

Appendix
Smoking Cessation for Smokers Not Ready to Quit: Meta-analysis and Cost-effectiveness Analysis
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Appendix Table 1. Summary of Studies Assessing Interventions for SNRTQ (2000–2011, Asfar)

Reference, country	Sample size	Eligibility criteria	Control/treatment conditions	Other treatment components	Follow-up (months)	Outcome	Smoking abstinence treatment %(n/N)	Smoking abstinence control %(n/N)	Effect size OR (95% CI)
Pharmacologic interventions									
Bolliger et al., 2000; Switzerland	400	Smoke ≥ 15 CPD for ≥ 3 years, have an exhaled-air CO level of at least 10 ppm, failed at least 1 serious quit attempt in past 12 months, unwilling or unable to quit at recruitment	Placebo; nicotine inhaler for 18 months	All subjects receive health information on smoking	24	PP ^a	10.5% (21/200)	8.5% (17/200)	1.26 (0.65, 2.47)
Wennike et al., 2003; Denmark	411	Smoke ≥ 15 CPD for ≥ 3 years, failed at least 1 serious quit attempt in past 2 years, have an exhaled-air CO level of at least 15 ppm, not intending to quit in next month	Placebo; nicotine gum for 12 months, randomized to 2 mg or 4 mg pieces	All subjects receive reduction information	24	PP ^a	9% (19/205)	3% (7/206)	2.90 (1.19, 7.07)
Etter et al., 2004; Switzerland	534	Smoke ≥ 20 CPD, not intending to quit in next 6 months	Placebo; NRT (free choice; patch, inhaler, or gum) for 6 months	All subjects receive 20-page booklets on reduction	26	30-day CA	11.7% (31/265)	9.3% (25/269)	1.29 (0.74, 2.26)
Hatsukami et al., 2004; U.S.	594	Smoke ≥ 20 CPD, not quit for >3 months in previous year,	Placebo; Bupropion for 26 weeks	All subjects receive written materials on	6	30-day CA ^a	7% (20/295)	5% (16/299)	1.29 (0.65, 2.53)

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		have at least 2 failed quit attempts including 1 with NRT		reduction. Additional treatment offered if a quit date is set					
Batra et al., 2005 Germany	364	Smoke >20 CPD for ≥3 years, have an expired-air CO level of at least 15 ppm, have at least 1 failed quit attempt within 2 years but not within the previous 6 months Not intending to quit in next month	Placebo; 4 mg nicotine gum for 12 months	13	1-day PP ^a	12% (22/184)	5% (8/180)	2.92 (1.26, 6.74)	
Rennard et al., 2006; U.S.	429	Smoke ≥20 CPD for ≥3 years, failed at least 1 serious quit attempt in past 2 years, exhaled-air CO level of at least 15 ppm, not intending to quit in next month	Placebo; nicotine inhaler for 12 months	15	PP ^a	8% (17/215)	2% (3/214)	6.04 (1.74, 20.92)	
Behavioral interventions									
Glasgow et al., 2009; U.S.	320	Age ≥18 years, currently ≥10 CPD, scheduled for outpatient surgery or diagnostic procedure, not	Enhanced usual care (generic newsletters); telephone counseling + tailored newsletters	–	12	PP ^a	6.7% (11/164)	4.4% (7/156)	1.53 (0.58, 4.05)

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		interested in quitting, can read/understand English									
Combination of behavioral and pharmacological interventions											
Carpenter et al., 2003; U.S.	67	Smoke ≥ 10 CPD, interest in quitting eventually but not in next 30 days, at least 1 previous quit attempt	Usual care (i.e., brief advice to quit); smoking reduction + free choice of NRT (gum or patches) for 6 months + brief advice to quit	All subjects received brief advice to quit. Additional treatment offered if a quit date is set	6	PP ^a	13% (4/32)	9% (3/35)	1.52 (0.31, 7.40)		
Carpenter et al., 2004; U.S. ^b	616	Smoke ≥ 10 CPD, no interest in quitting	No intervention; Arm 1: smoking reduction + free choice of NRT (gum or patches) for 6 months + brief advice to quit; Arm 2: Motivational intervention (brief advice to quit + NRT if a quit date is set)	–	6	PP ^a	20% (83/409)	4% (9/207)	4.65 (2.18, 9.91)		
Joseph et al., 2008; U.S.	152	Smokers with cardiovascular disease, not interested in quitting in next 30 days	Usual care (i.e., brief advice to quit); rate reduction + nicotine gum for 18 months	–	18	PP ^a	12% (9/78)	12% (9/74)	0.94 (0.35, 2.52)		

Note: Original table published in Asfar et al. (2011); where statistics vary from original published papers, we present those from the original studies. ORs and 95% CI presented here have been calculated by the authors and may differ from those published in Asfar et al. (2011) due to rounding error. Outcome measures are Continuous Abstinence (CA), Point Prevalence Abstinence (PP).

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^aChemically-validated outcomes using expired CO <10ppm.

^b Indicates studies with multiple treatment arms which have been pooled to estimate the overall effect of treatments versus control.

