Grading of Recommendations Assessment, Development and Evaluation (GRADE)

for

Systematic Review of Caries Risk Factors in Adults: Toward a Population-Based Screening Tool

Contents

1. Tobacco use and caries increment in young adults A prospective observational study (1)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The overall risk of bias for this study is categorized as "serious." This classification is based on the information provided in the document, which indicates potential concerns related to the selection of the reported result and the possibility of bias due to uncontrolled confounding factors. While the study design was longitudinal and aimed to investigate the association between tobacco use and dental caries increment in young adults, the presence of some concerns regarding bias in the selection of the reported results and uncontrolled confounding factors warrants this classification.
	Indirectness	⊖"serious." This impacts the certainty of evidence for each outcome and raises concerns about the applicability of the study to the PICO (Population, Intervention, Comparison, Outcome) interest. 1. Population: The study focused on a specific cohort of 19-year-old individuals from particular socioeconomic strata and geographic locations. The narrow demographic scope may limit the generalizability of the findings to broader populations, affecting the direct applicability of the study to diverse age groups, socioeconomic backgrounds, and geographic regions. 2. Intervention and Comparison: The study primarily investigated the association between smoking and smokeless tobacco (Swedish snus) use and dental caries increment. While the study addressed the specified interventions, the comparison groups, and the outcomes of interest, the narrow focus on tobacco use and caries in young adults may limit the direct applicability of the findings to broader research questions or diverse patient populations. 3. Outcome: The study outcomes specifically examined the relationship between tobacco use and caries increment over a 3-year period. While relevant to the PICO interest, the limited focus on this specific outcome may restrict the direct applicability of the findings to broader dental health or tobacco-related research questions. The indirectness of the included study is considered "serious," as the narrow focus on a specific population, limited interventions and comparisons, and specific outcomes may impact the direct applicability of the findings to the broader PICO interest and raise concerns about the certainty of evidence for each outcome.
	Inconsistency	○"not serious"

		The study results were consistent and showed the same direction of effect, with a statistically significant relationship between smoking and caries increment. 1. Direction of Effect: The study found a statistically significant relationship between smoking and caries increment, with a relative risk of 1.5 (95% CI 1.2-1.7) and a number needed to harm of 6.8 (95% CI 4.5-14.2). The study did not find a significant relationship between smokeless tobacco (Swedish snus) use and caries increment. The consistent direction of effect for smoking and the lack of effect for smokeless tobacco suggest that the study results were consistent. 2. Magnitude of Effect: The study results showed a moderate effect size for smoking, with a relative risk of 1.5 and a number needed to harm of 6.8. While the effect size was not large, the statistically significant relationship between smoking and caries increment suggests that the study results were consistent. The inconsistency of the included study can be considered "not serious," as the study results were consistent and showed the same direction of effect for smoking and smokeless tobacco. The moderate effect size for smoking suggests that the study results were reliable and consistent with previous research on the topic.
	Imprecision	○"not serious" The confidence intervals provided in the study were relatively narrow, indicating a reasonable level of precision in the effect estimates. 1. Precision of Effect Estimates: The study reported 95% confidence intervals for the relative risk associated with smoking and caries increment, with a range of 1.2-1.7. Additionally, the number needed to harm for smoking was reported as 6.8, with a confidence interval of 4.5-14.2. These confidence intervals, while not extremely narrow, provide a reasonable level of precision in the effect estimates, allowing for a more accurate assessment of the true underlying risk. 2. Study Power: Although the study did not explicitly conduct a formal power calculation, the relatively large sample size (1295 19-year-olds at baseline) and the follow-up of 982 patients over a 3-year period suggest that the study was adequately powered to detect the observed effects. The precision of the effect estimates, as indicated by the confidence intervals, supports the notion that the study was not underpowered. The imprecision of the effect estimates from the included study can be considered "not serious," as the reported confidence intervals were relatively narrow, indicating a reasonable level of precision in the effect estimates. The study's sample size and the precision of the effect estimates suggest that the study was adequately powered to detect the observed effects, further supporting the assessment of imprecision as "not serious."
	Publication Bias	○"not serious"

		This assessment is based on the availability of the study in a peer-reviewed journal and the absence of obvious publication bias. 1. Peer-Reviewed Publication: The study was published in a peer-reviewed journal, indicating that it underwent rigorous evaluation by experts in the field. This suggests that the study's findings were deemed to have scientific merit, reducing the likelihood of publication bias. 2. Absence of Obvious Publication Bias: The study's reporting of both statistically significant and non-significant findings related to smoking and smokeless tobacco use suggests that the authors did not selectively report only positive results. Additionally, the study's transparent reporting of methods and results further reduces the likelihood of publication bias. 3. Missing Studies or Outcomes: While the study focused on the specific relationship between tobacco use and caries increment in young adults, it is possible that there are other related studies or outcomes not captured in this particular investigation. However, the study's focus on a specific research question does not necessarily indicate publication bias, as it may reflect the deliberate scope of the research. The likelihood of publication bias in the included study is considered "not serious." The study's publication in a peer-reviewed journal, absence of obvious publication bias, and transparent reporting contribute to this assessment. While there may be other related studies or outcomes not included in this specific investigation, the study's focus on a specific research question does not inherently suggest publication bias.
Upgrading Factors		
	Large Effect Size	⊕ moderate with a relative risk of 1.5 for smoking and caries increment. While this effect size is not large, it is statistically significant and suggests a meaningful relationship between smoking and caries increment in young adults. 1. Effect Size: The study found a statistically significant relationship between smoking and caries increment, with a relative risk of 1.5 (95% CI 1.2-1.7) and a number needed to harm of 6.8 (95% CI 4.5-14.2). While this effect size is not large (e.g., risk ratio >2 or <0.5), it is statistically significant and suggests a meaningful relationship between smoking and caries increment in young adults. 2. Plausible Confounders: The study did not explicitly control for all potential confounding variables, such as diet, oral hygiene, or socioeconomic status. However, the study's longitudinal design and large sample size suggest that the observed relationship between smoking and caries increment is unlikely to be solely due to confounding factors.

		3. Certainty of Evidence: The moderate effect size and statistical significance of the observed relationship between smoking and caries increment suggest a moderate level of certainty in the evidence. While the study did not control for all potential confounding variables, the study's longitudinal design and large sample size support the validity of the observed relationship. The effect size in the included study can be considered moderate, with a statistically significant relationship between smoking and caries increment in young adults. While the study did not control for all potential confounding variables, the study's longitudinal design and large sample size support the validity of the observed relationship and suggest a moderate level of certainty in the evidence.
	Dose-Response Relationship	○ The study did not investigate the presence of a dose-response relationship between smoking and caries increment. Therefore, the certainty of evidence for this outcome is not influenced by the presence or absence of a dose-response relationship, and there is no dose-response gradient to consider.
	Opposing Plausible Residual Bias and Confounding	⊕ The design used allows for the assessment of tobacco use at baseline in relation to the actual caries development over the study period, reducing the potential for residual bias and confounding. 2. Large Sample Size: The study included a large sample size, with 982 patients being reexamined after 3 years. A large sample size provides greater statistical power and precision, reducing the impact of residual bias and confounding on the observed relationship between smoking and caries increment. 3. Statistical Analysis: The study conducted statistical analyses to assess the relationship between tobacco use and caries increment, including reporting relative risks and confidence intervals. This rigorous approach to data analysis enhances the validity of the study's findings and mitigates the influence of residual bias and confounding. 4. Transparent Reporting: The study provided transparent reporting of methods, results, and statistical analyses. This transparency allows for a clear assessment of the study's methodology and results, reducing the potential for residual bias and confounding to impact the certainty of evidence. The factors mentioned above, including the longitudinal design, large sample size, rigorous statistical analysis, and transparent reporting, collectively oppose plausible residual bias and confounding. These factors positively affect the certainty of evidence for the observed outcome of the relationship between smoking and caries increment, enhancing the validity and reliability of the study's findings.

Quality of Evidence
⊕⊕⊕○ moderate. 1. Study Design: The study utilized a longitudinal design, which is generally considered to be a strong study design for assessing causal relationships. However, the study did not control for all potential confounding variables, which may limit the strength of the evidence. 2. Sample Size: The study included a large sample size, which provides greater statistical power and precision. However, the study was conducted in a specific population (young adults in Sweden), which may limit the generalizability of the findings. 3. Effect Size: The observed effect size (relative risk of 1.5) is statistically significant and suggests a meaningful relationship between smoking and caries increment in young adults. However, the effect size is not large (e.g., risk ratio >2 or <0.5), which may limit the strength of the evidence. 4. Certainty of Evidence: The study's longitudinal design, large sample size, and statistical analyses support the validity of the observed relationship between smoking and caries increment. However, the study did not control for all potential confounding variables, and the effect size is not large. Therefore, the overall quality of the body of evidence can be considered moderate. The overall quality of the body of evidence based on the included study can be considered moderate. While the study's longitudinal design, large sample size, and statistical analyses support the validity of the observed relationship between smoking and caries increment, the study did not control for all potential confounding variables, and the effect size is not large.

2. Diabetes status affects long-term changes in coronal caries - The SHIP Study (2)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	○"not serious" The study demonstrated a low overall risk of bias through various strengths in its design and execution. Conducted on a large-scale population-based sample with 11-year follow-up data, the research provided a comprehensive assessment of the long-term effects of diabetes status and HbA1c levels on coronal caries outcomes. Results were reported for each objective and all groups, and mixed models were utilized for a detailed analysis, enhancing the understanding of the associations between diabetes status, metabolic control, and caries progression. Additionally, the well-trained and calibrated dental examiners ensured data accuracy, while appropriate statistical methods were employed for analysis. The study also transparently acknowledged potential limitations, further supporting the reliability and credibility of the findings regarding the impact of diabetes on coronal caries.

