Silver diamine fluoride (SDF) in the management of root caries in elders

A systematic review and meta-analysis

KEYWORDS
Silver diamine fluoride
Root caries
Prevention
Elders
Geriatric dentistry

SUMMARY
This systematic review was undertaken to address the PICO question: Is silver diamine fluoride (SDF) effective in preventing and arresting root caries lesions (RCL) in elders? Systematic literature searches were conducted of electronic databases (PubMed, Embase, and CENTRAL [Cochrane Controlled Register of Trials]) and searches by hand were performed to identify studies reporting on the use of SDF in elders to prevent and arrest root caries. Prospective clinical studies were included. Two independent investigators performed the literature search and data extraction. A total of 277 studies were identified; of those 3 randomized controlled clinical trials (RCT) were included for data extraction and analysis. A meta-analysis, using a fixed-effects model, was performed on the mean active RCL present after SDF intervention compared to controls at 24 months (3 studies), and 30–36 months (2 studies) post intervention. The fixed-effects model revealed a significant decrease in the mean new active RCL post intervention with SDF compared to controls at both 24 months (95%CI: 0.265–0.638; I² = 0.0%; overall: Z = 4.749, p < 0.001), and at 30–36 months (95%CI: 0.329–0.812; I² = 0.0%; overall: Z = 4.629, p < 0.001). A funnel plot ruled out any publication bias and the risk of bias was judged to be low. This systematic review and meta-analysis provides evidence that the application of silver diamine fluoride prevents and arrests root caries in elders.
Introduction
A large number of epidemiological dental surveys have indicated that tooth retention has increased as more elders retain natural teeth into old age (White et al. 2012; Steele et al. 2011). Whilst increasing tooth retention is seen as a leap forward in the oral health of the older population it also brings with it the challenges of managing chronic dental diseases including caries and periodontal disease especially in dependent/institutionalised older adults (Budtz-Jøgensen et al. 1996). Due to factors such as diet, reduced manual dexterity and xerostomia, these chronic diseases can cause considerable pain and suffering amongst elderly patients and impair oral function (Hayes et al. 2016). In particular, dental caries remains a problem for this age group with a high prevalence of coronal and root surface caries (Damata et al. 2019; Hayes et al. 2017; Mojon et al. 1995). In the 1998 UK Adult Dental Health Survey, the proportion of adults with 18 or more sound and unrestored teeth was only 5% among those aged 55 years and over. The 2009 UK Adult Dental Health Survey indicated that this figure had improved but still remained at only 13% (Kelly et al. 2000; Fuller et al. 2011). The 2009 UK Adult Dental Health Survey reported that 27% of adults aged 65–74 years had evidence of dental caries whilst this figure increased to 40% for those aged 75–84 years (Fuller et al. 2011).

The 1998 UK Dental Health Survey showed that almost 25% of the older adults had twelve or more teeth with a root surface that was either exposed, worn, filled or decayed. The 2009 Survey reported that 73% of all adults had exposed root surfaces and this increased to 90% for those aged over 55 years. The same survey reported that 11% of 55– to 64-year-olds had