SNRTQ, smokers not ready to quit; CPD, cigarettes per day; CO, carbon monoxide; NRT, nicotine replacement therapy.

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Appendix Table 2. Summary of Recent Studies of Cessation Interventions for SNRTQ

Reference, country	Sample size	Eligibility criteria	Control / Treatment	Other treatment components	Follow-up (months)	Outcome	Smoking abstinence in treatment % (n/N)	Smoking abstinence in control % (n/N)
Pharmacological								
Ebbert et al., 2015; 10 countries	1,510	Smoked ≥ 10 cigarettes/day, no CA > 3 months, exhaled CO ≥ 10 ppm, not willing/able to quit in 30 days, but were willing to reduce smoking and make attempt to quit within next 3 months	Placebo/ Varenicline 1 mg twice daily for 24 weeks	Additional treatment offered if a quit date is set	7	10-week CA ^a	27.0% (205/760)	9.9% (74/750)
Hughes et al., 2011; U.S.	218	Daily smoking ≥ 8 cigarettes/day, want to quit eventually but no intention to quit in 30 days, no history of varenicline use, not currently on smoking cessation	Placebo/ Varenicline 1 mg twice daily for 2–8 weeks	All subjects receive four brief (10–15 minute) counseling sessions. Additional treatment offered if a quit date is set	6	7-day PP ^a	14% (15/107)	7% (8/111)
Jardin et al., 2014; U.S.	157	Daily smoking ≥ 10 cigarettes/day, no previous use of quitline or NRT for > 1 day in past 6 months. Not motivated to quit in 30 days	Quitline referral only/ 2-week NRT sample and referral to quitline	–	3	7-day PP	15% (8/53)	5% (3/51)
Carpenter et al., 2011; U.S.	849	Daily smoking ≥ 10 cigarettes/day, no non-cigarette tobacco use, no previous use of NRT, no quit attempt longer than 1 week in past year, not motivated to quit in 30 days	Usual care/ 2 boxes of NRT lozenges	All subjects receive counseling for practice quit attempt	6	7-day PP	16% (68/426)	14% (60/423)
Behavioral								
Davis et al., 2011; U.S.	218	Smoke a pack a day and are not ready to quit	15-minute prescriptive interview/ 15-	Additional treatment offered if a quit date is set	Both 1 and 6 months	PP ^b	0% (0/109)	0.9% (1/109)

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Catley et al., 2016; U.S. ^c	255	Smoking ≥ 1 cigarettes/day, exhaled CO ≥ 7 ppm, no current use of cessation medication, no cessation plans in next 7 days, unmotivated to quit smoking	minute motivational interview Brief advice/ Arm 1: Motivational interviewing/ Arm 2: Health education	Additional treatment (varenicline, NRT patch or lozenge) offered if a quit date is set	6	7-day PP ^d	5.4% (11/204)	0.0% (0/51)
Huang et al., 2015; China	148	Smoked at least 5 cigarettes/week, exhaled CO ≥ 8 ppm, not motivated/ready to quit, had a family member who would participate as a supporter, had not been in another smoking cessation program	Usual care: cessation advice/ Individual, tailored MI consisting of four weekly 20-minute sessions	All subjects receive self-help manual and 25-minute group session	3 months	PP ^a	2.8% (2/72)	0% (0/76)
Danan et al., 2016; U.S.	1929 SNRTQ (3,006 total)	Current smoker, in preparation (35.8%), contemplation (38.2%), or precontemplation (26.0%) stage of change	Usual care/ Proactive mailing, telephone outreach, and offer of in-person or telephone counseling	All subjects have access to smoking cessation services through VA and state quitline services. Additional treatment offered if a quit date is set	12	6-month CA	6.6% (63/948)	5% (49/981)
Klemperer et al., 2016; U.S. ^c	560	Smoked ≥ 10 cigarettes per day, desire to quit someday but not ready to quit in the next 30 days, no change in CPD by more than $\pm 25\%$, no other nicotine or tobacco products nor cessation treatment	Usual care / Arm 1: Motivational intervention: Three 10–15 minute counseling calls in weeks 0, 2, and 4; Arm 2: Reduction intervention: Three 10–15	–	6 months	PP	9.4% (35/371)	5% (10/189)

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				minute counseling calls					
Combination									
Chan et al., 2011; China ^c	1,154	Smoke ≥2 cigarettes per day, no intention to quit in near future, but interested in reducing smoking, no contraindication to NRT, not following any other smoking cessation or reduction interventions	Cessation advice only/ (Arm 1 and Arm 2) Four sessions in-person counseling +8 weeks free NRT	All subjects receive baseline “Tips for Quitting Smoking” pamphlet	6	PP ^a	8.0% (74/928)	4.4% (10/226)	

Note: Outcome measures are Continuous Abstinence (CA), Point Prevalence Abstinence (PP).

^aChemically-validated outcomes of expired CO <10ppm.

^bUrine analysis cotinine <100 mm,

^cIndicates studies with multiple treatment arms which have been pooled to estimate the overall effect of treatments versus control.

^dSaliva cotinine ≤15 ng/mL.