	Indirectness	○"not serious" The included studies directly address the research question by investigating the effects of diabetes status and metabolic control on long-term changes in coronal caries, enhancing the relevance of the findings and strengthening the certainty of evidence. The studies' applicability to the PICO interest is evident as they focus on individuals aged 20 to 79 years, comparing the impact of diabetes mellitus on coronal caries outcomes. By analyzing diabetes status and metabolic control in relation to various caries variables, the studies directly align with the PICO framework, providing valuable insights into the associations between diabetes and coronal caries progression.
	Inconsistency	○"not serious" The results of the included studies consistently demonstrate associations between diabetes status, metabolic control, and long-term changes in coronal caries outcomes. This consistency in findings strengthens the certainty of evidence for each outcome assessed, indicating a robust relationship between diabetes and caries progression. The studies show a consistent direction of effect, highlighting the impact of diabetes on caries variables such as DMFS, DFS, and MS components. The overall trend supports the notion that diabetes status and metabolic control have significant implications for coronal caries experience. The consistency in results enhances the reliability and validity of the evidence, reinforcing the importance of addressing diabetes management in relation to oral health outcomes.
	Imprecision	○"not serious" The confidence intervals provided in the study were relatively narrow, indicating a reasonable level of precision in the effect estimates. The study found that the progression rate of the DMFS (Decayed Missing Filled Surfaces) index per year was 0.716 surfaces for subjects with poorly controlled diabetes, with a 95% confidence interval (CI) ranging from 0.552 to 0.880. This means that, on average, individuals with poorly controlled diabetes experienced an increase of 0.716 surfaces affected by decay, missing, or fillings each year.
	Publication Bias	○"not serious" The study underwent thorough evaluation by experts in the field before being published in a peer-reviewed journal, indicating its scientific validity and reducing the risk of publication bias. The study's inclusion of both statistically significant and non-significant results indicates that the authors did not selectively report positive findings. Moreover, the transparent presentation of methods and results in the study minimizes the likelihood of publication bias
Upgrading Factors		
	Large Effect Size	⊕ Based on the information provided from the study, it is indicated that subjects with poorly controlled diabetes had statistically significantly higher rates of progression in the DMFS index compared to subjects without diabetes. Specifically, subjects with

		poorly controlled diabetes had a progression rate of 0.716 surfaces per year, which was higher than the progression rate of 0.473 surfaces per year for subjects without diabetes. While the study did not explicitly mention a risk ratio or relative risk, the difference in progression rates between subjects with poorly controlled diabetes and those without diabetes suggests a notable effect size in terms of the impact of diabetes status on the progression of dental caries. The statistically significant difference in progression rates indicates a substantial effect of poorly controlled diabetes on the development of caries over time.
	Dose-Response Relationship	⊕ There is evidence suggesting a potential dose-response relationship between diabetes status and changes in coronal caries. Specifically, the study highlighted that increasing levels of fasting blood glucose and HbA1c were associated with a higher prevalence of untreated caries in individuals with uncontrolled diabetes compared to metabolically healthy individuals. This finding implies that as the levels of blood glucose and HbA1c increase, there is a corresponding increase in the prevalence of untreated caries, indicating a potential dose-response relationship.
	Opposing Plausible Residual Bias and Confounding	⊕ Various measures were taken to mitigate bias and confounding, enhancing the certainty of evidence. The large-scaled population-based design increased the generalizability of findings to the adult Caucasian population, minimizing biases related to sample size and population representation. Additionally, the 11-year follow-up period allowed for the evaluation of prolonged effects, reducing biases from short-term fluctuations and providing a more comprehensive understanding of the relationship between diabetes status and coronal caries progression. Rigorous training of dental examiners ensured data accuracy, minimizing measurement bias and increasing the reliability of study results. The use of mixed models in statistical analysis addressed individual-specific time intervals and unbalanced data, reducing selection bias and improving parameter estimation accuracy, thereby enhancing the certainty of evidence for each outcome. Overall, the study's meticulous approach in study design, long-term follow-up, examiner training, and statistical analysis effectively countered potential bias and confounding. By incorporating these strategies, the certainty of evidence for each outcome was strengthened, ensuring robust and reliable study results that are less susceptible to biases that could compromise result validity.
Quality of Evidence		
⊕⊕⊕⊕ high The study "Diabetes status affects long-term changes in coronal caries - The SHIP Study" rates as moderate quality using GRADE for the quality of evidence. This rating is supported by the significant difference in progression rates between subjects with poorly controlled diabetes and those without diabetes, indicating a substantial effect size in the impact of diabetes status on caries progression. Additionally, evidence suggests a potential dose-response relationship between diabetes status and changes in coronal caries, with increasing levels of fasting blood glucose and HbA1c associated with a higher		

prevalence of untreated caries in individuals with uncontrolled diabetes compared to metabolically healthy individuals. The study's meticulous measures to mitigate bias and confounding, such as the large-scaled population-based design, 11-year follow-up period, rigorous examiner training, and advanced statistical analysis using mixed models, further enhance the certainty of evidence by minimizing potential sources of bias and strengthening the reliability of study results.

3. Access to Fluoridated Water and Adult Dental Caries: A Natural Experiment (3)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The overall risk of bias for this study is categorized as "Some concerns." This assessment is based on several factors contributing to potential biases in the study, including concerns about uncontrolled confounding, measurement of exposure, and selection of participants. While efforts were made to control for important confounding factors and conduct sensitivity analyses to address selection biases, there are still some uncertainties and limitations in the study design that raise concerns about the potential impact on the estimated effect of exposure on the outcome. Therefore, the overall risk of bias is considered to have some concerns.
	Indirectness	⊖"serious." as the study directly addresses the research question and is applicable to the PICO (Population, Intervention, Comparison, Outcome) interest. The study directly investigates the association between lifetime access to fluoridated water and dental caries experience among adults in a specific geographic area (Florianópolis, Brazil). The research question aligns with the study's objectives, and the findings are directly relevant to understanding the impact of fluoridated water exposure on adult dental caries. The study's population includes adults residing in a specific city, the exposure of interest is lifetime access to fluoridated water, and the outcome is dental caries experience. The study's design and methods align with the PICO elements, making the findings directly applicable to the research question and relevant to the PICO interest. The direct applicability of the study to the research question and its alignment with the PICO elements enhance the certainty of evidence for each outcome. By directly addressing the specific population, exposure, and outcome of interest, the study's findings are more relevant and applicable to informing the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries.

	Inconsistency	○"not serious" The study's findings are consistent with previous research in the field, which has also found a significant association between lifetime access to fluoridated water and reduced dental caries experience in adults. The study's results are also consistent with the expected direction of effect, as increased exposure to fluoridated water is associated with lower dental caries experience. The consistency of the study's findings with previous research enhances the certainty of evidence for each outcome. By aligning with the existing body of evidence, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries. The inconsistency of the included study is not serious, as the study's findings are consistent with previous research in the field and support the expected direction of effect. This strengthens the certainty of evidence for each outcome and supports the study's relevance to addressing the research objectives.
	Imprecision	○"not serious" The study has a large sample size (over 1,000 participants) and narrow confidence intervals for the effect estimates, indicating a high level of precision. The study's effect estimates are also statistically significant, further supporting the precision of the findings. Therefore, the risk of imprecision is low. The precision of the study's effect estimates enhances the certainty of evidence for each outcome. By having a large sample size and narrow confidence intervals, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries. The imprecision of the included study is not serious, as the study has a large sample size and narrow confidence intervals. This strengthens the certainty of evidence for each outcome and supports the study's relevance to addressing the research objectives.
	Publication Bias	○"not serious" The study's methods and findings are transparent, and the study is publicly available, reducing the likelihood of publication bias. Additionally, the study's authors have provided detailed information about the research design, data collection, and analysis, which enhances the transparency of the study and reduces the potential for publication bias.

		The reduced likelihood of publication bias enhances the certainty of evidence for each outcome. By having transparent methods and publicly available findings, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries. There is no indication that relevant studies or outcomes are missing from the analysis. The study's comprehensive approach to investigating the association between lifetime access to fluoridated water and dental caries experience in adults suggests that relevant studies and outcomes have been appropriately considered. The likelihood of publication bias in the included study is not serious, as the study's methods and findings are transparent and publicly available. This strengthens the certainty of evidence for each outcome and supports the study's relevance to addressing the research objectives.
Upgrading Factors		
	Large Effect Size	⊕ The study found a large effect size (rate ratio of 2.70 for <50% lifetime access to fluoridated water) in the absence of plausible confounders, which enhances the certainty of evidence for each outcome. The large effect size enhances the certainty of evidence for each outcome. By having a strong association between fluoridated water access and reduced dental caries experience in adults, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries.
	Dose-Response Relationship	⊕ The study provides evidence of a dose-response relationship between lifetime access to fluoridated water and dental caries experience in adults. The study found that longer lifetime access to fluoridated water was associated with lower levels of dental caries, indicating a dose-response gradient. The evidence of a dose-response relationship enhances the certainty of evidence for each outcome. By demonstrating a dose-response gradient between lifetime access to fluoridated water and dental caries experience, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's results and their potential implications for understanding the relationship between fluoridated water access and adult dental caries.
	Opposing Plausible Residual Bias and Confounding	⊕ The study addresses potential sources of bias and confounding, which enhances the certainty of evidence for each outcome. The study's approach to mitigating these factors supports the validity of the research findings.

		The study employed strict selection criteria, including only residents living at the same address since the age of 7 years or before. This criterion reduces the potential for selection bias and exposure misclassification, thereby strengthening the validity of the study's findings. The study controlled for well-known confounders such as socioeconomic status (SES) and pattern of dental visiting. By addressing potential confounding variables, the study enhances the validity of the research outcomes. The factors that oppose plausible residual bias and confounding enhance the certainty of evidence for each outcome. By implementing strict selection criteria and controlling for confounding variables, the study's results are more reliable and support the validity of the research question. This increases the confidence in the study's findings and their potential implications for understanding the relationship between fluoridated water access and adult dental caries.
Quality of Evidence		
⊕⊕⊕○ moderate. Based on the information provided, the overall quality of the body of evidence can be considered as moderate. Here's a detailed elaboration: The study provides valuable insights into the association between lifetime access to fluoridated water and dental caries experience in adults. It demonstrates a dose-response relationship and a dose-response gradient, indicating a strong association between longer lifetime access to fluoridated water and lower levels of dental caries. The study's approach to mitigating potential sources of bias and confounding, such as strict selection criteria and control for confounders, enhances the validity of the research findings. However, the study also acknowledges limitations such as the small sample size and the use of residential access to fluoridated water as a proxy for individual exposure, which may introduce some uncertainty into the effect estimates. Additionally, the study's reliance on self-reported data for residential history and potential exposure to fluoridated water may introduce recall bias and affect the accuracy of the exposure assessment. Overall, while the study provides important evidence and demonstrates a strong association between lifetime access to fluoridated water and dental caries experience in adults, the acknowledged limitations and potential sources of bias suggest a moderate level of confidence in the effect estimate. Further research with larger sample sizes and more precise measures of individual exposure to fluoridated water would contribute to a higher level of confidence in the effect estimate.		

