



## Systematic Review



## The Impact of School-Based Caries Prevention Programs on DMFT Scores and Oral Health Behaviors in School Children

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## ABSTRACT

Oral health promotion is recognized as one of the fundamental components of health-promoting schools. However, few studies have demonstrated the efficacy of supportive school environments for school children's Oral health. This systematic review evaluates the impact of school-based caries prevention programs on DMFT scores and Oral health behaviours in school children. **Objective:** To evaluate the impact of school-based caries prevention programs on DMFT Scores and Oral Health Behaviors in school children. **Methods:** Databases like PubMed, Google Scholar, Cochrane Library, Springer, and Science Direct were searched from January 2009 to February 2024. Prisma guidelines were followed; 1,950 studies were identified on the first search, titles, and abstracts of 500 papers were screened, 500 full-text papers were screened for eligibility, and 25 studies meeting the inclusion criteria were evaluated, relevant information was extracted, and a systematic review was conducted. Twenty-five studies were included in the systematic review. **Results:** These results indicate the significant role of SCPP among school-going children. Children with school-based caries prevention programs compared to those with no school-based caries prevention programs showed improved DMFT scores, reduced caries increment, healthy oral health behaviours, consistent Oral health hygienic habits, frequent use of flossing, fluoride toothpaste and mouth rinsing, and increased caries prevention knowledge. **Conclusions:** It was concluded that based on the pooled results, school-based caries prevention programs provide better, easily accessible, and sustainable caries prevention activities to school children to improve DMFT scores and Oral health behaviours.

## INTRODUCTION

Oral diseases, also known as non-communicable diseases (NCDs), are preventable oral health conditions. It is a major public health problem affecting 60-90% of school-going children and adults in developing countries [1]. Dental caries is the major chronic disease affecting more than 600 million children globally and 135 million children in the Southeast Asian region. [2]. 35% of the world's population is affected by caries. Of which, 2.4 billion and 486 million populations are reported with caries of permanent and primary teeth, respectively [3]. Dental caries is caused by

the bacterial fermentation of dietary carbohydrates in the susceptible host. Smooth surface caries in primary maxillary anterior teeth, and missed, or decayed surfaces are indicative of early childhood caries (ECC) in children <6 years [4]. Oral health (OH) conditions, if left untreated, may lead to gingivitis, oral submucous fibrosis, and oral cancer. It can cause pain, discomfort, poor ability of children to eat or drink, malnutrition, speaking and sleeping issues, impaired social and behavioural patterns, and low self-esteem [5]. Caries potentially contribute to reduced school



attendance rates, lack of children's proper concentration, and poor participation in school activities. OH is recognized as equally important as general health conditions like cardiovascular disease (CVD), mental health conditions, diabetes mellitus (DM), and cancers. Due to increased cost and uneven distribution of OH services in developing countries; developed countries are now reported to be well below the WHO's goal of less than 3 decayed, missing, or filled teeth (DMFT) per 12-year-old child [6]. DMFT index is a valuable and simple tool used to determine, measure, and monitor the oral health status in a community. Preventive behaviours play a pivotal role in ensuring proper OH for children. The scale of the preventive behaviour may include aspects such as oral health hygiene, accessibility to OH services, appropriate oral care, use of clean objects and fluoridated toothpaste. These dimensions along with access to caries prevention programs should be conducted periodically from an early age to prevent the occurrence of poor OH conditions in school children. The limited OH education (OHE) includes caries preventive measures, inadequate access to OH services, increased sugar consumption, and reduced exposure to fluoride products compound ECC risk over time. Public health managers and stakeholders, especially in lower-middle-income countries (LMICs), should take evidence-based preventive steps to prevent ECC and concurrently promote OH. OHE is an important and effective public health prevention program tool as it provides not only caries education but also curative, preventive, and promotional dental health activities [7]. Promoting OH in children by using health-promoting schools (HPS) has been recommended by the World Health Organization (WHO). HPS is a comprehensive school-based concept focused on developing healthy lifestyles, and behaviour, and preventing diseases by engaging schoolchildren in healthy school activities using a multi-sectoral approach. WHO first launched the Global School Health Initiatives in 1995 [8]. This key intervention helps countries, especially LMICs, to develop caries prevention programs and build partnerships between health and educational organizations [9]. Globally, schools have been identified as an ideal environment and opportunity for caries prevention as children spend maximum time in their school. A school-based caries prevention program (SCPP) is a preventive strategy aimed at improving the OH status of school children during school years. It exclusively focuses on providing accessible and appropriate caries prevention guidance during school years that last a lifetime. They are considered supportive settings to promote OH in terms of implementing policies and caries prevention programs in schools to improve caries awareness, nutritional intake, school safety for dental injuries, caries screening and dental referral facilities [10]. According to Tahani et al., active involvement of school children and their caregivers in SCPPs are more likely to report improved caries knowledge and lower DMFT scores [11]. SCPPs may consist of a range of initiatives such as integrating OH services and caries prevention programs as part of the curriculum,