<table>
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<th>PICO focused question, criteria for inclusion, sources of information, search terms, search strategy, search filters, and search dates</th>
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<td><strong>Focus question</strong></td>
<td>Is silver diamine fluoride effective in preventing and arresting caries in elderly patients?</td>
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<td><strong>Criteria</strong></td>
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| **Inclusion criteria** |  - Professional silver diamine fluoride intervention in elders  
- Root caries  
- Patients must have been clinically examined during recall  
- Prospective clinical trials |
| **Exclusion criteria** |  - Age < 65 years  
- Minimum follow up of six months  
- Sample size of less than ten cases |
| **Information sources** |  |
| **Electronic databases** | PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL) |
| **Journals** | All peer reviewed dental journals available online in databases: PubMed, Embase, CENTRAL |
| **Others** | Popular online internet search engines (e.g. Google, Yahoo, etc.), online internet research community websites (www.researchgate.net), reference crosschecks, personal communications, searches by hand, etc. |
| **Search Terms (PICO)** |  |
| **Population** |  
#1: MeSH – (Elderly adults) OR (65+ Aged) OR (Older patient) OR (Aged patients) OR (Aged) OR (Root caries)  
#2: All fields – (Dependent elders) OR (Dependent adults) OR (Institutionalized elders) OR (Institutionalized adults) OR (Community dwelling adults) |
| **Intervention or exposure** |  
#3: All fields – (Silver Diamine Fluoride) OR (Diammine Silver Fluoride) OR (Ammoniacal Silver Fluoride) OR (Silver Ammonia Fluoride) OR (Silver Fluoride) OR (Quaternary Ammonium Compounds) OR (Saforide) OR (Riva-Star) OR (Silver Nitrate) |
| **Comparison** | No comparison was done |
| **Outcome** |  
#4: All fields – (Caries reduction) OR (Arrested Caries) OR (Caries Inactivated) |
| **Filters** |  |
| Language | Not applied |
| Species | Humans [MeSH] |
| Ages | 65+ Aged [MeSH] |
| Journal categories | Dental journals |
| **Search builder** | Search combination  
#1 OR #2 AND #3 AND #4 AND Humans AND 65+ Aged AND Dental journals |
| **Search dates** | January 1980 until 14 August 2019  
Last confirmatory online final search was performed on 14 August 2019. No further online searches were performed after this date |
active root caries compared with 20% of those aged 75–84 years (Fuller et al. 2011).

The concept of minimal intervention dentistry (MID) has evolved with an increased understanding of the caries process and the development of adhesive restorative materials. It is recognized that early carious lesions confined to enamel can be reversed and that the ‘extension for prevention’ approach is no longer appropriate in modern dentistry. The key principle of minimal intervention dentistry is early disease control and the avoidance of surgical intervention until it is absolutely essential (Frencken et al. 2012). One non-invasive medicament which has gathered interest in caries prevention and management in children and older adults is silver diamine fluoride (SDF). It is reported that silver and fluoride in an alkaline solution act synergistically to arrest carious lesions through a variety of mechanisms (Zhao et al. 2018). SDF has a bactericidal action and decreases the growth of cariogenic microorganisms; it has a re-mineralizing effect on enamel and dentine (Zhao et al. 2018). SDF has a protective effect on the dentine collagen and prevents its destruction (Zhao et al. 2018).

The aim of this review was to undertake a systematic appraisal and meta-analysis of the evidence available on the effectiveness of SDF in caries management for older adults. The focused PICO question for this systematic review was “Is silver diamine fluoride (SDF) effective in preventing and arresting root caries lesions (RCL) in elders?”

Methodology
Protocol and Registration
This systematic review and meta-analysis were conducted and reported according to the PRISMA guidelines (Moher et al. 2015). The review protocol was registered with PROSPERO: International prospective register of systematic reviews (CRD42020175693).

Eligibility Criteria
All prospective clinical studies reporting on the professional application of SDF in dependent older adults (aged 65 years and older) which satisfied the listed predefined inclusion criteria (Tab. I) were included in the systematic review.

Information Sources
Three electronic databases were searched: Medline (PubMed), Embase, and CENTRAL. Searches by hand of relevant dental journals were performed for records that were not accessible electronically or for those without an electronic abstract available. Further searches resulting from reference cross-checks were performed to identify studies that were not discovered online. The final update for all the electronic searches was performed on 14 August 2019.

Search Strategy
The search strategy was designed and set up by an expert in database searches (MS) (Tab. I). An initial electronic search was performed by a single reviewer (MS). Then the search was repeated by a second reviewer (MLG) to confirm the number of discovered articles by the search strategy. The search terms employed were either medical subject headings (MeSH) terms or keywords classified under general (all fields) category. The search terms were then combined with an “OR” and PICO categories were combined using “AND” to create a final logic search query.