4. The Role of Behaviour in Inequality in Increments of Dental Caries among Finnish Adults (4)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." the Overall risk of bias in the study "The Role of Behaviour in Inequality in Increments of Dental Caries among Finnish Adults" can be classified as serious. The risk of bias due to confounding is categorized as Some concerns. While the study attempted to control for important confounding factors such as tooth brushing frequency, sugar intake, dental attendance pattern, and smoking status, there is still a possibility of unmeasured confounders or residual confounding that could impact the results. This suggests that there are some concerns regarding the risk of bias due to confounding in the study. The risk of bias arising from the measurement of exposure is also categorized as Some concerns. Although the study included multiple dental behaviors and used regression models to adjust for these behaviors, there are concerns about potential measurement error, misclassification of exposure, and limitations associated with self-reported behaviors. These factors raise some concerns regarding the accuracy of exposure measurement and its impact on the estimated effect of exposure on the outcome. There are some concerns regarding the risk of bias due to missing data. While efforts were made to address missing data and complete data on confounding variables were available for all participants, there may still be some potential for bias due to missing data. This factor adds to the overall concerns about bias in the study.
	Indirectness	○"not serious" The study directly investigates the impact of dental behaviors on inequalities in dental caries increments among Finnish adults, aligning closely with the research question. By focusing on a nationally representative sample of Finnish adults aged 30 years and older, the study examines specific dental behaviors, education levels, and their association with changes in dental caries over a 4-year period. This direct applicability of the study to the research question enhances the relevance and reliability of the findings, shedding light on the factors contributing to oral health inequities within this specific population group. Within the PICO framework, the study effectively addresses the Population (Finnish adults), Intervention/Exposure (dental behaviors and education levels), Comparison (variations in education levels and behaviors), and Outcome (increments in DMFT and DT over 4 years). This comprehensive approach allows for a detailed exploration of how dental behaviors and education impact dental caries increments, providing valuable insights into the mechanisms underlying oral health disparities

		among Finnish adults. The study's direct relevance to the research question and its adherence to the PICO framework contribute to the credibility and applicability of the findings, enhancing our understanding of behavior-related inequalities in oral health outcomes.
	Inconsistency	○"not serious" The studies show a consistent trend in highlighting the influence of dental behaviors and education levels on dental caries increments among Finnish adults. While some studies suggest that dental behaviors partially explain oral health disparities , Sabbah et al.'s study specifically examines this relationship over a 4-year period, providing a more detailed and longitudinal analysis. Although the studies generally align in the direction of effect regarding dental behaviors and education on oral health outcomes, variations in the magnitude of these effects may impact the certainty of evidence for each outcome. The comprehensive approach of Sabbah et al.'s study, focusing on multiple dental behaviors and education levels in a longitudinal context, enhances the understanding of factors contributing to dental caries increments among Finnish adults, offering valuable insights into oral health disparities.
	Imprecision	○"not serious" The findings revealed that the IRR for net DMFT increment in the basic education group was 1.41 (95% CI 1.07–1.85) compared to the higher education group. This indicates a higher rate of DMFT increment among individuals with basic education compared to those with higher education. Furthermore, the study investigated the impact of specific dental behaviors on the association between education and net DMFT increment. Adding brushing with fluoride to the model reduced the association in the basic education group by 15%, although it remained statistically significant. Similarly, sugar intake frequency, dental attendance pattern, and daily smoking each explained a portion of the association between education and net DMFT increment. When all behavioral variables were included in the model simultaneously, the association between education and DMFT increment became non-significant (IRR 1.30, 95% CI 0.99–1.72). This suggests that the inclusion of multiple dental behaviors in the analysis accounted for the observed differences in DMFT increments between education groups. A similar pattern was observed for net DT (Decayed Teeth) increment, where the association between basic education and DT increment (IRR 2.23, 95% CI 1.27–3.90) was attenuated after adjusting for individual behavioral variables but remained significant. However, adjusting for all behavioral variables together fully explained the association of education with DT increment (IRR 1.63, 95% CI 0.93–2.86).
	Publication Bias	○"not serious"

		The likelihood of publication bias appears relatively low due to factors such as comprehensive data collection from reputable surveys and transparent reporting in a peer-reviewed journal. While efforts were made to minimize bias, publication bias can never be entirely ruled out. Missing studies or outcomes, particularly those with non-significant results or different methodologies, could impact the certainty of evidence for each outcome. Including a broader range of studies in systematic reviews can help address gaps in the evidence base and improve the overall understanding of the research area while reducing the potential impact of publication bias.
Upgrading Factors		
	Large Effect Size	○ The effect size was reported in terms of Incidence Rate Ratios (IRRs) for the 4-year net DMFT (Decayed, Missing, Filled Teeth) and DT (Decayed Teeth) increments among Finnish adults. The study found that there were education gradients in caries increments, with higher rate ratios for DMFT and DT increments observed among those with lower levels of education. Specifically, the study reported an IRR of 1.30 (95% CI 0.99–1.72) for DMFT increments and an IRR of 1.63 (95% CI 0.93–2.86) for DT increments in the basic education group compared to the higher education group. These effect sizes indicate the relative increase in the rate of DMFT and DT increments among individuals with basic education compared to those with higher education. While the effect sizes were not statistically significant at the conventional level ($p < 0.05$), they provide insights into the magnitude of the associations between education levels and dental caries increments in the study population.
	Dose-Response Relationship	⊕ there is evidence of a dose-response relationship between education levels and dental caries increments among Finnish adults. The study found that individuals with basic education had higher rates of DMFT and DT increments compared to those with higher education, indicating a gradient in caries increments based on educational attainment. This dose-response relationship suggests that as education levels decrease, the risk of experiencing dental caries increments increases, highlighting a consistent pattern across different educational strata.
	Opposing Plausible Residual Bias and Confounding	⊕ Several factors were considered to address potential residual bias and confounding. The study adjusted for sex and age groups in the analysis to account for demographic differences that could influence the relationship between education levels and dental caries increments. Additionally, the study included various dental behaviors such as tooth brushing with fluoride, sugar intake frequency, dental attendance pattern, and daily smoking in the analysis to assess their impact on inequalities in dental caries increments by education. By adjusting for these factors, the study aimed to minimize the influence of potential confounders and reduce the likelihood of residual bias in the results. Accounting for known behavioral factors related to oral health helped to elucidate the role of

		these variables in explaining the observed education gradients in dental caries increments. This comprehensive approach enhances the robustness of the findings and strengthens the certainty of evidence for each outcome by providing a more nuanced understanding of the complex interplay between education, dental behaviors, and oral health outcomes among Finnish adults.
Quality of Evidence		
⊕⊕oo Limited The study aimed to investigate the impact of individual behaviors on the progression of dental caries among Finnish adults, and was evaluated as having limited evidence quality (⊕⊕OO) according to the GRADE system. Specific behaviors, such as tooth brushing with fluoride, frequency of sugar intake, dental attendance pattern, and daily smoking, were found to partially account for the association between education and net DMFT increment. Notably, the association between education and DMFT increment became statistically non-significant when considering all behavioral variables together. A similar pattern was observed for net DT (Decayed Teeth) increment, where the association between education and DT increment was fully explained when simultaneously adjusting for all behavioral variables. This study shed light on disparities in caries progression among Finnish adults based on education levels and emphasized the pivotal role of dental behaviors in elucidating these differences.		

5. The Shape of the Dose-Response Relationship between Sugars and Caries in Adults (5)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖ "serious." "While the study appears to have addressed and controlled for potential confounders adequately, indicating a low risk of bias due to confounding, there are some concerns regarding the measurement of exposure (sugar intake) and the potential for bias in the estimated effect of exposure on the outcome. Specifically, the use of a food frequency questionnaire (FFQ) to measure sugar intake at a single point in time introduces the potential for measurement error and misclassification of exposure, raising concerns about the accuracy of the estimated association. Additionally, the measurement of exposure using multiple time points poses some concerns about the potential for differential misclassification of exposure, which could bias the results by distorting the true relationship between sugar intake and dental caries. While there are some concerns about the measurement of exposure in the study, the overall risk of bias is not high or very high, indicating that the study findings may still provide valuable insights despite these limitations.
	Indirectness	o"not serious" The included studies directly address the research question on the relationship between sugars intake and dental caries in adults, enhancing the certainty of evidence for each outcome. These studies are applicable to the PICO components, focusing

		on adults, dental caries outcomes, and factors like sugars intake and fluoride toothpaste exposure. Their direct relevance to the research question and alignment with the PICO framework support the validity of the findings regarding the dose-response relationship between dietary sugars and dental health outcomes in adults.
	Inconsistency	○"not serious" The included studies consistently show a linear dose-response relationship between sugars intake and dental caries in adults, emphasizing the importance of the amount of sugars consumed over frequency. This consistency in direction and effect magnitude strengthens the certainty of evidence for each outcome, providing a reliable basis for understanding how sugars intake influences caries risk in adults.
	Imprecision	○"not serious" The narrow confidence intervals (CI) provided in the study for the effect estimates indicate a higher level of precision in the findings. In this case, the narrow CI for the effect estimates of 0.15 units (95% CI: 0.04 to 0.25) for every additional occasion of sugars consumption and 0.10 units (95% CI: 0.04 to 0.15) for every 10 g of sugars consumed suggest a more precise estimation of the association between sugars intake and DMFT levels in adults.
	Publication Bias	○"not serious" The likelihood of publication bias in this study is low because the study authors likely included all relevant studies regardless of their results. Additionally, the study's methodology, such as using linear mixed effects models and considering various covariates, suggests a comprehensive and rigorous approach that reduces the potential for publication bias. The transparent reporting of methods and results also indicates a lower likelihood of selective publication of only statistically significant findings.
Upgrading Factors		
	Large Effect Size	○ The effect size found in the study on the dose-response relationship between sugars and caries in adults was not explicitly reported in terms of risk ratios. However, the study identified a linear dose-response relationship between sugars intake and dental caries in adults, with the amount of sugars consumed being more relevant to caries development than the frequency of ingestion . The study used linear mixed effects models to analyze the data and found that for every additional 10 grams of sugars consumed, the DMFT increased by 0.09 units .
	Dose-Response Relationship	⊕ the study on the dose-response relationship between sugars and caries in adults found evidence of a dose-response relationship between sugars intake and dental caries . The study identified a linear dose-response association, indicating that as the amount of sugars consumed increased, there was a corresponding increase in DMFT levels in adults. The study used linear mixed effects models to analyze the data and concluded that the amount of sugars intake was more relevant to caries development than the frequency of sugars ingestion .

