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# **Dental Caries among the Elderly in Iran: A Meta-analysis**

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# **Abstract**

**Background:** The prevalence of dental caries among the elderly is high worldwide, and dental caries cause the major burden of oral diseases. This meta-analysis aimed to determine the dental caries experience among the elderly in Iran.

**Methods:** A systematic review of the published and grey literature on Iranians aged 65 years or older was performed. Six international and local databases provided the most comprehensive population-based studies. National oral health surveys and national disease and health surveys were considered other primary data sources. The quality of remained studies was assessed by a modified tool designed based on the STROBE statement checklist to evaluate the cross-sectional studies. R Version 3.6.0 was used for statistical analysis. Heterogeneity was assessed using Cochran's Q and F statistics. Subgroup analysis was performed to detect the source of heterogeneity. Funnel plots and Egger's regression intercept test were used to assess publication bias and selective reporting.

**Results:** Overall, 3099 sources were found. After excluding ineligible studies, 46 data points with 10411 people ≥65 years were included in the meta-analysis. The mean pooled decayed, missing, and filled teeth (DMFT) among older people was 26.84 (range, 26.41-27.28). The DMFT was 26.78 (range, 26.12-27.43) in women and 26.91 (range, 26.32-27.50) in men. The mean number of decayed teeth was 1.48 (range, 1.32-1.65). The mean pooled missing teeth was 24.83 (range, 24.20-25.46), and the mean pooled filled teeth was 0.14 (range, 0.12-0.17). The majority (92%) of the DMFT was related to missing teeth.

**Conclusion:** Iranian elderly have almost 5 sound teeth in their mouth on average. The Iranian oral health policymakers should address this considerable burden of dental caries in designing and implementing better oral health policies for the population, especially older Iranian adults.

Keywords: Aged, Dental Caries, DMFT Index, Iran, Meta-analysis

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# Introduction

Dental caries is a global health condition affecting both children and adults, leading to disability (1). Despite being largely preventable, the prevalence of dental caries among adults is high worldwide, affecting almost 30% of the global population, making it the most prevalent health condition (2). According to the World Health Organization (WHO), dental caries among older adults aged 65 years or older remains a significant problem for countries within the WHO regions (3). The mean dental caries experience (decayed, missing, and filled teeth, or DMFT index) among this population group across the Eastern Med-

iterranean region is reported to be about 23, and the prevalence of edentulism is around 30% (4). According to studies conducted in Iran, the prevalence of edentulism was estimated to be between 60% and 78% among people aged >70 years (5, 6).

The impact of dental caries on individuals and communities includes pain and suffering, impairment of functions and communication, and reduced quality of life (7, 8). Dental caries could lead to edentulism and impairment of social functions (9-11). Furthermore, several oral conditions are linked to noncommunicable diseases (NCDs)

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# $\uparrow$ What is "already known" in this topic:

The prevalence and the number of decayed, missing, filled teeth (DMFT) among the Iranian elderly population are deemed to be high. However, there is no comprehensive subnational data available in the literature.

#### $\rightarrow$ What this article adds:

On average, the Iranian elderly had almost 5 sound teeth in their mouth, which was slightly higher in women. Iranian elderly lost more than three-fourths of their teeth, and less than 1% of their teeth were filled.

primarily because of their common risk factors (12). Older people often have multiple health conditions, which can affect oral health status and behavior. This may establish a vicious cycle and worsen the overall and oral health statuses. According to the latest Iran's National Population Census, the >60 age group accounted for 9.3% of the whole population—which was 13.4% more than the previous census (13). This means the oral health of older people needs more attention as time passes.

Advances in oral health care and treatment have reduced the number of edentulous individuals in the past decades. The proportion of adults who retain their natural teeth until late in life has increased substantially (14-17). Besides, a still growing number of dentate older people have tooth wear, oral implants, sophisticated tooth- and implant-supported restorations, and prostheses (18). Hence, they are in continuous need of both preventive and restorative oral health care. The complexity of oral health status, systemic diseases, and the use of multiple medications make older adults more vulnerable to oral problems than younger age groups, even more so in those who are cognitively impaired (19).

The magnitude of disease distribution provides a unique perspective for planning interventions and developing public health policies. One of the most crucial research methods to accurately estimate disease indicators (indices) in society is a structured review and meta-analysis. Based on our knowledge, no meta-analyses have been done to combine the results of the mean of DMFT among older adults in Iran's general population. The present study aimed to conduct a systematic review and meta-analysis to determine the mean DMFT among elderly Iranians.

