Rodrigo Hayashi Sakuma

EFEITO DO SAL FLUORETADO NA CÁRIE DENTÁRIA E FLUOROSE: REVISÃO SISTEMÁTICA E METANÁLISE

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Tese apresentada à Faculdade de Odontologia de Araçatuba da Universidade Estadual Paulista "Júlio de Mesquita Filho" – UNESP, como parte dos requisitos para a obtenção do título de Doutor em Ciências – Área Saúde Bucal da Criança.

Orientador: Prof. Dr. Juliano Pelim Pessan
Coorientadora: Profa. Dra. Cássia Cilene Dezan Garbelini

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Dedico este trabalho

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“O que vale na vida não é o ponto de partida e sim a caminhada. Caminhando e semeando, no fim, terás o que colher.”

Cora Coralina

Resumo

SAKUMA, R.H **Efeito do Sal Fluoretado na Cárie e Fluorose Dentária: Revisão Sistemática e Metanálise.** 2022. 90 f. Tese (Doutorado em Ciências, área de Saúde Bucal da Criança) - Faculdade de Odontologia de Araçatuba, Universidade Estadual Paulista, Araçatuba 2022.

O presente estudo avaliou o efeito do sal fluoretado como uma medida comunitária preventiva na prevalência de cárie dentária e fluorose dentária. Foram realizadas pesquisas nas seguintes bases de dados: Medline/PubMed, Scopus, Web of Science, Cochrane, Embase, Lilacs/BBO, ProQuest, além da plataforma Open Gray and Clinical Trials. A qualidade metodológica e o risco de viés foram avaliados usando as ferramentas Escala Modificada Newcastle-Ottawa, RoB-2 e ROBINS-1. Os dados referentes a chances de cárie, chances de fluorose e média de cáries foram plotados, e a análise apropriada foi realizada usando o Software Rev Man 5.3. A proporção de participantes livre de cáries foi calculada. A certeza da evidência também foi avaliada por média através da abordagem GRADE (Grading of Recommendations Assessment, Development, and Evaluation). Foram selecionados vinte estudos para síntese qualitativa, dos quais 15 estavam incluídos em 6 diferentes metanálises. Indivíduos que consumiam sal fluoretado (SF) apresentaram um menor risco de quando comparados aos controle negativo (nenhuma medida comunitária) (OR 0.41 [0.30; 0.57], I^2=99%, p<0.00001), mas não quando comparados à água fluoretada (AF) (OR 1.12 [0.97, 1.29], I^2=93%, p = 0.11). Um padrão inverso foi observado para fluorose, com o consumo de SF, aumentando o risco de fluorose quando comparado ao controle negativo OR 1.57 [1.26; 1.91], I^2=0%, p<0.0001), mas semelhante à AF (OR 0.76 [0.46; 1.27], I^2=62%, p=0.30). A qualidade da evidência foi muito baixa; muitos estudos incluídos eram transversais. Em conclusão, com as evidências disponíveis, é sugerido que o uso de SF promova um efeito na prevenção da cárie dentária comparável a AF, além de não promover aumento do risco de fluorose quando comparado a AF. Embora os resultados da presente Revisão Sistemática devam ser interpretados com cautela devido a baixa quantidade de ensaios clínicos e a baixa qualidade de

evidência (GRADE), a fluoretação do sal pode ser considerada uma estratégia efetiva e segura para a administração de flúor na comunidade.

Palavras–chave: Sais, Água, Fluoretação, Cárie Dentária, Fluorose dentária.

Abstract

Abstract

The present study evaluates the effect of salt fluoridation as a community preventive measure on the prevalence of dental caries and dental fluorosis. Searches were performed in Medline/PubMed, Scopus, Web of Science, Cochrane, Embase, Lilacs/BBO, ProQuest, in addition to Open Gray and Clinical Trials. Methodological quality and risk of bias were assessed using the modified Newcastle-Ottawa Scale, RoB-2 and ROBINS-1 tools. Data sets for fluorosis chance, caries chance and mean of caries were plotted, and the appropriate analyses were applied by using the Rev Man 5.3 software program. The proportion of caries-free participants was calculated. Certainty of evidence was also evaluated by means of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. Twenty studies were selected for qualitative synthesis, of which 15 were included in 6 different meta-analyses. Individuals consuming fluoridated salt (FS) were less likely to develop caries lesions compared to negative controls (no community measure) (OR 0.41 [0.30; 0.57], I^2=99%, p<0.00001), but not compared to fluoridated water (FW) (OR 1.12 [0.97, 1.29], I^2=93%, p = 0.11). An inverse pattern was observed for fluorosis, as consumption of FS increased the risk of fluorosis compared to negative control (OR 1.57 [1.26; 1.91], I^2=0%, p<0.0001), but not in comparison to FW (OR 0.76 [0.46; 1.27], I^2=62%, p=0.30). The quality of the evidence available was very low; most studies included were cross-sectional. In conclusion, with the available evidence, it is suggested that the use of FS promotes similar anti-caries effects compared with FW, without increasing the risk of fluorosis compared to FW. Although the results of the present systematic review should be interpretated with caution due to the low quantity of clinical trials and low certainty of evidence (GRADE), salt fluoridation can be considered as an effective and safe strategy for Community administration of fluoride.

Keywords: Fluoridation, salt; Fluoridation, water; Dental caries; Fluorosis, dental

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Lista de abreviaturas e símbolos

CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico/National Council for Scientific and Technological Development
CI	Confidence interval
DP	Desvio padrão
DMTF	decayed, missing, and filled teeth
Dmtf	decayed, missing, and filled teeth
F	Flúor
FS	Fluoridated salt
FW	Fluoridated water
g	Grama
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDI	Human development index
Kg	Kilograma
L	Liter/Litro
MA	Metanálise
MD	Mean difference
mg F/L	Miligrama de flúor por litro
NOS	Newcastle-Ottawa Scale

OR	Odds Ratio
p	Probabilidade
PCF	Proportion of caries-free
Ppm	Parte por milhão
SE	Standard errors
SF	Salt fluoridation
TF	Thylstrup e Fejerkov
UNESP	Universidade Estadual Paulista/São Paulo State University
WF	Water fluoridation
WHO	World Healthy Organization

Sumário

Introdução Geral

A saúde bucal tem impacto no bem-estar e na qualidade de vida das pessoas e, apesar dos avanços científicos e tecnológicos na odontologia, a cárie dentária continua sendo um problema de saúde pública em todo o mundo, principalmente em áreas mais carentes (Kassebaum et al., 2015). Trata-se de uma doença crônica, de etiologia multifatorial e com alta prevalência em dentes decíduos e permanentes. Ela é resultante do processo dinâmico de desmineralização e remineralização, causado pelo metabolismo de bactérias na superfície dentária (Petersen & Ogawa., 2016).

De acordo com o estudo da *Global Burden of Disease* em 2010, a cárie dentária era a condição odontológica mais prevalente nos adultos, afetando 2,4 bilhões de pessoas (Kassebaum et al., 2015). Entre as crianças, a prevalência global entre os pré-escolares era de 48% (Uribe et al., 2021), afetando em torno de 620 milhões de crianças (Kassebaum et al., 2015).

O tratamento dessa condição e suas consequências são custosos, além de trazerem potenciais complicações, como dor e infecções, com impacto nas atividades do dia a dia, tanto para crianças, quanto para adultos (Kassebaum et al., 2015; Irigoyen et al., 2012).

Nas últimas décadas, tem se observado uma queda da prevalência da cárie dentária na maioria dos países (Petersen., 2004; Fabruccini et al., 2016). Entre as intervenções mais reconhecidas para o controle da cárie dentária estão o uso de fluoreto em aplicações tópicas individuais (cremes dentais e enxaguantes bucais), aplicações tópicas para uso profissional (gel de flúor, verniz de flúor e diamino fluoreto de prata) e os métodos de base populacional, como por exemplo a fluoretação da água potável, sal de cozinha e leite (Sagheri et al., 2007; Meyer-Lueckel et al., 2010; Garcia- Perez et al., 2013; Fabruccini et al., 2016). Além disso, observou-se uma melhora da saúde bucal e menor gravidade da cárie nas últimas três décadas, decorrentes de programas de promoção de saúde bucal, com enfoque em educação, bem como o estímulo ao uso de produtos fluoretados (Petersen & Ogawa., 2016).

O acesso adequado a programas de fluoretação é uma das intervenções preventivas eficazes, econômicas e seguras utilizadas nos últimos 60 anos para controlar a cárie dentária (Yengopal et al., 2010). A exposição a mais de uma fonte de flúor tem sido a regra na maioria dos países desenvolvidos, sendo a mais comum o uso de dentifrícios fluoretados. Já os métodos populacionais mais comuns são os usos de água e sal fluoretados. A água fluoretada é de acesso

universal, enquanto o sal fluoretado depende da adesão individual ao seu uso. Além disso, algumas pessoas podem necessitar fazer restrição desse elemento, como crianças e portadores de algumas doenças (Sagheri et al., 2007).

O flúor protege os dentes contra a cárie dentária principalmente por dois mecanismos. Durante a formação dos dentes, ele é incorporado a sua estrutura, tornando-se mais resistente à ação cariogênica (O'Mullane et al., 2016). Já após a erupção, a ação direta do uso do flúor na redução da cárie dentária consiste, principalmente, em aumentar sua resistência, diminuindo a solubilidade do esmalte à ação do ácido produzido pelas bactérias e inibindo certos processos metabólicos (ação enzimática) das bactérias responsáveis pela formação da cárie dentária. (O'Mullane et al., 2016). O objetivo do uso do flúor é manter seus íons livres no meio bucal, incorporando o mais rápido possível e com maior frequência. O consumo de dentifrícios fluoretados, água e o sal tem esse efeito (Rojas, 2008).

Aproximadamente 90% do flúor ingerido ao dia é absorvido pelo Sistema digestivo e sua eliminação é predominantemente renal. Do flúor ingerido pelas crianças, aproximadamente 55% são retidos pelo organismo e em adultos aproximadamente 36%. O Flúor circula no plasma na sua forma iônica e sua concentração em tecidos moles e duros está diretamente relacionada à quantidade e duração da ingestão de flúor. Aproximadamente 99% da carga corporal de flúor está associada a tecidos calcificados. A concentração de flúor nos dentes reflete a disponibilidade geral de flúor durante a formação dos dentes e varia dependendo do tempo de exposição e ingestão de flúor. Ao contrário do esmalte, a dentina continua a acumular flúor ao longo da vida. O teor de flúor da dentina é derivado inteiramente pela via sistêmica. A maior parte do flúor no esmalte reflete sua disponibilidade no período pré-eruptivo e de formação dentária. A exposição pós-eruptiva se reflete principalmente na camada externa do esmalte (O'Mullane et al., 2016)

O objetivo de um programa de prevenção de cáries deve ser a manutenção dos níveis adequados de flúor na maior parte da população (Petersen & Ogawa., 2016). Historicamente, a fluoretação da água foi a primeira medida comunitária adotada para a prevenção da cárie dentária e está entre as 10 conquistas de saúde pública do século 20 (O'mullane et al.,2016). No entanto, outros métodos de fluoretação foram propostos pela Organização Mundial da Saúde, baseados na logística e custos, entre eles a fluoretação do sal de cozinha (Fabruccini et al., 2016). Essa foi introduzida primeiramente nos anos 60 na Suíça, como alternativa a fluoretação da água, já que essa última requer uma estação de tratamento, equipamento especial e monitorização diária. Após, essa estratégia se propagou para 43 países em diferentes continentes, sendo atualmente adotado como programa nacional de prevenção da cárie em 17 países (O'mullane et al., 2016).