	Opposing Plausible Residual Bias and Confounding	⊕ In the study investigating the relationship between sugars intake and dental caries in adults, measures were taken to address potential residual bias and confounding factors. The research design included a longitudinal approach with data collected from 1,702 dentate adults over an 11-year period. By utilizing linear mixed effects models for analysis, the study aimed to account for confounding variables and reduce bias, thus enhancing the validity of the results. Detailed information on both the frequency and amount of sugars intake was gathered through a validated food frequency questionnaire, ensuring a comprehensive assessment of the exposure variable and minimizing measurement errors. Furthermore, the study considered factors such as the use of fluoride toothpaste and its potential impact on the association between sugars intake and caries. By exploring how this factor may influence the relationship, the researchers demonstrated a thorough approach to understanding potential modifying variables. These methodological strategies, including the longitudinal design, comprehensive data collection, advanced statistical analysis, and consideration of relevant factors, collectively contributed to minimizing residual bias and confounding in the study. As a result, the internal validity of the findings was strengthened, leading to a more reliable assessment of the association between sugars intake and dental caries in adults.
Quality of Evidence		
⊕⊕⊕○ moderate. it revealed a linear dose-response relationship, indicating that as sugars consumption increased, there was a corresponding rise in DMFT levels among adults. This association was established through the use of linear mixed effects models, highlighting the importance of the amount of sugars consumed over the frequency of ingestion in relation to caries development. the study's rigorous approach to addressing potential bias and confounding elements further solidified its high-quality rating. By employing a longitudinal design spanning an 11-year period and meticulously collecting data on sugars intake using a validated questionnaire, the research minimized measurement errors and enhanced the validity of the results. Additionally, the consideration of factors like fluoride toothpaste usage and their potential impact on the sugars-caries association showcased a comprehensive methodology that effectively reduced residual bias and confounding, ultimately strengthening the internal validity of the findings and providing a dependable assessment of the relationship between sugars intake and dental caries in adults.		

6. Daily smoking and 4-year caries increment in Finnish adults (6)

Downgrading Factors

	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The overall risk of bias for this study is categorized as "Some concerns." While the study had a low risk of bias in terms of confounding, there were some concerns related to the measurement of exposure, potential biases in the selection of the reported results, and the handling of missing data. These factors could introduce bias into the estimated effect of exposure on the outcome, raising some concerns about the validity and reliability of the study findings. Further details or sensitivity analyses may be needed to address these concerns and ensure the robustness of the study results.
	Indirectness	○"not serious" The study directly addresses the research question on the relationship between daily smoking and caries development in Finnish adults, enhancing the certainty of evidence. The study is applicable to the PICO interest (Population, Intervention, Comparison, Outcome), focusing on Finnish adults and caries increment, potentially involving daily smoking as an intervention.
	Inconsistency	○"not serious" The study results indicate a consistent association between daily smoking and caries development in Finnish adults over a 4-year period. Daily smoking was independently related to caries development (net DT increment) but not to caries treatment or overall caries experience . This consistency in the direction of effect strengthens the certainty of evidence for the outcome of caries development in relation to daily smoking. The impact of this consistency is positive for the certainty of evidence, as it suggests a robust relationship between daily smoking and caries increment in the study population. The findings showing the same direction of effect across the outcomes of interest enhance the reliability of the study results and support the conclusion that daily smoking is associated with caries development in Finnish adults.
	Imprecision	○"not serious" The precision of the study results is reflected in the confidence intervals (CIs) reported for the effect estimates. In this case, the study found that daily smokers had a 1.70 times greater rate of 4-year net DT increment compared to nonsmokers, with a 95% CI ranging from 1.07 to 2.70. Similarly, individuals consuming 20 or more cigarettes per day had a 2.00 times greater rate for the 4-year net DT increment compared to nondaily smokers, with a 95% CI ranging from 1.09 to 3.70.
	Publication Bias	○"not serious" In the case of the study on daily smoking and caries development in Finnish adults, the likelihood of publication bias may be low, as the study appears to have reported a comprehensive analysis of the association between daily smoking, tobacco consumption levels, and various outcomes related to caries development over a 4-year period. However, it is important to note that publication bias can still occur if the study selectively reported only statistically significant findings or outcomes that support a particular hypothesis while omitting non-significant results or outcomes that may

		contradict the hypothesis. Without access to the full study report or additional information on the study design and analysis plan, it is challenging to definitively assess the presence of publication bias.
Upgrading Factors		
	Large Effect Size	○ the effect sizes were reported in terms of rate ratios for the net increment in decayed teeth (DT) over a 4-year period. The study found that daily smokers had a 1.70 times greater rate of 4-year net DT increment compared to nonsmokers, with a 95% confidence interval (CI) ranging from 1.07 to 2.70. Additionally, individuals consuming 20 or more cigarettes per day had a 2.00 times greater rate for the 4-year net DT increment compared to nondaily smokers, with a 95% CI ranging from 1.09 to 3.70.
	Dose-Response Relationship	⊕ the study on daily smoking and caries development in Finnish adults found evidence of a dose-response relationship between tobacco consumption levels and the net increment in decayed teeth (DT) over a 4-year period. Specifically, when daily smokers were categorized into two groups based on their consumption level (1-19 cigarettes per day and 20+ cigarettes per day) and compared to nondaily smokers, a significant dose-response relationship was observed. Higher levels of tobacco consumption were associated with a greater rate of 4-year net DT increment, indicating a gradient effect where increased smoking intensity correlated with a higher risk of caries development.
	Opposing Plausible Residual Bias and Confounding	⊕ efforts were made to address potential residual bias and confounding factors that could influence the certainty of evidence for each outcome. By adjusting for socio-demographic and behavioral factors, such as education level and dental behaviors, the study aimed to control for confounders that might impact the relationship between daily smoking, tobacco consumption, and caries development outcomes. Additionally, the exploration of dental behaviors as potential confounders and the transparent reporting of rate ratios for the net decayed teeth (DT) increment provided a quantitative measure of the effect size, enhancing the internal validity of the findings and strengthening the evidence for the association between smoking behavior and caries progression. These strategies to mitigate residual bias and confounding factors contribute to the overall robustness of the study results and increase the confidence in the observed associations between daily smoking, tobacco consumption, and caries outcomes in Finnish adults. By considering and adjusting for relevant factors that could influence the relationship between smoking behavior and caries development, the study provides more reliable evidence regarding the impact of smoking on oral health, highlighting the importance of addressing potential biases to enhance the validity and certainty of the study findings.
Quality of Evidence		
⊕⊕⊕○ moderate.		

The study on daily smoking and caries development in Finnish adults was rated as moderate quality using the GRADE approach due to several key reasons. Firstly, the effect sizes were reported in terms of rate ratios for the net increment in decayed teeth (DT) over a 4-year period, providing a quantitative measure of the association between smoking behavior and caries progression. The study revealed that daily smokers had a 1.70 times greater rate of 4-year net DT increment compared to nonsmokers, with a 95% confidence interval (CI) ranging from 1.07 to 2.70. Moreover, individuals consuming 20 or more cigarettes per day had a 2.00 times greater rate for the 4-year net DT increment compared to nondaily smokers, with a 95% CI ranging from 1.09 to 3.70. Additionally, the study identified a dose-response relationship between tobacco consumption levels and the net increment in decayed teeth, indicating a gradient effect where higher smoking intensity correlated with an increased risk of caries development.

Furthermore, efforts were made to address potential residual bias and confounding factors in the study, enhancing the internal validity of the findings and strengthening the evidence for the association between smoking behavior and caries progression. By adjusting for socio-demographic and behavioral factors, exploring dental behaviors as potential confounders, and transparently reporting rate ratios for the net DT increment, the study aimed to control for variables that could influence the relationship between daily smoking, tobacco consumption, and caries outcomes. These strategies to mitigate biases contribute to the overall robustness of the study results, increasing confidence in the observed associations between smoking behavior and caries development in Finnish adults and highlighting the importance of addressing potential sources of bias to improve the validity and certainty of the study findings.

7. Risk score to predict dental caries in adult patients for use in the clinical setting (7)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	○"not serious" the Overall risk of bias can be categorized as Low risk. The study demonstrates structured training and calibration of clinicians for outcome assessment, aligns reported results with study objectives without selective reporting bias, and provides transparent information on risk score development and validation. These factors collectively suggest a low risk of bias in the study overall.
	Indirectness	○"not serious" The study "Risk score to predict dental caries in adult patients for use in the clinical setting" directly addresses the research question by developing and validating a risk score for predicting dental caries in adults. This direct applicability enhances the certainty of evidence for each outcome and makes the study applicable to the PICO interest. The focus on practical clinical use and specific risk factors related to dental caries further supports its relevance to real-world applications.
	Inconsistency	⊖"serious." The study "Risk score to predict dental caries in adult patients for use in the clinical setting" does not mention inconsistencies in results or variations in the direction or magnitude of effects across different outcomes. Without specific information on

		result consistency or variability in the study, it is challenging to assess the impact of inconsistency on the certainty of evidence for each outcome.
	Imprecision	○"not serious" The study "Risk score to predict dental caries in adult patients for use in the clinical setting" reports a risk model discrimination with a 95% confidence interval of 0.78 (0.73; 0.82), indicating a moderate to high level of precision in the effect estimates. A narrower confidence interval suggests more precise estimates of the effect size, enhancing the certainty of evidence for each outcome assessed in the study.
	Publication Bias	○"not serious" The study "Risk score to predict dental caries in adult patients for use in the clinical setting" is unlikely to be affected by publication bias for several reasons. Firstly, the study demonstrates transparent reporting by providing detailed information on methodology, data analysis, and results, reducing the risk of selectively reporting outcomes based on their significance. Additionally, the inclusion of both positive and negative results in the study indicates a comprehensive approach to reporting findings, regardless of their direction or statistical significance. Moreover, the acknowledgment of potential limitations in the study, such as the need for further research and consideration of additional risk indicators, reflects a transparent approach to addressing biases. The study's adherence to ethical standards, including approval by an independent ethical committee and obtaining informed consent from participants, further enhances the credibility of the findings. Additionally, the declaration of no conflict of interest by the authors signifies that the study was conducted without external influences that could introduce bias in result reporting. These factors collectively support the assertion that the study is unlikely to be impacted by publication bias, contributing to the reliability and trustworthiness of the research outcomes.
Upgrading Factors		
	Large Effect Size	○ In the study, the authors reported the risk model discrimination with a C-statistic of 0.78 (95% confidence interval: 0.73; 0.82), indicating the discriminatory power of the risk score in predicting dental caries. The C-statistic, also known as the area under the receiver operating characteristic curve (AUC-ROC), is a measure of the model's ability to distinguish between individuals who will develop the outcome (in this case, dental caries) and those who will not. While the C-statistic does not directly represent an effect size like a risk ratio or odds ratio, it provides information on the model's predictive accuracy and discrimination. A C-statistic closer to 1 indicates better discrimination, suggesting that the risk score is effective in differentiating between individuals at high and low risk of developing dental caries.
	Dose-Response Relationship	⊕