#### **Methods**

This research is a subcomponent of the "National And Subnational Burden of Diseases" (NASBOD) study (20). In the NASBOD study, a systematic review of the published literature was conducted using unpublished and grey literature. We followed recommendations for reporting meta-analysis of observational studies in epidemiology (21).

# Search Strategy

Three international databases (PubMed, Web of Science, and Scopus) and 3 national databases (IranMedex, SID, and Irandoc) were used to find published studies from January 1, 1970, to March 17, 2019, and provide the most comprehensive epidemiological data bank. The search through international databases was performed using MeSH terms, Entry terms, Emtree, and related keywords. Persian keywords mainly were developed based on their English equivalents, and some expert panels were also conducted to review any probable keywords. The main English keywords included "dental caries," "DMFT," "dental restoration, permanent," "tooth diseases," and "dental health surveys." The detailed search strategy can be found in Appendix 1.

#### **Inclusion Criteria**

The following steps were based on title exclusion, ab-

stract exclusion, and reviewing full texts. The full texts of all relevant articles were extracted, and a comprehensive quality assessment form was designed to assess the quality of selected articles.

# Study Design

Only population-based studies reporting dental caries in Iran were included.

### **Participants**

The systematic review's target population was a representative Iranian population of any age to increase the research's sensitivity and not missing any possible data. However, we entered studies that reported dental caries for those aged >65 years for the meta-analysis. Another primary data source was the national oral health surveys providing dental caries for the elderly.

#### **Outcomes**

The primary outcome of interest was the DMFT. As the main component of the DMFT in older people is missing teeth, many studies have only reported this component. However, we reported all components altogether and separately.

#### Selection of Searched Articles

After entering the search results into EndNote 7X software (The EndNote Team), one of the authors (S.S.), with one of the participants involved in the more extensive NASBOD study (H.H.) selected articles according to the inclusion and exclusion criteria in 3 phases. In case of disagreement, reviewers discussed the indefinite articles to reach an agreement and select them. Otherwise, a third author (F.S.) decided whether to include or exclude the article. Full texts were obtained by referring to the Tehran University of Medical Sciences' digital library, contacting corresponding authors, or accessing the journal in which the article was published.

**Title Phase:** Reviewers scanned all titles according to the inclusion criteria. Titles in doubt were also included.

**Abstract Phase:** Reviewers scanned all abstracts according to the inclusion criteria. Articles with unclear methods were also included in this phase.

**Full-Text Phase:** To finalize the selection phase, reviewers evaluated all remaining articles to determine whether they were eligible.

#### **Data Extraction**

Author, province, year of publication, year of study, duration of the study, sex, age, DMFT, decayed teeth, missing teeth, filling teeth, DMFT index examiner, methods of examining decayed teeth, methods of reviewing missing teeth, and methods of examining filling teeth were independently extracted from included studies by 2 participants involved in the more extensive NASBOD study (A.G. and B.N.). If a disagreement could not be settled by consensus, a third author (S.S.) made the final decision. Although the DMFT index is usually determined by examining 28 teeth in the oral cavity—from the central incisor to the second molar in each quadrant—these data have

taken into account the third molars so that the highest end of the DMFT index in our data is 32 instead of 28.

# **Quality Assessment**

The quality of included studies was assessed by a form derived from the "Strengthening the Reporting of Observational studies in Epidemiology" (STROBE) (22). The risk of bias assessment was performed using the Risk of Bias Tool, developed by Hoy et al (23). During several sessions with the NASBOD group members, the main items for qualitative evaluation were identified, and the initial evaluation form was designed. Each item was defined and the group members calibrated to complete the form. The first assessment form was completed experimentally by 3 members of the NASBOD group so that each of them completed the evaluation form separately for 3 randomly selected articles. Problems in the initial form were reviewed during the group members' meeting, and the evaluation form was reviewed. During a meeting, a modified form of qualitative evaluation was designed. To further investigate and fix possible bugs, the modified evaluation form was completed by 3 group members so that each of them separately completed the evaluation form for ten randomly selected articles. A copy of this form is available in Appendix 2.

#### **Data Synthesis and Analysis**

We used R Version 3.6.0 for Windows (R Core Team, http://www.r-project.org) with meta (4.9-6) and metaphor (2.1-0) packages for statistical analysis. We calculated the mean of each parameter (DMFT and its components).