O sal de cozinha tem como vantagem ser um veículo que pode ser fortificado com micronutrientes na maior parte do mundo, devido a seu fácil acesso e baixo custo. O sucesso dos programas de fortificação do sal com iodo motivou a busca de outros componentes que pudessem trazer benefícios a saúde pública, entre elas o flúor (Yengopal et al., 2010).

A fluoretação do sal pode ser utilizada principalmente como um método de fluoretação alternativo à água, seja por questões técnicas, culturais ou sócio-econômicas (Fabruccini et al., 2016). Trata-se de uma estratégia comunitária custo-efetiva para a prevenção da cárie dentária. Essa intervenção é considerada prática, segura, de baixo custo e de fácil aplicação, especialmente em países onde a fluoretação da água não é utilizada (Petersen, 2004; Wennhall et al., 2014).

Estima-se que, aproximadamente 300 milhões de pessoas em todo o mundo recebam sal fluoretado, a maioria na América Latina (Marthaler, 2013). A fluoretação do sal foi adotada em países como Áustria, França, Alemanha, Bolívia, Colômbia, Jamaica, México, Costa Rica, República Dominicana, Honduras, Nicarágua, Panamá, Suíça e Venezuela (Peterson, 2004).

A eficácia e o impacto preventivo da fluoretação do sal dependem de como é realizada sua implementação. Fatores como distribuição, marketing e preços interferem no impacto preventivo da fluoretação do sal. Há variações nas políticas de implementação da fluoretação do sal dependendo da realidade de cada país, com variações na concentração de flúor no sal, distribuição do sal e disponibilidade de sal não fluoretados (O'Mullane et al., 2016). O flúor como mecanismo protetor de cáries dentárias já está bem estabelecido e difundido, portanto, o sal fluoretado é em geral bem aceito pela população (O'Mullane et al., 2016). A concentração do flúor no sal deve ser monitorada constantemente e pode ser ajustada, conforme a realidade local de exposição a outras fontes de flúor e consumo de sal, a fim de se evitar a fluorose dentária (Fabien, 1996; Betancourt-Lineares et al., 2013; O'Mullane et al., 2016).

Na América Latina, o flúor é utilizado no sal de cozinha em concentrações entre 180 a 220 ppm F/Kg de sal e, no caso da Europa, que tem um menor consumo de sal, as concentrações de F variam entre 200 a 350 ppm F/Kg. Em 1989, um estudo evidenciou que, para que o sal fluoretado tenha a mesma eficácia que a água fluoretada (0,8 ppm), a concentração deve ser de 250 ppm F/Kg (Ditterich et al., 2005). Alguns estudos mostram que as concentrações de flúor (F) no sal não estão dentro da faixa recomendada pelas autoridades governamentais e que diferentes concentrações de F foram relatadas na mesma embalagem ou saco (Kidd, 2011).

Em 2016, Fabruccini et al., publicou o primeiro estudo que mostrou uma diferença significativa entre a prevalência de cárie comparando com o uso da

água e sal fluoretados, com maior benefício da água fluoretada em crianças em idade escolar. Entretanto, os autores ressaltam que enquanto a água fluoretada alcança a todos, independente da vontade do indivíduo, o uso de sal fluoretado depende da adesão e de seu uso regular**.**

Apesar dos benefícios claros do flúor, seu excesso pode trazer consequências à saúde bucal. A fluorose dentária é outra patologia de interesse em saúde bucal, definida como a alteração do esmalte dentário relacionada ao consumo excessivo e prolongado de fluoreto durante o período de formação dentária, que inclui o período de nascimento até 6 ou 7 anos. Por isso, é necessário um controle das concentrações de flúor nos diversos meios (Meyer-Lueckel et al., 2010; Betancourt-Lineares et al.,2013)

Em geral, quatro fatores principais de exposição ao flúor em crianças são identificados na literatura: água potável fluoretada, cremes dentais com flúor, suplementos fluoretados e fórmulas para leite infantil. No entanto, um estudo realizado no México em crianças que vivem em áreas com diferentes concentrações de flúor na água e que recebem sal fluoretado, descobriu que a maior prevalência de fluorose estava associada à concentração de flúor na água e não a ingestão de sal (Garcia-Perez et al.,2013).

A maioria dos estudos que avaliam a fluoretação do sal de cozinha são estudos observacionais (Yengopal et al., 2010). Entre eles, um estudo avaliou o impacto da fluoretação do sal na França, após sua introdução, em dois momentos, nos anos 1987 e 1991. Havia pouca interferência de outras fontes de flúor nessa época. Foi constatado uma diminuição da prevalência de cárie na população avaliada (Cahen et al., 1993). Outro estudo conduzido na França nos anos 80, também avaliou como positiva a ação cariostática do flúor (Crousaz et al., 1985).

Há estudos em diversos países que evidenciaram benefício do uso do sal fluoretado (Menghini et al., 1995; Fabien, 1996; Irigoyen & Sánchez-Hinojosa 2000; Meyer-Lueckel et al. 2002). No ano de 2002, na Jamaica, um estudo, avaliou o impacto do sal fluoretado em crianças com idade entre 6 a 16 anos, doze anos após a introdução da fluoretação do sal. Foi identificada uma diminuição da prevalência da cárie dentária (Meyer-Luckel et at, 2002). Outro estudo, realizado no Peru em 2007, avaliou crianças de 12 anos e demonstrou prevalência de 100% de cárie, mas com índices menores na população que consumia sal fluoretado (Rojas, 2008). Esses dois estudos, os autores ressaltam que são observacionais, e, portanto, poderia haver influência de outros veículos com flúor.

Estudo realizado no México, nos anos 2000, mostrou que o programa de fluoretação do sal comtemplava mais de 11 milhões de pessoas. Os resultados também foram favoráveis, mostrando uma redução da prevalência e gravidade

da cárie dentária em dentes permanentes numa população de 6 a 10 anos. As razões para esses resultados incluem a fluoretação do sal e a melhora do acesso a serviços odontológicos (Irigoyen & Sánchez-Hinojosa 2000).

Além disso a última revisão sistemática sobre o assunto foi publicada há mais de 10 anos, relatando que a metanálise realizada favoreceu a fluoretação do sal em relação ao controle negativo. Essa Revisão Sistemática não incluiu ensaios clínicos randomizados, mas encontrou benefícios na prevalência de cárie dentária em diferentes faixas etárias, separando os estudos por idade, entre 6-8 anos, 9-12 anos e 13-15 anos (Yengopal et al., 2010).

Foram realizados novos estudos avaliando a fluoretação do sal na prevenção da cárie dentária, incluindo dois ensaios clínicos randomizados (Wennhall et al., 2014; Jordan et al.,2018). Em 2014, Wennhall et al., avaliou o efeito do uso domiciliar de sal de cozinha fluoretado em crianças de 12-14 anos na Suécia, não encontrando diferenças significativas entre os grupos. Entretanto, os autores ressaltam que podem ter ocorrido um problema na adesão ao uso do sal fluoretado.

Já Jordan et al., 2018, realizaram outro ensaio clínico randomizado, que avaliou o impacto da fluoretação do sal de cozinha na Gambia, em crianças de 3-5 anos com dentição decídua completa, após um ano de uso. Os autores verificaram um efeito benéfico da fluoretação do sal na prevenção da cárie dentária. O ponto positivo desse estudo é ser o primeiro a avaliar a fluoretação do sal sem influência de outras variáveis ou outras fontes de flúor, pois essas crianças não eram expostas a dentifrícios fluoretados. A desvantagem é que esses resultados não podem ser reproduzidos em muitos países.

Há poucos ensaios clínicos e revisões sistemáticas sobre o impacto da fluoretação do sal de cozinha no desenvolvimento da cárie dentária (Meyer-Lueckel et al., 2010). As dificuldades incluem as variações nas concentrações do flúor e a presença de outros fatores que contribuem para a cárie (Yengopal et al., 2010). Além do efeito preventivo dos diversos produtos fluoretados, um maior acesso à educação e a saúde bucal também contribuem para a diminuição da cárie dentária (Meyer-Lueckel et al., 2010).

A avaliação do impacto da fluoretação do sal na cárie dentária pode ser utilizada para formular e avaliar políticas públicas de prevenção de cárie dentária. A cárie tem etiologia multifatorial, e a monitorização de políticas públicas deve ser contínua. A avaliação do benefício da fluoretação do sal pode auxiliar alguns países a rever suas políticas públicas, principalmente em áreas de alta prevalência de cárie dentária (Irigoyen et al., 2012).

Considerando a disponibilidade de novos estudos e dados clínicos sobre o tema, o presente estudo tem como objetivo avaliar evidências científicas sobre

os efeitos da fluoretação do sal no controle de cárie e no risco de fluorose dentária, por meio de revisão sistemática e metanálise.

Salt fluoridation on dental caries and fluorosis: a systematic review and meta-analysis

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Salt fluoridation on dental caries and fluorosis: a systematic review and meta-analysis

Abstract

Objectives: To evaluate the effect of salt fluoridation as a community preventive measure on the prevalence of dental caries and dental fluorosis.

Data/Sources: Searches were performed in Medline/PubMed, Scopus, Web of Science, Cochrane, Embase, Lilacs/BBO, ProQuest, in addition to Open Gray and Clinical Trials. Methodological quality and risk of bias were assessed using the modified Newcastle-Ottawa Scale, RoB-2 and ROBINS-1 tools. Data sets for fluorosis chance, caries chance and mean of caries were plotted, and the appropriate analyses were applied by using the Rev Man 5.3 software program. The proportion of caries-free participants was calculated. Certainty of evidence was also evaluated by means of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

Study selection: Twenty studies were selected for qualitative synthesis, of which 15 were included in 6 different meta-analyses. Individuals consuming fluoridated salt (FS) were less likely to develop caries lesions compared to negative controls (no community measure) (OR 0.41 [0.30; 0.57], I^2=99%, p<0.00001), but not compared to fluoridated water (FW) (OR 1.12 [0.97, 1.29], I^2=93%, p = 0.11). An inverse pattern was observed for fluorosis, as consumption of FS increased the risk of fluorosis compared to negative control (OR 1.57 [1.26; 1.91], I^2=0%, p<0.0001), but not in comparison to FW (OR 0.76 [0.46; 1.27], I^2=62%, p=0.30). The quality of the evidence available was very low; most studies included were cross-sectional.