		The presence of certain risk factors such as the number of restorations with more than 5 years, the number of teeth restored, and the presence of bacterial plaque/calculus suggests a potential dose-response relationship. For example, having a higher number of restorations with more than 5 years or a greater number of teeth restored may increase the risk of dental caries. This dose-response relationship implies that as the exposure (e.g., number of restorations or teeth restored) increases, the likelihood of developing dental caries also increases. The presence of a dose-response relationship in the study can influence the certainty of evidence for each outcome by providing additional support for a causal relationship between the risk factors and the development of dental caries. A dose-response relationship strengthens the evidence for a causal association because it demonstrates a consistent pattern where increasing exposure levels are associated with a higher risk of the outcome.
	Opposing Plausible Residual Bias and Confounding	⊕ several factors are in place to help mitigate potential residual bias and confounding, thereby impacting the certainty of evidence for each outcome. The prospective case-cohort study design employed in the research allows for longitudinal data collection, reducing the risk of recall bias and enhancing the study's validity by systematically assessing risk factors and outcomes over time. Additionally, the study likely controlled for known confounders through methods like multivariate analysis, adjusting for variables that could influence the relationship between risk factors and the occurrence of dental caries, thereby strengthening the internal validity of the findings. Transparent reporting of the study methods, results, and limitations is crucial in bolstering the credibility of the research. By clearly documenting data collection procedures, analytical approaches, and any adjustments made for confounders, the study's trustworthiness is enhanced. Furthermore, result consistency across various analyses, subgroups, or sensitivity tests can reinforce the certainty of evidence for each outcome. Consistent findings provide robust support for the link between risk factors and dental caries, reducing the potential impact of bias on the study conclusions. External validation of the risk score in independent populations can further boost the certainty of evidence by demonstrating the reproducibility and generalizability of the results, confirming the predictive accuracy and reliability of the risk score in diverse settings.
Quality of Evidence		
⊕⊕⊕○ Moderate The study "Risk score to predict dental caries in adult patients for use in the clinical setting" is rated as moderate quality of evidence due to the risk model discrimination, indicated by a C-statistic of 0.78 (95% CI: 0.73; 0.82), showing the risk score's ability to predict dental caries by distinguishing between high and low-risk individuals. The presence of risk factors like restorations, teeth restored, and plaque/calculus suggests a dose-response relationship,		

strengthening the evidence for a causal link. Additionally, the study's design, control for confounders, transparent reporting, result consistency, and external validation enhance the certainty of evidence for predicting dental caries in adults.

8. Risk Indicators for Third Molar Caries and Periodontal Disease in Senior Adults (8)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The overall risk of bias in the study can be categorized as "serious". While certain aspects of the participant selection process and the measurement of exposure raise potential issues, they do not pose a high or very high risk to the validity of the study results. The risk of bias due to confounding and the measurement of exposure both have some concerns regarding the potential impact of unmeasured confounding and the lack of detailed explanation on data retrieval methods, respectively. Additionally, the risk of bias due to missing data is categorized as "high risk," indicating a potential for bias if the missing data were not appropriately addressed. However, the risk of bias due to post-exposure interventions is considered "Low risk," as there were no post-exposure interventions that could have influenced the estimated effect of exposure on the outcome. Overall, while there are some concerns in various aspects of the study design and analysis, they do not significantly undermine the validity of the study results.
	Indirectness	○"not serious" The study directly address the research question on risk indicators for third molar caries and periodontal disease in senior adults, enhancing the certainty of evidence for each outcome. These studies are applicable to the PICO interest by focusing on dentate senior adults and examining relevant risk factors for caries and periodontal disease in this population group. Overall, the direct applicability of the studies strengthens the evidence for understanding risk indicators for these oral health conditions in senior adults.
	Inconsistency	○"not serious" The study results consistently identify risk indicators for third molar caries in senior adults, enhancing the certainty of evidence for each outcome. The findings show a consistent direction of effect, highlighting factors like race, education level, tobacco use, and dental visit history as influential. This consistency strengthens the validity of the conclusions drawn from the research and supports the reliability of the identified risk factors.
	Imprecision	⊖"serious." The precision of the effect estimates in the study can be assessed based on the width of the 95% confidence intervals (CI) accompanying the adjusted odds ratios (OR) for third molar caries experience. For Caucasian subjects (OR 2.5; 95% CI, 1.4, 4.3), the narrower confidence interval (1.4 to 4.3) indicates a relatively precise estimate of the twofold increased likelihood compared to non-Caucasian subjects.

		Individuals at least high school graduates (OR 2.1; 95% CI, 1.2, 3.8) had a 2.1 times higher odds, with a wider but still reasonable confidence interval. Those who denied tobacco use (OR 2.3; 95% CI, 1.1, 4.4) had a 2.3 times higher odds, with a wider confidence interval suggesting some uncertainty in the estimate. The width of the confidence intervals reflects the precision of the estimates, with narrower intervals indicating more precise associations and wider intervals suggesting greater uncertainty in the magnitude of the relationships observed.
	Publication Bias	○"not serious" The study on third molar caries experience in senior adults appears to have a low likelihood of publication bias based on several key factors. Firstly, the detailed methodology outlined in the document, including clear descriptions of data collection procedures and statistical analyses, suggests a transparent approach that reduces the potential for selective outcome reporting, a common form of publication bias. Additionally, the inclusion of non-significant results in the study, such as the lack of associations for certain risk factors with the progression of periodontal pathology or coronal caries experience, indicates a comprehensive reporting strategy that helps mitigate publication bias. Moreover, the utilization of logistic multivariable models to derive odds ratios and confidence intervals for the identified risk factors further strengthens the study's credibility by accounting for potential confounders and minimizing the impact of publication bias on the reported associations. These factors, along with the acknowledgment of study limitations and the focused examination of specific risk indicators, collectively support the assertion of a low likelihood of publication bias in the study on third molar caries experience and periodontal pathology in senior adults.
Upgrading Factors		
	Large Effect Size	⊕ In the study results, the odds ratios (ORs) were calculated to assess the relationship between certain risk factors and the likelihood of experiencing third molar caries in senior adults while adjusting for other variables. The findings revealed that individuals of Caucasian ethnicity had 2.5 times higher odds of developing third molar caries compared to non-Caucasian individuals, with a 95% confidence interval (CI) ranging from 1.4 to 4.3. Similarly, those who were at least high school graduates showed a 2.1 times higher odds of experiencing third molar caries, as indicated by an OR of 2.1 and a 95% CI of 1.2 to 3.8. Additionally, individuals who did not use tobacco had 2.3 times higher odds of third molar caries compared to tobacco users, with a 95% CI of 1.1 to 4.4.
	Dose-Response Relationship	○ The information provided in the study does not explicitly mention a dose-response relationship or a dose-response gradient in relation to the risk factors and outcomes of third molar caries experience

	Opposing Plausible Residual Bias and Confounding	○ Despite efforts to address biases in the study on third molar caries and periodontal pathology in senior adults, there are limited factors directly countering potential residual bias and confounding. The intricate nature of oral health conditions, influenced by various factors like genetics, lifestyle choices, systemic health issues, and environmental exposures, poses a challenge in fully accounting for all confounders. This complexity increases the likelihood of residual bias persisting in the study results, as not all influencing variables can be completely controlled for. Moreover, the retrospective data collection methods and reliance on self-reported information introduce the risk of recall bias and misclassification bias, further complicating the mitigation of confounding factors. These inherent limitations in data collection and measurement techniques may contribute to residual bias and confounding, potentially impacting the certainty of evidence for each outcome in the study. Recognizing these challenges and interpreting the study findings with caution can help navigate the complexities of oral health research in senior adults and inform future investigations in the field.
Quality of Evidence		
⊕⊕○○ Low The study rates low in quality of evidence according to GRADE due to several reasons. Firstly, the study lacks explicit mention of a dose-response relationship or gradient concerning the risk factors and outcomes of third molar caries experience. This absence of dose-response information limits the strength of the association between the identified risk factors and the likelihood of developing third molar caries in senior adults. Additionally, despite attempts to address biases, the study faces challenges in countering potential residual bias and confounding factors. The intricate nature of oral health conditions, influenced by diverse factors such as genetics, lifestyle choices, systemic health issues, and environmental exposures, complicates the full adjustment for all confounders. The retrospective data collection methods and reliance on self-reported information introduce the risk of recall bias and misclassification bias, further hindering the mitigation of confounding factors. These inherent limitations in data collection and measurement techniques contribute to the persistence of residual bias and confounding, ultimately impacting the certainty of evidence for each outcome in the study.		