Heterogeneity was assessed using Cochran's Q and F statistics (24). We used funnel plots and Egger's regression intercept test to assess publication bias and selective reporting. Subgroup analysis was performed to detect resource heterogeneity. For this reason, the population of Iran was divided into 4 regions Southeast, North-Northeast, West, and Central (each region was homogeny in terms of socioeconomic variables based on years of schooling, employment rates, and family assets) (25). We also used meta-regression to detect the probable source of heterogeneity (year, province, sex, and sample size). No statistically significant level was considered, according to the statement by the American Statistical Association (26).

# **Results**

At first, we reached 3055 articles (917 English and 2138 Persian) reporting dental caries among all ages. Searching in other sources (eg, grey literature) provided 44 additional records. By removing duplicates, 991 articles remained. After screening based on the inclusion and exclusion criteria, 4 studies with 46 points of data (6, 27-29), including 2 from cross-sectional studies (conducted in 2 northern provinces in 2009) and 44 from 2 national data, 1 shown in 13 provinces in 1999, and the other in 31 provinces in 2012, were included in the meta-analysis (Figure 1). We also updated our search on May 3, 2022, and no new articles were found. The overall quality of all the studies was

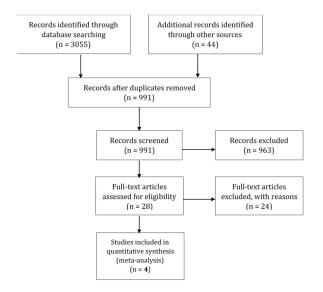


Figure 1. Study selection flowchart

Table 1. Risk of Bias Assessment of the Included Studies

Study (year) (reference)	ROB
Elderly dental health survey (1999)	Low
Gilan study (2009)	Moderate
Golestan study (2009)	Moderate
Iranian National Oral Health Survey (2012)	Low

judged to be fair and good (Table 1).

The total elderly population of this meta-analysis was 10411 (50.7% women). The pooled mean of the DMFT in the Iranian population at the national level using random effect method was 26.84 (95% CI, 26.41-27.28;  $I^2 = 87\%$ ; n = 9542). The mean DMFT according to sex was 26.78 (95% CI, 26.12-27.43;  $I^2 = 88\%$ ; n = 4862) for women and 26.91 (95% CI, 26.32-27.50;  $I^2 = 85\%$ ; n = 4680) for men. The mean of each DMFT component was as follows: decayed teeth: 1.48 (95% CI, 1.32-1.65;  $I^2 = 90\%$ ; n = 9339); missing teeth: 24.83 (95% CI, 24.20-25.46;  $I^2 = 91\%$ ; n = 10411); and filling teeth: 0.14 (95% CI, 0.12-0.17;  $I^2 = 77\%$ ; n = 9339). The forest plots for the DMFT and its components by sex are shown in Appendix 3-6.

On the subnational scale, Busher (18.44), Khuzestan (21.77), and Hormozgan (23.98) had the lowest mean DMFT and Kurdistan (30.21), Zanjan (29.72), and East Azarbaijan (28.93) had the highest mean DMFT (Figures 2-3). The highest male-to-female ratio for DMFT was in Hormozgan (1.171), Qom (1.163), and Tehran (1.132), whereas Razavi Khorasan (0.893), Alborz (0.908), and Chaharmahal and Bakhtiari (0.938) had the lowest ratio (Figure 4).

The measured  $I^2$  for the DMFT was 87% (P < 0.01). The map of the mean DMFT for each province is shown in Figure 3. The heterogeneity was also high for all DMFT components. The regional analysis was heterogeneous (Table 2 and Appendix 7).

The results of the Egger's test were significant for the DMFT and its components, showing considerable publication bias (Appendix 7).

