay after fluoridation compared to the non-fluoridated area. The reverse was found in one study and the remaining studies did not have conclusive results. The review estimated that six people needed to receive fluoridated water for one extra person to be free of tooth decay.

No additional studies were included in the 2007 NHMRC review.

u Note there can be more than one analysis in a single study.

The 2015 Cochrane review[24] included the same type of studies as the 2000 McDonagh review. However, unlike the 2000 McDonagh review, the results for dmft and DMFT were separated. Fifteen studies were included overall.[24] Results from individual studies were combined to generate findings (Table 1).

Table 1 Summary of findings from the 2015 Cochrane review[24]

Measure	No of studies	Findings
dmft	9	35% mean reduction with fluoridation
DMFT	10	26% mean reduction with fluoridation
% children without tooth decay (deciduous teeth)	10	15% mean increase with fluoridation
% children without tooth decay (permanent teeth)	8	14% mean increase with fluoridation

NB: dmft/DMFT are measures of severity of tooth decay. % children without tooth decay are measures of prevalence

Two further reviews were identified in the 2016 NHMRC Evidence Evaluation.[41, 42]

The first was assessed as low quality in terms of the AMSTAR criteria.[41] It included comparative studies which provided dmft, dft[v], dmfs, dfs[w], DMFT, DMFS and DFS[x] information for fluoridated and non-fluoridated communities. The results of the included studies were not combined. These are provided in Table 2.

Table 2 Summary of findings from Rugg-Gunn (2012)[41]

Measure	No of studies	Findings (range)
dmft	19	44% median reduction with fluoridation (29% - 68%)
dft	2	47% median reduction with fluoridation (34% - 59%)
dmfs	7	38% median reduction with fluoridation (14% - 66%)
dfs	1	17% reduction with fluoridation
DMFT	37	37% median reduction with fluoridation (5% - 85%)
DMFS	12	29% median reduction with fluoridation (0% - 50%)
DFS	2	27% median reduction with fluoridation (10% - 44%)

NB: these are all measures of severity of tooth decay

The second review, which focused on dental decay in adults, was assessed as acceptable quality.[41] It included a total of 9 comparative studies. The combined results of these studies showed that fluoridated water prevents 35% of tooth decay (measured using DMFT). When results were combined using only studies published after 1979 (when fluoridated toothpaste became widely available), the results showed that 27% of tooth decay was prevented in areas with fluoridated drinking water compared to areas without fluoridated drinking water (Table 3). This review included three studies from areas with higher levels of fluoride than current Australian levels; however when the analysis was repeated without these studies the findings remained similar.

Table 3 Summary of findings from Griffin et al (2007)[42]

Measure	No of studies	Findings (confidence interval)
DMFT	5	27.2% mean reduction with fluoridation (19.4% - 34.3%)

NB: this is a measure of severity of tooth decay.

v Number of decayed & filled deciduous teeth.

w Number of decayed & filled surfaces in deciduous teeth.

x Number of decayed & filled surfaces in permanent teeth.

Additional studies identified in the 2016 NHMRC Evidence Evaluation

All of the additional studies on tooth decay identified in the 2016 NHMRC Evidence Evaluation were ecological studies except for one prospective cohort study.[43]

Deciduous teeth

Three studies found that water fluoridation reduced tooth decay in children's deciduous teeth (as measured by dmft).[44-46] Two of these studies were conducted in Australia[45, 46] and one in England[44] (which has similar healthcare systems, dental care and income levels to Australia) so they are highly relevant. All of the studies made adjustment for known confounders.

Four studies found that water fluoridation reduced tooth decay in the deciduous teeth of children (as measured by dmfs).[43, 47-49] Two of these studies were conducted in Australia[47, 49] and one in the USA.[43] These studies were considered to be highly relevant to water fluoridation in Australia. One study was less relevant as it was conducted in Vietnam which has a different healthcare system, access to dental care and different levels of income among other factors.[48] All four studies made adjustments for known confounders.

One Australian study found more Aboriginal and Torres Strait Islander children without decay in areas with water fluoridation (27.3%) compared to children living in areas without water fluoridation (22.9%). However, the effect was not statistically significant[50] and the study did not adjust for all confounders including sugar consumption, tooth brushing and socio-economic status.

Seven studies found that water fluoridation reduced the percentage of children with tooth decay in deciduous teeth.[44, 46, 49, 51-54] There were small differences in how this was measured across the studies. Four of these studies were conducted in Australia[46, 49, 52, 53], one in the USA[51] and one in England[55] and so they are highly relevant. The other study was set in South Africa and is therefore less relevant.[54] All studies were of acceptable quality except one which was assessed as being of low quality.[51]

Of the studies conducted in Australia:

- the reduction of tooth decay ranged from 14% to 8.5% across three different time points in NSW[46]
- exposure to fluoridated water from birth to three years of age was estimated to prevent 34% of cases of tooth decay at six years of age in children in South Australia[53]
- lack of water fluoridation was estimated to account for 21% of tooth decay in Queensland children.[52]

Table 4 summarises the findings for deciduous teeth from the additional studies identified in the 2016 NHMRC Evidence Evaluation.

Table 4 Summary of findings for deciduous teeth

Measure	No of studies	Relevance	Findings
dmft	3	3/3 highly relevant	All studies found reduced tooth decay with fluoridation
dmfs	4	3/4 highly relevant	All studies found reduced tooth decay with fluoridation
% children without tooth decay (deciduous teeth)	1	Highly relevant	Increased % without tooth decay with fluoridation
% children with tooth decay (deciduous teeth)	7	6/7 highly relevant	All studies found a reduced % with tooth decay with fluoridation

NB: dmft/DMFT are measures of severity of tooth decay. Children with(out) tooth decay are measures of prevalence.

Permanent teeth

Six studies found that water fluoridation reduced tooth decay in permanent teeth (measured with DMFT).[44, 45, 56-59] Four of the studies were conducted in Australia[45, 57-59] and one in England[44] so they are highly relevant and all made adjustments for known confounders.

Three highly relevant studies from Australia found that water fluoridation reduced tooth decay in permanent teeth (measured with DMFS).[47, 49, 59] One other less relevant study found that water fluoridation did not significantly reduce tooth decay in Vietnam[47] but this study was of low quality and limited relevance to Australia.

One Australian study found that water fluoridation increased the percentage of children without tooth decay in their permanent teeth. This was found for both Aboriginal and Torres Strait Islander children and non-Aboriginal and Torres Strait Islander children.[50]

A second study from Brazil found that water fluoridation did not significantly change the percentage of children without decay in their permanent teeth.[56] This study was considered to be less relevant due to likely differences in Brazil's access to dental care, dental healthcare systems and other socio-economic factors (for example, levels of poverty, income and education).

Seven studies found that water fluoridation reduced the proportion of people with tooth decay in their permanent teeth.[44, 51, 52, 57, 58, 60, 61] There were small differences in how this was measured across the studies. One of these studies from Australia estimated that not having fluoride in drinking water contributes to 31% of all tooth decay.[51] Three studies were conducted in Australia[52, 57, 58], two in the UK[43, 60] and one in the USA[50] and so their findings were considered to be highly relevant to water fluoridation in Australia. The other was from Brazil and was less relevant.[60]

Two studies did not find any association between water fluoridation and the proportion of people with tooth decay in their permanent teeth.[49, 62] One study was from Australia[49] and the other from South Korea.[62]

Table 5 summarises the findings for permanent teeth from the additional studies.

Table 5 Summary of the findings for permanent teeth from the additional studies

Measure	No of studies	Relevance	Findings
DMFT	6	5/6 highly relevant	All studies found reduced tooth decay with fluoridation
DMFS	4	3/4 highly relevant	All of the highly relevant studies found reduced tooth decay with fluoridation
% children without tooth decay (permanent teeth)	2	1/2 highly relevant	The highly relevant study found an increased % without tooth decay with fluoridation
% children with tooth decay (permanent teeth)	9	7/9 highly relevant	Six of the highly relevant studies found a reduced % with tooth decay with fluoridation

NB: dmft/DMFT are measures of severity; & % children with or without tooth decay are measures of prevalence.

Additional considerations

The Fluoride Reference Group considered that a number of reports published after the cut-off date for inclusion in the Evidence Evaluation Report were relevant to water fluoridation in Australia. These are summarised below.

A recent report from Western Australia found that children from non-fluoridated areas had poorer dental health outcomes than children from the fluoridated area.[63] Specifically, they had 1.5 times greater odds of having a dmft score of one or greater, and 1.6 times greater odds of having a DMFT

score of one or greater. This report is based on a cross-sectional study of 10,825 children aged 5 to 12 years in 2011 and 2010 who presented to Dental Treatment Centres (DTC) in non-fluoridated areas of south west Western Australia and the Perth metropolitan area (which is supplied by fluoridated water). This study controlled for confounders including age, gender, Aboriginal status and having a record of an initial examination at a DTC.[63]

A recent systematic review looking at the effect of the cessation of water fluoridation on tooth decay suggests an increase in tooth decay after cessation of water fluoridation; however, this is not uniform across all studies.[64] Fifteen instances of cessation of fluoridation were included in the review. The research is of variable methodological quality and also varies in time and place.[64]

A 2015 review of benefits and costs of water fluoridation in New Zealand found that the benefits of fluoridation were:

- a 40% lower lifetime incidence of tooth decay for children and adolescents living in areas with water fluoridation
- a 21% reduction in tooth decay in adults aged 18 to 44 years and a 30% reduction in those 45 years and older.[65]

With respect to adult tooth decay, a recent study from Brazil of adults aged 20 to 59 years found that longer lifetime access to fluoridated water was associated with less tooth decay.[66]

Two Australian studies[67, 68] also found that access to fluoridated water across a lifetime was associated with lower tooth decay in young adults. One study conducted in South Australia collected data from young adults who were part of a 1991/2 study as children. This new data collection occurred between 2005/6 and 2009/11, when this group (cohort) were aged 20 to 35 years. The second study of adults analysed data from across Australia by cross matching results from over 5,500 dental examinations with information gained through 4,090 survey responses regarding residential history (and therefore their lifetime access to fluoride), tooth brushing behaviour and dental visits. The magnitude of the reduction in tooth decay was similar to that documented by the Griffin et al (2007)[42] systematic review of earlier studies of the effectiveness of water fluoridation among adults. The studies refer to difficulties in interpreting outcomes of analyses of the association of lifetime access to fluoridated water and tooth decay in adults, especially for middle-aged and older adults. These difficulties are due to limitations in available measurement of exposure to fluoride and the tools used to measure tooth decay.

Evidence Statement

There is consistent evidence[y] that water fluoridation at current Australian levels is associated with decreased occurrence and severity of tooth decay in children, adolescents and adults.

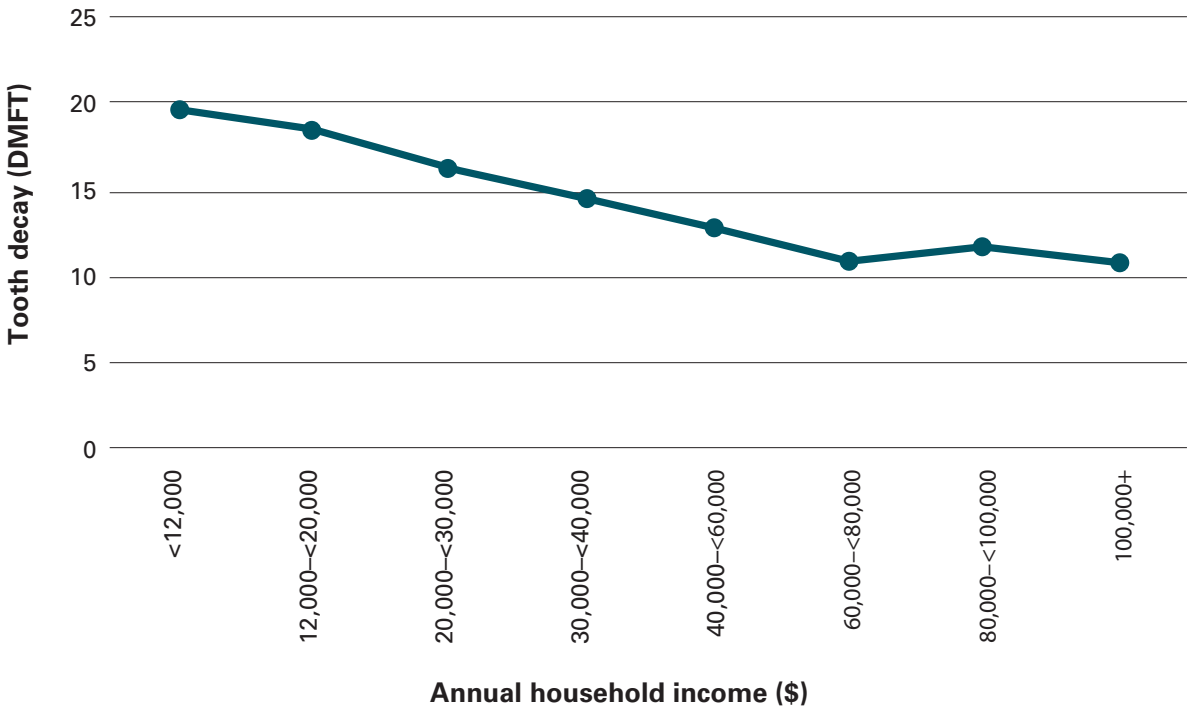
Inequality and tooth decay

Introduction

Health varies according to social factors such as income, education, Aboriginal and Torres Strait Islander status and where people live. In an Australia-wide survey, the average tooth decay (measured by DMFT) was much higher in people living in households with incomes of less than $12,000 per year compared to households with incomes of $60,000 per year. Above this income level there was less variation (see Figure 4).

y *Consistent evidence of an association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and consistently did show an association between water fluoridation and the dental or other human health outcome.

Figure 4 Tooth decay measured by average DMFT by household income (source: Chrisopoulos S, Harford JE 2013.[16]



A population-based survey of 24,644 Australian children aged 5-14 years was conducted in 2012-14 by the *Australian Research Centre for Population Oral Health* in collaboration with the states and territories (the *National Child Oral Health Study 2012-2014*). Findings from this survey indicate that children of low socio-economic background and Aboriginal and Torres Strait Islander children had significantly higher rates of tooth decay, unfavourable dental and general health behaviours and were less likely to access dental services for regular check-ups.[69]

Tables 6 and 7 present the unadjusted tooth decay (dmfs and DMFS) for children by household income. The average tooth decay in primary teeth (dmfs) was twice as high in children aged 5-8 years living in households with low incomes compared to those with high incomes. The average tooth decay in permanent teeth (DMFS) was twice as high among children aged 9-10 years and around 40-50% higher among children aged 11-14 years living in households with low incomes compared to those with high incomes.