implementing OH-enhancing social environments, supervised daily group dental brushing, and topical fluoride application programs [12]. The majority of these programs in school settings are delivered using either traditional approaches such as lectures, demonstrations, and models or the utilization of modern approaches such as flipcharts, videos, slide presentations, and other actionable tasks like daily brushing, fluoridated water, and toothpaste applications [13].

This study aims to evaluate the impact of school-based caries prevention programs on DMFT Scores and Oral Health Behaviors in school children.

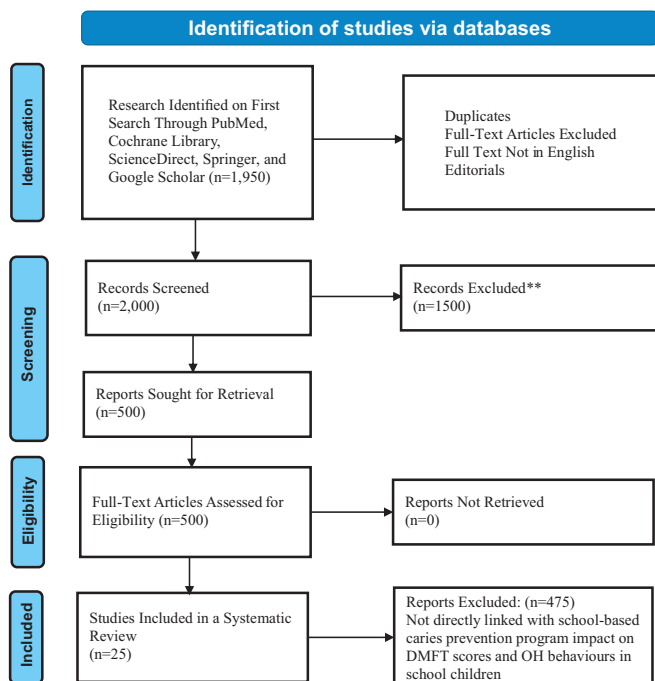
## METHODS

The final eligibility of papers was analyzed by using the inclusion and exclusion criteria (Table 1).

**Table 1:** Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Papers published between January 2009 to February 2024	Studies that have been previously included in the reviewer are duplicates of other included studies.
Directly linked to SBCPP, DMFT scores, and OH behaviours	Studies with inadequate methodological rigour, such as case reports or poorly designed observational studies.
Studies written in English language only	Studies with insufficient or unreliable data on SBCPP implementation, DMFT scores, or OH behaviours.
Studies conducted in school settings among school children (aged 5-14 years) as target population	Studies with a high risk of reporting bias, such as selective reporting of outcomes or lack of blinding.
Studies using SBCPP to address OH behaviors and improve DMFT scores	Studies with extreme or outlier results could significantly distort the overall findings.
Papers mentioning the impact of SBCPP on DMFT scores and OH behaviours in school children	Studies conducted in non-school settings that not accurately reflect the challenges and opportunities of school-based interventions.

PubMed and Google Scholar were systematically searched to detect all the relevant studies published during the last 15 years (January 2009 to February 2024) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement by using the following search key terms "caries", "school children", "decayed, missing, or filled teeth", "impact", "DMFT score", "oral health", "dental", "caries prevention", "oral health behaviours", "school-based program." Initially, a total of 1,950 studies were identified, a total of 2,000 potential studies were screened, and 1500 studies were excluded, followed by an in-depth reading of 500 remaining full-text articles led to the exclusion of 475 studies. 25 studies were included for qualitative synthesis (Figure 1).