Study Selection
All studies that fulfilled the inclusion criteria were included in this review. A title and abstract screening were performed by two investigators independently (MLG and MS). A final list of studies was put forth for full-text analysis and data extraction, only after a mutual agreement between the two investigators; disagreements, if any, were resolved by means of a consensus discussion. In cases of identified studies reporting on the same cohort at different time points, only the most recent publication was included in the review.

Data Collection Process
The investigators (MLG and MS) extracted data from the included studies independently and were reciprocally blinded. During data extraction, for any uncertainty involving the extracted variable, a consensus was always reached by both investigators before finalizing the extracted data. In cases of significant doubts, corresponding authors were contacted for confirmation of the extracted information.

Risk of Bias Assessment of Included Studies
The Cochrane collaboration’s tool was used for the assessment of the risk of bias of the included studies (Higgins & Green 2011).

Outcome Measure
The outcome measure in this review was the calculated mean new active carious root surfaces (or newly restored root surfaces) after SDF application compared to controls.

Synthesis of Results
Kappa (κ) statistics were calculated to confirm the inter-investigator agreement for the extracted data. A meta-analysis was performed on the included RCT for mean new active carious root surfaces after SDF application compared to controls at 24 months (3 studies included) and 30 months (2 studies included) post intervention. The weighted means across the studies were calculated using a fixed-effects model. Heterogeneity across the included studies was assessed using the I² statistics (I² statistics). The meta-analysis was performed using a meta-analysis software (CMA, version 3.0; Bio- stat, Englewood, NJ, USA), with confidence intervals set to 95% (95% CI).

Risk of Publication Bias
The risk of publication bias was explored across the included studies using a funnel plot.

Results
Study Selection
An initial search identified a total of 277 studies from the three databases. After title and abstract screening, 8 studies were selected for full text analysis and a further 12 were included from cross-checking references. Finally, three studies, all RCTs, were included for data extraction and further analyses. The flow chart of the entire search process is shown in Figure 1.

Study Characteristics
The three included RCTs (Tan et al. 2010; Zhang et al. 2013; Li et al. 2017) reported data on a total of 552 patients (SDF: n = 277; control: n = 275). All of the patients included were over 65 years old. The follow-up times for the three studies differed with one study reporting a 24-month follow-up, a second reporting at
30 months and the third one reporting at 36 months. The risk of bias for the three included studies was judged to be low (Tab. II).

**Synthesis of Results**

The calculated kappa scores ranged from 0.750 to 1.000 at the different stages of the search strategy process (Fig. 1). This indicated almost perfect to good inter-examiner reliability during the search process.

A meta-analysis was performed for the mean new active carious root surfaces (or newly restored root surfaces) after SDF application compared to controls. Due to the differing follow-up periods the two meta-analyses were undertaken, one for studies with a follow-up period of 24 months (3 studies) and one for studies with a follow-up period of 30–36 months (2 studies).

A fixed-effects model revealed a significant decrease in the mean new active RCL post intervention with SDF compared to controls at both 24 months (95%CI: 0.265, 0.638; I² = 0.0%; overall: Z = 4.749, p < 0.001) (Fig. 2), and at 30–36-months (95%CI: 0.329, 0.812; I² = 0.0%; overall: Z = 4.629, p < 0.001) (Fig. 3). According to the funnel plot analysis, a possible publi-
cation bias across the studies included in the meta-analysis was explored and ruled out (Fig. 4).