Table 6 Decayed, missing or filled primary (deciduous/baby) tooth surfaces (dmfs) per child (source: Ha DH, et al. 2016[102])

	dmfs (95%CI)		
Age (years)	**All ages**	**5-6**	**7-8**
All	3.1 (3.0 –3.3)	2.7 (2.5 –2.9)	3.6 (3.4–3.8)
Household income			
Income1(Lowest)	4.6 (4.3–4.9)	4.3 (3.9–4.7)	5.0 (4.6–5.4)
Income2	2.6 (2.4–2.7)	2.2 (1.9–2.5)	2.9 (2.7–3.2)
Income3 (Highest)	1.9 (1.7–2.1)	1.3 (1.1–1.6)	2.5 (2.2–2.8)

Abbreviation: 95%CI = 95% confidence interval. These estimates were computed using weighted data.

Table 7 Average number of decayed, missing or filled permanent (adult/secondary) tooth surfaces per child (DMFS) (source: Ha DH, et al. 2016[102])

		DMFS (95%CI)		
Age (years)	**All ages**	**9-10**	**11-12**	**13-14**
All	1.0 (0.9–1.0)	0.5 (0.5–0.6)	0.9 (0.9–1.0)	1.5 (1.4–1.6)
Household income				
Income1 (Lowest)	1.2 (1.1–1.3)	0.7 (0.6–0.8)	1.1 (1.0–1.2)	1.8 (1.6–2.0)
Income2	0.9 (0.8–0.9)	0.5 (0.4– 0.5)	0.8 (0.7–0.9)	1.4 (1.2–1.5)
Income3 (Highest)	0.8 (0.7–0.8)	0.3 (0.3–0.4)	0.8 (0.7–0.9)	1.2 (1.0–1.3)

Abbreviation: 95%CI = 95% confidence interval. These estimates were computed using weighted data.

Data from Queensland was collected at the start of the survey (in 2010-12) and published in 2014.[70] Queensland children were more likely to experience tooth decay if they were Aboriginal and Torres Strait Islander, consumed more than four sugary drinks per day, were from a low income household, their parents had only school education or they lived in an area without water fluoridation.[52]

In an Australia-wide survey of adult oral health involving 5,505 people aged 15-91 years, the average tooth decay (measured by DMFS) was strongly age-related. The number of surfaces with tooth decay increased from about ten surfaces among 15-34-year olds to 60 surfaces among 55+ year olds.[67]

An analysis of data from the *National Survey of Adult Oral Health 2004-06* revealed that adults were more likely to experience tooth decay if they were Aboriginal and Torres Strait Islander, lived outside a capital city, had only school education, consumed more than four sugary drinks per day, were from a low income household, were eligible for public dental care, and usually visited a dentist for a problem rather than for a check-up.[71]

While tooth decay varied by household income among 15-34-year-olds, the variation was greatest among those adults aged 35-44 years. In older age groups, the variation diminished. This reflects both a survivor issue (those people who continue to have some natural teeth from whom DMFS is observed) and a convergence issue (whereby more and more decay susceptible tooth surfaces have experienced decay and the count of surfaces does not increase with recurrence on already affected surfaces).[67]

Table 8 Decayed, missing or filled permanent tooth surfaces per adult (DMFS) (source: Do GL, et al. 2017[67])

	DMFS (95%CI)				
Age (years)	**All ages**	**15-34**	**35-44**	**45-54**	**55+**
All	36.4 (34.8–37.9)	9.8 (8.4–11.2)	24.4 (22.6–26.1)	51.8 (49.8–53.8)	59.9 (58.2–61.5)
Household income					
Income1 (Lowest)	44.4 (42.2–46.5)	10.0 (7.8–12.2)	30.9 (27.0–34.8)	51.8 (48.3–55.3)	57.8 (55.8–59.8)
Income2	33.6 (31.3–35.9)	10.3 (8.0–12.7)	23.1 (20.5– 25.6)	52.8 (49.5–56.1)	63.2 (59.8–66.5)
Income3 (Highest)	30.5 (27.8–33.2)	8.5 (6.6–10.5)	20.3 (17.3–23.4)	51.0 (47.5–54.6)	60.7 (57.0–64.4)

Abbreviation: 95%CI = 95% confidence interval.

Australians living in regional and remote areas are more likely to experience tooth decay compared with those living in major cities. Adults in these areas also have higher levels of tooth loss and untreated decay, and are more likely to report having difficulties paying dental bills compared with those living in urban areas.[40]

People in low income households are also likely to have more untreated decay reflecting poorer access to dental care. In 2012, the *National Advisory Council on Dental Health* reported that 39.8% of people in low income households had untreated decay compared to 17.3% of high income households. Untreated decay was also strongly associated with Aboriginal and Torres Strait Islander status.[35]

Adding fluoride to drinking water may reduce oral health inequalities because water fluoridation does not rely on individual actions or access to dental and/or health services. Water fluoridation therefore benefits everyone, especially lower socio-economic groups, given they have a higher risk of tooth decay[72] and are less likely to access dental services for routine check-ups.[73]

In the interest of focusing on evidence that is highly relevant to Australia, the introductory text above includes data from recent Australian surveys on inequalities and tooth decay in children and adults. It was not formally assessed in the 2016 NHMRC Evidence Evaluation.

The 2016 NHMRC Evidence Evaluation did not involve a separate search for evidence on the effect of water fluoridation in reducing inequalities in oral health. However, relevant evidence on this issue was collected from sub-populations included in the research studies[44, 50, 61] and existing reviews[23, 24] on tooth decay included in the 2016 NHMRC Evidence Evaluation.

Description of the evidence

The 2000 McDonagh review included 15 studies from the UK which reported on the effect of water fluoridation across different social groups.[23] Six studies reported on the percentage of children and young people without tooth decay. In five of the six studies, water fluoridation increased the number of children and young people without tooth decay across all social groups. However, water fluoridation did not reduce the gap in the occurrence of tooth decay between the most advantaged and least advantaged groups. When the review considered tooth decay measured using dmft/DMFT, the results were mixed. The review concluded that there appeared to be some evidence that water fluoridation reduced the inequalities in dental health across social classes in 5 and 12 year olds, but this effect was not found for children of other ages. The authors of this review were cautious in interpreting these results, given there was a small number of low quality studies with differences between them.

The 2015 Cochrane review[24] included three studies which considered the effect of the introduction of water fluoridation on inequality between socio-economic groups. However, the authors of this review were not able to draw any conclusions due to the poor quality of these studies.

The 2016 NHMRC Evidence Evaluation included three studies which reported on fluoride in drinking water and tooth decay inequalities.[44, 50, 61]

An Australian study described an association between water fluoridation and an increase in the difference in tooth decay between Aboriginal and Torres Strait Islander children and non-Aboriginal and Torres Strait Islander children.[50] This study was low quality and did not adjust for known confounders (for example sugar intake, use of fluoridated toothpaste, and family income). Although no reduction in inequality was found, water fluoridation was associated with less tooth decay for both Aboriginal and Torres Strait Islander children and non-Aboriginal and Torres Strait Islander children.[50]

The other two studies (one of acceptable quality and one of low quality) were conducted in the UK.[44, 61] These studies found that the gap in the rate of tooth decay (measured by DMFT) between the lowest socio-economic group and higher socio-economic groups was reduced in the areas with fluoridated water compared to areas without.[44, 61]

Additional considerations

The 2016 NHMRC Evidence Evaluation did not search for evidence about whether or not water fluoridation reduces inequalities in dental health due to the Evaluation's focus on dental and other human health outcomes.

Any studies about inequalities included in the 2016 NHMRC Evidence Evaluation were studies that met all the inclusion criteria for tooth decay but also included information about inequalities. Given that public water fluoridation appears to offer a dental health benefit across the population, the Fluoride Reference Group considered that it was important to look at additional studies relevant to Australia in order to assess the effect of fluoridation on oral health inequalities.

Studies from Australia and New Zealand conducted in the 1980s provided evidence that water fluoridation was effective in reducing tooth decay among low socio-economic groups. However, these studies were inconclusive regarding whether water fluoridation helped to reduce the gap in oral health between high and low socio-economic groups.[74-76] A New Zealand study, published in 1994, also found that while there were significant differences in tooth decay in 14-year-old children across socio-economic groups (measured by DMFT and DMFS), water fluoridation did not impact on this inequality.[77]

A 1990s Australian study looked at tooth decay (measured by dmfs and DMFS) in a large random sample of children from Queensland and South Australia who participated in school dental services. This study found that children from low income households, and children with parents who had a low level of education, were more likely to experience tooth decay. This inequality existed despite all children having access to free, regular dental care for prevention and treatment of tooth decay through school dental services. The inequality between children of lower and higher socio-economic status was most pronounced in non-fluoridated areas.[78] The authors of this study concluded that water fluoridation helped to reduce the gap in oral health amongst children from lower socio-economic groups.

A 2011 study conducted in Korea considered the impact of water fluoridation on socio-economic differences in tooth decay experienced by 11-year-old children. The authors found that tooth decay (measured by DMFT) was similar across different socio-economic groups in fluoridated and non-fluoridated areas. However, after adjusting for confounders, tooth decay was more common in lower socio-economic groups in non-fluoridated areas compared to non-fluoridated areas. The authors concluded that water fluoridation may have helped to reduce the disparity in tooth decay across socio-economic groups.[79] This finding was supported by an analysis of rates of tooth decay in 12-year-old children in two communities without water fluoridation in Northern England. Following the introduction of water fluoridation in one of these communities, the biggest reduction in tooth decay was seen amongst children living in socio-economically disadvantaged areas of this community.[80]

A more recent population-based study conducted in Queensland in 2010-12 also considered the effect of water fluoridation in reducing socio-economic inequalities in tooth decay (measured by dmfs/DMFS). This study found that children from lower socio-economic groups had significantly higher rates of tooth decay compared to other children, even when oral health behaviours and dental visiting patterns were taken into account. Rates of tooth decay were much higher among socially disadvantaged children in areas without water fluoridation but not in areas with water fluoridation. The study authors concluded that water fluoridation can deliver larger benefits for socially

disadvantaged children who are at higher risk of experiencing tooth decay. The findings of this study were presented to the *European Organisation for Caries Research* in 2015.[81]

Recent research has also been published on reducing the disparities in tooth decay between Australians living within and outside of capital cities. Data from the *Australian National Survey of Adult Health 2004-06* indicated that people located outside of capital cities experienced more dental decay than their urban counterparts. After taking into account differing socio-economic characteristics and dental visiting patterns, people living outside of Australian capital cities experienced more tooth decay only when they had not lived in an area with access to fluoridated water supply over the course of their life.[82]

A number of studies have considered the possible benefits of water fluoridation in helping to prevent tooth decay among Aboriginal and Torres Strait Islander Australians living in remote communities in the Northern Territory. The majority of these communities have naturally low levels of fluoride in their water supplies (less than 0.6 mg/L). A study that examined data from the Northern Territory School Dental Service estimated that the implementation of water fluoridation in these communities has the potential to reduce tooth decay in Aboriginal and Torres Strait Islander children by between 7% and 28%.[2, 83] A community-randomised controlled trial focused on the effectiveness of a dental health program in remote Aboriginal communities in the Northern Territory, but also took into account the impact of fluoride levels in the drinking water. This analysis was based on modelling and found that having optimal fluoride levels in drinking water may be associated with reduced tooth decay in Aboriginal and Torres Strait Islander children, independent of any benefits from the dental health program.[84]

An Israeli study found that the inequalities in hospitalisation due to tooth decay and periodontal disease in children younger than 18 years of age were reduced with water fluoridation.[85]

An analysis of national New Zealand data investigated inequalities in severity and prevalence of tooth decay between Maori and non-Maori.[86] This analysis showed that the proportion of 5 and 8 year old children who were free of tooth decay increased between 2004 and 2012 and the severity of tooth decay was also significantly reduced during this time period. However, water fluoridation by itself did not remove the inequalities in tooth decay levels between Maori and non-Maori children.[86]

A study from Canada with methodological limitations found that inequalities in tooth decay of children related to levels of deprivation were increased after the cessation of water fluoridation.[64, 87]

Data from the *National Child Oral Health Study 2012-14* has reasonably strong findings of an association of water fluoridation with a reduced gap in the occurrence of tooth decay between lower income groups compared to higher income groups, and between Aboriginal and Torres Strait Islander children and non-Aboriginal and Torres Strait Islander children.[88]

The Fluoride Reference Group identified the need for further high quality research within the Australian context on the impact of water fluoridation in reducing inequalities in tooth decay experienced across socio-economic groups, some Aboriginal and Torres Strait Islander people and in rural and regional areas.

Evidence Statement

Taking into account the findings of the 2016 NHMRC Evidence Evaluation and the additional considerations of the Fluoride Reference Group, there is consistent evidence[z] that water fluoridation reduces tooth decay for all socio-economic groups. The 2016 NHMRC Evidence Evaluation did not search for evidence about whether or not water fluoridation reduces inequalities in dental health as the focus was on dental and other human health outcomes.

However there is some additional evidence that suggests water fluoridation reduces inequality in tooth decay experienced by those in lower socio-economic groups and those living in regional areas. This evidence should be interpreted with caution given that previous reviews and the 2016 NHMRC Evidence Evaluation identified a limited amount of evidence from the Australian context and many of these studies were of low quality with varying results. Further, the additional material identified by the Fluoride Reference Group was not assessed through a systematic process, so all relevant material may not have been considered.

Hospital visits for tooth decay

Introduction

Treatment of tooth decay is a common cause of hospital admission in children. Hospital admission for treatment of tooth decay is costly for the health system and for the family involved who may need to take time off work and cover any out-of-pocket expenses.

While the 2016 NHMRC Evidence Evaluation did not involve a separate search for evidence on the effect of water fluoridation in reducing hospital admissions, relevant evidence on this issue was collected from the research studies and existing reviews on tooth decay included in the 2016 NHMRC Evidence Evaluation.

Description of the evidence

There were no studies in the 2000 McDonagh review or the 2007 NHMRC review that looked at hospital visits for tooth decay.

One ecological study of acceptable quality was identified in the 2016 NHMRC Evidence Evaluation.[44] This study was conducted in England and compared hospital admission for tooth decay in 1-4-year-old children in fluoridated and non-fluoridated areas. This study also looked at the inequality in the rate of hospital admissions for tooth decay across socio-economic groups. Among the most disadvantaged children, the rate of hospital admissions was 75% lower in areas with fluoridated drinking water compared with non-fluoridated areas. After adjusting for the socio-economic inequality between groups, there were 55% fewer hospital admissions for tooth decay among children in areas with fluoridated water. This provided no reliable evidence of a link between water fluoridation at current Australian levels and children's hospital admissions for tooth decay.