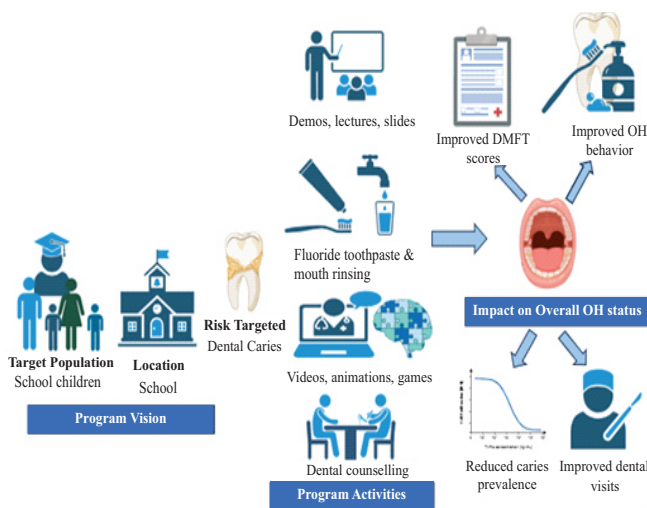
**Figure 1:** Screened Studies Included in the Systematic Review

The program components include 1): Program vision involving schoolchildren (aged 5-16 years) as the target population and school as the location for implementation of the prevention program 2) program activities imparted by schoolteachers or dentists using OHE methods such as OH demos, lectures, games, and dental counselling 3). The impact of SCPP on overall health statuses such as improved DMFT score, OH behaviors and hygiene, and

**Table 2:** Summary of Study Findings Evaluated

Sr. No.	Country	Total Participants / Studies	Intervention	Outcome	Evaluation Method	Reference
1	Japan	2573 Participants	After-Lunch Tooth-Brushing Program	Zero Excess DMFT	ZINB	[14]
2	Australia	34 Studies	SCPP	Improved DMFT Scores	DMFT Index	[15]
3	India	1,100 Participants	OHE	Improved Oral Hygiene Status	OHI-S	[16]
4	India	600 Participants	OHE	Improved OH Behaviors	KAP, DMFT Scores	[17]
5	Kuwait	440 Participants	OHE	Improved DMFT Scores	DMFT Indices	[18]
6	India	276 Participants	OHE	Improved Caries Status	DMFT Index	[19]
7	China	514 Participants	Monthly OHE Sessions	Improved OH Behaviours	DMFT Index	[20]
8	China	1,334 Participants	OHE	Reduced DMFT Increment	DMFT Index	[21]
9	Iran	12 Studies	OHE	Improved OH Behaviours	KAP Score	[22]
10	India	120 Participants	SCPP	Improved DMFT	Person Chi-Square	[23]
11	Taiwan	340 Participants	HPS Framework	Improved Hygienic Behaviours	Linear & Logistic Regression Model	[24]
12	Iran	470 Participants	OHE	Improved OH Behavior	SPSS	[25]
13	Iran	82 Participants	OHE	Improved Self-Care Behaviour	Mann-Whitney U-Test	[26]
14	Iran	200 Participants	OHE	Improved OH Behavior	SPSS	[27]
15	India	200 Participants	OHE	Improved OH Behavior	ALG	[28]
16	India	100 Participants	OHE	Improved Hygienic Behaviours	KAP Score	[29]
17	Sudan	423 Participants	OHE	Improved OH Behaviour	SPSS	[30]
18	USA	8,207 Participants	SCPSP	Improved DMFT Score	DMFT Index	[31]
19	Japan	173 Participants	OHE	Improved Hygienic Behaviours	OHI-S	[32]

reduced caries prevalence. The overview of the program design of the SCPP as per the systematic review was illustrated(Figure 2).