Conclusions: With the available evidence, it is suggested that the use of FS promotes similar anti-caries effects compared with FW, without increasing the risk of fluorosis compared to FW.

Clinical Significance: Although the results of the present systematic review should be interpretated with caution due to the low quantity of clinical trials and low certainty of evidence (GRADE), salt fluoridation can be considered as an effective and safe strategy for Community administration of fluoride.

1. Introduction

Despite all scientific and technological advances in Dentistry, dental caries remains a public health problem worldwide, especially in the most deprived areas [1]. According to the Global Burden of Diseases study in 2010, untreated caries was the first most prevalent condition evaluated in adults, affecting over 2.4 billion adults [2]. For children, it was the tenth most prevalent condition, affecting over 620 million children [2], with a global prevalence of 48% in preschoolers [3]. Treatment of its consequences is costly and, when untreated, it may cause pain and infection, affecting daily activities and productivity, both for children and adults [2].

Caries-preventive strategies have heavily relied on the effectiveness and safety of fluoridation schemes, when used as community vehicles or in products for self- or home-use. Water fluoridation (WF) was the first community-based fluoridation method and is regarded as one of the 10 most great public health achievements of the 20th century [4]. Nonetheless, other community-based fluoridation methods have been proposed in order to overcome financial and logistic issues, including salt, milk and supplements. In this context, salt fluoridation (SF) was first introduced in Switzerland in the 1960s, as an alternative to WF, as the latter requires a centralized water treatment station, special equipment and daily monitoring. Preventive strategies involving SF later spread to 43 countries in Europe, Americas, Asia and Africa, being currently adopted as a National Program for caries prevention in 17 countries [4].

Community-based fluoridation schemes have proven to be effective and safe in caries control. Nonetheless, it is widely known that the use of such methods (previously known as systemic fluoridation) is associated with unwanted side-effects, especially dental fluorosis. Despite this condition in mild form is usually not associated with effects on the quality of life of individuals [5], in more severe forms it may increase the risk of dental caries [6].

The majority of the studies assessing the effects of SF are of observational nature, mostly employing cross-over protocols, which have limitations inherent to the study design. Furthermore, the last systematic review on the topic was published over 10 years ago, reporting that the meta-analysis performed favored

SF in comparison with negative control (*i.e.*, no intervention) on caries control only [7]. Since then, new studies assessing the effects (preventive or adverse) of SF, including two randomized clinical trials [8,9] have been published, which brought new light to the issues on the efficacy and safety of this method.

Thus, based on the availability of new clinical and observational data on the effects of SF on dental caries, and considering the lack of evidence-based studies on the side-effects of this measure (*i.e.*, dental fluorosis), the present study aimed to evaluate scientific evidence about the effects of SF on caries control and on the risk of dental fluorosis, in addition to provide comparative data between SF and WF on both clinical conditions through a systematic review and meta-analysis.

2. Materials and Methods

Search strategy

The following databases were used to search the papers: PubMed, Scopus, Web of Science, Cochrane, Embase, Lilacs and BBO. Other soureces investigated included ProQuest, Open Gray and Clinical Trials. Additionally, a manual search for information was carried out on the reference list of the included studies, to identify manuscripts that could not have been recovered by the electronic search. The search strategy was guided by a specialized librarian (ACMGM) and adapted for each database (Appendix 1 – S1). There were no restrictions regarding the language or year of publication. The initial search was performed on May 16, 2019 and the latest updated, on November 1, 2022.

Eligibility criteria

The eligibility criteria followed the PICOS/PECOS strategy, in which observational studies and randomized/non-randomized trials that compared the prevalence of dental caries and/or dental fluorosis in individuals or populations consuming fluoridated salt with either individuals or populations with or without another measure of fluoridation were included. As inclusion criteria, individual or populations of all ages, who were examined by any indexes for dental caries and

dental fluorosis examinations, were selected. The exclusion criteria were: (1) lack of clear definition of the exposed and control groups; (2) literature reviews; (3) absence of a control group; (4) studies published more than once under different titles and in different journals; (5) case reports; (6) letters to editors; (7) animal studies; and (8) studies with missing data, even after contact attempts with the authors.

Study selection and data extraction process

After paper retrieval from the 7 databases and 3 additional sources, they were checked for duplicates using the online version of Endnote software and were considered only once. Titles and abstracts were analyzed independently by two reviewers (LCC and RHS). Potentially eligible papers, including those whose title and abstract did not provide enough information for either inclusion or exclusion, were read in full text to clearly determine their eligibility. Data were extracted individually by three independent researchers (LCBQ, LCC, and RHS) using a form based on other systematic reviews, in which the following data were recorded: study details (authors and year of publication); details of study methods (study design and follow-up period); details of participants (mean age and number of patients in each group); evaluation criteria; and results. Studies unavailable at electronic databases were retrieved by the institution's library via a switching service. For studies with missing data, the authors of each paper (corresponding author and coauthors) were contacted via e-mail, Research Gate and/or Linkedin) three times, at weekly intervals. For papers in languages other than English, Portuguese or Spanish, an online translation tool (Google Translator) was initially used, and the resulting material was assessed by collaborators with experience in those languages (listed in the acknowledgement section).

Risk of bias in individual studies

Two review authors (LCBQ and LCC) independently undertook the risk of bias assessment for the included studies. Disagreements were solved by discussion with a third review author (JPP) until a consensus was reached.

The risk of bias of each cross sectional included study was evaluated using an adapted version of the Newcastle-Ottawa Scale (NOS) [10]. This adapted

version includes three domains of risk of bias assessment: selection, comparability and outcome. Seven items compose the three domains. The score for each study can range from 0 to 10 stars, being that the higher the score (more stars) the lower the risk of bias.

For clinical trials, the risk of bias assessment was taken using Cochrane Risk of Bias Tools (https://www.riskofbias.info). A Revised Tool to Assess Risk of Bias in Randomized Trials (RoB-2) was used [11] for randomized controlled clinical trials. RoB-2 assesses quality in five domains of bias: randomization bias, deviation from intended intervention bias, missing outcome data bias, measurement of the outcome bias and selection of the reported results bias. For each domain, there are five options of response: yes, probably yes, probably no, no, and not informed.

Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) was used for clinical trials that did not perform randomization [12]. ROBINS-I assesses quality in seven domains: bias due to confounding factors, selection, classification, intervention, missing data, outcome measures and reported results. The response options are yes, probably yes, probably no, no, and not informed.

Quantitative synthesis

The studies data were analyzed using RevMan software (Review Manager v. 5.4.1, The Cochrane Collaboration; Copenhagen, Denmark) to evaluate the association between fluorosis and consumption of fluoride salt, as well as the association between caries and consumption of fluoride salt. Six analyses were performed, comparing people who consumed fluoride salt (exposed/treated) with those with or without another community fluoridation measure (positive and negative controls, respectively):

In fluorosis analysis, the number of people with fluorosis (events) and the total individuals evaluated in case and control groups were used to calculate the odds ratio (OR) and its 95% confidence interval (CI), subgrouping according to the indexes used (Thylstrup-Fejerkov or DEAN). To evaluate the influence of the 'questionable' score in DEAN's index, three analyses were performed considering "questionable" as with fluorosis (first data set) or without fluorosis

(second dataset), in addition to a third dataset excluding 'questionable'. Separated analyses were performed for negative and positive control.

It was considered negative control when the comparison was performed with participants groups not exposed to any other method of community fluoride, and positive control when the comparison was performed with participants group not exposed to fluoridated salt, however they were exposed to other method(s) of community fluoride.

In dental caries analysis with dichotomous data, the OR of caries between people who consumed fluoride salt (exposure group) and those exposed (positive control) or not (negative control) to another community fluoridation measure, 95% CIs and standard errors (SEs) were calculated for all studies included in this analysis. The pooled effect size was calculated by the generic inverse variance OR. Separated analysis were performed for negative and positive control group.

In dental caries analysis with continuous data, the mean difference (MD) of caries between people who consumed fluoride salt (exposed group) and those exposed (positive control) or not (negative control) to another community fluoridation measure, 95% CIs and SEs were calculated for all studies included in this analysis, in attempt to combine data from the largest possible number of studies. The pooled effect size was calculated by the generic inverse variance MD since the outcome was measured by the same index between studies. This analysis was performed to dmft and DMFT index. Separate analyses were performed for negative and positive control groups.

When necessary, the effect estimates were converted with the help of RevMan software tools. Fixed effects model was applied when extreme low number of studies were included (three or lass studies) and random effect were applied when four or more studies were included in the meta-analysis [13]. Heterogeneity was tested using the I^2 index and, when possible, the prediction intervals were calculated in analysis that random effect was applied.

The proportion of caries-free (PCF) participants was calculated for exposed/treated group (SF) and control groups through the formulae

$$\frac{\text{Total number of caries free participants} \times 100;}{\text{Total number of participants evaluated}}$$

And the increment of caries-free participants was calculated through the formulae: PCF for the group exposed to SF – PCF for control group (separately for positive and negative controls).

Certainty of evidence

The certainty of the evidence (certainty in the estimates of effect) was determined for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. With the GRADE approach, observational studies and clinical trials start as “low” and “high” certainty of evidence, respectively; however, the certainty of evidence decreases to “very low” if serious or very serious issues related to risk of bias, imprecision, inconsistency, indirectness, and publication bias are present [14].

The age of the participants in the intervention/exposed and control groups, the exposure to fluoride sources other than salt in the intervention/exposure group, kappa values for intra- and inter-examiner assessment, and diagnosis of the condition performed in a non-clinical way (exclusively by radiographs) were considered to evaluate de influence of risk of bias in the caries outcome. Exposure to fluoride sources other than salt in the intervention/exposure group, kappa values for intra- and inter-examiner assessment, and diagnosis of the condition performed in a non-clinical way (photographs) were considered to evaluate de influence of risk of bias in the fluorosis outcome. The age of participants was considered to evaluate indirectness.

3. Results

Selection of studies

After reading the titles and abstracts, 3,809 duplicates were removed, with identification of 4,991 studies (4,967 studies identified via databases and registers, and 24 via other methods). Among the 46 potentially eligible studies (read in full text), 26 were excluded due to the following aspects (Appendix 2 – S2): Same study published twice with different title, year and/or journal (n = 3), Literature review (n = 3), Descriptive Studies (absence of a control group) (n =

8), No groups exposed to fluoridated salt (n = 1), Overlapping sources of fluoride (n = 8), Missing data referred to the population of the study; contact with the author was tried but unsuccessfully (n = 3).