Additional considerations

The 2016 NHMRC Evidence Evaluation was not designed to specifically locate studies about water fluoridation and the prevention of hospital admissions for the treatment of tooth decay. All studies about hospital admissions included in the 2016 NHMRC Evidence Evaluation met all the inclusion

z *Consistent evidence of an association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and consistently did show an association between water fluoridation and the dental or other human health outcome.

criteria for tooth decay and also included information about preventing hospital admissions. The Fluoride Reference Group considered that additional material should be considered on the prevention of hospital admissions for the treatment of tooth decay, given the financial implications for individual patients and the health system.

The results of one Australian study were presented to the conference of the *International Association for Dental Research* in 2010.[89] This study looked at dental hospital admissions of children in an area that started water fluoridation in 2002. The study found a significant decrease in hospitalisation of children for dental treatment after the introduction of water fluoridation. A similar town which did not start water fluoridation also had reduced admissions, but this was not statistically significant. A study of population-based data from births in Western Australia found that children born between 1980-1998 were more likely to be admitted to hospital for treatment of tooth decay when they were under two years old if they lived in an area without fluoridated drinking water.[90]

The results of a further Australian study were presented to the conference of the International Association for Dental Research in 2016.[91] This study looked at dental hospital admission rates of 0-4 year olds related to access to community water fluoridation, access to dental health professionals, and socio-economic status. The study found that no access to community water fluoridation, poor access to dental health professionals, and lower socio-economic status were independently associated with higher dental hospital admission rates. After adjusting for socio-economic status, admission rates were 43% lower in areas with fluoridated water.

A study from Israel, previously mentioned in the section on inequalities, investigated whether water fluoridation was associated with a reduction in rates of hospitalisation due to tooth decay and periodontal disease in children younger than 18 years of age.[85] The cities with higher fluoride water levels had significantly lower rates of hospitalisation and this difference was more pronounced in populations with lower socio-economic status.

A 2015 review of benefits and costs of water fluoridation in New Zealand found that there was a 48% reduction in hospital admissions for treatment of tooth decay in children aged up to 4 years.[65]

Evidence Statement

The 2016 NHMRC Evidence Evaluation did not search for evidence about the effect of water fluoridation on hospital admissions as the focus was on dental and other human health outcomes. Only one study on tooth decay reported on hospital admissions. This provided no reliable evidence of an association[aa] between water fluoridation at current Australian levels and hospital admissions for tooth decay in children.

The additional material considered by the Fluoride Reference Group provides some evidence that children living in regions with water fluoridation may be less likely to be admitted to hospital for the treatment of tooth decay. However, this evidence was not identified through the systematic review process and its quality has not been formally assessed.

aa *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

Tooth loss

Introduction

Missing teeth may be an indicator that a person has experienced tooth decay, as severe decay may need to be treated by tooth extraction. However, tooth loss may also be due to trauma, gum disease or the result of treatment decisions.

Description of the evidence

The 2000 McDonagh review and the 2007 NHMRC review did not include tooth loss as an outcome.

The 2016 NHMRC Evidence Evaluation identified five studies that looked at water fluoridation and tooth loss. Three of these studies were from Brazil[56, 92, 93] one from the USA[94] and one from Australia.[95] The Australian and USA studies were highly relevant and the Brazilian studies were less relevant for the reasons discussed in the earlier section on tooth decay.

The three Brazilian studies found an association between water fluoridation and reduced tooth loss, but these studies have limited relevance to Australia. The USA study found an association between living in an area with water fluoridation at birth and reduced tooth loss.

In the one Australian study, no significant association was found between water fluoridation and tooth loss.

Evidence Statement

There is no reliable evidence of an association[ab] between water fluoridation at current Australian levels and tooth loss.

Delayed tooth eruption

Introduction

Delayed tooth eruption happens when teeth come through the gums later than usual. This may lead to orthodontic problems as the delayed teeth may be crowded by other teeth.

Description of evidence

One study was included in the 2000 McDonagh review that reported on the number of erupted teeth per child before and after water fluoridation was started.[96] The difference was very small and in opposite directions in the two age groups examined (8 and 12 year olds).

There were no studies in the 2007 NHMRC review that looked at delayed tooth eruption.

The 2016 NHMRC Evidence Evaluation located two studies that assessed levels of fluoride in drinking water and tooth eruption.[97, 98] One study looked at children aged from 5-17 years from three areas with different levels of fluoride in water and found no difference in the number of permanent teeth.[97] The study took place in the USA which has similar water fluoride levels to that used in Australia and so the results were considered very relevant to Australia. The second study from India suggested

ab *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

that children living in areas with high water fluoride levels had fewer permanent teeth. The level of fluoride was much higher [average level 2.7 mg/L] than that used in Australia for water fluoridation and so was not particularly relevant to the Australian situation. The dental healthcare system, access to dental care and other factors like levels of poverty also contribute to this study not being relevant to the Australian situation. The results could be caused by things other than fluoride in drinking water including confounding factors (for example, preterm birth or injuries), by chance alone or the way the teeth were assessed as being delayed.[98]

Evidence Statement

The evidence shows that there is no association[ac] between water fluoridation at current Australian levels and delayed tooth eruption.

Tooth wear

Introduction

Exposure to fluoride may make teeth less prone to wear.

Description of the evidence

The 2000 McDonagh review and the 2007 NHMRC review did not include tooth wear as an outcome.

One study was identified in the 2016 NHMRC Evidence Evaluation which compared water fluoridation exposure and tooth wear.[99] This study was conducted in Ireland and therefore is very relevant to the Australian context. The study did not find any association between water fluoridation and tooth wear.

Evidence statement

The evidence from a single study of acceptable quality shows that there is no association[ac] between water fluoridation at current Australian levels and the prevalence of tooth wear in adults and adolescents.

ac *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.

Water fluoridation and dental fluorosis

Summary

There is an increased risk of dental fluorosis with increasing fluoride levels in water supplies. However, most of the studies on this association are from countries where the levels of naturally occurring fluoride in water supplies are up to five times greater than levels used in Australia for water fluoridation. In addition, these studies used different measures and definitions of fluorosis levels and as such are less applicable to Australia. Fluorosis is measured using the Thylstrup and Fejerskov (TF) Index in Australia.

In Australia dental fluorosis has declined, from about 40% of children showing any dental fluorosis in the 1990s[100,101] to about 25% in the mid 2000s[53] and to 16.8% in 2012-14[102], over a time when the extent of fluoridation in Australia has expanded

Data from 2007-09 comparing fluoridated and non-fluoridated areas revealed that around 25% of children showing signs of any level of dental fluorosis lived in fluoridated areas compared with 17% of children who lived in non-fluoridated areas.[53, 103] Data from 2012-14 shows that around 21% of children showing signs of any level of dental fluorosis lived in fluoridated areas compared with around 8% of children who lived in non-fluoridated areas.[102]

Most of the dental fluorosis in Australia is very mild or mild (TF 1, 2 or 3).[53, 103] Research suggests that this level of dental fluorosis is not of aesthetic of concern to affected children and adolescents or their parents. Moderate dental fluorosis (TF 4) is uncommon and severe dental fluorosis (TF 5+) is rare in Australia.[36-39] Moderate dental fluorosis may cause aesthetic concern and severe dental fluorosis is generally accepted to be of aesthetic concern to those few people who have it.

Dental fluorosis

Introduction

Dental fluorosis affects the appearance of teeth. It can range from faint white areas (termed very mild or mild fluorosis) to pitting and loss of the enamel surface of teeth (termed severe fluorosis). Very mild and mild fluorosis in children often diminishes over time.[38] Dental fluorosis occurs when teeth are developing, before they emerge into the mouth. Therefore, children can only develop fluorosis during the first six years of life.[38]

Dental fluorosis is measured using a standard scale such as Dean's Fluorosis Index or the Thylstrup and Fejerskov (TF) Index.[3] In research studies, a score of more than or equal to 3 on the TF index or a Dean's score of 2 or worse has often been described as fluorosis that 'may be of aesthetic concern'.[3,23] More recent research has found that very mild or mild fluorosis (TF 1, 2 or 3) is not of aesthetic concern to affected children and adolescents, or their parents.[36-39] Moderate dental fluorosis (TF 4) may also not be of aesthetic concern.[37] Severe fluorosis (TF 5+) is generally accepted to be of aesthetic concern.[39] Therefore studies that use the earlier lower thresholds, described above, for fluorosis 'of aesthetic concern' may overestimate the impact of fluorosis on people's quality of life. See Appendix F Dental fluorosis indices for more details.

Description of evidence

The 2000 McDonagh review included 88 studies on dental fluorosis.[23] These studies included levels of fluoride in water from less than 0.3 mg/L to 4-7 mg/L (well above current Australian levels). The findings from this review suggested that at a fluoride level of 1.0 mg/L, approximately 12.5% of the population would have fluorosis 'of aesthetic concern'.

The 2007 NHMRC review included ten new studies published after the McDonagh review. These studies compared the amount of fluorosis in groups of people with non-fluoridated water with the amount of fluorosis in groups of people with fluoridated water at current Australian levels. The findings from this review suggested that there was about a fourfold risk of developing fluorosis 'of aesthetic concern' with fluoride levels of 0.8-1.2 mg/L compared to ≤ 0.4 mg/L.

The association of fluoride in water supplies and fluorosis was assessed in the 2015 Cochrane review.[24] The review included 90 studies and updated the 2000 McDonagh review. These studies compared two groups of people with different levels of fluoridated water, in which any level of fluoride was included. The findings of the 2015 Cochrane review suggested that about 12-15% of people would have fluorosis 'of aesthetic concern' with water fluoridation at current Australian levels.

There are serious limitations in how the three reviews considered the relationship between levels of fluoride in water and dental fluorosis. The McDonagh[23] and Cochrane[24] reviews investigated the dose-response relationship between water fluoride levels and dental fluorosis. The Fluoride Reference Group raised concerns that some of the fluoride levels were much higher than current Australian levels (up to 5 mg/L). In addition, all three reviews did not consider other sources of fluoride (for example, toothpaste). The Fluoride Reference Group also noted that the cut-off point used to define the level of fluorosis 'of aesthetic concern' in these reviews was set too low.[3,23,24]

Recent evidence suggests that mild and very mild fluorosis in children is not of aesthetic concern to children or their parents.[36-39] Moderate fluorosis, if represented by a TF score of 4 may be of aesthetic concern to some people. Severe dental fluorosis represented by a TF score of 5 or above is generally accepted to be of aesthetic concern. These issues limited the applicability of these reviews' dental fluorosis evidence to the Australian context. The Fluoride Reference Group decided to address these concerns by including some of this recent evidence under 'additional considerations'.

Additional considerations

Dental fluorosis has declined from about 40% of children showing signs of any dental fluorosis in the 1990s[100,101] to about 25% in the mid 2000s[53] and down to 16.8% in 2012-14[102], over a time when the extent of fluoridation in Australia has expanded.

The most recent Australian data from the National Child Oral Health Study 2012-14 (NCOHS)[102] shows that in Australian children aged 8 to 14 years:

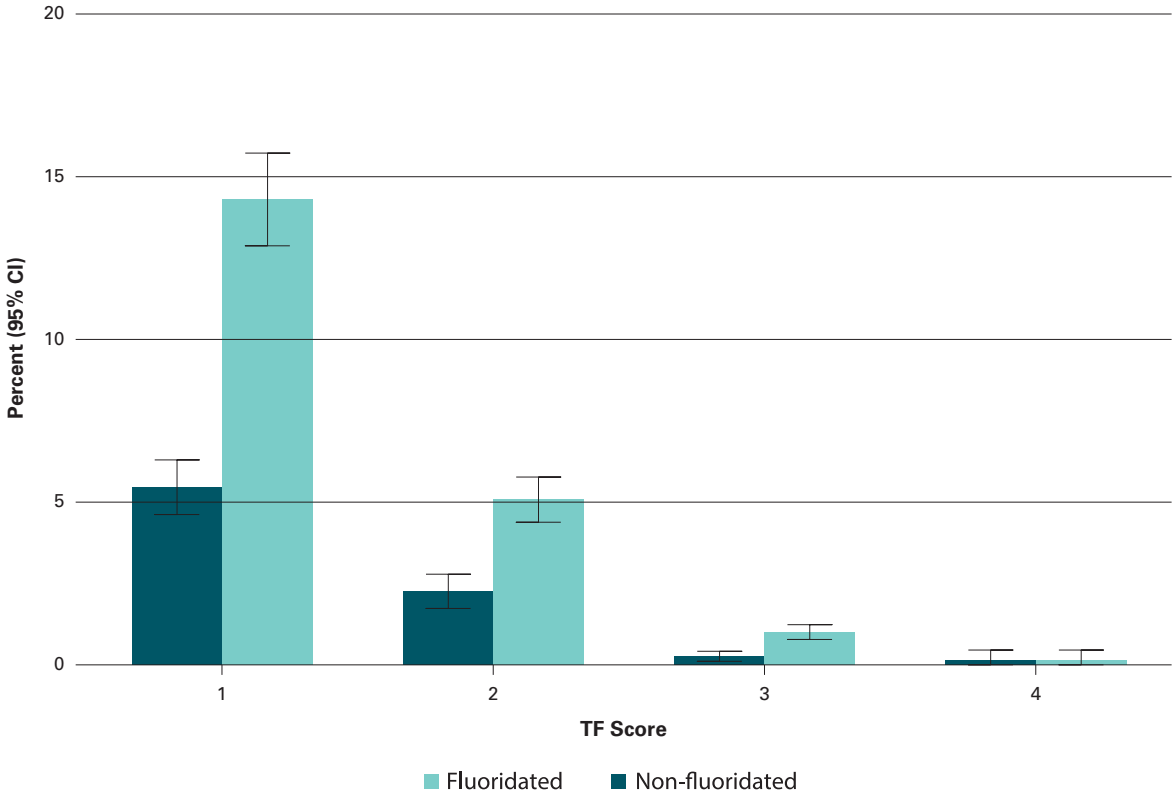
- 16.8% have signs of any dental fluorosis (TF1+)
- nearly all dental fluorosis is very mild (TF 1 or 2)
- only 0.8% have mild fluorosis (TF 3)[ad]
- very few children (0.1%) have moderate to severe dental fluorosis (TF 4+).[ad]

Fluorosis is more common in children who live in areas with fluoridated water. Figure 5 compares the prevalence of dental fluorosis by fluoridation status in Australian children aged 8-14 years based on unpublished data from the NCOHS.[ad] It shows that:

- very mild to mild fluorosis (TF 1, 2 and 3) is more common in children who live in areas with fluoridated water
- most cases of fluorosis are very mild (TF 1 or 2)
- the prevalence of moderate and severe dental fluorosis (TF 4+) is very low and is not statistically different between fluoridated and non-fluoridated areas.

ad Sourced from further analysis of the NCOHS data in 2017 by the study authors, as requested by NHMRC.

