Supplementary Table 1: Inclusion Criteria for Selecting Studies on Nicotine Replacement Therapy for Oral Smokeless Tobacco (OST) Cessation

PICOS	Inclusion criteria
Participants	Oral Smokeless tobacco (ST) users of both gender
Intervention	Nicotine Replacement Therapy (NRT)
Comparison	Generic intervention (education, advice, self-help), Placebo or no intervention
Outcome	1. 7-day point prevalence ST abstinence rate at week 12 2. ST reduction rate at week 12
Study design	Randomized controlled trial and non-randomized trial

Supplementary Table 2: Summary judgment determination by risk of bias numbers per study

Amount of 'Low risk'	Amount of 'High risk'	Amount of 'Unclear risk'	Summary judgment
0	0,1 or 2	3,4 or 5	Unclear risk
0	3, 4 or 5	0,1 or 2	High risk
1	0 or 1	3 or 4	Unclear risk
1	2, 3 or 4	0,1 or 2	High risk
2	0	3	Unclear risk
2	1, 2 or 3	0,1 or 2	Intermediate risk
3	0,1 or 2	0,1 or 2	Intermediate risk
4	0 or 1	0 or 1	Low risk
5	0	0	Low risk

Supplementary Table 3: Interpretation Framework for Effect Sizes: Standardized Mean Differences (Cohen's *d*) and Odds Ratios

Effect Size (ES)	**Standardized mean difference (*d*)** (Cohens' *d*, 1988)[a]	**Odds ratio (*OR*)** (Lipsey and Wilson, 1993)[b]
Small	.10 to .49	1.50 to 2.49
Medium	.50 to .79	2.50 to 4.29
Large	≥.80	≥ 4.30

a: Cohen J. Statistical Power Analysis for the Behavioral Sciences. Hove: Lawrence Erlbaum Associates; 1988.

b: Lipsey MW, Wilson DB. The efficacy of psychological, educational, and behavioral treatment: Confirmation from meta-analysis. Am Psychol. 1993;48(12):1181-1209. doi:10.1037//0003-066X.48.12.1181

Material 1: Data abstraction form

Authors, year, country	
Publication status	Published/ In Press /Unpublished/ Not reported
Study design	RCT/ Non-randomized trial
Nicotine replacement therapy	yes / no
Smokeless tobacco intervention	yes / no
Outcome measure	1. ST Abstinence rate: Yes/No 2. ST reducing consumption rate: Yes/No 3. Others:
Sample Size	1. Number of participants at baseline 2. Number of participants at the end of intervention
Intervention setting	
Intervention group	
Placebo or Comparison group	
Instrument used	
Time point	
Analysis	
Co-variates used	
Results for outcome	
The size of effect	

The direction of effect	
Type of Bias	(Selection/ performance/ detection/ attrition/ reporting) bias
Risk of bias	(low/ high/ Unclear)
Summary judgement of bias risk per article	(Low risk/ intermediate risk/ high risk/ unclear risk)
Note	
This form was filled with	