**Figure 2:** Program Design of the SCPP as Per the Systematic Review

## RESULTS

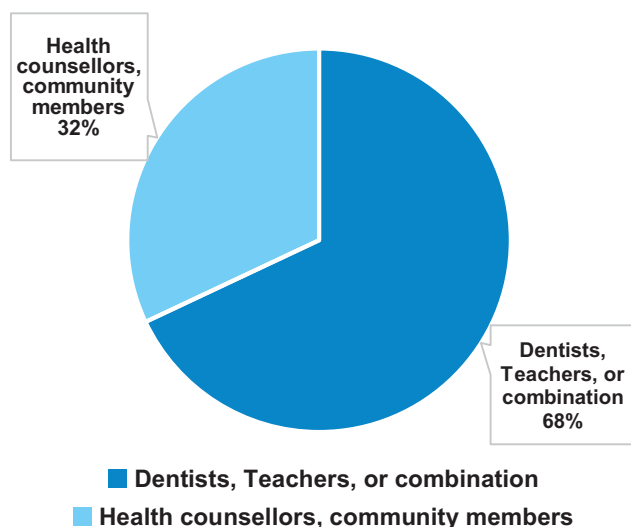
This systematic review yielded a total of 23 studies, of which, 6 were RCT studies, 5 were cross-sectional studies, and 5 were cohort studies. The remaining studies were clinical trials, longitudinal studies, quasi-experimental studies, and follow-up studies. A combined total of 28,882 schoolchildren included in the studies have been evaluated in this systematic review. A comprehensive summary of the included study findings in 23 studies is presented (Table 2).

20	Pakistan	175 Participants	OHE	Higher Combined KBS Scores	GEE	[33]
21	Bangladesh	944 Participants	OHE	Reduced Caries Prevalence	McNemar's Chi-Square	[34]
22	USA	6,927 Participants	SCPP	Reduced Caries Prevalence	DMFT Index	[35]
23	Kuwait	300 Participants	SOHP	Better OHRQoL	X <sup>2</sup> Analysis	[36]

Zero-inflated negative binomial (ZINB); OHI-S, oral hygiene index simplified; OHE, oral health education; RCT, randomized controlled trial; HPS, health-promoting school; GEE, generalized estimating equations; FMR, fluoride mouth rinse; SOHP, school-based OH program; OHRQoL, oral health-related QoL; SPSS, statically package for the social science; ALG, absolute learning gain; SCPP, school-based caries primary and secondary prevention program; SCPP, school-based caries prevention program; DMFT, decayed, missing, or filled teeth.

Seventeen studies used OHE interventions in the SCPP. Three strategy types were used in the studies evaluated (Figure 1). Among these, 11 studies used OHE interventions comprising OH lectures, practical demonstrations, caries prevention booklets, OH talks and counselling sessions. The remaining 6 studies used OHE based on OH-related animations, games, and videos. These interventions were delivered by either dentist, teacher, peer, or a combination of teacher and dentist. Eight studies included SCPP strategies consisting of the topic antibacterial therapy, after-lunch tooth-brushing, daily teacher-supervised group tooth-brushing, and fluoride mouth rinse (Figure 3).

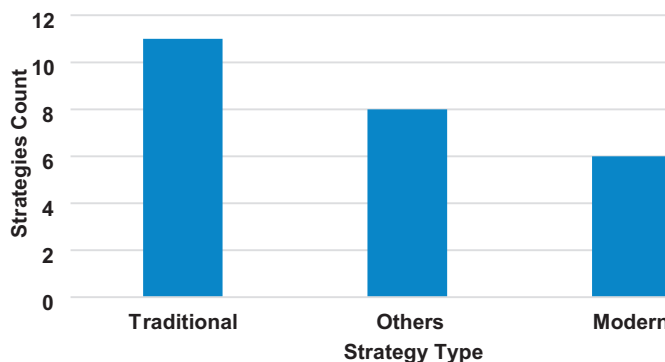
### SCPP Key Actors



**Figure 3:** OHE Interventions Delivered by Key Actors As Per Systematic Review

SCPP strategies implemented in the included studies as per systematic review are studied. Traditional strategies include lectures, demonstrations, and OHE talk. Modern activities include caries animation, videos, and games. Others include fluoride mouth rinsing, daily supervised toothbrushing, and flossing practice (Figure 4).

### SCPP Strategies Delivered



**Figure 4:** SCPP Strategies Implemented in the Included Studies

The WHO-modified DMFT index and KAP scores were used by the majority of the studies to measure the changes in DMFT scores and OH behaviours. Other studies used OHI-S, Person chi-square, linear & logistic regression model, SPSS, Mann-Whitney U-test, ALG, McNemar's chi-square, and X<sup>2</sup> analysis to assess the improvements in levels of OH hygiene status, OHRQoL, and caries prevalence (Table 3).