Figure 5 Prevalence of dental fluorosis by fluoridation status in Australian children aged 8-14 years. (source: the National Child Oral Health Study 2012-14 produced on request by NHMRC)



Dental fluorosis causes visible signs on tooth surfaces but does not affect dental function. The main concern is how people who have fluorosis feel about the appearance of their teeth. Recent research has asked people about this and whether dental fluorosis affects their quality of life. They then compared the answers to these questions with the amount of dental fluorosis people have. These studies found that:

- in both Australian and international studies very mild and mild fluorosis were not of aesthetic concern. In some cases, people reported increased satisfaction with dental appearance and a small improvement in oral health and quality of life[ae 36-39, 104]
- moderate dental fluorosis may be of aesthetic concern to some of those who have it[36-39]
- severe dental fluorosis causes aesthetic concern to some people who have it and may affect their quality of life.[36-39]

These studies show that the definition of 'fluorosis of aesthetic concern' that was used in the 2000 McDonagh review and 2015 Cochrane review may not be relevant to the Australian context. Some of the dental fluorosis included in 'fluorosis of aesthetic concern' in these reviews is not of any concern to Australians. A TF score of 3 is not of concern to Australians,[105] but was not considered separately in the McDonagh or Cochrane reviews. Moderate fluorosis, a TF score of 4 may be of aesthetic concern to some people. It is generally accepted that severe fluorosis, a TF score of 5, is of aesthetic concern to people who have it, because this level of fluorosis involves pitting or loss of tooth enamel. In Australia, moderate dental fluorosis is very uncommon and severe dental fluorosis is rare.

ae This reflects people's comfort when eating, sleeping and engaging in social interaction; their self-esteem; and their satisfaction with respect to their oral health.

Rates of dental fluorosis increased in Australia in the 1980s. This increase was associated with the addition of fluoride to toothpaste and the use of other fluoride containing products such as supplements in the form of drops or tablets. Other countries, such as Canada and the USA, are observing these trends now and amending their 'optimal' level of water fluoridation accordingly. Current rates of dental fluorosis in Australia, however, are lower due to the availability and promotion of low fluoride toothpastes for children, and public health messages about the appropriate use of these products (e.g. use only a small pea-sized amount; encourage children not to swallow toothpaste).[105] This reduction in rates has been achieved over a period when the extent of fluoridation in Australia has expanded.

Concern is often raised about the possibility of dental fluorosis affecting babies who are fed using infant formula powder that is mixed with fluoridated water. The *Australia New Zealand Food Standard Code 2016* ensures that infant formula products exceeding the prescribed level of fluoride are labelled to highlight of the potential to cause dental fluorosis (for more details, see Appendix E).[106] An Australian study conducted in 2011, found that in non-fluoridated areas children who were fed with infant formula had an increased probability of very mild and mild dental fluorosis, compared with children who were breastfed. Children in fluoridated areas had an increased probability of very mild and mild dental fluorosis compared with children in non-fluoridated areas, regardless of whether or not they were fed with infant formula. Children in fluoridated areas also had lower rates of tooth decay.[107] Mild to very mild dental fluorosis has been associated with a protective benefit against tooth decay in adult teeth.[108]

Evidence Statement

There is consistent evidence[af] that an increased level of fluoride in the water supply is associated with an increase in the occurrence and severity of dental fluorosis. However, the majority of this evidence applies to countries where naturally occurring fluoride levels are up to five times greater (5 mg/L) than water fluoridated at current Australian levels.

In Australia, at current water fluoridation levels, dental fluorosis of any level has declined from about 40% in the 1990s[100,101] to about 25% in the mid 2000s[53], to 16.8% in 2012-14[102], over a time when the extent of fluoridation in Australia has expanded. The dental fluorosis found in Australia is predominantly very mild or mild (TF 1, 2 or 3), and is not of aesthetic concern to those who have it.[36-39] Moderate dental fluorosis (TF 4) is uncommon and severe fluorosis (TF 5+) is rare in Australia. Moderate dental fluorosis may be of aesthetic concern to some people who have it. It is generally accepted that severe fluorosis (TF 5+) is of aesthetic concern to people who have it.

af *Consistent evidence of an association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and consistently did show an association between water fluoridation and the dental or other human health outcome.

Water fluoridation and other human health outcomes

Summary

The evidence shows that there is no association[ag] between water fluoridation at current Australian levels and:

- Cancer (overall cancer incidence, osteosarcoma, Ewing sarcoma)
- Down syndrome
- Cognitive function and IQ
- Hip fracture.

There is no reliable evidence of an association[ah] between water fluoridation at current Australian levels and:

- Chronic kidney disease
- Kidney stones
- Heart disease and high blood pressure
- Low birth weight
- Mortality
- Certain muscle and skeletal effects (musculoskeletal pain, osteoporosis, skeletal fluorosis)
- Thyroid function
- Self-reported health outcomes (gastric discomfort, headache, insomnia).

Cancer

Introduction

Cancer is a disease in which cells in the body grow in an uncontrolled way. This can be caused by exposure to harmful substances but can also be due to chance, genetics or due to lifestyle factors or a combination of these factors. Cancer can affect different parts of the body. Cancer that develops in the bone is relatively rare (for example, 120 new cases recorded in Australia in 2012 compared to 8,239 new cases of bowel cancer in the same year).[109] Two types of bone cancer are considered here, osteosarcoma and Ewing sarcoma.

Description of the evidence

Ten studies in the 2000 McDonagh review assessed the relationship between water fluoridation and the occurrence of any type of cancer and death due to any cancer.[110-119] The results from eight of these studies suggested no association. One other study suggested higher rates of cancer in areas with fluoridated water, while another one suggested a lower death rate due to cancer in fluoridated areas.

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ag *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.

ah *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

The review authors' concluded that there was no clear association between water fluoridation and overall cancer occurrence and death from any cancer.

The 2007 NHMRC review included three additional ecological studies.[120-122] The authors of the 2007 NHMRC review rated these studies as poor quality (largely due to no consideration of confounders) and noted the limited applicability of the fluoride levels considered in these studies compared with current Australian levels. Two of these studies looked at the occurrence of cancer.[120, 121] One study found an increase in the occurrence of cancer in 23 of 36 body sites, a decrease in four sites and no change in nine sites.[121] The other study found that the lower the fluoride level in drinking water, the higher the deaths from cancer.[120] The review authors advise that these results should be interpreted with caution. The third study found that the death rate from cancer was generally similar in fluoridated and non-fluoridated areas.

The 2000 McDonagh review included seven studies assessing water fluoridation and osteosarcoma in their review.[123-129] Five of these studies found no association between water fluoridation and osteosarcoma, one study found a reduced risk of developing osteosarcoma, and the final study reported an increase in osteosarcoma in men only. The 2000 McDonagh review concluded that, overall, there was no clear association between water fluoridation and osteosarcoma. Four other studies assessed other bone related cancers and the results suggested no clear association.

The 2007 NHMRC review included one study that suggested a higher risk of osteosarcoma associated with water fluoridation in 7-year-old boys.[130] This was part of a larger study that was incomplete at the time and the results could be explained by factors other than water fluoridation. Final analysis of the full data was published in 2011 and concluded that there was no association between water fluoridation and osteosarcoma.[131]

The 2016 NHMRC Evidence Evaluation included two studies that assessed water fluoridation and the occurrence of cancers (other than bone cancer).[44,132] One was a large study that found no difference between the rate of all cancers in fluoridated and non-fluoridated areas. This study also found that the rate of bladder cancer was lower in fluoridated areas.[44] The authors considered the result for bladder cancer was possibly due to confounding or bias. The other study suggested that the number of people with cancer of the eye was less in areas with fluoridated water compared to non-fluoridated areas.[132] However, the Fluoride Reference Group considered that this result was most likely due to chance. The countries in which these studies were done (UK and USA) have fluoride levels similar to current Australian levels. Levels of income and health systems are also similar in these countries, which therefore make these results very relevant to Australia.

The 2016 NHMRC Evidence Evaluation included six studies that assessed osteosarcoma and water fluoridation.[44,55,133-136] Five of these studies were conducted in four different countries (the UK, USA, Republic of Ireland and New Zealand) and included large numbers of people. These studies found no association between water fluoridation and osteosarcoma.[44,55,133,135,136] These five studies used highly reliable information about cancer drawn from large and well established cancer registries in countries that collect data over long term periods and on a regular basis. These registries collect information on 98% to 100% of all cancers. The results are very relevant to Australia because the countries reported in the studies all fluoridate their water to levels very similar to current Australian levels. The sixth study suggested that osteosarcoma was related to fluoride levels in drinking water. However, the Fluoride Reference Group considered that the result from this low quality study was most likely due to the high risk of bias in the study or due to chance, given the small numbers of people included (twenty: ten with osteosarcoma and ten without).[134]

The 2016 NHMRC Evidence Evaluation identified one study that assessed another type of bone cancer, called Ewing sarcoma, in relation to water fluoridation.[55] This study used highly reliable national data that was collected from large and well established cancer registries from 10 regions, which collect data over long term periods and on a regular basis. The results suggested no association between Ewing sarcoma and water fluoridation.

Evidence Statement

The evidence shows that there is no association[ai] between water fluoridation at current Australian levels and overall cancer incidence or mortality.

The evidence shows that there is no association[ai] between water fluoridation at current Australian levels and incidence of osteosarcoma.

The evidence from a single study of acceptable quality shows that there is no association[ai] between water fluoridation at current Australian levels and incidence of Ewing sarcoma.

Down syndrome

Introduction

Down syndrome (also referred to as Trisomy 21) is a genetic disorder caused by an extra copy of all or part of chromosome 21. The biggest risk factor for Down syndrome is maternal age. Older mothers have a greater risk of having a baby with Down syndrome.

Description of the evidence

The 2000 McDonagh review included six studies that considered the relationship between fluoride exposure and Down syndrome.[137-142] All six studies were assessed as being of poor quality and most did not control for confounders. The authors concluded that the evidence for an association between water fluoride level and the incidence of Down syndrome is weak.

The 2007 NHMRC review identified the six studies in the 2000 McDonagh review and one additional ecological study of poor quality that found no significant association between water fluoridation and Down syndrome.[143]

The 2016 NHMRC Evidence Evaluation found one additional population-based ecological study of acceptable quality on Down syndrome.[44] After adjustment for maternal age, there was no association between water fluoridation at current Australian levels and Down syndrome.

Evidence Statement

The evidence from a single study of acceptable quality shows that there is no association[ai] between water fluoridation at current Australian levels and incidence of Down syndrome.

Cognitive function and IQ

Introduction

Cognitive function refers to a broad set of skills including visuo-spatial and verbal abilities, memory and learning, executive skills and processing speed. There are a wide variety of tests that measure these individual skills. Measures of intellectual ability, known as IQ tests, tap into some of these cognitive skills and provide a summary score (i.e. IQ) for level of cognitive function, which represents a person's overall intellectual ability. IQ scores reflect not only a person's innate ability, but also their

ai *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.

access to education and other social factors which influence learning and development. These are important confounders which should be measured in studies that investigate the association between IQ and water fluoridation.

Description of the evidence

Both the 2000 McDonagh review and the 2007 NHMRC review included the same study that assessed the relationship between fluoride and cognitive function.[144] Both reviews reported a decreased risk of cognitive impairment with exposure to fluoride. However, no measure of the statistical significance of this effect was provided.

One additional study of acceptable quality was identified in the 2016 NHMRC Evidence Evaluation which reported no association between fluoride levels in drinking water and cognitive performance.[145]

The same two studies on IQ were identified in the 2000 McDonagh review and the 2007 NHMRC review.[146,147] Both studies found a decrease of IQ in children exposed to fluoride in water; however, they were of insufficient quality to allow definitive conclusions about any relationship between water fluoride levels and IQ to be determined. In one study the levels of fluoride were much higher (4 mg/L) than current Australian levels. The results of the other study were likely to have been confounded by iodine exposure.[aj148] Neither of the studies took account of other confounders known to influence IQ such as parental education.

The 2016 NHMRC Evidence Evaluation found 11 additional studies investigating the relationship between water fluoride levels and IQ.[7, 9, 11, 149-156] Eight of these studies found that average IQ was lower in the areas that had higher levels of fluoride (all higher than current Australian levels) in their drinking water. Three studies found no difference in IQ between areas with different water fluoride levels.

One study was a high quality prospective cohort study, with a low risk of bias.[149] This study took account of known confounding factors including sex, socio-economic status, breastfeeding, childhood maltreatment, perinatal insults, birth weight and educational achievement. The fluoride levels in this study were similar to current Australian levels and the study was done in a country with similar socio-economic and healthcare system characteristics (New Zealand). This study found that there was no significant difference in IQ scores at ages 7-13 years and 38 years between those exposed to water fluoridation and those that are not.

The remaining studies were of low quality or at a high risk of bias and all were of limited applicability to Australia. All studies included groups with water fluoride levels above current Australian levels. Only two studies adjusted for potential confounding, one of which showed no significant differences in the adjusted analysis[145] and the other one remained confounded by exposure to arsenic.[153]

Evidence Statement

The evidence from a single study of acceptable quality shows that there is no association[ak] between water fluoridation at current Australian levels and the cognitive function of children or adults.

The evidence from a single study of acceptable quality shows that there is no association[ak] between water fluoridation at current Australian levels and the IQ of children or adults.

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aj Some evidence suggests that chronic and severe iodine deficiency can significantly reduce children's IQ.

ak *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome.

Chronic kidney disease

Introduction

Chronic kidney disease refers to all conditions in which there is loss of function of the kidneys.

Description of the evidence

Both the 2000 McDonagh review and the 2007 NHMRC review did not include any studies that assessed the association of water fluoridation and chronic kidney disease.

One ecological study of low quality was identified in the 2016 NHMRC Evidence Evaluation.[157] This study found no clear association between water fluoride levels and the prevalence of chronic kidney disease of unknown aetiology.

Evidence Statement

There is no reliable evidence of an association[al] between water fluoridation at current Australian levels and chronic kidney disease.

Kidney stones

Introduction

The kidneys filter blood and remove waste and water from the body. Kidney stones are crystals that can form from salts in the kidney and can cause severe pain and require treatment.

Description of the evidence

The 2000 McDonagh review did not include any studies that assessed the association between water fluoridation and kidney stones.

The 2007 NHMRC review identified one poor quality cross-sectional study that reported an increased prevalence of kidney stones in an area with fluoride concentrations higher than that observed with water fluoridation in Australia.[158]

The 2016 NHMRC Evidence Evaluation included one additional acceptable quality ecological study that reported a significantly lower prevalence of kidney stones in areas with water fluoridation.[44]

Evidence Statement

There is no reliable evidence of an association[al] between water fluoridation at current Australian levels and kidney stones.

al *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

Heart disease and high blood pressure

Introduction

The cardiovascular system includes the heart, arteries and veins of the body. Diseases of the cardiovascular system include high blood pressure, heart disease and hardening of the arteries (atherosclerosis), which are common causes of illness and death in Australia.