Thus, 20 papers remained for the qualitative synthesis, and 15 for the quantitative analysis. The flowchart of study selection, following the PRISMA 2020 statement [15], is presented in Fig. 1.

Characteristics of studies included

The characteristics of the 20 included studies are listed in Table 1. Among them, 18 studies were cross-sectional [16–33] and 2 were prospective (one randomized [8] and one non-randomized [9]). All included studies had a control group (among which 5 were exposed to fluoridated water, 1 exposed to fluoridated tablets and 14 not exposed to any community fluoridation measure) and a group exposed to fluoridated salt. Two studies (published in three separate papers) evaluated both dental caries and fluorosis indexes in the same population [27–29]. Regarding fluorosis, three studies used the Dean's index [28,32], while two used Thylstrup and Fejerskov's index [17,29].

For dental caries, 10 studies evaluated only permanent teeth (DMFT/DMFS) [18,19,22,23,25–27,29,30,33], 1 evaluated only primary teeth (dmft) [8], and 4 studies evaluated both permanent and primary teeth (DMFT/DMFS/dmft) [20,21,24,31]. Nine studies are comparisons of National surveys carried out in different periods of time (*i.e.*, before and after salt fluoridation implementation) [16,18–20,23,24,31–33].

Risk of bias within studies

The included articles varied regarding of risk of bias. For cross-sectional studies, the overall quality score ranged from 3 to 9. Ascertainment of the exposure in the selection section was the main bias, considering that 13 [16–18,21,24–32] of the 18 studies did not fit the criteria (did not measure the fluoride concentrations in the table salt, nor in water or tablets), followed by lack of appropriate statistical tests (Odds Ratio – OR). The randomized controlled study [8] was classified as "some concerns" risk of bias because of missing data about plans for the analysis elaboration. The non-randomized controlled study [9] was

evaluated as having serious concerns about risk of bias due to confounding factors and deviations from intended interventions (table 2).

Meta-analyses and certainty of evidence

Four studies were excluded from the meta-analyses. Marthaler *et al.* [33], was excluded since caries outcomes were only measured in DMFS. Betancourt-Lineares *et al.* [16], and De Crousaz *et al.* [19] Fabien *et al.* [21] were excluded due to insufficient data. Furthermore, despite the study by Stephen *et al.* [29] presented data for both caries and fluorosis, it was only considered in the meta-analysis of fluorosis, given that the study population was exposed to fluoride tablets after the age of 4. This makes it impossible to assess the effects of fluoridated salt alone on dental caries.

Fluorosis

Four studies were included in these analyses, comprising 3,731 individuals. The chance to present fluorosis was similar between the exposure (fluoridated salt) and positive control (fluoridated water), with OR values ranging from 0.76 to 0.84 (Table 3). Also, the use of fluoridated salt significantly increased the chance of fluorosis compared with negative controls (without any F-based community measure), with OR values ranging from 1.50 to 1.58. For both comparisons, the data related to the “questionable” score of Dean’s index was shown to exert negligible influence.

Caries – dichotomous data

Mansila *et al.* [25] was not included in this analysis since all participants (100%) in both exposure and control groups presented dental caries, so that the OR could not be estimated. Nine studies (from 10 papers) were included in this analysis, accounting for 226.220 people, out of which 7 were compared against negative controls (without any F-based community measure) and 2, against positive control (fluoridated water). Individuals exposed to fluoridated salt presented lower chance of dental caries compared to negative controls OR 0.41 [0.30, 0.57] $p<0.00001$, $I^2=99\%$, with prediction interval range from 0.13 to 1.29. On the other hand, individuals exposed to fluoridated salt or to fluoridated water

presented similar chance of dental caries OR 1.12 [0.97, 1.29] p=0.11 I^2=99% (figure 2). The certainty of evidence was very low (table 2).

Caries – continuous data

Nine studies (from 10 papers) were included in the analysis of DMFT data (7 compared with negative control, and 2 with positive control), and four were included in the analysis of dmft data (all compared with negative control). Individuals exposed to fluoride salt presented lower mean DMFT (MD -1.98 [-2.84, -1.11], p<0.00001, I^2=99% - prediction interval range from -2.77 to 0.30) and dmft (MD -1.45 [-2.62, -0.29], p=0.01, I^2=99% - prediction interval range from -6.99 to 4.09) compared to negative controls, as shown in Figures 3 and 4, respectively. Conversely, individuals exposed to fluoridated salt and fluoridated water (positive controls) presented similar mean DMFT (MD 0.00 [-0.17, 0.17] p=97 I^2=73 (Figure 3). The certainty of evidence of these analyses were classified as very low (table 2).

Proportion of caries-free

Overall, there was a 10.8% increase in the proportion of caries-free in populations exposed to fluoridated salt compared with those not exposed to any community fluoridation measure (negative control), for both dentitions considered together. For the permanent dentition (DMFT), there was an increase of 14.8% in the proportion of caries-free in populations exposed to fluoridated salt compared to negative control [9,18,23,25]. On the other hand, there was a 3.8% reduction in the proportion of caries-free individuals compared to positive controls (exposure to fluoridated water) [22,27].

4. Discussion

With the increase in access, acceptance, and development of vehicles with fluoride for home and/or professional use, the question about the effectiveness, safety and maintenance of community vehicles for the control of dental caries has been raised, especially due to concerns on risks of chronic toxicity (*i.e.*¸dental

fluorosis). The results of the six MAs analyzed together attest the higher protective effect of fluoridated salt on dental caries compared with negative controls, reaching levels similar to those achieved by the use of fluoridated water, both for caries control and chance of fluorosis. These results, however, must be interpreted with caution, due to the very low level of evidence, as detailed below.

Regarding the effects of fluoride salt as a preventive measure against dental caries, three MAs were conducted. In the first MA, dichotomized data (i.e., without caries versus presenting any number of lesions) was used to calculate the OR, demonstrating a lower chance of presenting dental caries in individuals exposed to fluoridated salt compared with negative control, and a similar chance compared to individuals exposed to fluoridated water. For the second and third MAs, continuous data were used, finding that individuals exposed to fluoridated salt presented lower means of DMFT/dmft compared to groups not exposed to any community fluoridation measure. However, compared to groups exposed to fluoridated water, similar means of DMTF were observed. The use of community fluoridation measures is endorsed by the World Health Organization, which regards the implementation of programs for the automatic administration of fluoride through water, salt, or milk among the urgent actions of governments to improve the oral health of populations [34]. A previous systematic review and meta-analysis found a 35% reduction in dmft and 26% in DMFT in children exposed to fluoridated water dentition [35]. This corresponds to a 15% increase in caries-free children in deciduous dentition and 14% in permanent dentition [35], what is in line with the data obtained in the present review.

The certainty of evidence of these analyses was classified as very low, mainly due to the cross-sectional nature of the majority of studies included (in Table 2), in addition to issues related to imprecision, external validity and inconsistencies. Also, the studies were conducted in different continents, comprising 11 European, seven North American, two South American and one African country, whose specific socioeconomic and cultural features might have played an important role on the outcomes obtained in each study. The quality assessment also identified that most of the studies presented some type of risk of bias that could influence in outcome, in addition to high heterogeneity and wide variations in the effect estimates. Another important aspect was that exposure to other

fluoride sources such as dentifrices, gels and varnishes was not investigated or was not clearly described neither for the exposed nor the negative/positive control groups, with the exception of one study [21]. These aspects, analyzed together, reduce the strength of the suggestions from the present review and should, therefore, be taken into consideration.

In fact, the present systematic review identified only two prospective clinical trials assessing the effects of fluoridated salt on dental caries. The first was conducted in Sweden [9] and found no significant difference between adolescents who consumed fluoridated salt and those who did not. Some methodological aspects, however, must be emphasized for a better understanding of such results. Firstly, wide variations in the consumption of fluoridated salt at home were reported for the exposed group (ranging from 1 to 37 kg per household throughout the 2-year study period), in addition to ad libitum consumption of fluoridated salt at school during meals. Secondly, and perhaps most importantly, the study was conducted in a high HDI country, in which both groups (exposed and control) regularly used fluoride toothpaste, and had access to routine preventive and restorative treatments, which are likely to have played a major role in the results observed. Despite this study represents a more realistic condition of modern lifestyle concerning the simultaneous use of different sources of fluoride, the points highlighted above hinder the estimation of the actual effects of fluoridated salt on caries control.

On the other hand, a prospective, controlled and interventional study conducted in 3-5 year-old children in Gambia [8], where the drinking water had a low fluoride content (0.1 mg F/L) and children did not use fluoridated toothpastes, concluded that salt fluoridation was an effective measure to reduce caries incidence. This study was extremely controlled regarding the amount of fluoridated salt administered to the children (1.6 g of salt containing 250 ppm F per child, once a day at school, only in schooldays). This allowed a clear determination of the preventive effects of fluoridated salt on caries control in a low HDI country, in which this measure provided the only source of fluoride to the study population. Nonetheless, the extent to which these results could be extrapolated to children from countries with higher HDI and/or with access to other sources of fluoride (i.e., toothpastes or mouthrinses), is still unknown. The

analysis of the information above (both from cross-sectional and prospective studies) clearly point out to the need for more well controlled clinical trials. This is reinforced by the widespread availability of fluoridated products and industrialized foods and beverages, which can also contribute to total daily fluoride exposure. The use of logistic regression models under well controlled exposure conditions might also bring new light into this important issue.

To evaluate the effect of fluoridated salt on the chance of dental fluorosis, four cross-sectional articles were included in the meta-analysis, out of which two used the Dean's index [28,32] and two, TF's index using clinical photographs [17,29]. As for the comparison between fluoridated salt and fluoridated water, two studies included in the MAs [17,28] compared these vehicles in 12-year-old children, showing that the chance of fluorosis was similar in both groups. These results are in line with data from a comprehensive study assessing urine as a biomarker of fluoride exposure, in 4- to 6- year-old children exposed to different sources of systemic fluoride, showing no significant differences in mean 24-hour urinary fluoride excretion between individuals exposed to fluoridated water (0.69 mg) and fluoridated salt (0.81 mg) [36]. Furthermore, Sagheri et al. [28] concluded that the fluorosis resulting from both measures (assessed by the Dean's index) did not represent a public health problem, given that most of the cases were not of esthetical concern. The level of this evidence, however, was considered as very low for the type of studies included, for similar reasons presented for the studies assessing dental caries.