**Discussion**

This systematic review includes the first meta-analysis examining the effect of SDF in preventing and arresting root caries lesions (RCL) in dependent elders. Whilst other reviews have been published in this field, none have included a meta-analysis of the extracted data (Seifo et al. 2019; Hendre et al. 2017). This study clearly demonstrates the significant protective impact of SDF on root caries lesions in older adults at both 24 months (95% CI: 0.265-1.050; I² = 0.0%; overall: Z = 4.749, p < 0.001) and 30 months (95% CI: 0.329-0.812; I² = 0.0%; overall: Z = 4.629, p < 0.001). Similar findings are mirrored in pooled analyses for children, which clearly confirm the significant protective impact of SDF on caries (Trieu et al. 2019).

A protective non-invasive medicament for preventing root caries lesions is of particular interest due to the nature of this destructive dental disease. Not only is it progressive and leads to tooth loss when left untreated, it may also present a life-threatening challenge to elders who present with cognitive impairment or swallowing disorders. Root caries may disconnect the clinical crown from the root, which remains in the dental socket. Unfortunate cases have been reported, where multi-unit bridges have been aspirated after being disconnected from the roots by root caries, leading to serious complications or even death (Oghalai 2002). Hence prevention in dependent elders is not limited to tooth conservation and prevention of disease, it also implies assuring a “safe” oral environment, when it comes to aspiration and aspiration pneumonia.

Root caries may exhibit mixed cavity margins positioned in enamel as well as dentine (Wefel et al. 1985). Restoration of this cavity type is extremely challenging with respect to the lack of restorative materials which bond equally well to both dental tissues. The evidence base for the selection of a restorative material for the restoration of a root surface lesion is neither plentiful nor convincing. Most of the scientific literature examines lesions restored with amalgam, glass ionomer cement (GIC), resin-modifi-
fied glass ionomer cement (RMGIC), modified polyacid resins ("compomers") or composite resins. A systematic review published in 2016 concluded that there was insufficient evidence to recommend any specific material (Hayes et al. 2016). Difficulties in treating root caries are not limited to the choice of the restorative material. The shape of the lesions is often circular, rendering the application of the restorative material a serious challenge. The proximity to the gingival margin often precludes an operation site free from saliva, crevicular fluid or even blood. Placing a rubberdam may be difficult where the lesion reaches beyond the gingival margin. Furthermore, rubberdam may not be suitable in frail geriatric or bedbound patients with a limited capacity to undergo restorative treatments.

However, failure rates of root caries restorations across all materials was extremely high; 82% of GIC restorations were considered a “failure” after just 24 months. 25% of all composite restorations had developed recurrent caries after two years. Despite the poor survival rates of GIC restorations, many authors still concluded that GIC was the material of choice for root caries as conventionally setting glass ionomer cements were associated with protection against secondary caries – even after the filling itself had been lost (De Moor et al. 2011). Clinical judgement is essential in each individual case and the choice of restorative material to restore a carious lesion on a root surface is influenced by the location of the lesion, aesthetic requirements of the patient, moisture control and future caries risk.

In order to avoid further tooth tissue loss and enhance prevention among elderly individuals, MID should always be the first line of treatment for caries. It prioritises prevention, patient’s information and guidance to empower them to be responsible for their own oral health and intervene as conservatively as possible when a surgical approach is judged necessary, thus avoiding unnecessary tooth tissue removal. It was born from the evolution in the understanding of the caries process and the mechanisms involved in its beginning, progression and control, together with improved dental materials. According to the MID concept, early caries detection and caries risk assessment, remineralization of demineralized enamel and dentine and optimal caries-preventive measures should always be used throughout an individual’s life, and operative interventions should only be employed when all of these have failed (Frencen et al. 2012). For older patients with a high caries rate or poor compliance with oral hygiene instruction, there are a number of surgery-based interventions to reduce caries risk including SDF. Unfortunately, in many countries, including the United Kingdom, SDF is not currently licensed for prevention or arrest of dental caries. One of reasons why SDF is not widely used may be that, despite its undoubted efficiency and efficacy in arresting RCL, its application on the dental tissues leads to a persistent black staining. Such aesthetically displeasing appearances will have obvious psycho-social implications when occurring in the visible zone, which precludes its use in patients with high aesthetic demands, where optically more pleasing preventive and restorative measures could readily be applied. This situation is different in children and dependent elders, where operative dentistry does not often meet the compliance needed for performing a state-of-the-art procedure. When functional impairment and chronic diseases dominate daily life, the advantages of a fast and non-invasive intervention to arrest root caries may seem an attractive alternative to long and invasive restorative procedures, even if the aesthetic outcome of the latter may be more favourable. However, the RCL sites are often not within the visible area, and therefore do not create the above-mentioned disadvantages. However, ethical aspects of a potential stigmatisation of patients with “black” teeth must always be considered and it seems particularly important to obtain the patient’s informed consent before applying the procedure.