Description of the evidence

The 2016 NHMRC Evidence Evaluation included one study from China that assessed levels of fluoride in drinking water and the presence of atherosclerosis in neck arteries (carotid arteries).[6] The results suggested that the risk of having atherosclerosis was greater in areas with high water fluoride levels. As this study included fluoride levels that were well above current Australian levels (>3.0 mg/L), these results have limited applicability to Australia. In addition, there were a number of potential confounding factors not included in the study such as levels of income, living conditions and high rates of smoking.

Four studies assessed water fluoride levels and high blood pressure.[157, 159-161] Two studies had opposite results and their findings could be explained by other factors that are known to be related to high blood pressure.[159, 160] Another study found an increased risk of having high blood pressure in areas with high fluoride levels in water. These levels were up to two times higher than current Australian levels. The final study simply reported how common high blood pressure was in two regions. These results can be explained by chance or by other factors known to be related to high blood pressure.

Evidence Statement

There is no reliable evidence of an association[am] between water fluoridation at current Australian levels and atherosclerosis.

There is no reliable evidence of an association[am] between water fluoridation at current Australian levels and hypertension.

Low birth weight

Introduction

Low birth weight babies are those born weighing less than 2.5 kg. This is usually due to the baby being born early (prematurely) or due to the baby not growing well in the womb.

Description of the evidence

There were no studies that investigated the association between water fluoride levels and the prevalence of low birth weight in the 2000 McDonagh review or the 2007 NHMRC review.

The 2016 NHMRC Evidence Evaluation identified one low quality case-control study that reported an increased risk of having a low birth weight baby at fluoride levels almost five times greater than current Australian levels.[4]

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am *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

Evidence Statement

There is no reliable evidence of an association[an] between water fluoridation at current Australian levels and low birth weight.

Mortality

Introduction

Death from any cause is measured by all-cause mortality. This is a broad measure which may show an association but is also likely to be at risk of confounding as many social, economic and environmental factors can affect mortality.

Description of the evidence

Five studies were identified in the 2000 McDonagh review that assessed the association between water fluoride levels and all-cause mortality.[138, 162-165] Three of these studies found an increase in mortality associated with water fluoridation, one found a decrease in mortality and one found no association. No measures of the statistical significance of these associations were provided. However, for two of the studies that found an increase in mortality, the adjusted rate-ratio was 1.01, and the authors did not consider the results to be statistically significant. Due to the small number of studies, the study designs used and the low quality of studies, the 2000 McDonagh review concluded that there was insufficient evidence to reach a conclusion. The 2007 NHMRC review included the same five studies only and provided the same conclusion as the 2000 McDonagh review.

The 2016 NHMRC Evidence Evaluation included a single ecological study of acceptable quality that assessed exposure to water fluoridation and overall mortality.[44] Mortality in the areas supplied with fluoridated water was found to be slightly less than that in the non-fluoridated areas, after taking into consideration age, gender, deprivation and ethnicity. The authors concluded that the effect was so small that this was likely to have occurred as a result of chance, or possibly confounding.

Evidence Statement

There is no reliable evidence of an association[an] between water fluoridation at current Australian levels and all-cause mortality.

an *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

Muscle and skeletal effects

Introduction

Consuming large amounts of fluoride over a long period of time can lead to skeletal fluorosis, which, in its most severe form involves deformities, pain and serious disability.[166, 167] It is generally found in parts of the world where people are exposed to relatively high levels of naturally occurring fluoride (>5 mg/L) over many years (e.g. 5 to 10 years or longer), such as China, Ethiopia, India, South Africa, and Tanzania.

Osteoporosis, which leads to fragile bones, is one of the most common conditions affecting bones. There are many known risk factors for osteoporosis such as age, sex and dietary factors. Osteoporosis is often diagnosed following a bone fracture so measuring bone fractures is a means of assessing any association between fluoride and osteoporosis.

Musculoskeletal pain is not a specific disease; it is a self-reported health outcome characterised by pain in joints or muscles. Studies based on self-reported health outcomes, particularly those that are poorly defined, have a high risk of bias.

Description of the evidence

The 2000 McDonagh review identified one low quality study that assessed skeletal fluorosis in areas of India with naturally high fluoride levels in drinking water (0.7 to 9.4 mg/L, with an average of 4.1 mg/L). Skeletal fluorosis was more common at higher fluoride levels in this study.[168] The 2007 NHMRC review included a study on the effects on fracture risk, but did not locate any additional studies on skeletal fluorosis.

The 2016 NHMRC Evidence Evaluation identified two low quality ecological studies that assessed the occurrence of skeletal fluorosis in areas with different levels of fluoride in drinking water.[5,8] Both studies were from areas of India where skeletal fluorosis is found and where the levels of fluoride in the drinking water are much higher than current Australian levels (>5.0 mg/L in one study and ranging from 1.5 to 3.7 mg/L in the other). The results did not show any clear increase in the occurrence of skeletal fluorosis with increasing fluoride levels.

Two systematic reviews were included in the 2007 NHMRC review that investigated the relationship between bone mineral density or bone mass and water fluoridation.[169, 170] These studies were of poor methodological quality. The authors concluded that water fluoridation at current Australian levels had little effect on bone mineral density. The 2007 NHMRC review located one additional study that found no increased risk of hip fracture at fluoride levels similar to current Australian levels.[171]

The 2000 McDonagh review included 18 studies with 30 analyses undertaken[ao] that investigated the relationship between water fluoridation and the occurrence of hip fracture.[171-188] Most of the studies either had a high risk of bias or did not account for confounders. Twenty-one of the analyses did not find an association between water fluoridation and hip fractures. Five of them suggested that water fluoridation was associated with fewer hip fractures and four of them indicated an association with increased hip fractures. The review authors concluded that, overall, there was no clear association between water fluoridation and hip fracture.

The 2016 NHMRC Evidence Evaluation included two studies that investigated the number of hip fractures in areas with and without fluoridated water.[44, 189] Both studies involved large numbers of people and also looked at other factors known to be associated with hip fractures including sex and age. The results found no difference in the occurrence of hip fracture at current Australian levels.

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ao A single study may have more than one analysis within it.

The 2016 NHMRC Evidence Evaluation identified one study that assessed fluoride levels in water and osteoporosis.[190] The results of this study suggested that there was no association between fluoride levels in water and osteoporosis. However, the fluoride levels considered in this study were significantly higher than the current Australian levels, and therefore the results were unlikely to be relevant to water fluoridation in Australia. Furthermore, this study assessed osteoporosis using a plain x-ray of the shin and forearm, which would not commonly be used for diagnosing osteoporosis in Australia as it may be inaccurate. In Australia, osteoporosis is usually diagnosed using a bone density test.

The 2000 McDonagh review and the 2007 NHMRC review did not report any studies that investigated the association between water fluoridation and musculoskeletal pain.

The 2016 NHMRC Evidence Evaluation included two studies that looked at the association between water fluoridation and self-reported musculoskeletal pain.[191, 192] One study from Thailand reported higher rates of joint pain with high levels of fluoride (>1.5 mg/L).[192] However these results could be explained by other known causes of joint pain that were not considered in this study. In addition, the levels of fluoride in Thailand were higher than current Australian levels.

The other study was from India and it reported an association between higher levels of water fluoride (>0.7 mg/L) and lower back pain.[191] Fluoride water levels were not associated with knee pain and leg pain. No important risk factors for lower back pain (such as lack of exercise, smoking, and excessive weight) were considered. The Fluoride Reference Group considered that it was very likely that these other factors could explain the study's findings.

Evidence Statement

There is no reliable evidence of an assocation[ap] between water fluoridation at current Australian levels and skeletal fluorosis.

There is no reliable evidence of an assocation[ap] between water fluoridation at current Australian levels and osteoporosis.

The evidence shows that there is no association[aq] between water fluoridation at current Australian levels and incidence of hip fracture.

There is no reliable evidence of an assocation[ap] between water fluoridation at current Australian levels and musculoskeletal pain.

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ap *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

aq *The evidence shows no association* – this wording was used when the Fluoride Reference Group was confident that the body of evidence was valid, applicable to the Australian context and demonstrated that there was no association between water fluoridation and the dental or other human health outcome

Thyroid function

Introduction

The thyroid gland is in the neck and releases hormones to regulate growth and energy expenditure.

Description of the evidence

The 2000 McDonagh and 2007 NHMRC reviews did not include any studies that assessed the association of water fluoride concentrations and thyroid function.

The 2016 NHMRC Evidence Evaluation included two low quality studies (one ecological and one cross-sectional) that investigated thyroid function in children.[98, 193] Both studies reported an association between levels of fluoride above current Australian levels and an increase in thyroid stimulating hormone (TSH). However, all TSH levels were within the normal range. There was no difference in the other thyroid function tests.

Additional considerations

One study published after the cut-off date for inclusion in the Evidence Evaluation Report was provided via Public Consultation to the Fluoride Reference Group. This ecological study used secondary data from three databases to investigate any association between levels of fluoride in water supplies and the prevalence of hypothyroidism in English GP practices.[194] The authors found a significantly higher prevalence of hypothyroidism in areas with fluoride water levels >0.3 mg/L compared to areas with ≤0.3 mg/L. This study had some serious limitations which restricted drawing conclusions based on its finding. The authors accounted for some confounding factors but the study was criticised for not considering more important confounders (such as iodine intake which is associated with hypothyroidism). Other methodological limitations included potential selection bias, arbitrary categorisation of some variables, making errors in analyses and over-interpreting the findings.[195, 196] The Fluoride Reference Group concluded that this study did not change the overall evidence about the effect of fluoridated water on thyroid function.

Evidence Statement

There is no reliable evidence of an association[ar] between water fluoridation at current Australian levels and thyroid function.

Self-reported health outcomes

Introduction

Self-reported health outcomes are assessed by asking someone whether they have experienced them. Hence, they are less reliable than an outcome which can be measured such as number of decayed teeth. The self-reported outcomes included here are not associated with any specific disease and are complaints which most people would be likely to experience from time to time.

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ar *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

Description of the evidence

The 2000 McDonagh and 2007 NHMRC reviews searched for any potential harms or negative health outcomes associated with water fluoridation. In regards to self-reported health outcomes, no studies were identified that met the inclusion criteria.

Two low quality ecological studies were identified in the 2016 NHMRC Evidence Evaluation.[192, 197] Both studies reported that the prevalence of gastric discomfort/problems was higher in villages with higher water fluoride levels. No statistical analysis was conducted and no other factors that could explain the symptoms that were elicited. Therefore it is possible that the reported findings may be due to chance or other unmeasured confounding factors.

The 2016 NHMRC Evidence Evaluation identified two low quality ecological studies that investigated the association between water fluoride levels and headache.[192, 197] Both studies found that people in the villages with the higher water fluoride levels recalled having headaches more often. No statistical analysis was reported and possible confounding factors were not considered.

Two low quality ecological studies were identified in the 2016 NHMRC Evidence Evaluation that assessed the association between fluoride water levels and the prevalence of insomnia.[192, 198] Both studies reported a higher prevalence of insomnia in villages with water fluoride levels >1.5 mg/L, although in one study[192] this was only seen in adults. There was no statistical analysis and no possible confounding factors were considered.

Evidence Statement

There is no reliable evidence of an association[as] between water fluoridation at current Australian levels and gastric discomfort.

There is no reliable evidence of an association[as] between water fluoridation at current Australian levels and headache.

There no reliable evidence of an association[as] between water fluoridation at current Australian levels and insomnia.

Health outcomes identified in earlier reviews with insufficient evidence to enable a GRADE assessment

The 2016 NHMRC Evidence Evaluation identified no new evidence for some health outcomes included in the 2000 McDonagh and 2007 NHMRC reviews. Interpreting the results was difficult due to the small number of studies, the study designs, lack of control for possible confounding factors, and the low quality of these earlier studies. Therefore, there was insufficient evidence or additional information to suggest an association between water fluoridation at current Australian levels and any of the following health outcomes:

- age of menarche
- Alzheimer's disease
- anaemia during pregnancy

as *No reliable evidence of an association* – this wording was used when the Fluoride Reference Group was not confident that the body of evidence was sufficiently valid or relevant to Australia to accept any association between water fluoridation and the dental or other human health outcome. Confidence in the body of evidence can be affected by several issues including the small number of studies, the study designs, the low quality of the studies and the lack of control for possible confounding factors. Confounding factors can include a lack of consideration of: fluoride from other sources; socioeconomic status; and iodine exposure.

- birth rates
- childhood behavioural problems
- congenital malformations
- coronary heart disease mortality
- foetal and perinatal mortality
- fractures (other than hip fractures)
- goitre
- otosclerosis
- primary degenerative dementia
- slipped epiphysis
- sudden infant death syndrome
- thyroid cancer.

Ethical considerations

Ethics is about doing the right thing, which can involve weighing up benefits and harms. For a public health intervention like adding fluoride to drinking water, it is important to consider the advantages, such as improved oral health and the disadvantages, such as affecting access to non-fluoridated drinking water for people who wish to avoid the added fluoride.

Ethical justifications for water fluoridation

The main ethical justification for fluoridating water is that it provides an important dental health benefit across the population. The 2016 NHMRC Evidence Evaluation confirms that water fluoridation provides a benefit to health by reducing occurrence and severity of tooth decay in children, adolescents and adults.[23, 24, 42-46, 49, 51, 52, 54, 56-59, 150] Prevention of tooth decay reduces infection, pain, avoidable treatment (including hospitalisation[44, 89, 90]) and other consequences of tooth decay. This is an important benefit for children and adults. Better oral health also provides a cost saving as less money has to be spent on tooth restoration.[199-201]

Water fluoridation provides a benefit to all members of society, including those who might be less likely to adopt preventive dental behaviours or who struggle to pay for dental care.[44, 50, 61, 74-78, 80, 82] This is important in Australia where there are differences in dental health between different sectors of the community.[16, 35, 40, 202] There is some evidence that water fluoridation may help to reduce inequalities in oral health, but further high quality research in Australia is needed.

Water fluoridation demonstrates community solidarity, as it is an action taken by the government to look after the dental health of all citizens, especially children. It is a generally acknowledged responsibility of governments to act in support of good health by ensuring things like clean air and safe foods. Many people see water fluoridation in the same way.

Ethical concerns about water fluoridation

Even if water fluoridation provides benefits, it would not be justified if it caused serious harms. At current Australian water fluoridation levels, dental fluorosis of any level is found in one in six children, but most is very mild or mild and not of aesthetic concern to children and parents. Dental fluorosis that may be of aesthetic concern is uncommon, and not associated with water fluoridation in Australia. There is no reliable evidence that water fluoridation at current Australian levels causes health problems.