Regarding the studies comparing fluoridated salt with a negative control, the MAs showed that consumption of fluoridated salt increased the chance of fluorosis in the study population (OR ranging from 1.50 to 1.58, depending on the approach used for the "questionable" score of Dean's index). The individual analysis of these two studies deserves some comments, given their opposite outcomes. First, despite Stephen et al. [29] reported no significant differences in fluorosis prevalence between adolescents exposed or not to fluoridated salt, this study only accounted for 5.4% of the total weight of the analysis, in addition to presenting a wide confidence interval of the estimates (0.30 – 11.53). On the other hand, the study by Salas-Pereira et al. [32] reported an increased chance of fluorosis in the exposed group. The study population comprised Costa Rican

adolescents who were born before or after the implementation of salt fluoridation (15 or 12 year-olds, respectively). For this reason, only the upper anterior teeth were considered in the MAs, this since the onset of mineralization of these teeth occurs around 2.5 years of age. Interestingly, these individual studies reported that 6.1% [29] and 26.3% [32] of the participants consuming fluoridated salt had dental fluorosis (at any level), while the reported figure obtained in a Cochrane systematic review [35] indicated that 40% of the population using fluoridated water was affected by enamel opacities at any level (aesthetic and no aesthetic concern). Despite the different review protocols and scopes of both reviews, in addition to the higher number of studies included in the Cochrane review [35] impede a direct comparison of the figures reported, the present results indicate that the consumption of fluoridated salt can be regarded to be as safe as fluoridated water.

Salt fluoridation is a method usually well accepted by the population, as it presents greater geographical reach than with fluoridated water, longer shelf life than fluoridated milk, in addition to allowing the freedom of choice by individuals, the latter being in high demand over recent decades. Furthermore, the estimated range of costs for salt fluoridation varies from US$0.026 to 0.0412 per capita/year versus US$0.46 per capita/year for water fluoridation [37], assuming a cost-benefit ratio of 1:10 to 1:14 [38]. All these aspects allow the implementation of this community-based method of fluoridation in virtually any settings. The disadvantages of salt fluoridation, nonetheless, are related to wide variations in fluoride concentrations in commercially available salts [39], which can lead to under or over exposure to fluoride, both of which are undesirable situations considering benefits and risks, respectively. Such variations might be associated with difficulties in the manufacturing process and/or lack of adequate inspection by health authorities. In this sense, it is important to stand out that fluctuations in fluoride concentrations have also been reported for fluoridated water, and that the implementation of strategies for external control over the fluoridation has shown to be effective in reducing such variations [40]. This suggests that similar approaches could be adopted for fluoridated salt in order to assure concentrations that are effective for caries, and safe concerning the risk of fluorosis.

Another disadvantage is related to the amount of salt consumed on a daily basis by each individual. Since this aspect is strongly influenced by personal preference, a precise estimation of daily fluoride exposure from this source becomes difficult, which constitutes a challenge for health authorities when balancing risks and benefits. Furthermore, due to growing concerns on cardiovascular diseases related to over consumption of sodium choride [41], the WHO recommends that the daily intake of salt should not exceed 5 g [42]. Given that fluoride concentrations in table salts were based on a daily consumption of 10-12 g per day [43], it is rational to assume that the reduction in salt consumption endorsed by the WHO may impact the protective effect of this measure. This scenario, therefore, would demand new estimates of fluoride concentrations in table salts, which would have to be tested in short- and long-term protocols to assess total fluoride exposure and bioavailability. Protocols assessing historical and recent biomarkers, including saliva, dental biofilm, hair, nails and urine, could bring important data concerning the safety of such changes [44].

While dental fluorosis has specific window of susceptibility (ranging from 11 months to 7 years of age) [45], dental caries is a biofilm- and sucrose-dependent disease caused by fluctuations in biofilm pH, which lead to de- and re-mineralization of tooth surfaces [46]. Thus, the window of susceptibility to dental caries spams the entire individual's life, from the eruption of the first tooth to death, if the risk factors exceed the protective factors [47]. In this sense, despite the present review only included studies conducted in children and/or adolescents, a study was carried out with recruits demonstrated that individuals who consumed fluoridated salt from the age of 5 years presented ~30% fewer caries lesions compared with those who did not [48]. This indicates that the benefits of fluoride exposure from this source are not restricted to the first two decades of life, but instead are reflected throughout life, including adults and the elderly. However, given the limited scope of the present review regarding age of the participants, studies assessing the benefits of this community-based measure in the adult population could be instructive in directing public health measures. This is especially needed considering that preventive measures (such as topical fluoride application) for caries control are usually focused on pre-school and school children, with lesser or no measures directed to other age groups.

A final point that deserves comment is related to the novelty of the present review. The last systematic review on the effectiveness of fluoridated salt for the prevention of caries was published in 2010 [7]. The 12-year period between the present and the previous review allowed the inclusion of six new studies, out of which two had longitudinal protocols, the latter bringing unprecedented information under more controlled experimental conditions. In addition, to the best of our knowledge, this is the first systematic review assessing the effects of fluoridated salt on dental fluorosis. This is extremely important from clinical and epidemiological standpoints, as it simultaneously assessed both risks and benefits of this community-based measure.

To sum up, the low quality of evidence and the cross-sectional nature of most of the studies included in the review indicated limited evidence on the risks and benefits of salt fluoridation, so that any conclusions should be interpreted in light of these limitations. Nonetheless, the results of the MAs clearly indicated that use of fluoridated salt is an effective strategy for the control of dental caries, being comparable to water fluoridation. Furthermore, it can be regarded to be as safe as fluoridated water concerning the risk of dental fluorosis, despite the low number of studies that contributed for this analysis. Thus, based on the evidence gathered in the present review, there is reason to believe that this strategy should be maintained in countries in which salt fluoridation is already present as a community-based fluoridation scheme. It could also be implemented in countries where the access to dental health services is precarious, especially in those where no other systemic sources of fluoride are available.

5. Other Information

Protocol and registry

This study was registered in PROSPERO database (registry CRD42015027689) and followed the PRISMA guidelines on the Preferred Reporting Items for Systematic reviews and Meta-Analyses [49].

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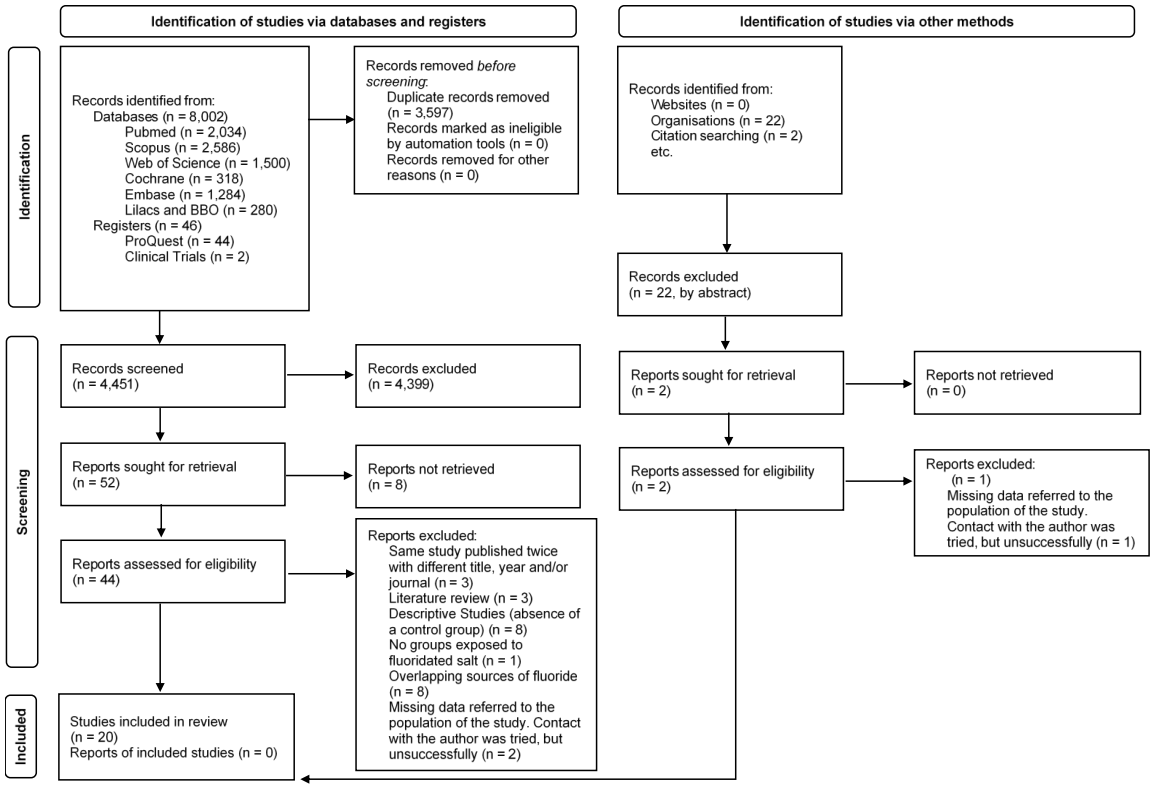

Figure 1. Flow diagram of the study.

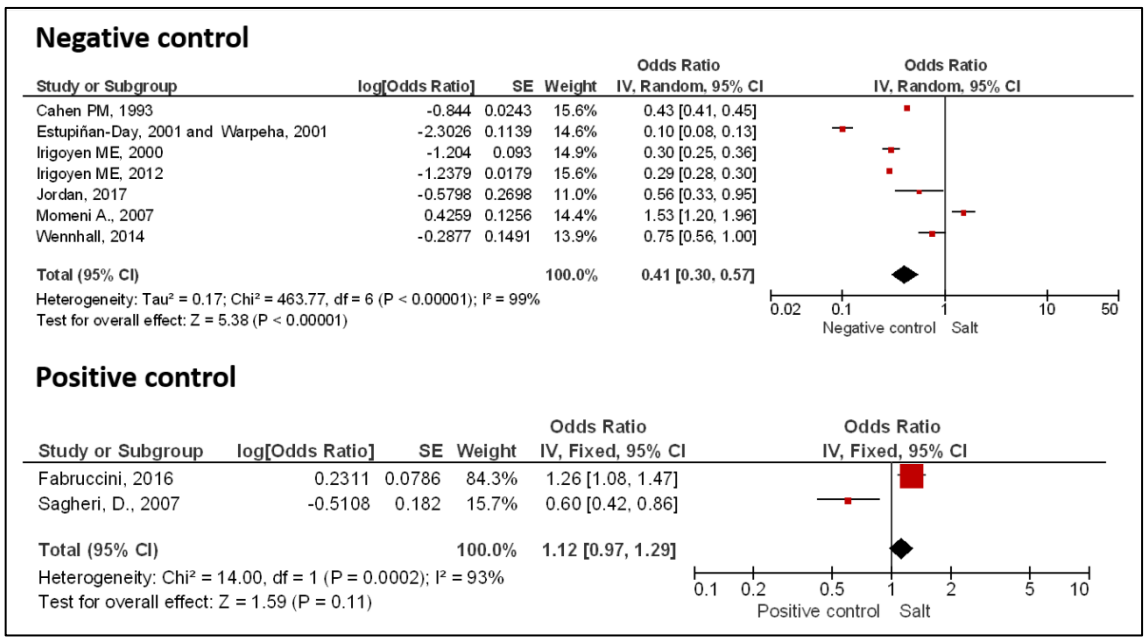

Figure 2. Chance of dental caries in individuals exposed to fluoridated salt, compared to positive (fluoridated water) and negative (no community measure) controls.