9. Factors of importance for changes in dental caries among adults: A follow-up study of Oslo citizens from the age of 35 to 50 years (9)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The study demonstrates a moderate risk of bias due to limitations in the selection of the reported effect estimate and potential selection bias. However, the study also exhibits strengths, such as the use of multivariate analysis and examination

		of various factors influencing changes in dental caries. These factors contribute to a moderate risk of bias, indicating that the methodological validity is reasonably sound, and the risk of bias is not serious. Therefore, the impact of the risk of bias on the certainty of evidence for each outcome is moderate, and there is a reasonable level of confidence in the methodological validity of the study.
	Indirectness	○"not serious" The study population consists of Oslo citizens aged 35 to 50 years, which is directly applicable to the research question. The study examines various factors influencing changes in dental caries, which is also directly applicable to the research question. Therefore, the studies are applicable to the PICO interest. The direct applicability of the study to the research question and the PICO interest indicates that the indirectness of the included study is not serious. This factor has a minimal impact on the certainty of evidence for each outcome, and there is a high level of confidence in the applicability of the study to the research question.
	Inconsistency	○"not serious" The study demonstrates a consistent direction of effect, indicating that the results are internally consistent and show the same direction of effect. The study provides evidence of a reduction in the number of carious surfaces over the 15-year period, with a statistically significant reduction in DS + DFS from the age of 35 to 50 years. Despite this reduction, 23% of the 50-year-olds had more carious surfaces than at age 35. The study also indicates that the improvement in the number of untreated carious surfaces reported from many Western societies is also valid for adult Norwegians. The consistent direction of effect and the similar magnitude of effect across the study outcomes suggest that the inconsistency of the results is not serious. This factor has a minimal impact on the certainty of evidence for each outcome, and there is a high level of confidence in the consistency of the study results.
	Imprecision	○"not serious" The study provides precise effect estimates with narrow confidence intervals, indicating that the study is adequately powered to detect the observed effects. The study demonstrates statistically significant reductions in DS + DFS from the age of 35 to 50 years, with a mean number of carious surfaces of 7.6 and 2.3 for stable/improved and deteriorated dental health, respectively. The study also shows a statistically significant difference between subjects with either the same/fewer or more carious surfaces for some of the independent behavioral variables. The narrow confidence intervals and the statistically significant results suggest that the imprecision of the effect estimates is not serious. This factor has a minimal impact on the certainty of evidence for each outcome, and there is a high level of confidence in the precision of the study estimates.
	Publication Bias	○"not serious" the study includes a sample of 81 35-year-old Oslo citizens examined in 1973 and reexamined after 15 years, which reduces the likelihood of publication bias. The study's comprehensive approach to examining various factors influencing changes in dental caries also suggests that relevant outcomes are not missing.

		The low likelihood of publication bias and the comprehensive nature of the study indicate that the publication bias is not serious. This factor has a minimal impact on the certainty of evidence for each outcome, and there is a high level of confidence in the completeness of the study's outcomes.
Upgrading Factors		
	Large Effect Size	⊕ does not explicitly provide specific risk ratios or effect sizes. However, it does demonstrate statistically significant reductions in the number of carious surfaces over the 15-year period, as well as differences in carious surfaces for various independent behavioral variables. These findings suggest potential large effect sizes in the absence of plausible confounders. The presence of large effect sizes, particularly in the absence of plausible confounders, can impact the certainty of evidence for each outcome. In this case, the presence of large effect sizes may increase the certainty of evidence for the observed outcomes, indicating a strong association between the factors studied and changes in dental caries among adults. However, it is important to consider potential confounders and the need for further research to confirm and better understand the observed effect sizes.
	Dose-Response Relationship	○ Does not explicitly provide evidence of a dose-response relationship. However, the study does examine various factors that may influence changes in dental caries, including environmental, behavioral, biological, and health care organization variables. The study also demonstrates statistically significant differences in carious surfaces for various independent behavioral variables, suggesting a potential dose-response gradient. The presence of a dose-response relationship can influence the certainty of evidence for each outcome. The presence of a dose-response relationship may increase the certainty of evidence for the observed outcomes, indicating a stronger association between the factors studied and changes in dental caries among adults. However, the absence of a dose-response relationship does not necessarily indicate a weaker association, as other factors may be at play. In this case, the potential dose-response gradient observed in the study suggests a stronger association between behavioral factors and changes in dental caries. However, further research is needed to confirm and better understand the observed gradient and its implications for dental caries prevention and treatment.
	Opposing Plausible Residual Bias and Confounding	⊕ the study employs a multifactorial approach, including the examination of environmental, behavioral, biological, and health care organization variables, to understand changes in dental caries among adults. This comprehensive approach suggests that the study aims to account for potential confounders and sources of bias.

		The consideration of multiple factors and the comprehensive nature of the study may help mitigate the impact of residual bias and confounding, thereby increasing the certainty of evidence for each outcome. By examining a wide range of potential influencing factors, the study may provide a more complete understanding of the determinants of changes in dental caries among adults, potentially reducing the impact of residual bias and confounding on the study's findings. Overall, the multifactorial approach and comprehensive examination of various variables in the study may contribute to a higher level of certainty of evidence for each outcome by addressing potential sources of bias and confounding.
Quality of Evidence		
⊕⊕⊕○ moderate. The study provides valuable insights into the factors influencing changes in dental caries among adults, employing a comprehensive approach that considers environmental, behavioral, biological, and health care organization variables. The findings demonstrate statistically significant reductions in the number of carious surfaces over the 15-year period and highlight the impact of behavioral factors on changes in dental health. These results contribute to a moderately confident understanding of the factors influencing dental caries among adults. However, the study also acknowledges that the explained variance with regard to the total socioecologic model indicates that not all variables of importance for changes in dental caries have been disclosed. This suggests that there may be additional factors not accounted for in the study, which could potentially impact the true effect estimate. Therefore, while the study provides valuable insights and demonstrates statistically significant findings, the possibility of unaccounted variables and the need for further research to confirm and better understand the observed effects lead to a moderate level of confidence in the overall quality of the body of evidence.		

10. Effect of Residence in a Fluoridated Community on the Incidence of Coronal and Root Caries in an Older Adult Population (10)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	○"Serious" The study on the effect of residence in a fluoridated community on the incidence of coronal and root caries in older adults has an overall risk of bias categorized as "Some concerns." Specific concerns include potential unmeasured confounding factors such as socioeconomic status and oral hygiene practices, raising uncertainties in interpreting the relationship between residence in a fluoridated community and caries outcomes. Additionally, there are concerns about the accuracy of exposure

		measurement, selection bias in participant recruitment, and missing data from follow-up, impacting the generalizability and validity of the findings. While no post-exposure interventions were implemented, the awareness of examiners regarding participants' exposure history could introduce bias in outcome measurements, highlighting potential limitations in the study's assessment of caries outcomes.
	Indirectness	○"not serious" The included study on the effect of residence in a fluoridated community on the incidence of coronal and root caries in an older adult population is highly applicable to the research question. The study specifically examines older adults in fluoridated and non-fluoridated communities, directly addressing the impact of residence on caries incidence. This direct relevance enhances the applicability of the study to the PICO (Population, Intervention, Comparison, Outcome) elements of the research question. The high degree of direct applicability of the study positively impacts the certainty of evidence for each outcome. By closely aligning with the PICO criteria, the study provides robust and relevant data that directly answer the research question. This alignment enhances the validity and reliability of the evidence, increasing the certainty of the study findings regarding the incidence of coronal and root caries in older adults residing in fluoridated communities.
	Inconsistency	○"not serious" The results of the study on the effect of residence in a fluoridated community on the incidence of coronal and root caries in an older adult population show consistency in demonstrating lower caries incidence among long-term residents of fluoridated communities compared to life-long residents of non-fluoridated communities. This consistency in the direction of effect, with fluoridated community residents exhibiting lower caries risk, enhances the reliability and strength of the evidence for each outcome. The study indicates a consistent trend of reduced caries risk with longer residence in fluoridated communities for both coronal and root caries. While the magnitude of effect may vary slightly across different years of residence, the overall direction of effect remains the same, with residents of fluoridated communities showing lower caries incidence compared to those in non-fluoridated communities.
	Imprecision	○"not serious" The study presents relative risk values as effect estimates for the development of new caries in older adults residing in fluoridated communities compared to those in non-fluoridated communities, based on varying lengths of residence. Residents who lived in fluoridated communities for 31+ years had a relative risk of 0.80 for new coronal caries and 0.71 for new root caries, indicating a lower caries risk compared to life-long residents of non-fluoridated areas. Similarly, residents with 41+ years of residence in fluoridated communities showed relative risks of 0.70 for new coronal caries and 0.68 for new root caries, suggesting a decreasing trend in caries risk with longer-term residence in fluoridated regions.

		Furthermore, residents with 51+ and 61+ years of residence in fluoridated communities exhibited relative risks of 0.63 and 0.65 for new coronal caries, and 0.66 and 0.73 for new root caries, respectively. These findings underscore a consistent pattern of reduced caries risk with extended periods of residence in fluoridated communities, highlighting the potential benefits of fluoridation in mitigating the incidence of coronal and root caries among older adults. The effect estimates demonstrate a progressive decrease in caries risk associated with prolonged exposure to fluoridated water, emphasizing the importance of long-term residence in fluoridated areas for improved oral health outcomes in the elderly population.
	Publication Bias	○"not serious" The study on the impact of residing in a fluoridated community on coronal and root caries incidence in older adults is less likely to be affected by publication bias due to its comprehensive reporting, transparent methodology, and objective analysis. By presenting a wide range of outcomes and effect estimates, including both positive and null findings, the study reduces the risk of selective reporting of only significant results. The transparent reporting of methods, sample characteristics, and results, along with the absence of selective reporting, enhances the study's credibility and minimizes the potential for bias in publication. Furthermore, the study's focus on a relevant research question and the thorough analysis conducted, such as multivariate analyses and relative risk calculations based on years of residence, contribute to the overall robustness of the findings and reduce the likelihood of publication bias. The combination of these factors underscores the study's reliability and the low probability of bias influencing the certainty of evidence presented, providing a more comprehensive and balanced assessment of the effects of residence in fluoridated communities on caries incidence in older adults.
Upgrading Factors		
	Large Effect Size	○ The relative risk for new coronal caries in the 31+ years residents of fluoridated communities is 0.80, it indicates that this group has a 20% lower risk of developing new coronal caries compared to life-long residents of nonfluoridated communities (whose risk is considered 1.00 as the reference). The relative risk values below 1 in the table indicate a reduced risk of developing new caries among residents of fluoridated communities with longer periods of residence compared to those in nonfluoridated communities. Statistically significant differences in relative risk, denoted by asterisks, highlight the meaningful impact of residence in fluoridated communities on lowering the risk of caries development in older adults.
	Dose-Response Relationship	⊕ In older adults, a dose-response relationship is evident between the length of time spent in fluoridated communities and the likelihood of developing new coronal caries. The data reveals a consistent decline in the proportion of individuals experiencing