Meta-regression results showed that none of the coeffi-

	Location	dmft	Location	dmft	Location	dmft	Location	dmft
	National	26.84	llam	25.95	Semnan	27.20	Ardabil	27.98
	Bushehr	18.44	Kohgiluyeh and Boyer- Ahmad	26.29	Kermanshah	27.37	Markazi	28.09
	Khuzestan	21.77	Alborz	26.70	North Khorasan	27.44	West Azerbaijan	28.15
	Hormozgan	23.98	Razavi Khorasan	26.83	Lorestan	27.73	Yazd	28.73
Sist	tan and Baluchistan	24.28	Fars	26.90	Kerman	27.74	Chahar Mahaal and Bakhtiari	28.84
	Gilan	24.72	Qom	26.91	Golestan	27.74	East Azerbaijan	28.93
	South Khorasan	24.88	Mazandaran	26.97	Qazvin	27.82	Zanjan	29.72
	Tehran	25.51	Hamadan	27.12	Isfahan	27.84	Kurdistan	30.21

Figure 2. Mean DMFT index of the elderly in all provinces of Iran

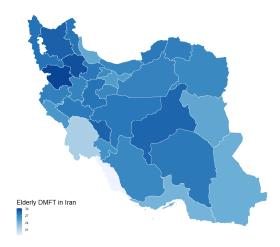


Figure 3. Map of mean DMFT index of the elderly in all provinces of Iran

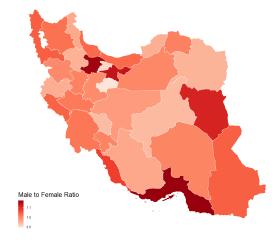


Figure 4. Map of male-to-female ratio for DMFT of the elderly in all provinces of Iran

cients were statistically significant in relation to the mean DMFT ( $\tau^2 = 5.418$ ; I<sup>2</sup> residual = 87%; adjusted R<sup>2</sup> = -4.32%). More details are illustrated in Table 3.

# Discussion

This pooled analysis is the first study reporting the DMFT index of Iranian elderly nationally and subnation-

ally. We found a high mean DMFT index in the elderly Iranian population (26.84); missing teeth accounted for 24.83 (92.5% of DMFT). On average, the Iranian elderly have about 7 sound teeth in their mouth, counting third molars.

We found little information regarding the DMFT index of older people in the literature. Indeed, most studies we found had only reported the number of missing teeth.

Table 2. DMFT index based on socioeconomic regions and sex

Region (number of provinces)	Sex	DMFT Index (95% CI)	I <sup>2</sup> (%)	P-value
West (14)	Female	26.83 (25.75 – 27.92)	91	< 0.01
	Male	26.72 (25.69 – 27.75)	90	< 0.01
	Both	26.78(26.05 - 27.52)	90	< 0.01
Central (8)	Female	27.23 (26.17 – 28.29)	75	< 0.01
	Male	27.60(27.05 - 28.15)	18	0.28
	Both	27.42(26.84 - 28.00)	60	< 0.01
North-Northeast (5)	Female	27.47(26.51 - 28.43)	71	< 0.01
	Male	26.89 (25.67 – 28.11)	82	< 0.01
	Both	27.22 (26.52 – 27.92)	77	< 0.01
Southeast (4)	Female	24.32 (21.26 – 27.38)	90	< 0.01
	Male	26.36 (25.08 – 27.63)	52	0.10

*Table 3.* The results of the meta-regression

Coefficient	В	Standard error	T-value	P-value	Lower bound	Upper bound
Year	0.013	0.0885	0.15	0.885	-0.163	0.189
Province	-0.029	0.0314	-0.92	0.360	-0.091	0.034
Sex	-0.076	0.5509	-0.14	0.890	-1.172	1.019
Sample size	0.004	0.0083	0.47	0.637	-0.013	0.020
Constant	0.914	176.9754	0.01	0.996	-350.961	352.789

Hence, we used 2 extensive studies conducted nationwide in 1999 and 2012 and data from a survey conducted in 1 province in 2009.

The calculated mean DMFT is high; however, studies from other countries have reported DMFT in their elderly population in a range near our results. For example, this index was 25.8 in Turkish (30), 25.4 in Norwegian (31), and 27 in Croatian (32) elderly. Some studies reported a higher or lower DMFT, such as 30.2 for Brazil (33), 13.3 for China (34), and 21.9 for Hungary (35), 18.9 for Australia (36). Similar to this study, missing teeth were responsible for most DMFT in all these populations.

The portion of filled teeth in developed countries is relatively higher than in developing countries (31, 37), which may be due to more disciplined oral health care systems. This study's mean number of filled teeth is 0.14, which accounts for 0.5% of the whole mean DMFT. This can show 2 things: first, there is limited access to operative dentistry services. The other is that there still may be a belief in the Iranian community that they should extract carious teeth instead of filling them and the appeal to remove all remaining decayed or even sound teeth to wear a denture for the rest of their lives.