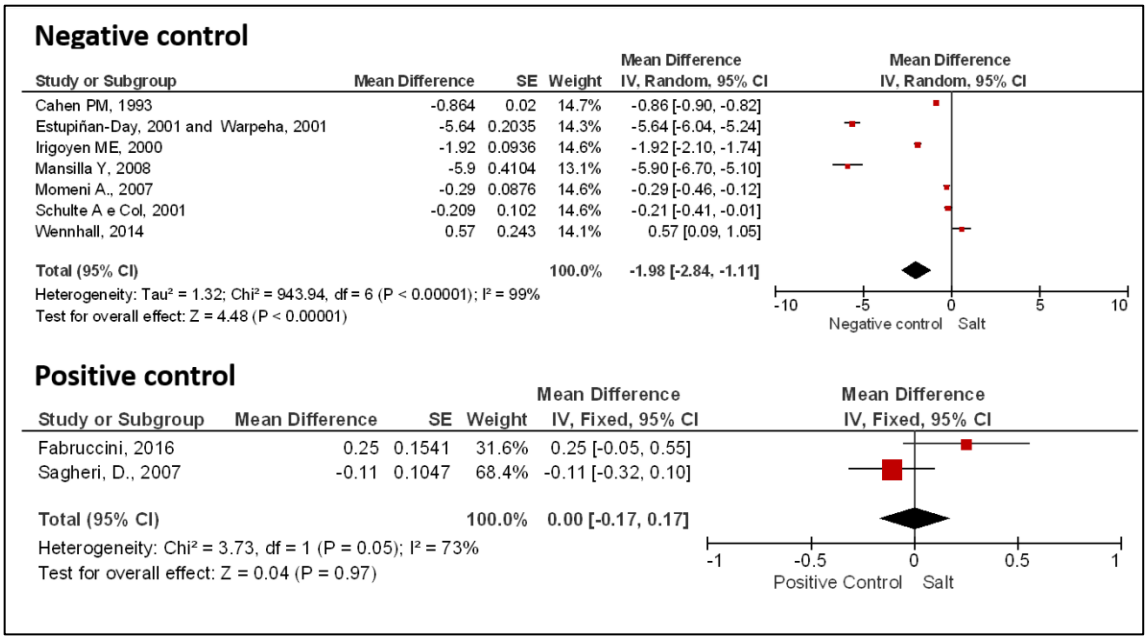

Figure 3. Mean difference of DMFT of in individuals exposed to fluoridated salt, compared to positive (fluoridated water) and negative (no community measure) controls.

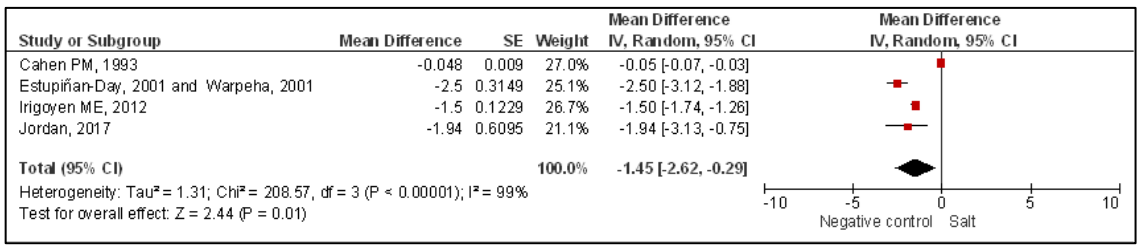

Figure 4. Mean difference of dmft of in individuals exposed to fluoridated salt, compared to negative control (no community measure).

Table 1. Summarized data collected from the selected studies

Author, year	Country	Study design	Age of participants	Number of participants using fluoridated salt	Number of participants NOT using fluoridated salt	Evaluation Criteria	Control group	Results	Main conclusions
Betancourt-Lineares *et al.*, 2013	Mexico	Cross-sectional	12-15 years old	4,793	12,218	Dental fluorosis (Dean's index)	Fluoridated water	Mean fluorosis prevalence of 27.9% (95% CI 24.4, 28.5). The lowest prevalence was detected in Morelos (3.2%, exposed to FS) and the highest, in Durango (88.8%, exposed to naturally fluoridated water at above-optimum fluoride levels).	Fluorosis prevalence and severity was higher in states consuming fluoridated water at above-optimum fluoride levels.
Büchel Kathrin *et al.*, 2011	Switzerland	Cross-sectional	12 years old	365	373	Dental fluorosis (TF index)	Fluoridated water	31.9% of schoolchildren studied in 1999 in Basel-Stadt (fluoridated water) and Basel-Landschaft (FS) showed fluoride-associated enamel opacities.	The fluorosis prevalence was identical in both cantons, regardless the fluoridation scheme used.
Cahen *et al.*, 1993	France	Cross-sectional	6-15 years old	18,786	19,366	Dental caries (DMFT/DMFS indexes)	Negative control*	After introduction of salt fluoridation, a decrease of 28.7% in dmft score was shown in children 6-years old. For 12-years old children the corresponding decrease was 38,0%.	A significant decline in dental caries in France became evident after salt fluoridation, both for primary and in permanent teeth.
de Crousaz *et al.*, 1985	Switzerland	Cross-sectional	8-14 years old	842	875	Dental caries (DMFT/DMFS indexes)	Negative control*	At the age of 12-years, children had a DMFT score of 5.65 in 1970 (negative control) and 2.96 in 1982 (FS).	The average caries prevalence of the test group (FS) was lower than that of the corresponding control groups (negative control).
Estupiñan-Day *et al.*, 2001	Jamaica	Cross-sectional	6, 12 and 15 years old	1,113	1,220	Dental caries (DMFT/dmft indexes)	Negative control*	The mean DMFT scores in children 6, 12 and 15 years of age were lower (0.22, 1,08 and 3.02, respectively) in 1995 (FS) than the corresponding scores of 1.71, 6.72 and 9.60 obtained at the baseline examination in 1984 (negative control).	A significant decline in dental caries was observed comparing the findings of 1984 (negative control) and 1995 (FS).
Fabien *et al.*, 1996	France	Cross-sectional	9 years old	3,600	107	Dental caries (DMFT/DMFS /dmft indexes)	Negative control*	At the age of 9-years, children consuming FS had DMFT score of 0.53 and children in the negative control group had a DMFT score of 0.61. Considering primary teeth, the dmft scores were 0.91 and 1.41, respectively.	A significant reduction observed for dmft in children exposed to FS. No significant differences observed for DMFT and DMFS data.

Fabruccini *et al.*, 2016	Brazil and Uruguai	Cross-sectional	12 years old	1,154	1,528	Dental caries (DMFT index)	Fluoridated water	For children at age 12-years, DMFT scores were 1.29 in Porto Alegre (fluoridated water) and 1.70 in Montevideo (FS).	Schoolchildren exposed to FS had significantly higher likelihood of having caries than those exposed to fluoridated water.
Irigoyen and Sánchez-Hinojosa, 2000	Mexico	Cross-sectional	12 years old	1,138	2,275	Dental caries (DMFT/DMFS indexes)	Negative control*	The mean DMFT index was 4.39 in 1988 (negative control) and 2.47 in 1997 (FS); caries reduction after implementation of salt fluoridation was 43.7%.	Since the implementation of FS, the caries prevalence and treatment needs in the State of Mexico have decreased.
Irigoyen *et al.*, 2012	Mexico	Cross-sectional	6-10 and 12 years old	16,882	9,798	Dental caries (DMFT/dmft indexes)	Negative control*	For the negative control group (first survey), dmft and DMFT values were 3.86 and 1.03, respectively. For the FS group (second survey), the corresponding values were 2.36 and 0.35, corresponding to reductions of 38.9% and 66.0%, respectively.	A decrease in dental caries rates was detected, especially in permanent dentition. The increase in fluoride availability probably contributed to this decrease.
Jordan *et al.*, 2017	Gambia	Prospective, controlled, interventional 2 years follow-up	3-5 years old	304	137	Dental caries (dmft index)	Negative control*	After 12 months, mean caries incidence per person was 1.29 $\Delta d_{3/4}$mft in the test group (FS) and 3.83 $\Delta d_{3/4}$mft in the control group (negative control). The caries-prevented fraction was 66.3%.	The use of FS in the schools in Gambia resulted in a caries-protective effect in 3-5 year-old children.
Mansilla, 2008	Peru	Cross-sectional	12 years old	104	78	Dental caries (DMFT index)	Negative control*	The average caries index (DFMT) in schoolchildren was 8.18 (FS) and 14.80 (negative control).	The population consuming FS had a significant reduction in the presence of carious lesions.
Marthaler *et al.,* 1977	Switzerland	Cross-sectional	7-15 years old	501	596	Dental caries (DMFT/DMFS indexes)	Fluoridated tablet	In the community of Yverdon (canton of Vaud), the percentage of children with caries decreased by 30.1% after the introduction of FS as the only fluoridated measure (1974), compared with data obtained in 1970 (use of fluoridated tablets). In other 3 communities (from the cantons of Fribourg and Neuchâtel) where fluoridated tablets were still used in association with other preventive measures, the corresponding decreases were 19.6, 22.3 and 28.2%.	Children from the canton of Vaud presented lower percentage of caries compared with those from the cantons of Fribourg and Neuchâtel.