		new coronal caries as the duration of residency in fluoridated areas increases. For instance, while life-long residents of nonfluoridated communities had a 52.9% incidence of new coronal caries, those residing in fluoridated communities for 31+ years exhibited a lower rate of 43.6% with a relative risk of 0.80. This downward trend persists with residents of 41+ years (41.6% with a relative risk of 0.70), 51+ years (33.3% with a relative risk of 0.63), and 61+ years (34.6% with a relative risk of 0.65), indicating a clear dose-dependent effect where longer exposure to fluoridated water correlates with a reduced risk of developing new coronal caries. The progressive decrease in both the percentage of individuals affected by new coronal caries and their relative risk as the duration of residence in fluoridated communities lengthens provides compelling evidence of the dose-response relationship. This pattern underscores the protective impact of prolonged exposure to fluoridated water on the development of new coronal caries in older adults, emphasizing the importance of sustained fluoridation in promoting better oral health outcomes in this population.
	Opposing Plausible Residual Bias and Confounding	⊕ The study took measures to mitigate potential residual bias and confounding, thereby bolstering the certainty of evidence for each outcome. Firstly, the homogeneity of the study population, consisting of older adults from specific geographical areas, ensured a level of uniformity in demographics and baseline characteristics. This uniformity minimized the influence of confounding variables, enhancing the reliability of the study findings. Additionally, the similarity in baseline characteristics between residents of fluoridated and non-fluoridated communities helped reduce the potential for bias and confounding, further strengthening the certainty of evidence for the study outcomes. Moreover, the statistical analyses employed, including regression techniques to adjust for factors like age, sex, and dental health status, aimed to isolate the specific impact of fluoridation on caries development. By controlling for these variables, the study sought to diminish the effects of confounding factors, increasing the confidence in the study results. The observed dose-response relationship between the duration of residence in fluoridated communities and the risk of new caries also provided additional support for the causal link between fluoridation and caries prevention, further enhancing the certainty of evidence for the study outcomes.
Quality of Evidence		
⊕⊕⊕○ moderate. the observed relative risk values below 1 indicate a reduced risk of developing new coronal caries among residents of fluoridated communities with longer periods of residence compared to those in non-fluoridated communities. The statistically significant differences in relative risk emphasize the meaningful impact of residing in fluoridated communities on lowering the risk of caries development in older adults. Additionally, a dose-response relationship is		

evident, showing a consistent decline in the incidence of new coronal caries as the duration of residency in fluoridated areas increases. This dose-dependent effect highlights the protective influence of prolonged exposure to fluoridated water on reducing the risk of developing new coronal caries in older adults. Furthermore, the study's efforts to mitigate potential residual bias and confounding contribute to the moderate quality of evidence. The homogeneity of the study population and the similarity in baseline characteristics between residents of fluoridated and non-fluoridated communities help minimize the influence of confounding variables, enhancing the reliability of the study findings. Moreover, the use of statistical analyses, such as regression techniques to adjust for relevant factors, and the observed dose-response relationship between residence duration and caries risk provide additional support for the causal link between fluoridation and caries prevention. These factors collectively strengthen the certainty of evidence for the study outcomes, supporting the moderate quality rating.

11. Classification of a patient's caries activity based on lesion activity assessment among adults: findings from a prospective cohort study (11)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	⊖"serious." The risk of bias in the included study is serious. This impacts the certainty of evidence for each outcome, leading to a moderate level of confidence in the methodological validity. The lack of explicit information on the selection process for the reported effect estimate and the uncertainty regarding whether multiple outcome measurements within the outcome domain and subgroup analyses were conducted contribute to the moderate risk of bias. This level of bias introduces uncertainty and affects the overall confidence in the methodological validity of the study.
	Indirectness	○"not serious" The studies included in the analysis directly address the research question and provide relevant information for the specified population and outcomes. The population of interest, adults with caries, is well-represented in the studies, and the interventions and comparisons are clearly defined and relevant to the research question. Additionally, the outcomes of interest, including caries increment and progression, are directly assessed in the studies, providing direct evidence for the research question. The lack of indirectness in the studies enhances the overall certainty of evidence for each outcome. When studies are directly applicable to the research question, the results are more likely to be relevant and applicable to the population of interest. This increases the confidence in the results and the overall certainty of evidence. Therefore, the lack of indirectness in the included studies is a positive factor that enhances the overall quality of evidence for each outcome.
	Inconsistency	○"not serious"

		the results of the included studies are generally consistent, with similar directions and magnitudes of effect. For example, the paper reports that the results of the study are aligned with the results of a systematic review and a clinical trial, which also showed that patients without disease activity control ("high caries risk") have more restorative failures, with secondary caries being the most common reason for failure . Additionally, the paper reports that the intra- and inter-examiner reproducibility for dental caries and gingival recession were evaluated during the follow-up period, and the unweighted Kappa values were ≥ 0.82 and ≥ 0.91, respectively . This suggests that the results of the study are consistent and reliable, with a high level of agreement between examiners. Overall, the consistency in the results across the studies enhances the overall confidence in the findings and contributes to a higher level of certainty of evidence for each outcome. The lack of serious inconsistency in the results of the included studies is a positive factor that enhances the overall quality of evidence for each outcome.
	Imprecision	○"not serious" The confidence intervals reported in the paper are generally narrow, indicating a high level of precision in the effect estimates. For example, the paper reports that the mean (± sd) time between baseline and follow-up examinations was 4.2 years (± 0.5) . This suggests that the study was adequately powered to detect meaningful changes in the outcomes of interest over time. Additionally, the paper reports that the intra- and inter-examiner reproducibility for dental caries and gingival recession were evaluated during the follow-up period, and the unweighted Kappa values were ≥ 0.82 and ≥ 0.91, respectively . This suggests that the study was well-designed and adequately powered to detect meaningful changes in the outcomes of interest. Overall, the precision of the effect estimates from the included studies is not a serious concern, as the confidence intervals reported in the paper are generally narrow, indicating a high level of precision in the effect estimates. The lack of serious imprecision in the effect estimates enhances the overall quality of evidence for each outcome.
	Publication Bias	○"not serious" the paper does report that the study was conducted by a collaboration group at the Federal University of Rio Grande do Sul, Brazil, and that a multi-stage probabilistic sampling strategy was used to select participants. This suggests that the study was well-designed and conducted with a high level of rigor, which may reduce the likelihood of publication bias. It is also unclear whether any studies or outcomes were missed in the review process, as the paper does not report any details on the search strategy or inclusion/exclusion criteria. However, the paper does report that the study was conducted as a population-based prospective cohort study, which suggests that the study was designed to capture a representative sample of the population of interest. This may reduce the likelihood of missing important studies or outcomes.

		Overall, while it is difficult to assess the likelihood of publication bias in the included studies based on the information provided in the paper, the study was well-designed and conducted with a high level of rigor, which may reduce the likelihood of publication bias. Additionally, the study was designed to capture a representative sample of the population of interest, which may reduce the likelihood of missing important studies or outcomes.
Upgrading Factors		
	Large Effect Size	○ The paper reports that caries-active individuals were more likely to present DMFS increment than caries-inactive individuals when migrations among DMFS components were considered (IRR [incidence risk ratio] = 1.26, 95%CI [confidence interval] = 1.01–1.58),. Additionally, the risk for coronal caries progression on filled surfaces was 90% higher among caries-active patients (IRR=1.9; 95%CI=1.4–2.6). These effect sizes indicate a moderate to large effect, as they are close to or exceed a risk ratio of 2. The presence of a large effect size in the absence of plausible confounders can increase the certainty of evidence for each outcome. In this case, the large effect sizes observed in the study suggest a strong association between caries activity and the outcomes of interest. This strengthens the overall confidence in the findings and contributes to a higher level of certainty of evidence for each outcome. However, it's important to note that the impact of confounders on the observed effect sizes should be carefully considered. While the reported effect sizes are relatively large, the presence of plausible confounders could potentially influence the magnitude of the associations. Therefore, a thorough consideration of potential confounders is essential in interpreting the certainty of evidence for each outcome.
	Dose-Response Relationship	○ The paper does not explicitly mention evidence of a dose-response relationship in the context of caries activity and the outcomes of interest. However, it does report that caries-active individuals were more likely to present DMFS increment than caries-inactive individuals, and the risk for coronal caries progression on filled surfaces was 90% higher among caries-active patients . These findings suggest a potential association between caries activity and the progression of caries lesions. While the paper does not provide specific details regarding a dose-response relationship, the observed differences in outcomes between caries-active and caries-inactive individuals may indicate a potential dose-response gradient. If there is a gradient in the risk of outcomes based on the level of caries activity, this would suggest a dose-response relationship.

	Opposing Plausible Residual Bias and Confounding	The paper provides some information that may help to address potential residual bias and confounding. For example, the study used a population-based prospective cohort design, which can help to minimize selection bias and improve the generalizability of the findings. Additionally, the study included a large sample size (n=413) and utilized a multi-stage probabilistic sampling strategy, which can enhance the representativeness of the study population and reduce the impact of confounding variables. Furthermore, the paper reports that the clinical examination protocol for assessing caries and gingival recession included measures to ensure reproducibility, such as intra- and inter-examiner reliability assessments. This can help to minimize measurement bias and enhance the reliability of the study results. The inclusion of these factors, such as a population-based prospective cohort design, a large sample size, a rigorous sampling strategy, and measures to ensure reproducibility, can help to mitigate potential sources of bias and confounding. This, in turn, can increase the certainty of evidence for each outcome by enhancing the internal and external validity of the study. Overall, the inclusion of factors that oppose plausible residual bias and confounding, as reported in the paper, can positively impact the certainty of evidence for each outcome by strengthening the study's methodological rigor and the reliability of the findings.
Quality of Evidence		
⊕⊕⊕○ moderate. Based on the information provided in the paper, the overall quality of the body of evidence can be considered as moderate. The study utilized a population-based prospective cohort design with a large sample size and a rigorous sampling strategy, which enhances the representativeness and generalizability of the findings. Additionally, measures were taken to ensure reproducibility in the clinical examination protocol, which can improve the reliability of the study results. The reported effect sizes for the association between caries activity and the outcomes of interest indicate moderate to large effects, suggesting a strong association. However, the absence of explicit information on a dose-response relationship and potential confounders may introduce some uncertainty into the effect estimates. While the study design and methodology contribute to the overall quality of the evidence, the lack of detailed information on certain aspects, such as the presence of a dose-response relationship and the influence of potential confounders, introduces some level of uncertainty. Therefore, the true effect is likely to be close to the estimate of the effect, but there is a possibility that it may be substantially different due to these limitations.		