**Table 3:** Table of Reference Used in Included Studies to Analyze DMFT Scores and OH Behaviors

Characteristics	Standard Reference Used In Studies
DMFT Scores and OH Status	WHO Modified DMFT* Index (Reference Values=0-12)
OH Behaviors	KAP** Score
Oral Hygiene Status	OHI-S (Reference Values =1-10, Ranging from Very Poor to Perfect Oral Hygiene)
Mean Plaque and Gingival Score	Silness And Loe Plaque Index, Low and Silness Gingival Index
Combined OH Knowledge, Behavior, and Hygiene Status	KBS*** Score (Ranging From 0 To 36)
Caries Prevalence (Follow-Up Data Compared to Baseline)	McNemar's Chi-Square Analysis
Ohrqol	X <sup>2</sup> Analysis
Statistical Analysis	The Linear and Logistic Regression Model, Person Chi-Square, Quasi-Likelihood Poisson Regression

DMFT, Decayed, Missing and Filled Teeth; OH, oral health; KAP, Knowledge, attitude, and practice; OHI-S, Oral hygiene index simplified; KBS, knowledge, behaviour, and hygiene status; OHRQoL, OH-related quality of life \*DMFT score is a useful index in determining OH status by taking the sum of several D (decayed), M(missing) due to caries, and F (filled) teeth in the permanent teeth. \*\*KAP, also known as knowledge, attitude, behaviour, and practice surveys. It is a quantitative method that involves a predefined standardized questionnaire. It provides valuable

insights into qualitative and quantitative information in health-related behavioural research. \*\*\*The KBS index is constructed by combining scores of OH knowledge, behaviour, and hygiene status.

## DISCUSSION

Oral health (OH) is a fundamental part of general health. Several chronic illnesses such as asthma, diabetes, and oral cancer. Globally, the DMFT scale has been used as an important index for over 70 years to assess overall OH status and dental health. School-based caries prevention programs (SCPP) can positively impact the DMFT scores and OH behaviours in school children. A cross-sectional study consisting of 2573 children aged 10-11 years was conducted by Tashiro *et al.*, in Japan. The study found that children exposed to supervised after-lunch toothbrushing programs compared to children from schools without it showed higher odds ratio (OR) for zero excess DMFT (OR=1.47, 95% CI=1.00-2.15,  $p=0.049$ ) as indicated by zero-inflated negative binomial (ZINB) [14]. A systematic review and meta-analysis of 34 studies published between 1996 and 2021 was conducted by Guray *et al.*, in Australia. Among them, 30 studies were experimental studies and 4 were observational studies conducted in LMICs. The study showed that SCPPs had a positive impact on dental caries as measured by DMFT index (standardized mean difference (SMD)=- 0.33; 95% CI - 0.56 - 0.10;  $p=0.005$ , DMFT and DMFT/ S (decayed, missing, and filled teeth/ surfaces) score >1 Risk ratio (RR)=0.70; 95% CI 0.53 to 0.94;  $p=0.02$ ) and plaque scores (SMD=-0.32; 95% CI - 0.46 to -0.18;  $p<0.00001$ ) [16]. A meta-analysis of 7 RCTs published between 2010 and 2019 (A combined total of 1,100 children aged 5-16 years) was undertaken by Karuveetil *et al.*, in India. The Intervention group (IG) received OHE methods such as demos, videos, posters, and oral hygiene instructions given by dental health professionals and the control group (CG) received traditional OHE methods such as OH talk or counselling. The study found that children exposed to IG compared to CG showed improved oral hygiene status and dental caries as indicated by oral hygiene index simplified (OHI-S), debris status, and DMFT index (cumulative mean difference (CMD); -0.37 (-0.74, 0.00), -0.20(0.33, -0.07), and -0.17(0.73, 0.38), respectively) [17]. A non-randomized controlled trial consisting of 600 school children (Group A; OHE imparted by a dental professional=300 school children, group B; OHE imparted by schoolteacher=300 children) was conducted by Alsumait *et al.*, in India. The results of the data analysis using knowledge, attitude, and practice (KAP) and DMFT scores indicated that curriculum-based educational OH intervention significantly improved OH behaviours and