Some people are concerned that fluoride is a poison, medication or drug which should not be added to the drinking water. However, fluoride is found widely in the earth's crust and occurs naturally in water and many foods. Regulatory bodies (like the Therapeutic Goods Administration) do not consider fluoridated drinking water to be a therapeutic good or medicine.[203]

The most common ethical argument against water fluoridation is that it affects people's autonomy, or right to self-determination. This argument has two claims. The first is that fluoride is added to drinking water without the explicit consent of the people who drink the water, which may be seen as a breach of their rights. However, the UNESCO Universal Declaration on Bioethics and Human Rights (2005) specifically exempts laws for the protection of public health from seeking consent for public health

interventions like water fluoridation.[204] The second claim is that fluoridating drinking water imposes a cost and/or inconvenience on people who choose to drink water which is not fluoridated.[205,206] However, it should be noted that water supplies may naturally contain some level of fluoride. Water fluoridation certainly reduces choices about drinking fluoridated water in areas where naturally occurring levels are lower than intentionally fluoridated water. It is possible to avoid drinking fluoridated water by using rain water, bottled water or a reverse osmosis filter, but these measures can be expensive so may not be available to everyone.

Other government actions to improve public health raise similar ethical issues, such as the addition of iodine to salt, or the addition of folic acid to bread flour.[207] Even though these measures may not improve the health of all members of the community, there is a view that it is reasonable to accept a restriction on some choices, so that other members of the community may be protected from potentially serious health problems.

In order to reach a decision about whether it is ethical to provide water fluoridation to the community, the following issues were considered:

1. **Is there a need for water fluoridation?** Yes. As tooth decay is a significant health problem in Australia, we do need strategies to improve and safeguard dental health.
2. **Is water fluoridation at current Australian levels effective in reducing tooth decay?** Yes. The 2016 NHMRC Evidence Evaluation found that water fluoridation is effective in reducing tooth decay.
3. **Is water fluoridation at current Australian levels harmful?** No. Water fluoridation in Australia is associated with very mild or mild dental fluorosis which research suggests is not of aesthetic concern to people. There is no reliable evidence of an association between water fluoridation at current Australian levels and other human health outcomes.
4. **Does water fluoridation affect individual choice?** Yes. Water fluoridation does make it more difficult for people who wish to drink non-fluoridated water. It may be difficult and/or expensive for people to avoid fluoridated water in areas with water fluoridation programs. Again it should be noted that most 'non-fluoridated' water naturally contains some level of fluoride.
5. **Are the values of equity and solidarity important in the Australian community?** Yes. These values are important. Water fluoridation may reduce health inequalities as it offers dental benefits to everyone, including people who may find it difficult to adopt preventive dental behaviours or may not be able to access or afford dental care.
6. **Is water fluoridation a proportionate response to the problem of tooth decay?** The answer to this question depends on the value placed on helping to reduce tooth decay across the population versus the value placed on people's choices about the water they drink. The Fluoride Reference Group considered that the benefits of water fluoridation outweigh the costs and/or inconvenience imposed upon people who prefer to drink non-fluoridated water. But this is a matter over which people may disagree. Of note, the large majority of the Australian public support water fluoridation.[208, 209]
7. **Finally, the Fluoride Reference Group considered what would happen if we stopped providing water fluoridation.** If drinking water was not fluoridated, individuals who wished to have the dental health benefits of fluoride would have to undertake extra measures to obtain these. It is not possible to buy fluoride supplements, and it can be difficult to buy fluoridated bottled water. Fluoride treatments from dentists are not affordable for all members of society. The likely outcome would be higher rates of tooth decay and the complications of tooth decay in children and adults. The impact may be greatest for people who struggle financially, as they would be least able to afford other forms of fluoride. In turn, this may increase differences in health between well off and disadvantaged groups. Given the government has limited funding

to dedicate to health care, increased costs in the treatment of preventable tooth decay and other associated diseases may reduce the resources that could otherwise be used for other health care measures. Moreover, water fluoridation is cost-effective and can save individuals and communities money by reducing the need for dental treatment.

Overall conclusion

The evidence shows that water fluoridation at current Australian levels reduces the occurrence and severity of tooth decay.

Water fluoridation at current Australian levels is associated with dental fluorosis. In Australia, however, most dental fluorosis is very mild or mild, does not affect the function of teeth and is not of aesthetic concern to those who have it.

There is evidence that water fluoridation at current Australian levels is not associated with cognitive dysfunction, lowered IQ, cancer, hip fracture and Down syndrome. There is no reliable evidence of an association between water fluoridation at current Australian levels and other human health outcomes.

Appendices

A Membership and terms of reference of the Fluoride Reference Group

Membership

Members	Job title and other relevant roles
Emeritus Professor Judith Whitworth AC FTSE (Chair)	Emeritus Professor, John Curtin School of Medical Research, Australian National University
Professor Vicki Anderson	Director, Clinical Sciences Research, Murdoch Childrens Research Institute Director, Psychology, The Royal Children's Hospital Professorial Fellow, School of Psychological Sciences, University of Melbourne
Doctor Meenakshi Arora	Lecturer in Environmental Engineering, Melbourne School of Engineering, University of Melbourne
Associate Professor Stephen Corbett	Director, Centre for Population Health, Western Sydney Local Health District Conjoint Associate Professor, School of Public Health, University of Sydney and Western Clinical School, Westmead
Professor Dallas English	Professor of Epidemiology and Biostatistics, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, University of Melbourne Research Fellow, Cancer Epidemiology Centre, Cancer Council Victoria
Professor Matthew Gillespie	Professor, Faculty of Medicine, Nursing and Health Sciences, Monash University
Professor Sharon Goldfeld	Paediatrician, Centre for Community Child Health, Royal Children's Hospital Co-Group Leader, Policy Equity and Translation, Murdoch Childrens Research Institute Professor, Department of Paediatrics, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne
Professor Alison Jones	Executive Dean, Faculty of Science, Medicine and Health, University of Wollongong Clinical Toxicologist, Blacktown Hospital
Associate Professor Frederic Leusch	Associate Professor and Head of Discipline, Soil Water and Energy, School of Environment, Griffith University
Professor Mike Morgan[at]	Head of School, Melbourne Dental School, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne
Ms Debra Petrys	Member, Consumers Health Forum Australia
Adjunct Professor Kaye Roberts-Thomson	School of Dentistry, University of Adelaide
Professor Wendy Rogers	Professor of Clinical Ethics, Department of Clinical Medicine and Department of Philosophy, Macquarie University
Emeritus Professor A. John Spencer	Emeritus Professor, Australian Research Centre for Population Oral Health, School of Dentistry, University of Adelaide
Professor Clive Wright	Associate Director (Oral Health) and Clinical Professor, Centre for Research and Education on Ageing, Concord Clinical School, the University of Sydney and Concord Repatriation General Hospital, Sydney Local Health District

at Resigned on 25 July 2016 due to other work commitments.

Terms of reference

1. The Fluoride Reference Group will guide the development of an evaluation of the evidence on the health effects of water fluoridation, focusing on studies published since 2006.
2. The Fluoride Reference Group will consider the outcomes of this evaluation, and use these findings to:
    a. inform the development of an evidence evaluation report that synthesises the evidence and identifies critical gaps in the current evidence base
    b. guide the identification of key issues to be considered by the Council and CEO of NHMRC as the Office of NHMRC translates the 2016 NHMRC Evidence Evaluation into an Information Paper on the artificial fluoridation of drinking water.
3. The Fluoride Reference Group will consider comments received during consultation on the draft Information Paper.
4. The Fluoride Reference Group will report to the Council of NHMRC.

B Quality assurance processes

Rigorous quality assurance processes support the development of all NHMRC health advice. The quality assurance processes used to support the quality of the 2016 NHMRC Evidence Evaluation and the Information Paper are outlined below.

- **Declaration of interests** — As part of their formal appointment to the Fluoride Reference Group, each member and observer was required to disclose any factors that may cause, or be perceived to cause, a conflict of interest with their duties as members of the Fluoride Reference Group. The declared interests of all Fluoride Reference Group members are published on NHMRC's website. Under the *Public Governance, Performance and Accountability Act* 2013, members have a responsibility to declare any interests to the whole committee and members have a joint responsibility to decide on the management of any perceived or real conflict. No unmanageable conflicts were identified by the Fluoride Reference Group or NHMRC. Meetings of the Fluoride Reference Group involved a quorum of members and decision-making was consensus-based.
- **Independent evidence evaluation** — The 2016 NHMRC Evidence Evaluation was conducted by independent evidence reviewers with expertise in systematic review methodology. The evidence reviewers were selected from NHMRC's Health Evidence Panel through a competitive tender process. The 2016 NHMRC Evidence Evaluation team completed a declaration of interest process before being appointed by NHMRC and no conflicts of interest were identified.
- **Methodological review** — Independent reviewers examined the methodological quality of the report of the evidence review to ensure that the review followed the systematic and rigorous approach documented in the review protocol. The methodological reviewers were appropriately qualified in systematic review processes and methodology. The methodological review team completed a declaration of interest process before being appointed by NHMRC and no conflicts of interest were identified.
- **Public consultation** — The draft Information Paper was released for public consultation. The public consultation process allowed members of the public to make submissions about the document, comment on the evidence-based approach that was undertaken and provide any relevant additional evidence for consideration. The draft Information Paper was revised in light of the submissions received during public consultation.

- **Expert review** — The Information Paper has undergone expert review to ensure that the evidence was appropriately interpreted and synthesised.
- **Consideration by the Council of NHMRC** — The consultation draft and final Information Paper were considered by the Council of NHMRC for its recommendation to the Chief Executive Officer that the documents be released. The Council has a broad range of experience and expertise in health and medical research. Council's final approval of NHMRC health advice documents ensures that the checks and balances at all stages of the process have been met and that any material issued by NHMRC is evidence-based, robust and meets international standards.

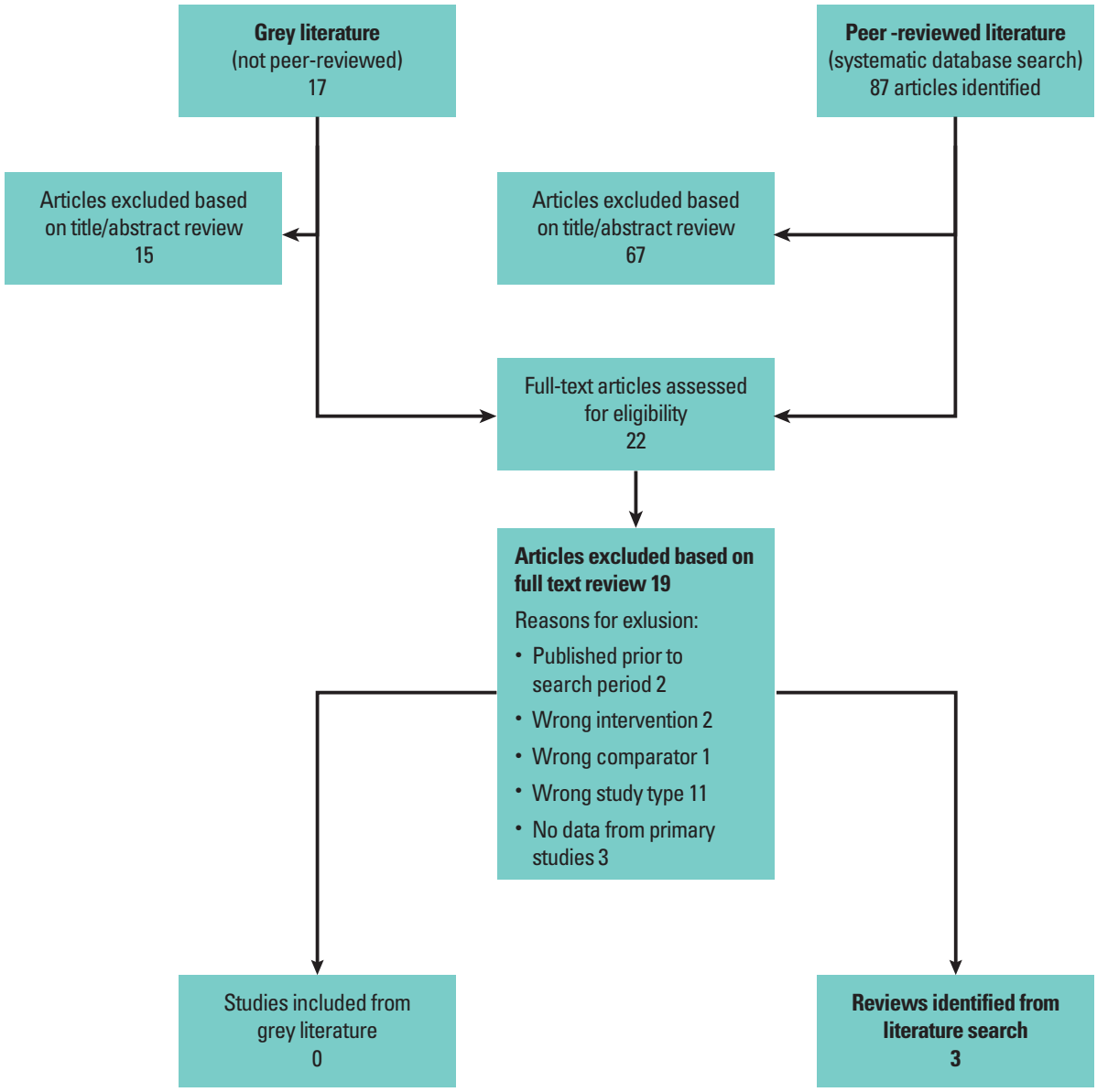
C Selection of literature

All literature searches in the 2016 NHMRC Evidence Evaluation were conducted from 2006 onwards (up to 12 November 2015 for tooth decay, and 14 October 2014 for other health effects) to update the 2007 NHMRC review.

Existing reviews on the effect of water fluoridation on tooth decay

Search terms used to search electronic databases for the review of existing reviews which followed a systematic approach to evaluate studies on water fluoridation and tooth decay included: *fluoridation*, *water supply* and *systematic review*. This search was undertaken on 12 November 2015 and the process for selecting existing reviews to be included in this component of the 2016 NHMRC Evidence Evaluation is provided in Figure 6.