Given the advantages of a chemical management of root caries in frail and geriatric patients over invasive and restorative measures, it seems obvious that SDF is not the only agent ever been tested for this purpose. Contemporary chemical management of root caries comprise high concentration fluoride tooth pastes and varnishes (Srinivasan et al. 2014). However, their effectiveness to arrest RCL seems to fall only second to the therapeutic effect of SDF (Gluzman et al. 2013). Still, these agents gain in popularity, given that they do not stain the tooth structure in an unpleasing and permanent manner.

Given the above-mentioned regional restrictions, it is not surprising that the studies included in this systematic review and meta-analysis arise from a small number of geographical locations. All three included RCTs were carried out in Hong Kong where SDF is licensed for prevention or arrest of dental caries (Tan et al. 2010; Zhang et al. 2013; Li et al. 2017). Whilst all three studies were well designed RCTs, with a low risk of bias, the external validity of this work must be questioned. Future research should target undertaking well designed clinical studies of SDF in other countries and settings around the world.

Conclusion
This systematic review and meta-analysis provides evidence that application of SDF prevents and arrests root caries in elders.

Zusammenfassung
Einleitung

Material und Methoden
Systematische Literatursuchen wurden in elektronischen Datenbanken (PubMed, Embase und CENTRAL [Cochrane Controlled Register of Trials]) sowie per Handrecherche durchgeführt, um Studien zu identifizieren, die über die Verwendung von SDF bei älteren Menschen zur Prävention und zur Arretierung von Wurzelkaries berichteten. Zwei unabhängige Prüfer führten die Identifizierung, das Screening sowie die Einbeziehung der Artikel durch. Die Datenextraktion wurde von den beiden Untersuchern unabhängig und gegenseitig verblindet.
durchgeführt. Die Zuverlässigkeit zwischen den Ermittlern wurde unter Verwendung des Cohens-Kappa-Koeffizienten (κ) berechnet. Es wurde eine Metaanalyse über aktive Wurzelkarischesionen durchgeführt, die nach der Intervention mit SDF vorhanden waren.

**Resultate**

Insgesamt wurden 277 Studien identifiziert und 20 Studien für die Daten-Volltextanalyse eingeschlossen. Schliesslich wurden drei randomisierte kontrollierte klinische Studien zur Datennextraktion und -analyse eingeschlossen. Der berechnete Cohens-Kappa-Koeffizient (κ) wurde als gut bis perfekt angesehen und lag zwischen 0,750 und 1,000. Zwei Metaanalysen über die aktiven RCL, die nach der SDF-Intervention vorhanden waren, wurden unter Verwendung eines Paneldatenmodells mit fixen Effekten gegen Kontrollen durchgeführt. Eine Metaanalyse wurde an drei Studien mit einer Nachbeobachtungszeit von 24 Monaten nach der Intervention mit SDF durchgeführt. Die zweite Metaanalyse wurde an zwei Studien mit einer Nachbeobachtungszeit von 30 bis 36 Monaten nach der Intervention mit SDF durchgeführt. Das Paneldatenmodell mit fixen Effekten zeigte eine signifikante Abnahme der neuen aktiven RCL nach der Intervention mit SDF im Vergleich zu den Kontrollen, sowohl nach 24 Monaten (95% CI: 0,265–0,638; I² = 0,0%; Total: Z = 4,749, p < 0,001) als auch nach 30 bis 36 Monaten (95% CI: 0,329–0,812; I² = 0,0%; Total: Z = 4,629, p < 0,001). Gemäss der Trichterdiagrammanalyse wurde ein möglicher Publikationsbias in den in der Metaanalyse einbezogenen Studien entdeckt und ausgeschlossen. Das Verzerrungspotenzial der eingeschlossenen Studien wurde als gering eingestuft.