reduced caries experience among Indian school children (DMFT score; preintervention =  $0.98 \pm 1.69$  and post intervention= $0.75 \pm 1.51$ , KAP score; Group A= $10.74 \pm 0.60$  and group B= $10.64 \pm 0.60$ ) [18]. A cross-sectional study comprising 440 primary school students (aged 11-12 years) was conducted by Bhardwaj *et al.*, in Kuwait. Study participants were classified into 2 groups; the school OH program (SOHP) group received at least 1 OHE session on the application of fluoride varnish and fissure sealants and the non-SOHP group without any OHE activity. The study found that SOHP children compared to non-SOHP children reported statistically significant differences in mean DMFTs as determined by DMFT indices (mean DMFTs for SOHP and non-SOHP children= $1.41$  (1.66) and  $7.24$  (7.78), respectively, ( $p<0.001$ )[19]. Gurav *et al.* conducted a cohort study consisting of 276 schoolchildren (aged 12-15 years old) in the Government Senior Secondary School, Sajauli India. The study found that the OHE program significantly improved mean plaque and gingival score, and caries status among participants irrespective of gender ( $p>0.05$ ) as assessed by Silness and Loe plaque index, Low and Sillness gingival index, and WHO-modified DMFT index, respectively [16]. A clinical trial comprising 514 kindergarten children (aged 1-3 years) was conducted by Shan *et al.* The study reported that IG compared to CG showed a higher percentage of daily toothbrushing twice a day (87.6% vs. 69%,  $p<0.001$ ), and reduced DMFS increment as determined by DMFT index ( $p=0.09$ )[20]. Similar findings were also reported in a RCT consisting of 1,334 preschool children (aged 3 years) by Alsumait *et al.*, in China [18]. A cluster RCT comprising 2021 schoolchildren (aged 6-12 years) was conducted in Switzerland. IG participants ( $n=1107$ ) received a 21-day brush day & night brush program and CG participants ( $n=915$ ) did not receive it. The study revealed that IG compared to CG showed a 45% increased probability of no worsening in the DMFT score as indicated by the DMFT index [19-21]. OH behaviours and beliefs are built during childhood, therefore schools can provide an ideal environment to prevent caries increment [25]. SCPP aims to promote healthy OH behaviours and the adoption of healthy lifestyles such as daily toothbrushing, fluoride nutrition, and fissure sealant application [37]. A two-decade systematic review and meta-analysis of 12 studies (5 were individual RCTs, 4 cluster-RCTs, and 3 Quasi-experimental research work), including 2,838 students (aged 6-18 years) were performed by Dadipoor *et al.*, in Iran. IG received educational interventions such as lectures, albums, movies, and dental instructional models and the comparison group (CG) received any OHE intervention. The results of the RevMan 2014 analysis demonstrated that IG

compared to CG showed improved OH behaviours and outcomes in terms of knowledge, attitude, behaviour, plaque and gingival index (SMD; knowledge=3.31, 95% CI 2.52 to 4.11, attitude=1.99, 95% CI 0.43 to 3.54, behaviour = 4.74, 95% CI 3.70 to 5.77, plaque index (PI)=-1.01, 95% CI -0.36 to 1.02, gingival index (GI)=0.33, 95% CI -0.36 to 1.02) [38]. A longitudinal study comprising 120 schoolchildren (aged 8 to 10 years) was conducted by You et al., in India. The results of the study found that children with parental participation compared to children without parental participation in SCPP showed statistically significant changes, after the 36<sup>th</sup> week of program implementation, in mean DMFTS, lower caries increments, improved OHI, as assessed by person chi-square, quasi-likelihood Poisson regression ( $p < 0.001$ ) [39]. A quasi-experimental study comprising 340 schoolchildren (IG with HPS framework=166 children, CG without HPS framework=174) in rural high caries (>68%) elementary school was conducted by Wei et al., in Taiwan. The study found that IG compared to CG reported increased participation in follow-up to OH-related knowledge (95% CI=0.27 to 3.28), improved hygienic behaviours (95% CI=0.76 to 2.15), self-efficacy regarding flossing and fluoride toothpaste (aOR=5.88, 95% CI=2.31 to 14.93) as determined by linear and logistic regression model [24]. Similar findings were also reported in a cluster RCT conducted by Salahshour et al., among 470 elementary students in Iran [25]. An RCT consisting of 82 schoolchildren (aged 6-12 years) (IG; OHE games and animations=38 students, CG; routine school OHE=44 students) was conducted by Hashemi et al., in Iran. The study revealed that IG compared to CG showed improved OH self-care education and behaviour, and self-efficacy, as indicated by data analysis, performed 5 months post-intervention using Mann-Whitney U-test (3.8 to 4.8, 36.8 to 48.9, and 17.07 to 18.29, respectively,  $p > 0.05$ ) [26]. These findings were similar to a quasi-experimental study comprising 200 schoolchildren conducted by Mohamad Khan et al., in Iran, a cross-sectional study undertaken by Sinha et al., among 200 schoolchildren, RCT by Gauba et al., in India among 100 children (10-12 years), cross-sectional study by Albani et al., among 423 schoolchildren in Sudan [27-30]. A prospective cohort study comprising 8,207 schoolchildren (aged <12 years) was conducted by Ruff & Niederman., in the USA. Two caries prevention programs were designed: primary and secondary prevention program (6584 participants); glass ionomer sealant and interim therapeutic restoration activities, primary prevention program only (1623 participants); glass ionomer sealant. The study found that students in primary and secondary prevention programs compared to primary