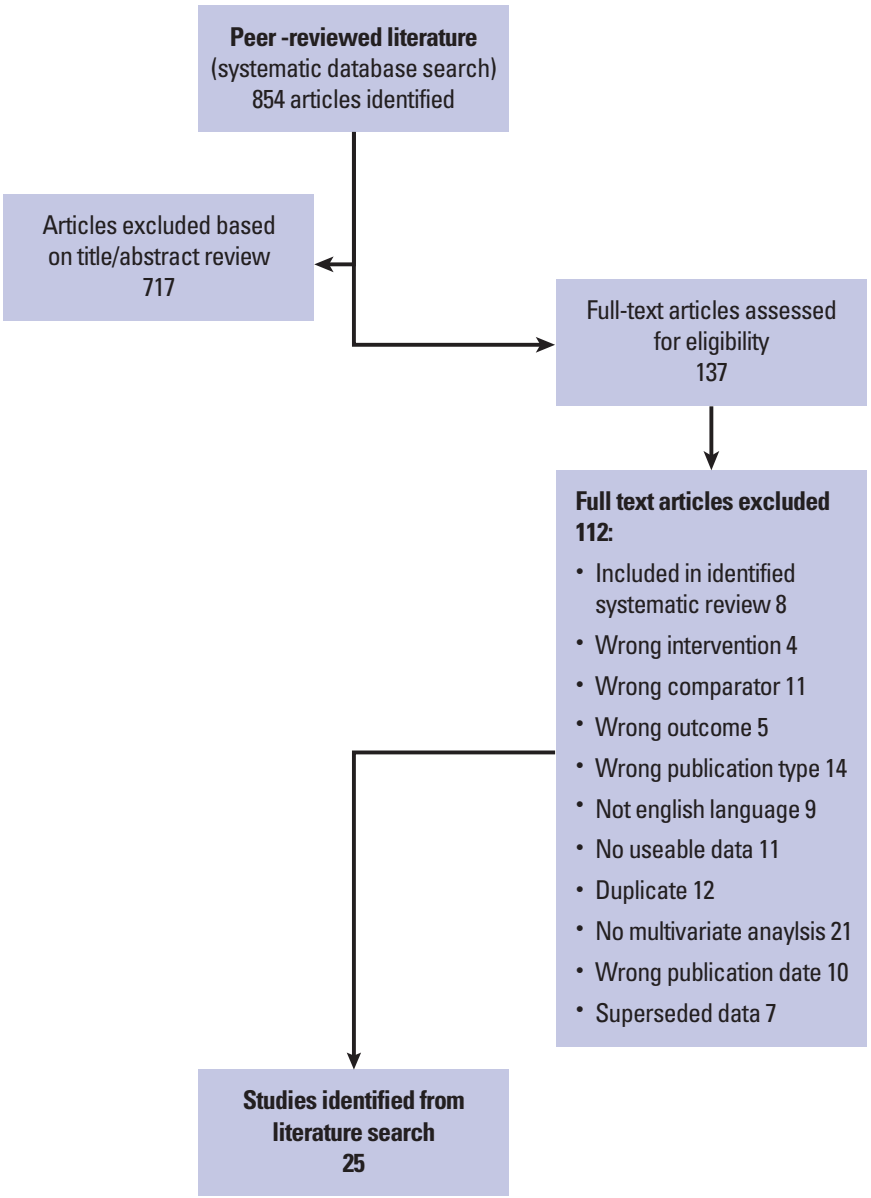
Figure 6 Process for selecting literature for inclusion in the NHMRC evaluation of existing reviews on the effects of water fluoridation on tooth decay



Research studies on the effect of water fluoridation on tooth decay

Search terms used for the review of research studies on water fluoridation and tooth decay included: *fluoridation*, *water supply* and *dental caries*, *tooth demineralisation*, *decay*, *dmft* or *dmfs*. This search was undertaken on 12 November 2015 and the process for selecting literature for inclusion in this component of the 2016 NHMRC Evidence Evaluation is provided in Figure 7.

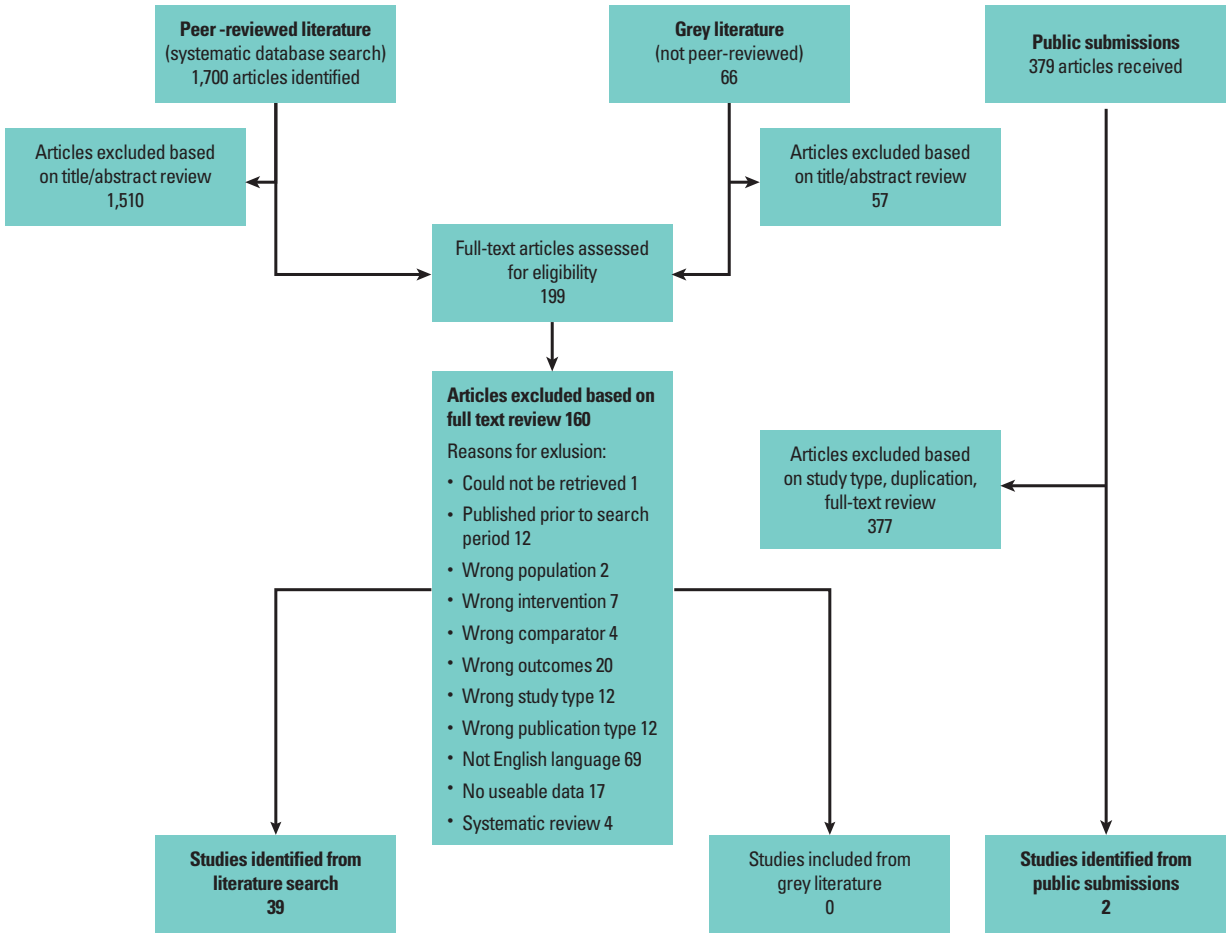
Figure 7 Process for selecting literature for inclusion in the NHMRC review of primary studies looking at tooth decay



Research studies on any other health effects of water fluoridation

Search terms used for the review of any other health effects of water fluoridation included: *fluoridation* and *water supply*. This search was undertaken on 14 October 2014 and the process for selecting literature for inclusion in this component of the review is provided in Figure 8.

Figure 8 Process for selecting literature for the systematic review of the health effects of water fluoridation



D Current state and territory regulations

Table 9 State and territory fluoride legislation and regulations

State or Territory	
Australian Capital Territory	***Licenced condition issued under the Public Health Act 1997*** http://www.legislation.act.gov.au/a/1997-69/ ***Clause 36 of the Utilities (Technical Regulation) Act 2014*** http://www.legislation.act.gov.au/a/2014-60/
New South Wales	***Fluoridation of Public Water Supplies Act 1957*** ***Fluoridation of Public Water Supplies Regulation 2012*** ***NSW Code of Practice for Fluoridation of Public Water Supplies*** http://www.health.nsw.gov.au/environment/water/Pages/fluoridation.aspx
Northern Territory	***The Use of Fluorides in the Northern Territory – position statement 2010*** http://hdl.handle.net/10137/569
Queensland	***Water Fluoridation Act 2008 (current as at 1 November 2013)*** https://www.legislation.qld.gov.au/LEGISLTN/CURRENT/W/WatrFluorA08.pdf ***Water Fluoridation Regulation 2008 (current as at 21 December 2012)*** https://www.legislation.qld.gov.au/LEGISLTN/CURRENT/W/WatrFluorR08.pdf ***Water Fluoridation Code of Practice (revised September 2013)*** https://www.health.qld.gov.au/public-health/industry-environment/environment-land-water/water/fluoridation/default.asp
South Australia	Water fluoridation is implemented by South Australia Water as a matter of Government policy and maintained by Ministerial direction under the Public Corporations Act.
Tasmania	***Fluoridation Act 1968*** http://www.thelaw.tas.gov.au/tocview/content.w3p;doc_id=87++1968+AT@EN+20111005000000;rec=0 ***Fluoridation (Interim) Regulations 2009*** http://www.thelaw.tas.gov.au/tocview/index.w3p;cond=ALL;doc_id=%2B14%2B2009%2BAT%40EN%2B20160817150000;histon=;pdfauthverid=;prompt=;rec=;rtfauthverid=;term=fluoride;webauthverid= ***Tasmanian Code of Practice for the Fluoridation of Public Water Supplies (2017)*** http://www.dhhs.tas.gov.au/publichealth/water/drinking/mains/fluoride
Victoria	***Health (Fluoridation) Act 1973*** ***Code of practice for fluoridation of drinking water supplies 2009*** https://www2.health.vic.gov.au/public-health/water/water-fluoridation/water-fluoridation-legislation
Western Australia	***Fluoridation of Public Water Supplies Act 1966 (24 January 2017 version)*** https://www.slp.wa.gov.au/legislation/statutes.nsf/main_mrtitle_348_homepage.html

E Other government policy advice relating to fluoride

Safe drinking water

NHMRC's *Australian Drinking Water Guidelines 2011* (ADWG) provide guidance to Australia's state and territory governments, councils, and the water supply industry on what constitutes good quality drinking water and how it can be achieved and assured.[210] The guidelines are based on the best available scientific evidence and provide a framework for good management of drinking water supplies to ensure safety at the point of use. In addition, the guidelines also set maximum impurity levels to ensure a high level of purity is maintained.

The ADWG are not mandatory standards. However, they are relied upon by agencies with responsibilities associated with the supply of drinking water, and are referred to in state and territory legislation on water quality.

Drinking water suppliers, water regulators and health authorities closely monitor the addition of fluoride to public water supplies. The ADWG recommend that fluoride levels should not exceed 1.5 mg/L. This value is not a recommended value for fluoridation of water supplies. Rather, it is an upper limit that has been set to protect children from the risk of dental fluorosis. It is considered that this level would also protect against any other unwanted health outcomes which may occur at higher exposures and at different life stages.

The ADWG contain fact sheets on the acceptable use of hydrofluorosilic acid, sodium fluoride, and sodium fluorosilicate to fluoridate drinking water to the optimal level for dental health, including guidance on their use in controlled doses to ensure safe, good quality drinking water.

Fluoride in food and drinks

In Australia, fluoridated water is the main source of fluoride. The average Australian adult receives between 19% and 32% of their recommended daily intake of fluoride through drinking water. This increases if you include tea, coffee and other drinks.

Nutrient Reference Values

NHMRC's *Nutrient Reference Values for Australia and New Zealand* (2006 NRVs)[au] provide information on the amount of individual nutrients that are needed to ensure optimal health and prevent chronic disease. This resource is used by health professionals to assess dietary requirements of individuals and population groups, in developing nutritional advice, and by health policy areas and food legislators. The NRVs include recommended Adequate Intake (AI) and Upper Levels of Intake (UL) for fluoride for different age and gender groups, taking into account the sources of fluoride from food, beverages and toothpaste.[211]

The Australian Government Department of Health, in conjunction with the New Zealand Ministry of Health is undertaking an ongoing review of the NRVs to ensure that they remain relevant, appropriate and useful. The NRVs for fluoride for infants and young children (0 to 8 years) were revised in early 2017 as part of this process using the most recent data on standardised body weights for the various age/gender groups.[211] This was considered the critical age group for dental caries and fluorosis as this is the period of time when permanent teeth are formed.

The AI for fluoride is high enough to ensure substantial prevention of tooth decay but low enough to avoid dental fluorosis of aesthetic concern. This is based on an estimate of fluoride intake from

au available at https://www.nrv.gov.au/

drinking water at 1.0 mg of fluoride per litre (F/L). The AI for fluoride for infants and children seven months to eight years old is based on an intake of 0.05 milligrams per kilogram of bodyweight (bw) per day (mg/kg bw/day). In line with international recommendations, an AI has not been established for infants less than six months of age as the preventive effect (reduction in dental caries) associated with fluoride intake could not be observed.

The UL for fluoride is based on evidence that at this level of intake the risk of an adverse effect, in this case severe dental fluorosis, is reduced to an acceptable level. The UL is based on the 95th percentile of fluoride intake (representative of high consumers) and a theoretical water fluoridation level of drinking water of 1.9 mg F/L. Beyond this UL, severe enamel fluorosis is likely to appear.

The UL for infants up to six months of age applies to fluoride intake among infant formula fed infants, as the review of evidence found that breast milk is low in fluoride and fluoride intakes for breastfed infants of this age are unlikely to exceed the UL. Given this, the UL for fluoride for infants and children up to eight years old is based on an intake of 0.20 mg/kg bw/day.

Infant formula

Infant formula products sold in Australia are safe to be fed to infants when made up with drinking water fluoridated at the levels used in Australia.

NHMRC's *Infant Feeding Guidelines: Information for health workers* (2012)[212] advise that tap water should be used for preparing infant formula and when offering extra water to drink. This should be boiled and cooled for food safety reasons, as the immune system of infants is not fully developed, making them more susceptible to foodborne illness. Infant formula should be reconstituted according to the instructions of the formula package label to ensure the correct concentration is prepared. In meeting infant fluoride requirements, it is assumed that tap water is fluoridated to approximately 1 mg/L. For children aged 6-24 months living in areas where water is not fluoridated, parents should seek the advice of a dentist.