Material 2: List of included interventions

1) Ebbert JO, Severson HH, Croghan IT, Danaher BG, Schroeder DR. A randomized clinical trial of nicotine lozenge for smokeless tobacco use. Nicotine Tob Res. 2009;11(12):1415-1423. doi:10.1093/ntr/ntp154
2) Severson HH, Danaher BG, Ebbert JO, Van Meter N, Lichtenstein E, Widdop C, Seeley JR. Randomized trial of nicotine lozenges and phone counseling for smokeless tobacco cessation. Nicotine Tob Res. 2014;17(3):309-315. doi:10.1093/ntr/ntu157
3) Schiller R, Luo X, Anderson A, Jensen J, Allen S, Hatsukami D. Comparing an immediate cessation versus reduction approach to smokeless tobacco cessation. Nicotine Tob Res. 2012;14(8):902-909. doi:10.1093/ntr/ntr296
4) Raja M, Saha S, Krishna-Reddy V, Mohd S, Narang R, Sood P. Effectiveness of oral health education versus nicotine replacement therapy for tobacco cessation—a parallel randomized clinical trial. J Clin Exp Dent. 2016;8(1):e64-e69. doi:10.4317/jced.52752
5) Ebbert JO, Severson HH, Croghan IT, Danaher BG, Schroeder DR. Comparative effectiveness of the nicotine lozenge and tobacco-free snuff for smokeless tobacco reduction. Addict Behav. 2013;38(5):2140-2145. doi:10.1016/j.addbeh.2013.01.012
6) Ebbert JO, Severson HH, Croghan IT, Danaher BG, Schroeder DR. A pilot study of mailed nicotine lozenges with assisted self-help for the treatment of smokeless tobacco users. Addict Behav. 2010;35(5):522-525. doi:10.1016/j.addbeh.2009.12.014
7) Ebbert JO, Dale LC, Patten CA, Croghan IT, Schroeder DR, Moyer TP, Hurt RD. Effect of high-dose nicotine patch therapy on tobacco withdrawal symptoms among smokeless tobacco users. Nicotine Tob Res. 2007;9(1):43-52. doi:10.1080/14622200601078505
8) Danaher BG, Severson HH, Crowley R, van Meter N, Tyler MS, Widdop C, Ebbert JO. Randomized controlled trial examining the adjunctive use of nicotine lozenges with MyLastDip: an eHealth smokeless tobacco cessation intervention. Internet Interv. 2015;2(1):69-76. doi:10.1016/j.invent.2014.12.005
9) Wallström M, Bolinder G, Hassèus B, Hirsch JM. A cessation program for snuff-dippers with long-term, extensive exposure to Swedish moist snuff: A 1-year follow-up study. Acta Odontol Scand. 2010;68(6):377-384. doi:10.3109/00016357.2010.514728
10) Ebbert JO, Croghan IT, Schroeder DR, Hurt RD. A randomized phase II clinical trial of high-dose nicotine patch therapy for smokeless tobacco users. Nicotine Tob Res. 2013;15(12):2037-2044. doi:10.1093/ntr/ntt088

11) Siddiqui F, Kanaan M, Croucher R, et al; ASTRA Global Health Research Group. Behavioural support and nicotine replacement therapy for smokeless tobacco cessation in Bangladesh, India and Pakistan: A pilot randomized controlled trial. Addiction. Published online May 20, 2024. doi:10.1111/add.16515

Material 3: Search String

The search string was the following:
((("nicotine"[MeSH Terms]) AND ("replacement") AND ("therapy"[Subheading] OR "therapy" OR "therapeutics"[MeSH Terms])) OR ("tobacco use cessation products"[MeSH Terms] OR ("tobacco" AND "cessation" AND "products") OR ("nicotine" AND "lozenge") OR ("nicotine lozenge") OR ("nicotine" AND "patch") OR ("nicotine patch") OR ("nicotine" AND "gum") OR "nicotine gum")) AND (("tobacco, smokeless"[MeSH Terms] OR "smokeless tobacco" OR ("smokeless" AND "tobacco")) OR ("tobacco" AND "smokeless") OR ("oral" AND "tobacco") OR "oral tobacco") OR ("chewing" AND "tobacco") OR "chewing tobacco"))) AND (cessation OR quitting OR abstinence OR reduction)) AND (rates OR ("utilization"[Subheading] OR "use"))) NOT ("smoking"[MeSH Terms]).

Material 4: PRISMA 2020 Main Checklist

Topic	No.	Item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pages 1 and 2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pages 2 and 3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pages 3 and 31 (Material 3)

Topic	No.	Item	Location where item is reported
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 3 and 4

Topic	No.	Item	Location where item is reported
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pages 3 and 4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)).	Page 3
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 3
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 3

Topic	No.	Item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Pages 3 and 4
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Pages 3 and 4
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pages 4 and 5

Topic	No.	Item	Location where item is reported
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	NA
Study characteristics	17	Cite each included study and present its characteristics.	Pages 5, 6 and Table 4 (Pages 14-17)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 6 and Table 5 (Pages 19-23)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 6. Pages: 24 - 28.
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pages 6 and 7
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA

Topic	No.	Item	Location where item is reported
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 7
	23b	Discuss any limitations of the evidence included in the review.	Page 8
	23c	Discuss any limitations of the review processes used.	Page 8
	23d	Discuss implications of the results for practice, policy, and future research.	Pages 8 and 9
OTHER INFORMATION			

Topic	No.	Item	Location where item is reported
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Submitted to PROSPERO [586624]
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	NA
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 9
Competing interests	26	Declare any competing interests of review authors.	Page 9
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Material 1 to 4

PRIMSA Abstract Checklist

Topic	No.	Item	Reported?
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesize results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes

Topic	No.	Item	Reported?
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

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