**Fazit**

Dieses systematische Review und die Metaanalyse liefern Hinweise darauf, dass die Anwendung von Silberdiaminfluorid Wurzelkaries bei älteren Menschen verhindert und arretiert.

**Résumé**

**Introduction**

Le fluorure diamine d’argent (SDF) a suscité un intérêt pour la prévention et la prise en charge des caries chez les enfants. Il a été rapporté que l’argent et le fluorure contenues dans une solution alcaline agissent en synergie pour arrêter les lésions cariées par divers mécanismes. Le SDF une action bactériicide et diminue la croissance des microorganismes cariogènes. Il a un effet reminéralisant sur l’émail et la dentine. De plus, le SDF a un effet protecteur sur le collagène dentinaire et aide à prévenir sa destruction. Des études ont démontré des résultats prometteurs avec le SDF dans l’arrêt des caries radiculaires chez les personnes âgées. Le but de cette revue systématique était d’entreprendre une évaluation systématique et une méta-analyse des preuves disponibles sur l’efficacité du SDF dans la prise en charge des caries chez les personnes âgées. La question PICO formulée aux fins de cet examen était : « Le fluorure diamine d’argent (SDF) est-il efficace pour prévenir et arrêter les lésions carieuses des racines (RCL) chez les personnes âgées ? »

**Matériaux et méthodes**

Des recherches documentaires systématiques ont été menées dans des bases de données électroniques (PubMed, Embase et CENTRAL [registre Cochrane des essais contrôlés]) pour identifier les études faisant état de l’utilisation du SDF chez les personnes âgées pour prévenir et arrêter les caries radiculaires. Deux enquêteurs indépendants ont procédé à l’identification, au dépistage ainsi qu’à l’inclusion des articles. L’extraction des données a été réalisée par les deux chercheurs de manière indépendante et réciproquement en aveugle. Une fiabilité inter-investigateur a été calculée en utilisant le kappa de Cohen (κ).

**Résultats**

Au total 277 études ont été identifiées, 20 études ont été incluses pour l’analyse du texte intégral des données. Enfin, trois essais cliniques contrôlés randomisés ont été inclus pour l’extraction et l’analyse des données. Le kappa calculé (κ) a été considéré comme bon à parfait et varié entre 0,750 et 1000. Deux méta-analyses ont été réalisées à l’aide d’un modèle à effets fixes sur les RCL actifs moyens présents après l’intervention SDF contre les contrôles. Une méta-analyse a été réalisée sur trois études avec une période de suivi de 24 mois après l’intervention avec SDF ; et la deuxième méta-analyse a été réalisée sur deux études avec une période de suivi de 30 à 36 mois après l’intervention avec SDF. Le modèle à effets fixes a révélé une diminution significative de la moyenne des nouveaux RCL actifs après intervention avec SDF par rapport aux témoins à 24 mois (95 % CI : 0,265–0,638 ; I² = 0,0 % ; Globalement : Z = 4,749, p < 0,001), et à 30–36 mois (95 % CI : 0,329–0,812 ; I² = 0,0 % ; Globalement : Z = 4,629, p < 0,001). Le risque de biais des études incluses a été jugé faible.

**Conclusion**

Cette revue systématique et méta-analyse fournit des preuves que l’application du fluorure diamine d’argent prévient et arrête les caries radiculaires chez les ainés.

**References**