Momeni *et al.*, 2007	Germany	Cross-sectional	12 years old	627	571	Dental caries (DMFT index)	Negative control*	Children using FS presented a DMFT score of 0.63, while those not exposed to this measure (negative control) had a DMFT index of 0.92.	Significantly lower DMFT in children exposed to FS compared to those who did not.
Sagheri *et al.*, 2007	Ireland/Germany	Cross-sectional	12 years old	206	377	Dental caries (DMFT index)	Fluoridated water	In Dublin (fluoridated water) the mean DMFT was 0.80, while in Freiburg (FS), the corresponding value was 0.69.	The use of FS should be adopted where water fluoridation is not feasible.
Sagheri *et al.*, 2007	Ireland/Germany	Cross-sectional	12 years old	206	377	Dental fluorosis (Dean's index)	Fluoridated water	The prevalence of fluorosis in children of Dublin (fluoridated water) was 25.5%, and in Freiburg (children using FS) it was 19.4%.	The prevalence of aesthetically important DF ('Mild' and 'Moderate') was low and similar in both communities (using either FS or water).
Salas-Pereira *et al.*, 2008	Costa Rica	Cross-sectional	12 and 15 years old	1,250	1,249	Dental fluorosis (Dean's index)	Negative control*	Prevalence of enamel fluorosis (very mild or higher) at the age of 12 year was 17% (for teeth 13 to 23) and 32% (when teeth 14 and 24 were included). At the age of 15 years, the corresponding figures were 12% and 25%, respectively.	The prevalence and severity of enamel fluorosis increased in the cohort born after FS implementation.
Schulte *et al.*, 2001	Germany and France	Cross-sectional	12 years old	927	716	Dental caries (DMFT/DMFS indexes)	Negative control*	DMFT scores of children living in Heidelberg and Montpellier consuming FS was 1.32 and 1.84, respectively. For children in the same cities but not using FS (negative control), the corresponding scores were 1.71 and 1.38, respectively.	Increasing the use of FS would be a good strategy to reduce the dental caries levels in children in both cities.
Stephen *et al.*, 1999	Hungary	Cross-sectional	14 years old	49	59	Dental caries (DMFT/DMFS indexes) Dental fluorosis (TF index)	Negative control*	In 1997, mean DMFS score was 9.18 for children who were exposed to FS from birth to the age of 2.3-4.8 years in 1985 (when the measure was ceased). The corresponding value for children not exposed to FS was 4.51. Prevalence of fluorosis was very low in both groups (3 children exposed to FS and 2 from the negative control). Fluoridated tablets were available to both groups in 1987.	No difference was found in the presence of fluorosis in anterior teeth between the two groups. No caries-preventive benefit was apparent after 11.5 years after the use of FS was ceased. Caries prevalence was social class-related (higher scores in children living in rural areas).

Warpeha *et al.*, 2001	Jamaica	Cross-sectional	6, 12 and 15 years old	1,049	1,220	Dental caries (DMFT/dmft index)	Negative control*	Data from 1984 and 1995 showed reductions of 52% in dfmt, and 84% and 68% in DMFT in 6-, 12- and 15-year-old children, respectively. FS was introduced in 1987.	An epidemiological transition was observed between 1984 (severe and highly prevalent dental caries), and 1995 (less prevalent and concentrated in a smaller proportion of the population).
Wennhall *et al.*, 2014	Sweden	Prospective study 2-year follow-up	12-14 years old	384	349	Dental caries (DMFT index)	Negative control*	The ΔDFS score in children attending a school where FS was available was 1.05, while that for children attending a school without this measure (negative control) was 1.12.	There were no significant differences in total caries increment or proximal progression rate between the two schools. A negative correlation between the amount of delivered salt and caries progression rate was noted.

*Negative control: those exposed (positive control) or not (negative control) to another community fluoridation measure.

FS: fluoridated salt.

Table 2. Certainty of evidence of the studies included in the meta-analyses using the GRADE tool

Certainty assessment						Effect		Certainty
Number of studies and study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	**Absolute (95% CI)**	
Dmft								
4 observational studies	serious [a]	serious [b]	serious [c]	serious [d]	none	-	MD **1.45 lower** (2.62 lower to 0.29 lower)	⊕◯◯◯ VERY LOW
Caries OR - Negative control								
7 observational studies	very serious [e]	very serious [b,f]	serious [c]	serious [g]	strong association	**OR 0.41** (0.30 to 0.57)	**0 fewer per 1.000** (from 1 fewer to 0 fewer)	⊕◯◯◯ VERY LOW
Caries OR - Positive control								
2 observational studies	not serious	very serious [b,f]	serious [c]	not serious	none	**OR 1.12** (0.97 to 1.29)	**1 fewer per 1.000** (from 1 fewer to 1 fewer)	⊕◯◯◯ VERY LOW
DMFT - Negative control								
8 observational studies	not serious	very serious [b,f]	serious [c]	serious [d]	none	-	MD **1.98 lower** (2.84 lower to 1.11 lower)	⊕◯◯◯ VERY LOW
DMFT - Positive control								
2 observational studies	not serious	serious [b,h]	serious [c]	not serious	none	-	MD **0** (0.17 lower to 0.17 higher)	⊕◯◯◯ VERY LOW

Legends: CI: Confidence interval; **MD:** Mean difference; **OR:** Odds ratio. (**a**) All studies included presented some type of risk of bias that could influence in outcome; (**b**) Considerable heterogeneity; (**c**) Results could not be extrapolated to adults; (**d**) Upper and/or lower confidence limit crosses the effect size of 0.5 in either direction; (**e**) Analysis including only 'low risk of bias' studies change result significance; (**f**) Wide variation in the effect estimates across studies with little overlap between studies confidence interval; (**g**) Upper and/or lower limits of confidence interval is greater than 25% of effect; (**h**) Some variation in the effect estimates across studies.

Table 3. Quantitative results and certainty of evidence for chance of fluorosis in individuals exposed to fluoridated salt, compared to positive (fluoridated water) and negative (no community measure) controls, using fixed effects

Approach regarding the "questionable" classification of Dean's index	Number of studies	OR	CI	*p* value	I^2	Certainty of evidence
"Questionable" considered as with fluorosis						
Negative Controls *	2	1.58	1.31 – 1.91	<0.0001	0%	⊕○○○
Positive controls	2	0.84	0.64 – 1.11	0.22	15%	⊕○○○
"Questionable" considered as without fluorosis						
Negative Controls	2	1.50	1.21 – 1.88	<0.0003	0%	⊕○○○
Positive controls	2	0.77	0.47-1.25	0.29	60%	⊕○○○
"Questionable" excluded						
Negative Controls	2	1.57	1.26 – 1.97	<0.0001	0%	⊕○○○
Positive controls	2	0.76	0.46 – 1.27	0.3	62%	⊕○○○

*Negative control: comparison with participants not exposed to any type of community fluoride.

Positive control: comparison with participants not exposed to fluoridated salt however, were exposed to other methods of community fluoride

Appendix S1

Table 1. Description of the search strategy for each database

Database	Search Strategy
PubMed	#1 ((((((((((((((Child[MeSH Terms]) OR Child[Title/Abstract]) OR Adolescent[MeSH Terms]) OR Adolescent[Title/Abstract]) OR Adult[MeSH Terms]) OR Adult[Title/Abstract]) OR Children[Title/Abstract]) OR Preschool[Title/Abstract]) OR Adolescents[Title/Abstract]) OR Adults[Title/Abstract]) OR Young[Title/Abstract])) AND ((prevalence[MeSH Terms]) OR prevalence[Title/Abstract])) #2 ((((((((((((((((((((sodium chloride, dietary[MeSH Terms]) OR Sodium chloride, dietary[Title/Abstract]) OR Fluorides[MeSH Terms]) OR Fluorides[Title/Abstract]) OR Fluoridation[MeSH Terms]) OR Fluoridation[Title/Abstract]) OR Cariostatic Agents/administration and dosage[MeSH Terms]) OR Cariostatic Agents/administration and dosage[Title/Abstract]) OR Cariostatic Agents/therapeutic use[MeSH Terms]) OR Cariostatic Agents/therapeutic use[Title/Abstract]) OR Fluorides/administration and dosage[MeSH Terms]) OR Fluorides/administration and dosage[Title/Abstract]) OR Fluorides/therapeutic use[MeSH Terms]) OR Fluorides/therapeutic use[Title/Abstract]) OR Table Salt[Title/Abstract]) OR Salt, Table[Title/Abstract]) OR Fluorine[Title/Abstract]) OR Fluoride[Title/Abstract]) OR Salt Fluoridation[Title/Abstract]) OR Fluoridated Salt[Title/Abstract]) OR Systemic Fluoride[Title/Abstract]))) #3 ((((((((((animal experimentation[MeSH Terms]) OR animal experimentation[Title/Abstract]) OR iodine[MeSH Terms]) OR iodine[Title/Abstract]) OR Hypertension[MeSH Terms]) OR Hypertension[Title/Abstract]) OR Thyroid Gland[MeSH Terms]) OR Thyroid Gland[Title/Abstract]) OR in vitro[Title/Abstract]) OR in situ[Title/Abstract]) OR iodization[Title/Abstract]) #1 AND #2 NOT #3
Scopus	#1 ((TITLE-ABS-KEY (child) OR TITLE-ABS-KEY (adolescent) OR TITLE-ABS-KEY (adult) OR TITLE-ABS-KEY (children) OR TITLE-ABS-KEY (preschool) OR TITLE-ABS-KEY (adolescents) OR TITLE-ABS-KEY (adults) OR TITLE-ABS-KEY (young))) AND (TITLE-ABS-KEY (prevalence))

	#2 ((TITLE-ABS-KEY (sodium chloride, dietary) OR TITLE-ABS-KEY (fluorides) OR TITLE-ABS-KEY (fluoridation) OR TITLE-ABS-KEY ("Cariostatic Agents/administration and dosage") OR TITLE-ABS-KEY ("Cariostatic Agents/therapeutic use") OR TITLE-ABS-KEY ("Fluorides/administration and dosage") OR TITLE-ABS-KEY ("Fluorides/therapeutic use") OR TITLE-ABS-KEY ("Table Salt") OR TITLE-ABS-KEY ("Salt, Table") OR TITLE-ABS-KEY (fluorine) OR TITLE-ABS-KEY (fluoride) OR TITLE-ABS-KEY (salt fluoridation) OR TITLE-ABS-KEY (fluoridated salt) OR TITLE-ABS-KEY (systemic fluoride))) #3 ((TITLE-ABS-KEY (animal experimentation) OR TITLE-ABS-KEY (iodine) OR TITLE-ABS-KEY (hypertension) OR TITLE-ABS-KEY (thyroid gland) OR TITLE-ABS-KEY (in vitro) OR TITLE-ABS-KEY (in situ) OR TITLE-ABS-KEY (iodization))) #1 AND #2 AND NOT #3
Web of Science	#1 (Child) OR (Adolescent) OR (Adult) OR (Preschool) OR (Children) OR (Adolescents) OR (Adults) OR (Young) #2 (prevalence) #3 ("Sodium chloride, dietary") OR (Fluorides) OR (Fluoridation) OR ("Cariostatic Agents/administration and dosage") OR ("Cariostatic Agents/therapeutic use") OR ("Fluorides/administration and dosage") OR ("Fluorides/therapeutic use") OR ("Table Salt") OR (Fluorine) OR (Fluoride) OR ("Salt Fluoridation") OR ("Fluoridated Salt") OR ("Systemic Fluoride") #1AND #2 AND #3
Cochrane	#1 Child OR Adolescent OR Adult OR Children OR Preschool OR Adolescents OR Adults OR Young #2 prevalence