The mean DMFT index varied significantly between the Bushehr provinces (18.44), which had the lowest, and Kurdistan (30.21), which had the highest. To explain this, we ran a secondary analysis based on the socioeconomic status of each region. This analysis did not address this difference, either. Evidence shows that water fluoridation may prevent dental caries in children and adults (38). In a study measuring the amount of fluoride in groundwater resources in Iran, Bushehr had the highest fluoride level, and Kurdistan was among the provinces with the lowest amount of fluoride (39, 40). Overall, provinces by the Persian Gulf and Oman Sea have the highest fluoride concentration in their water and, as our study showed, have the lowest DMFT in their older people. This can be an explanation; however, further investigations are needed.

A slightly higher mean DMFT index was observed in men (26.91 compared with 26.78). Men had slightly high-

er decayed teeth but slightly lower missing and filled teeth. These differences were not clinically significant. Although there is no evident sex-based inequality, it should not be assumed to be favorable since both sexes have unfavorable mean DMFT index. In other words, both "fairness" and "goodness" are essential to health systems' performance (41), and we do not see "goodness" in elderly dental caries in both sexes.

Generally, DMFT increases with age. The mean DMFT index of 12- and 18- year-olds in Iran is reported to be 1.9 (42) and 4.3 (43), respectively. In these ages, decayed teeth are responsible for most of the DMFT index. In people aged 35 to 44, DMFT is rising to 11—60% because of missing teeth (43). The findings of our study show that elderly DMFT is over twofold of the reported adult DMFT. Besides, the number of decayed teeth decreases from 2.6 to 1.45, and the number of filled teeth is almost one-thirteenth (0.14 compared with 1.8). This means many sound, filled, and decayed teeth will become hopeless and be extracted with aging for different reasons, including dental caries, periodontal diseases, the inadequate functional ability of the remaining teeth, tendency to replace natural teeth with complete dentures because of cultural or economic factors, or little public or insurance support for oral health services. Furthermore, insurance coverage for complete dentures encourages older people to extract their teeth and wear a denture.

# **Limitations**

Our analysis showed a high publication bias in the data. The data were mainly from 2 national studies, and there was limited data in the literature reporting the DMFT of older people and its components. Another limitation was the quality of the data. Although the last national survey reported their methods before the study, there was limited data regarding the previous one. Moreover, there is no definite assurance that the missing teeth component of the DMFT index in the elderly is majorly due to dental caries or other factors such as periodontal diseases or dental trauma.

#### **Policy Implications**

The finding of the high DMFT index in the elderly and the vast disparity between provinces is of interest to policymakers. With the growing number of the elderly in the Iranian population, which is estimated to elevate to 11% by 2036, there should be more efforts to decrease the level of caries experience among the elderly. Dental caries is highly preventable; thus, preventive programs should be encouraged first and then restorative services, and many teeth can be saved. Furthermore, targeted approaches may be attractive to policymakers since they can restrict resource allocation. They may be determined as addressing essential determinants such as behavior and access to dental care (with dental insurance coverage) (44).

Oral health care is mainly private in Iran, especially in urban areas (80% private), and in rural areas, 70% of oral health care, mainly essential oral services, is delivered by the public sector (45). Although it is estimated that nearly 90% of Iranians have social insurance coverage (46), insurance funds for oral health care are limited. However, there are few dental insurance plans that everyone, including older people, can use to cover their out-of-pocket expenditures, but it is insufficient. We encourage oral health policymakers to advocate for an oral health plan at a national- or provincial level considering the nature of the oral disease, which has significant differences with other health conditions (47); for example, deductibles and copayments should be avoided in some cases, and patients should be encouraged to use their oral health insurance regularly as delayed treatment can worsen their oral health status.

As the elderly population suffers from many other NCDs, it is an excellent practice to follow the common risk factor approach (48). This approach addresses risk factors that are in common with other chronic conditions. However, this factor slightly impacted promoting oral health, and there should be more radical actions such as "strike out independently of the other NCDs" (49, 50). In any case, we urge Iranian decision-makers to apply the most recent data and international best practices to lower the incidence of dental caries, which is a useful indicator of a person's socioeconomic status. For instance, functional capacity may be preserved by reducing tooth loss (51); as a result, the overall burden of diseases would decline.