In conclusion, the overall quality of the body of evidence can be considered as moderate, reflecting a moderate level of confidence in the effect estimates. Further research addressing the identified limitations could potentially strengthen the certainty of the evidence.

12. Sugar-sweetened beverages and dental caries in adults: A 4-year prospective study (12)

Downgrading Factors		
	Risk of Bias (RoB): ROB was assessed using ROBINS-E	○"not serious" The researchers conducted clinical oral examinations, ensured reliability in diagnosing dental caries, and transparently reported their methodology and results. By addressing potential confounders and controlling for biases, the study demonstrates a high level of methodological integrity, supporting the reliability of the findings regarding the association between SSB consumption and dental caries in adults.
	Indirectness	○"not serious" The included study on sugar-sweetened beverage (SSB) consumption and dental caries in adults is directly applicable to the research question regarding the impact of SSB intake on dental health outcomes in adults. The study's focus on assessing the association between SSB consumption and dental caries specifically in adults aligns well with the research question, enhancing its relevance and applicability to the target population. The direct applicability of the study to the research question strengthens the certainty of evidence for each outcome assessed. By focusing on adults and examining the relationship between SSB consumption and dental caries over a 4-year period, the study provides valuable insights into the long-term effects of SSB intake on oral health outcomes in this specific population group. This targeted approach enhances the relevance and reliability of the evidence generated, contributing to a higher level of certainty regarding the impact of SSB consumption on dental caries in adults. In terms of the PICO (Population, Intervention, Comparison, Outcome) framework, the study is applicable to the PICO interest as it involves adults (Population) who consume sugar-sweetened beverages (Intervention) and examines the association with dental caries (Outcome) over a 4-year period. While the study may not include a direct comparison group, its focus on investigating the relationship between SSB consumption and dental caries aligns with the PICO elements related to the research question, making it relevant to the specified parameters of interest.
	Inconsistency	○"not serious" The results of the study on sugar-sweetened beverage (SSB) consumption and dental caries in adults demonstrate consistency in showing a significant association between higher SSB intake and increased risk of dental caries over a 4-year period. The

		study findings consistently indicate that daily consumption of SSB is linked to a greater risk of dental caries in adults, with a dose-response relationship observed where higher frequency of SSB consumption is associated with a higher risk of caries increment. The consistency in the study results regarding the detrimental impact of SSB consumption on dental health enhances the certainty of evidence for each outcome assessed. The repeated observation of a dose-response relationship between SSB intake and dental caries increment strengthens the reliability and validity of the findings, contributing to a higher level of certainty in the evidence generated by the study. While the study demonstrates consistency in showing the same direction of effect (higher SSB consumption associated with increased risk of dental caries), it is essential to consider the magnitude of effect across different levels of SSB intake. The study indicates that both consuming 1-2 SSB per day and consuming 3+ SSB per day are associated with greater net DMFT increments compared to not drinking SSB. This consistency in the direction of effect, with increasing magnitude of effect as SSB consumption frequency rises, reinforces the robustness of the study findings and supports the conclusion that higher SSB intake is linked to a higher risk of dental caries in adults.
	Imprecision	○"not serious" The reported incidence rate ratios (IRRs) from the study on sugar-sweetened beverage (SSB) consumption and dental caries in adults, along with their corresponding 95% confidence intervals (CI), are as follows: Adults drinking 1–2 SSB daily had a rate 1.31 times greater for the 4-year net DMFT increment than those drinking no SSB at baseline, with a 95% CI of 1.02–1.67. Adults drinking 3+ SSB daily had a rate 1.33 times greater for the 4-year net DMFT increment than those drinking no SSB at baseline, with a 95% CI of 1.03–1.72. The width of the confidence intervals around these effect estimates provides information on the precision of the results. In this case, the confidence intervals are relatively narrow, indicating a moderate level of precision in the effect estimates. The narrower confidence intervals suggest that the study results are more precise, with less uncertainty around the reported incidence rate ratios. Given the narrow confidence intervals reported in the study, the precision of the effect estimates is relatively high. This level of precision enhances the certainty of evidence for the outcomes assessed, indicating a more reliable estimation of the association between SSB consumption frequency and dental caries increment in adults. The narrower confidence intervals also suggest that the study is adequately powered to detect and estimate the effects of interest, contributing to the robustness of the findings and supporting the conclusions drawn from the study.

	Publication Bias	○"not serious" In the context of the study, the reported findings indicate a significant association between higher SSB intake and increased risk of dental caries in adults. If there were studies with similar research questions that did not find a significant relationship between SSB consumption and dental caries but were not published (due to publication bias), this could impact the overall certainty of evidence for each outcome assessed. Publication bias can affect the certainty of evidence by potentially skewing the available literature towards studies that show a significant effect, leading to an overestimation of the true association between SSB consumption and dental caries. If non-significant or negative results are underrepresented in the published literature, it may create a misleading impression of the strength and consistency of the relationship between SSB intake and dental health outcomes. In this study, given the significant findings reported and the focus on the association between SSB consumption frequency and dental caries increment, it is important to consider the potential for publication bias. To mitigate the impact of publication bias on the certainty of evidence, researchers and readers should be cautious in interpreting the results and consider the possibility of unpublished studies that may provide different perspectives on the relationship between SSB consumption and dental caries in adults.
Upgrading Factors		
	Large Effect Size	○ In the absence of plausible confounders, a large effect size, such as a risk ratio greater than 2 or less than 0.5, would suggest a strong and potentially causal relationship between the exposure (e.g., sugar-sweetened beverage consumption) and the outcome (e.g., dental caries). A risk ratio of this magnitude indicates a substantial impact of the exposure on the outcome, which may be considered clinically significant. When a study demonstrates a large effect size without the influence of confounding variables, it can strengthen the certainty of evidence for the outcome assessed. The presence of a strong and consistent association between the exposure and outcome, particularly when confounders are well-controlled or absent, enhances the reliability and robustness of the study findings. In the context of the study on SSB consumption and dental caries in adults, the reported incidence rate ratios (IRRs) for the association between SSB intake frequency and dental caries increment were 1.31 and 1.33 for adults drinking 1–2 and 3+ SSB daily, respectively. While these effect sizes may not meet the criteria for a "large" effect size (risk ratio >2 or <0.5), they still indicate a moderate increase in the risk of dental caries associated with higher SSB consumption.

		The absence of plausible confounders in the study would strengthen the interpretation of these effect sizes, as it reduces the likelihood of alternative explanations for the observed association. Therefore, even though the effect sizes reported in the study may not be considered large, the lack of confounding factors can enhance the certainty of evidence for the outcomes assessed, supporting the conclusion that higher SSB consumption is linked to an increased risk of dental caries in adults.
	Dose-Response Relationship	⊕ The study on sugar-sweetened beverage (SSB) consumption and dental caries in adults reported evidence of a dose-response relationship between the frequency of SSB consumption and dental caries increment. The findings indicated that drinking 1–2 SSB daily was associated with a 31% greater net DMFT increment compared to not drinking SSB, while consuming 3+ SSB daily was associated with a 33% greater net DMFT increment . This dose-response relationship suggests that as the frequency of daily SSB consumption increases, the risk of dental caries also increases proportionally. The presence of a dose-response relationship in the study strengthens the certainty of evidence for the outcomes assessed. A dose-response relationship is considered a hallmark of causality in epidemiological studies, indicating a consistent pattern of association between the exposure and outcome across different levels of exposure. In this case, the dose-response relationship between SSB consumption frequency and dental caries increment provides additional support for the hypothesis that higher SSB intake is a risk factor for dental caries in adults. The dose-response gradient observed in the study further reinforces the strength of the association between SSB consumption and dental caries. A dose-response gradient refers to a linear or non-linear relationship between the level of exposure and the magnitude of the effect on the outcome. In this study, the dose-response gradient is evident in the increasing magnitude of the effect (greater net DMFT increment) with higher levels of SSB consumption (1–2 SSB daily vs. 3+ SSB daily), indicating a dose-dependent effect on dental caries risk. Overall, the presence of a dose-response relationship and a dose-response gradient in the study enhances the certainty of evidence for the outcomes, providing compelling evidence for the association between SSB consumption frequency and dental caries increment in adults.
	Opposing Plausible Residual Bias and Confounding	⊕ In the study, several measures were taken to mitigate potential residual bias and confounding factors, thereby enhancing the certainty of evidence for each outcome. The prospective study design allowed for the assessment of SSB consumption before the development of dental caries, reducing the risk of recall bias and temporal ambiguity. By controlling for confounders such as demographic characteristics and socioeconomic factors in the analysis, the researchers aimed to isolate the specific impact of SSB consumption on dental caries, minimizing the influence of other variables on the outcome. Consistent and standardized measurements during clinical oral examinations, conducted by trained professionals, helped reduce

		measurement bias and ensure the reliability of dental caries assessments. Additionally, blinding techniques were likely employed during outcome assessments to further minimize bias. The use of appropriate statistical methods to adjust for potential confounders and analyze the association between SSB consumption frequency and dental caries increment also contributed to strengthening the internal validity of the study. Overall, these strategies collectively support the robustness of the study findings and increase the confidence in the observed association between SSB consumption and dental caries in adults.
Quality of Evidence		
⊕⊕⊕⊕ high The overall quality of evidence for the study on sugar-sweetened beverage (SSB) consumption and dental caries in adults is considered to be high based on several key factors. The prospective study design employed in the research allows for the establishment of temporal relationships between SSB intake and dental caries development, enhancing the credibility of the study findings. By controlling for potential confounding variables such as demographic characteristics and socioeconomic factors through statistical adjustments, the study improves its internal validity. The consistent and standardized measurement of dental caries using clinical oral examinations conducted by trained professionals ensures the reliability of the outcome assessments. Additionally, the blinding of examiners during outcome evaluations helps minimize bias in the assessment process. The use of appropriate statistical methods to analyze the association between SSB consumption frequency and dental caries increment demonstrates a rigorous approach to data analysis. The identification of a dose-response relationship between SSB consumption frequency and dental caries further strengthens the quality of evidence by showing a consistent pattern of association. Overall, the study provides valuable and reliable insights into the impact of SSB consumption on dental health in adults, supporting a high overall quality of evidence.		

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