prevention programs only demonstrated a reduced risk of untreated decay on permanent dentition (OR=0.77, 95% CI=0.60, 0.98) [31]. A 6-month follow-up study comprising 173 schoolchildren (aged <12 years) was conducted by Nguyen et al., in Japan. The WHO-modified debris index (DI) showed that OHE IG compared to CG (with no OHE intervention) reported improved OH knowledge ( $p < 0.01$ ), behaviour ( $p < 0.05$ ), and hygiene ( $p < 0.001$ ) [32]. A 2-year cluster RCT was conducted by Haleem et al., among 175 schoolchildren in Pakistan. The generalized estimating equations showed that IG (OHE imparted by either a dentist or a teacher) compared to CG (did not receive any form of OHE) reported higher combined OH knowledge, behaviour, and hygiene status (KBS) scores ( $p < 0.001$ ) [33]. A cohort study conducted by Haque et al., among 944 schoolchildren in Bangladesh compared baseline data regarding OH knowledge, attitude, and practice scores with 6 months of follow-up. The results of McNemar's chi-square analysis revealed that follow-up compared to baseline showed OHE intervention significantly reduced caries prevalence among study participants to 42.5% ( $p < 0.01$ ), higher healthy OH practices (AOR=1.64; 95% CI=1.12, 3.38), OH knowledge (95% CI=1.87, 3.45), and OH attitude (95% CI=1.44-2.87) [34]. A clinical trial comprising 1,363 children (grade 1-5) was conducted in the USA. The study found that the fluoride mouth rinse (FMR) program reduced caries prevalence and improved mouthwash practice in high-risk schools ( $\geq 1$  untreated carious teeth) compared to low-risk schools (<1 untreated carious teeth) (55% vs. 10% caries reduction in 5-6 years of FMR participation compared to none). Starr et al. conducted a 6-year prospective open cohort study consisting of 6,927 children exposed to SCPP in 33 US public elementary schools. The study found that SCPP activities such as fluoride varnish, teacher-supervised daily toothbrushing, fluoride toothpaste, and oral hygiene instructions reduced untreated caries prevalence by >50% (95% CI) [35]. A cross-sectional study consisting of 300 schoolchildren (aged <13 years) was conducted by Alsumait et al., in Kuwait. The X<sup>2</sup> analysis showed that children attending SOHP compared to non-SOHP demonstrated better oral health-related QoL (OHRQoL) and overall OH status (OR=2.28, 95% CI=1.41 - 3.68,  $p < 0.001$ , OR=2.85, 95% CI=1.31-6.18,  $p = 0.008$ , respectively) [18].

## CONCLUSIONS

It was concluded that this systematic review provides a detailed comprehensive review of the impact of SCPP on DMFT scores, OH behaviours in terms of daily toothbrushing, flossing, OH hygiene habits, use of dental care products, and a routine visit to the dentist in school children. The study found that SCPP demonstrated a

positive correlation with the DMFT scores and OH behavioural patterns among school children.

### Authors Contribution

Conceptualization: SM

Methodology: SM, NI, ZNM, SA, ME

Formal analysis: MAAA

Writing review and editing: PM, AM

All authors have read and agreed to the published version of the manuscript

### Conflicts of Interest

All the authors declare no conflict of interest.

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