	#3 (sodium chloride, dietary) OR Fluorides OR Fluoridation OR (Cariostatic Agents) OR (Table Salt) OR (Salt, Table) OR Fluorine OR Fluoride OR (Salt Fluoridation) OR (Fluoridated Salt) OR (Systemic Fluoride) #4: (animal experimentation) OR iodine OR Hypertension OR (Thyroid Gland) OR (in vitro) OR (in situ) OR iodization #1 AND #2 AND #3 NOT #4
Embase	#1: 'child'/exp OR (child of impaired parents) OR children OR (single parent child) OR 'adolescent'/exp OR (adolescent, institutionalized) OR (institutionalised adolescent) OR (institutionalized adolescent) OR teenager OR 'adult'/exp OR (grown-ups) OR grownup OR grownups #2: 'prevalence'/exp OR (prevalence study) #3: 'salt intake'/exp OR (dietary salt) OR (dietary sodium chloride) OR (intake, salt) OR (sodium chloride intake) OR (sodium chloride, dietary) OR 'fluoride'/exp OR (fluoride binding) OR (fluoride content) OR (fluoride derivative) OR (fluoride uptake) OR (fluorides) OR (hydrofluoride) OR (karitane fluoride tablets) OR 'fluoridation'/exp OR (drinking water fluoridation) OR (fluoridation, water) OR (fluoridization) OR (water fluoridation) OR 'anticaries agent'/exp OR (anticaries vaccine) OR (cariostatic agent) OR (cariostatic agents) #4: 'animal experiment'/exp OR (animal experimentation) OR (animal studies) OR (animal study) OR (animal trial) OR (experiment, animal) OR (physical conditioning, animal) OR 'iodine'/exp OR 'hypertension'/exp OR 'thyroid gland'/exp OR (glandula thyroidea) OR thyroid #1 AND #2 AND #3 AND [embase]/lim NOT #4
Lilacs and BBO	#1: MH:Criança OR Criança$ OR Child OR Niño OR MH:C26.130$ OR MH:F03.080.931.124$ OR MH:Adolescente OR Adolescente$ OR Adolescent OR MH:M01.060.057$ OR MH:Adulto OR Adulto$ OR Adult OR MH:M01.060.116$

	#2: MH:Prevalência OR Prevalência OR Prevalence OR Prevalencia OR MH:E05.318.308.985.525.750$ OR MH:L01.280.975.525.750$ OR MH:N01.224.935.597.750$ OR MH:N06.850.505.400.975.525.750$ OR MH:N06.850.520.308.985.525.750$ OR MH:SP4.001.012.153.244.155$ OR MH:SP5.001.032.063$ #3: MH:"Cloreto de Sódio na Dieta" OR (Cloreto de Sódio na Dieta) OR (Sodium Chloride, Dietary) OR (Cloruro de Sodio Dietético) OR (Sal de Cozinha) OR MH:D01.857.650.705$ OR MH: D01.857.700.705$ OR MH: VS2.001.001.002.003$ OR MH: Fluoretos OR Fluoretos OR Fluorides OR Fluoruros OR MH:D01.248.497.158.380$ OR MH: D01.303.350.300$ OR SP4.011.097.039.764$ OR MH: Fluoretação OR Fluoretação OR Fluoridation OR Fluoruración OR MH:E06.761.382$ OR MH:E06.761.382$ OR MH:N06.890.235$ OR MH:SP4.021.202.133.779$ OR MH:VS4.001.001.002.002.002$ OR MH: Cariostáticos OR Cariostáticos OR (Cariostatic Agents) OR Cariostáticos OR MH:D25.223$ OR MH:D27.505.696.706.222$ OR MH: D27.720.102.223$ OR MD:D27.720.799.113$ OR MD:J01.637.051.223$ #4: MH:"Experimentação Animal" OR (Experimentação Animal) OR (Animal Experimentation) OR (Experimentación Animal) OR MH:E05.017$ OR MH:H01.770.644.053$ OR MH:VS3.003.001.006.005.003.002$ OR MH:Iodo OR Iodo OR Iodine OR Yodo OR MH:D01.268.380.400$ OR MH:SP4.011.097.063.999$ OR MH:SP4.021.202.133.794.825$ OR MH:Hipertensão OR Hipertensão OR Hypertension OR Hipertensión OR MH:C14.907.489$ OR MH:Glândula Tireoide OR Glândula Tireoide OR Thyroid Gland OR Glándula Tiroides OR HM:A06.407.900$ #1 AND #2 AND #3 NOT #4
ProQuest	"salt fluoridation" AND Fluoridation AND prevalence
Open Gray	(prevalence) AND (Sodium chloride, dietary OR fluorides OR Fluoridation OR Cariostatic Agents)

Clinical Trials	salt fluoridation

Appendix S2

Table 1. Description of the studies excluded from the review

Author	Year of publication	Reasons for exclusion
Angulo *et al.*	2019	A descriptive, cross-sectional study. All participants consumed fluoridated salt and therefore, no control group was evaluated.
Cahen *et al.*	1989	National survey assessing dental caries prevalence in children of 6-to-15-years-old consuming fluoridated salt for one year. No control group was evaluated.
Casanova-Rosado *et al.*	2013	The study assessed the prevalence of dental fluorosis in eight birth cohorts in Mexican schoolchildren. Data referred to the number of children evaluated by age groups were missing. Author was contacted, but unsuccessfully.
Cook *et al.*	2008	The study assessed the dental caries experience in children living in 5 villages in Mexico. In all villages there was both fluoridated water and salt available. Excluded due to overlapping of fluoride sources.
El Mir *et al.*	2020	Participants were exposed to fluoridated water, fluoride suplements and fluoridated salt. Excluded due to overlapping of fluoride sources.
García-Perez *et al.*	2013	A descriptive, cross-sectional. All participants were examined in 2010 and consumed fluoridated salt and fluoridated water and therefore, there was an ovellaping of fluoride sources and no control group.

Irigoyen-Camacho	1997	All participants consumed fluoridated salt and therefore, no control group was evaluated.
Jimenez-Farfan *et al.*	2011	Participants were exposed to fluoridated water and fluoridated salt. Excluded due to overlapping of fluoride sources.
Marthaler *et al.*	1975	Same study published in 1977 (included) with different title, language and journal.
Marthaler *et al*.	2005	Literature review.
Mejia *et al.*	1976	Missing data referred to population of the study. Author was contacted, but unsuccesfully.
Menghini *et al.*	1991	The study assessed dental caries in military recruits from three cantons (Zurich, Vaud and Basileia). Fluoridated salt was only available in the canton of Vaud but another preventive measures were also available and, therefore, an overlapping was identified.
Menghini *et al.*	1994	Participants consumed fluoridated salt and also had access to other preventive measures. Therefore, there was as an ovellaping of fluoride sources and control group not well established.
Menghini *et al.*	1995	Participants consumed fluoridated salt, but had access to other preventive measures. Therefore, there was as an ovellaping of fluoride sources and control group not well established.
Menghini *et al.*	2005	Not all participants of the study consumed fluoridated salt, and dental caries prevalence did not separate the groups considering this variable.
Meyer-Lueckel *et al.*	2002	Descriptive and cross-sectional study. All participants consumed fluoridated salt and, therefore, no control group was evaluated.
Meyer-Lueckel *et al.*	2010	Children evaluated consumed fluoridated salt and fluoridated tablets. Excluded due to overlapping of fluoride sources.
Obry-Musset	1998	Literature review.

Pérez-Pérez *et al.*	2017	Participants were exposed to fluridated salt and fluoridated water. Excluded due to overlapping of fluoride sources.
Solórzano *et al.*	2005	Descriptive study. All participants consumed fluoridated salt and, therefore, no control group was evaluated.
Stephen *et al.*	1998	Same study published in 1999 (included) with different title, language and journal.
Tramini	2005	Literature review.
Tubert-Jeannin *et al.*	2009	Only 29.5% of the families included in the study were sure about the consumption of fluoridated salt, and 17.8% did know whether they used it or not. Therefore, the group exposed was not clearly defined.
Vallejos-Sanchez et al.	2006	Missing data about the number of children per age group (6-12-years old). Author was contacted, but unsuccesfully.
Clerehugh *et al.*	1983	Population was only exposed to fluoridated water, and no groups were exposed to fluoridated salt.
Velázquez *et al.*	2003	The study used the same data of national surveys of Mexico published in other studies included in the present review. Author was contacted, but unsuccesfully.

*Negative control: those exposed (positive control) or not (negative control) to another community fluoridation measure.

FS: fluoridated salt.

Considerações Finais

CONSIDERAÇÕES FINAIS

A fluoretação do sal é uma medida comunitária em geral bem aceita pela população com o objetivo de prevenção de cárie dentária. Está atualmente presente em muitos países, tem um bom custo-benefício e possibilidade de promover uma exposição adequada ao flúor. As desvantagens desse método incluem as variáveis concentrações de flúor encontradas no sal de cozinha e também a orientação de restrição de sal que alguns indivíduos necessitam fazer.

Considerando todos esses fatores, a última revisão sistemática que havia sido publicada anteriormente a essa, que avaliava a eficácia do sal fluoretado na prevenção da cárie dentária foi publicada em 2010. Além disso, essa é a primeira que avaliou o efeito do sal fluoretado na fluorose dentária.

Esses resultados são muito importantes do ponto de vista epidemiológico e de saúde pública, pois avaliou os riscos e benefícios dessa medida comunitária. Embora a qualidade da evidência seja baixa, com a inclusão de poucos ensaios clínicos, foi possível sugerir que o uso de SF promova um efeito na prevenção da cárie dentária comparável a AF, além de não promoter aumento do risco de fluorose quando comparado a AF.

Portanto, baseado nas evidências atuais, há razões e benefícios da manutenção da fluoretação do sal nos países onde ela já está popularizada. Ademais, pode ser uma estratégia complementar em países com altos índices de cáries dentárias, com dificuldade de acesso ao Sistema de saúde bucal, especialmente onde não há outras fontes de flúor disponíveis.

Anexos

ANEXO A

REFERÊNCIAS INTRODUÇÃO GERAL

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ANEXO B

JOURNAL OF DENTISTRY
Guide for authors

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[5] Cancer Research UK, Cancer statistics reports for the UK. http://www.cancerresearchuk.org/ aboutcancer/statistics/cancerstatsreport/, 2003 (accessed 13 March 2003).

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[7] E. Coon, M. Berndt, A. Jan, D. Svyatsky, A. Atchley, E. Kikinzon, D. Harp, G. Manzini, E. Shelef, K. Lipnikov, R. Garimella, C. Xu, D. Moulton, S. Karra, S. Painter, E. Jafarov, S. Molins, Advanced Terrestrial Simulator (ATS) v0.88 (Version 0.88), Zenodo, March 25, 2020. https://doi.org/10.5281/ zenodo.3727209.

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