# **Conclusion**

This meta-analysis showed that the level of DMFT in Iranians aged >65 years old is very high and that the Iranian elderly have almost 5 sound teeth in their mouth on average. Tooth loss is the primary cause of DMFT. The Iranian society is headed toward edentulousness due to a lack of a properly designed strategy for promoting oral health among the elderly and to the limited dental insurance coverage available to them, which is limited to complete dentures and tooth extractions. Consequently, dental caries ought to be Iran's top concern when it comes to health care, and funds for oral health care should be allocated to developing policies, plans, and initiatives for elderly oral health. The oral health and quality of life of this demographic group may be sufficiently improved by in-

corporating oral health into national general health programs. Overall, more emphasis should be placed on oral health policies and preventive oral care principles in Iran.

#### **Abbreviations**

DMFT: decayed, missing, filled teeth; NCDs: noncommunicable diseases; WHO: World Health Organization.

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#### **Authors' Contributions**

S.S. conceived, designed, and conducted the study, wrote and revised the manuscript, and interpreted the data. F.S. interpreted the data and wrote and revised the manuscript. P.G. conducted the research and wrote and revised the manuscript. AS-M. conducted the study, wrote and revised the manuscript, and interpreted the data.

# **Conflict of Interests**

The authors declare that they have no competing interests.

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#### Appendix 1. Search Strategy

Search keywords for articles about "<u>Dental Caries</u>" in 3 databases including PubMed, Scopus, ISI were used as follows: PubMed:

((("Dental Caries"[Mesh]) OR "DMF Index"[Mesh]) OR "Dental Restoration, Permanent"[Mesh]) OR "Tooth Diseases"[Mesh]) OR "Dental Health Surveys"[Mesh]

ISI OR Scopus: "Dental Caries" OR "dental decay" OR "dental white spot" OR "DMF Index" OR "decayed, missing and filled teeth" OR "Dental Restora-

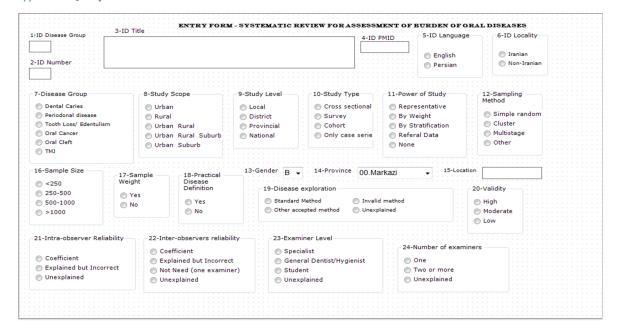
tion, Permanent" OR "dental filling, permanent" OR "Tooth Diseases" OR "Dental Health Surveys"

Also Search keywords for articles about "Dental Caries" in 3 databases including SID, IranMedex, IranDoc, which include persian and english articles, were used as follows:

پوسیدگی دندان/ پوسیدگی های دندان/ پوسیدگیهای دندان/ شاخص دندانهای پوسیده افتاده و پر شده/ شاخص دندانهای پوسیده از دست رفته و پرشده/ دندان های پوسیده افتاده و پرشده/ دندان های پوسیده از دست رفته و پرشده/ شاخص دی ام اف/ DMF/ DMF/ شاخص / ترمیم دندان/ بیماری های دندان/ بیماریهای دندان/ مطالعات بهداشت دندان

Dental Caries / DMF Index / Dental Restoration, Permanent / Tooth Diseases / Dental Health Surveys

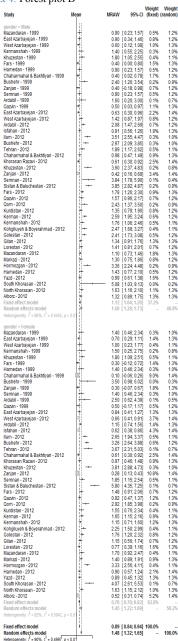
Appendix 2. Quality assessment tool based on STROBE