Food Standards Australia New Zealand (FSANZ) is responsible for developing standards that regulate the use of ingredients, additives, vitamins and minerals. FSANZ is also responsible for some labelling requirements for packaged and unpackaged food, e.g. specific mandatory warnings or advisory labels.[213] The Australia New Zealand Food Standards Code covers the composition of some foods and recommends that the concentration of fluoride in infant formula powder should be low enough to allow for reconstitution with fluoridated water.[106] Under Standard 2.9.1 (Clause 23) of the code, infant formula products that exceed the limits of fluoride (more than 17 µg/100 kJ in powdered or concentrated product prior to reconstitution, or more than 0.15 mg/100 mL (1.5 mg fluoride/L) in ready to drink formula products) are required to contain a label indicating the potential to cause dental fluorosis and recommending discussion with a medical practitioner or other health professional before use.

Bottled water

For bottled or packaged drinking water, the Australia New Zealand Food Standards Code allows between 0.6 and 1.0 mg/L (including naturally occurring and added fluoride) to align with the NHMRC's 2007 Public Statement (Standard 2.6.2, Clause 4.c).[214]

Fluoridated bottled water (at the approved levels) is nutritionally equivalent to fluoridated tap water. Not many bottled waters contain fluoride. However, all bottled water with fluoride added must be clearly labelled. FSANZ states that bottled water with added fluoride is safe for everyone and can be used to make up infant formula.[215]

Fluoride is not a therapeutic good

The Therapeutic Goods Administration (TGA) is the Australian regulator responsible for making sure that therapeutic goods used to prevent or manage health conditions in Australia are safe and meet specified quality standards. Fluoridated drinking water is not considered to be a therapeutic good or medicine by the TGA.[203]

International recommendations

In 2014, Public Health England[44] reported that water fluoridation at England's optimal range of 1mg/L is safe and effective. Ireland has a range of 0.6 to 0.8 mg/L, with a report released by its Health Research Board in 2015 that found no strong evidence of any association with negative health effects.[av] In 2014, New Zealand's (NZ) Royal Society of NZ released a review that stated that for the levels of fluoride used in NZ, it provides protection against tooth decay and there are no health risks.[166]

The Public Health Service in the USA decided in 2015 to change its 1962 recommended range from 0.7 to 1.2 mg/L to a single optimal level of 0.7 mg/L. The USA decision was largely due to data that showed an increasing trend in the prevalence of dental fluorosis at least up to the late 1990s, an increase in the availability of other fluoride sources (such as toothpaste, mouth rinse, fluoride supplements), and that children's fluid intake did not vary with outdoor air temperatures as much as previously thought. Canada revised its optimal concentration of fluoride in drinking water to 0.7 mg/L in 2011 for similar reasons.[aw] This is different to the situation in Australia where there is evidence of decreasing dental fluorosis. Australia also has fluoride guidelines that aim to reduce total fluoride intake by children up to six years of age,[ax] the age at which most teeth are developed.

F Dental fluorosis indices

The Thylstrup & Fejerskov (TF) Index

This TF index aims to make any dental fluorosis easier to see. Dental enamel is a microporous solid. Fluoride ingested during tooth development causes slight increases in the porosity of the outer layers of dental enamel. Such porosities are usually filled with water. When they are filled with water they are difficult to see. In observing dental fluorosis with the TF Index teeth are air dried making the signs of dental fluorosis more obvious. The TF Index has 9 levels: 1, 2, 3, 4, 5, 6, 7, 8, and 9. In many studies in countries comparable to Australia grades 5 and above are not differentiated.

Dean's Index of Dental Fluorosis

Dean's Index of Dental Fluorosis was developed in the 1930s and has been widely used in the US. In observing dental fluorosis with Dean's Index the teeth are examined while they are wet and in good natural light. Dean's Index has five levels: Questionable (0.5), Very mild (1.0), Mild (2.0), Moderate (3.0), and Severe (4.0).

Prevalence of dental fluorosis

The presence of dental fluorosis at or above TF 1 or Dean's 1.0.

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av Health effects of water fluoridation: An evidence review 2015. Available at http://www.hrb.ie/uploads/tx_hrbpublications/Health_Effects_of_Water_Fluoridation.pdf

aw https://www.canada.ca/en/health-canada/services/healthy-living/your-health/environment/fluorides-human-health.html

ax Australian Research Centre for Population Oral Health. The use of fluorides in Australia: guidelines. Australian Dental Journal. 2006; 51: 195-9. Available at https://www.adelaide.edu.au/arcpoh/downloads/publications/journal/2006-spencer-aj.pdf

Dental fluorosis of aesthetic concern

The presence of dental fluorosis at or above a threshold level associated with lower satisfaction with appearance of anterior teeth. The comparator is teeth without dental fluorosis.

The threshold level has previously been regarded as Dean's Mild or a TF 3.[216]

Recent research has indicated that neither Dean's Mild or TF 3 level fluorosis is rated less satisfactory in appearance than teeth with no fluorosis. The threshold level for aesthetic concern may be at Dean's Moderate or TF 4 grade fluorosis. It is generally agreed that Dean's Severe or TF 5 level of fluorosis is of aesthetic concern to people. Severe dental fluorosis involves pitting or loss of some of the outer layers of dental enamel. These changes to the dental enamel are of aesthetic concern and involve a macro-structural change in the enamel of the tooth.

Relationship between TF and Dean's Index for fluorosis

The TF Index captures signs of dental fluorosis not readily seen when teeth are wet and under natural light. It is more sensitive to any white areas in the tooth, recording the presence of a lower grade of dental fluorosis than would be recorded by Dean's Index. Each TF Index score corresponds to a lower level score by Dean's Index up to TF 5. A conversion from one index to another has been published by Mabelya et al (1994).[217]

Table 10 Comparison of TF and Dean's indices for dental fluorosis

TF Index	Conversion to Dean's Index[ay]	Palin English descriptoray[az]
0	0	normal
1	0.3	very mild
2	0.8	
3	1.4	mild
4	2.4	moderate
5-9	4	severe

G Resource use and cost-effectiveness

Providing fluoridated water to a population requires an investment. The costs involved in establishing and maintaining a fluoridated water supply are significantly lower than the savings that occur as a result of water fluoridation. These savings come from reduced dental treatments and less time lost from work for dental-related reasons. Water fluoridation is cost-effective.

Australian studies on the cost-effectiveness of water fluoridation have found:

- that for every dollar spent on fluoridation, between $7 and $18 is saved in avoided treatment costs.[199, 200, 218]
- over 25 years, water fluoridation had saved the state of Victoria about $1 billion through avoided dental costs, days away from work or school and other costs.[202]
- a recent unpublished study on the cost-effectiveness of extending water fluoridation in Victoria to an additional 127,000 people found it would achieve $7.2 million in expected annual benefits.[219] This comprises $5.1 million in reduced dental treatment costs, $1.7 million in saved patients' and carers' time and $0.4 million in hospitalisations prevented.

ay These descriptors are the approximately equivalent to Dean's Index grades of fluorosis.

az Dean's Index score 0.5 is labelled Questionable and is not included in estimates of the prevalence of dental fluorosis.

- unpublished Queensland data indicated that the operating costs for fluoride dosage units (including costs such as labour, fluoride chemicals, electricity, water analysis, equipment calibration, maintenance, waste disposal, building insurance and staff training) range from $0.57 per person per year in a large regional town to $11.98 per person per year for a cluster of five small towns each with their own fluoride dosing infrastructure (2015-16 figures). In other words, the recurrent costs for operating small dosing units are much higher per person than large units.[ba]

A 2015 cost-effectiveness analysis of water fluoridation in New Zealand found:

- the total cost per person was between NZ$0.37 to NZ$5.63 per year depending on the size of the community (the cost per head was higher in smaller communities).
- water fluoridation resulted in a cost saving for the total population and children in all communities of over 5,000 people.[220]

Another New Zealand study concluded that water fluoridation is cost-saving for populations over 5,000 and likely to be cost-saving for populations over 500.[65] The study found that for populations over 500:

- the net discounted saving over 20 years is about NZ$1,401 million, made up of fluoridation costs of NZ$177 million and savings of NZ$1,578 million from reduced tooth decay.
- the 20-year discounted net saving of water fluoridation is approximately NZ$334 per person, made up of NZ$42 for the cost of fluoridation and NZ$376 savings in reduced dental care. Dental care benefits are made up of reduced fillings, fewer tooth extractions, and a reduction in childhood hospitalisations for treatment of tooth decay.[64]

Evidence on the cost-effectiveness of USA water fluoridation was systematically reviewed in 2015.[201] The study found that:

- the annual cost of providing water fluoridation ranged from $0.11 to $4.92 per person for communities with at least a population of 1,000
- the annual savings ranged from $5.49 to $93.19 per person in avoided costs such as health care savings and avoided days off work.[201]

Another report from the USA found that water fluoridation saves about US$30 per person annually in reduced dental treatment.[221]

ba Data provided by Queensland Health.

Glossary

Association: a statistical relationship in which two or more events, attributes or other variables occur together either more or less often than expected by chance.

Bias: any influence or action at any stage of a study that systematically distorts the findings, leading to invalid results (see also selection bias).

Blinding: procedures intended to keep participants in a study from knowing some facts or observations that might bias or influence their actions or decisions regarding the study.

Case-control study: a study in which participants are selected by whether they have the outcome of interest ('cases') or not ('controls') and the exposure levels of each group is compared.

Chance: the probability or likelihood of an event occurring.

Chromosome: structures inside a cell nucleus that contain genetic material.

Cohort study: see Prospective cohort study.

Confounding: a type of bias where a third factor distorts the relationship between the outcome and exposure of interest and can lead to invalid results.

Cross-sectional study: a study in which the outcome(s) of interest is measured in two groups of participants at a single points in time, one exposed to the outcome of interest (in this review, water fluoridation) and the other not exposed.

Deciduous teeth (synonym: primary teeth): the first set of teeth which start to come through the gums at about the age of six months and is complete around 2½ years; when complete it consists of 20 teeth. Deciduous teeth are gradually replaced by the permanent teeth.

Dental caries: see Tooth decay.

Dental fluorosis: A change in the appearance of teeth that most commonly appears as white lines or areas on tooth surfaces. Dental fluorosis is caused by a high intake of fluoride from one or more sources during the time when teeth are developing.

Dose-response relationship: a change in dose is associated with a correlated change in effect.

Ecological study: a study which looks for an association between a particular exposure and an outcome at a population level. In this review, the exposure is of a population or community to a level of fluoride in drinking water.

Economic benefit: a benefit to a person, business or society that can be expressed numerically as an amount of money that will be saved or generated as the result of an action.

Epidemiology: the study of the occurrence and distribution of health and disease in populations, including the study of what influences them, and the application of this knowledge to control relevant health problems.

Equity: the absence of avoidable or remediable differences among groups of people.

Ethics: to do with beliefs, morals and values, and understanding right and wrong. Ethical principles and values are used in the development and assessment of health care systems, policies and practices.

These principles and values include beneficence (doing good, acting in the best interests of an individual or population); non-maleficence (preventing harm); respecting autonomy (supporting a range of individual freedoms); equity (fair distribution of benefit and burdens); procedural justice (fairness in the processes of decision making); solidarity (the commitment to "share costs" to assist others); and, effectiveness and efficiency (adopting measures that are likely to achieve healthcare aims and avoiding those that do not work or are unproven).

Exposure: this is when a person comes into contact with an intervention or event of interest that has the capacity to influence the health outcome of interest. For this review, exposure relates to people drinking or ingesting fluoride through water, whether or not through a community water fluoridation program, or through other sources.

Fluoridation: for this review, this refers to water fluoridation.

Fluoride: naturally occurring inorganic ion of fluorine, a non-metallic gaseous element.

Grey literature: multiple document types and literature produced by government, academia, business and other organisations in electronic or print format; it is not always peer-reviewed and is not controlled by commercial publishing.

Health outcome: a defined disease, state of health or health related event that has been measured in a study.

Incidence: the number of new health related events in a defined population within a specified period of time.

Inequality: for this review, inequalities are differences in health status or in the distribution of health determinants between different population groups.

Ingestion: the taking of food, drugs, liquids, or other substances into the body by mouth.

Mean: the average (the sum of all the individual values in a set of measurements divided by the number of values in the set).

Median: the value on the scale that divides the number of observations into two equal parts.

Mortality: death rate (an estimate of the portion of a population that dies during a specified period).

Neurodevelopment: refers to the processes that generate, shape, and reshape the nervous system, from the earliest to the final years of life.

Observational study: a study where the investigator does not assign the participants to an intervention or exposure and simply observes the course of events. (See also ecological study). An ecological study is a type of observational study defined by the level at which data are analysed, namely at the population level, rather than individual level.

Outcome: see Health outcome.

Participants: people who have taken part in a trial or study or have responded to a survey questionnaire or interview.

Peer-reviewed literature: published literature that, before it was published, was reviewed critically by other people in the same field of research and revised in response to the critical review as a condition of publication.

Prevalence: a measure of occurrence or disease frequency that refers to the proportion of individuals in a population who have a disease or condition.

Prospective cohort study: a study in which a group of participants are followed over a period of time and the outcome(s) of interest in the participants exposed to water fluoridation are compared to the outcome(s) in the participants not exposed.

Randomised controlled trial: a study in which participants are randomly assigned to one of two or more treatment groups and the outcome(s) of interest of each treatment groups is compared.

Selection bias: distortions in outcomes of a study that result from the procedures used to select participants and from factors that influence participation in a study.

Self-report: information about a person's history or personal characteristic that a person themselves provides, generally from memory.

Socio-economic status: refers to the social standing of an individual or group. It is usually based on criteria including income, level of education attained, occupation, and value of dwelling place.

Synthesis: This is the compilation and integration of different sources of information including the results of current and past research as well as expert opinion in order to summarise and interpret existing knowledge and inform decision making. Systematic reviews and meta-analysis are tools employed to synthesise evidence.[222] For this review, combining the results of individual studies and systematic reviews together to make conclusions about the body of evidence.

Systematic review: review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.[223] A key characteristic of a systematic review is that it is reproducible, as it results from systematic search and synthesis methods being applied.

Tooth decay: (synonym: dental caries): the breakdown of the outer layers of teeth caused by acid produced by bacteria in the mouth.

Toxicology: the science of the study of actual or potential hazards of chemicals on living organisms and ecosystems.

List of acronyms and abbreviations

dmfs	number of decayed, missing and filled surfaces in deciduous teeth
DMFS	number of decayed, missing and filled surfaces in permanent teeth
dmft	number of decayed, missing and filled deciduous teeth
DMFT	number of decayed, missing and filled permanent teeth
GP	General Practitioner
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IQ	Intelligence quotient
mg/L	milligrams per litre (equivalent to ppm)
NHMRC	National Health and Medical Research Council
ppm	parts per million (equivalent to mg/L)
TF	Thylstrup-Fejerskov Index
TSH	thyroid stimulating hormone
UK	United Kingdom
USA	United States of America

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