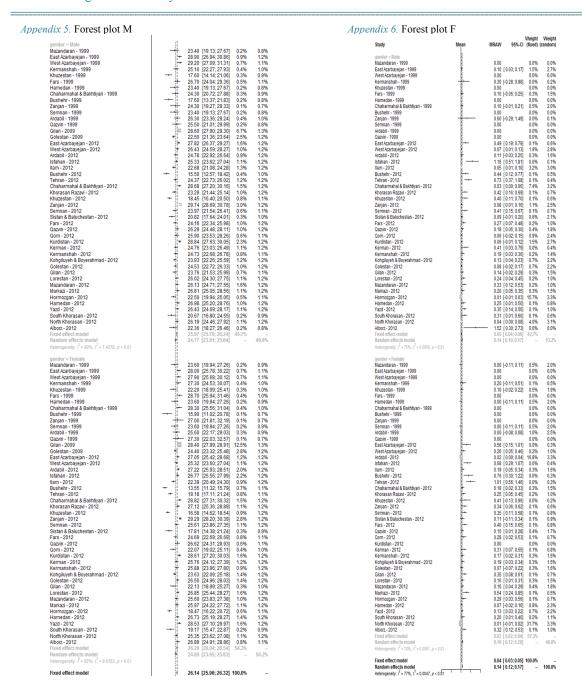


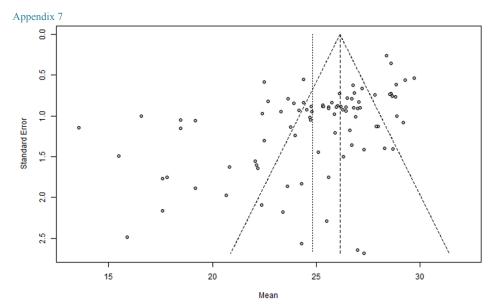
# Appendix 3. Forest plot DMF

# Weight Weight 95%-CI (fixed) (random) MRAW 2430 (2017; 31.43) 2380 (2017; 31.43) 2380 (2017); 31.43) 2380 (2017); 31.43) 2380 (2017); 31.43) 2380 (2017); 31.43) 2430 (2018); 2017); 2017) 2430 (2018); 2017); 2017) 2430 (2018); 2017) 2430 (2018); 2017); 2018) 2530 (2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2017, 2018); 2018, 201 0.7% 1.2% 1.0% 0.6% 0.6% 0.6% 0.6% 1.13% 1.2% 1.13% 1.2% 1.13% 1.2% 1.13% 1.2% 1.13% 1.2% 1.13% 1.2% 1.14% 1.15% 1 49.9% gender – Female Mazandraun 199 Mazandraun 199 Mazandraun 1999 West Azanbejen 1999 West Azanbejen 1999 Koluzesten 1999 Koluzesten 1999 Hamedran 1999 Hamedran 1999 Zanjan 1999 Zanjan 1999 Gazin 1999 2500 (21-83, 28.17) 28.27 (21-0.2% 0.6% 0.6% 0.6% 0.6% 0.3% 0.3% 0.3% 0.2% 0.1% 0.2% 0.1% 0.2% 0.1% 0.9% 0.15% 1.16% 0.9% 1.4% 0.9% 1.50% 0.9% 1.4% 0.9% 1.15% 0.9% 1.16% 0.9% 1.16% 0.9% 1.16% 0.9% 1.16% 0.9% 0.16% 0. Clabin - 1992 Seal Audiopigian - 2012 Weet Audiopigian - 2012 Aradiopigian - 2012 Aradiopigian - 2012 Aradioli - 2012 Islahan - 2012 Islahan - 2012 Besahetr - 2012 Seal - 2012 Khorasan Razawi - 2012 Khorasan Razawi - 2012 Cangian - 2012 Zangian - 2012 Seminan - 2012 Cangian - 2012 Kerman -Kurdstan. 2012 Keman. 2012 Keman. 2012 Keman. 2012 Golsstan. 2012 Golsstan. 2012 Golsstan. 2012 Golsstan. 2012 Golsstan. 2012 Homogan. 2012 Homogan. 2012 Homogan. 2012 Homogan. 2012 Homogan. 2012 Homosan. 2012 Homosan. 2012 Fad. 2012 Tad. 2012 Ta 27.82 [27.68; 27.97] 100.0% --26.84 [26.41; 27.28] -- 100.0%

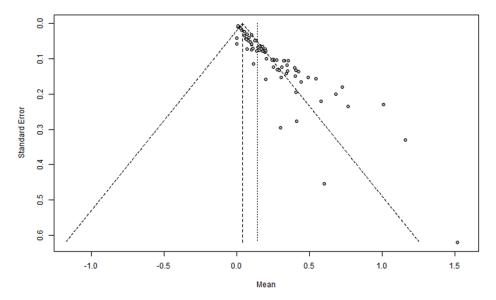
## Appendix 4. Forest plot D







Egger's Test – Test for funnel plot assymetry -  $M:P \leq .0001\,$ 



Egger's Test – Test for funnel plot assymetry -  $F: P \le .0001$