SNRTQ, smokers not ready to quit; CO, carbon monoxide; NRT, nicotine replacement therapy; MI, motivational interviewing

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Appendix Table 3. Estimates of Effectiveness of Cessation Interventions for SNRTQ

Intervention	Treatment		Treatment		Control		Weight	OR M-H fixed (95% CI)	NNT	Cost per smoker	Cost per quit
	Type	Duration	Quits	Total	Quits	Total					
Pharmacological interventions											
Bollinger et al. 2000	NRT inhaler	18 months	21	200	17	200	14.20%	1.26 (0.65, 2.47)	50	\$5,166.43	\$258,321.69
Wennike et al. 2003	NRT gum	12 months	19	205	7	206	5.90%	2.90 (1.19, 7.07)	17	\$1,046.16	\$17,784.72
Hatsukami et al. 2004	Bupropion	6.5 months	20	295	16	299	13.80%	1.29 (0.65, 2.53)	70	\$1,436.62	\$100,563.46
Batra et al. 2005	NRT gum	12 months	22	184	8	180	6.60%	2.92 (1.26, 6.74)	13	\$1,046.16	\$13,600.08
Rennard et al. 2006	NRT inhaler	12 months	17	215	3	214	2.60%	6.04 (1.74, 20.92)	15	\$3,444.29	\$51,664.34
Ebbert et al. 2015	Varenicline	6 months	205	760	74	750	50.60%	3.37 (2.53, 4.50)	6	\$1,650.05	\$9,900.32
Hughes et al. 2011	Varenicline	2 months	15	107	8	111	6.30%	2.10 (0.85, 5.18)	15	\$550.02	\$8,250.26
Etter et al. 2004 ^a	NRT inhaler, gum, or patch	6 months	31	265	25	269	0.00%	1.29 (0.74, 2.26)	42	\$833.29	\$34,998.10
Carpenter et al. 2011 ^a	NRT lozenges	2 boxes	68	426	60	423	0.00%	1.15 (0.79, 1.67)	56	\$64.56	\$3,615.36
Jardin et al. 2014 ^a	NRT sample	2 weeks	8	53	3	51	0.00%	2.84 (0.71, 11.40)	11	\$85.78	\$943.58
Pooled pharmacological			319	1,966	133	1,960	100.00%	2.72 (2.19, 3.37)	10	\$2,021.79	\$19,510.24
Heterogeneity: $\chi^2 = 13.78$, $df=6$ ($p=0.03$); $I^2 = 56\%$											
Test for overall effect: $z = 9.10$ ($p < 0.00001$)											
Behavioral interventions											
Glasgow et al. 2009	RC + newsletters	4 sessions, telephone + mailings	11	164	7	156	71.10%	1.53 (0.58, 4.05)	45	\$268.48	\$12,081.40
Davis et al. 2011	MI	1 session, telephone	0	109	1	109	15.90%	0.33 (0.01, 8.20)	–	\$86.98	–
Catley et al. 2016 ^b	MI or HE	4 sessions, in-person	11	204	0	51	8.00%	6.12 (0.35, 105.62)	19	\$275.13	\$5,227.51
Huang et al. 2016	MI	4 sessions, in-person	2	72	0	76	5.00%	5.43 (0.26, 114.97)	36	\$275.13	\$9,904.75

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Danan et al. 2016 ^a	Mailings and telephone outreach	1 session, telephone + mailings	63	948	49	981	0.00%	1.35 (0.92, 1.99)	61	\$101.00	\$6,160.75
Klemperer et al. 2016 ^{a,b}	MI	4 sessions, telephone	35	371	10	189	0.00%	1.86 (0.90, 3.85)	24	\$254.46	\$6,107.03
Pooled behavioral			24	549	8	392	100.00%	1.90 (0.86, 4.23)	47	\$240.48	\$11,415.74
Heterogeneity: $\chi^2 = 2.43$, $df=3$ ($p=0.49$); $I^2 = 0\%$											
Test for overall effect: $z = 1.58$ ($p=0.11$)											
Combination interventions											
Carpenter et al. 2003	RC + NRT gum or patches	4 sessions, in-person + 6 months NRT	4	32	3	35	7.20%	1.52 (0.31, 7.40)	25	\$1,108.42	\$27,710.51
Carpenter et al. 2004 ^b	RC + NRT gum or patches	4 sessions, telephone + 1.5 months NRT	83	409	9	207	27.20%	5.60 (2.75, 11.39)	6	\$462.78	\$2,776.69
Chan et al. 2011 ^b	Counseling + NRT choice	4 sessions, in-person + 2 months NRT	74	928	10	226	42.30%	1.87 (0.95, 3.68)	28	\$552.89	\$15,481.05
Joseph et al. 2008	RC + NRT gum	5 sessions, telephone + 18 months NRT	9	78	9	74	23.30%	0.94 (0.35, 2.52)	–	\$2,098.83	–
Pooled combination			170	1,447	31	542	100.00%	2.64 (1.76, 3.97)	16	\$928.59	\$14,662.36
Heterogeneity: $\chi^2 = 9.99$, $df=3$ ($p=0.02$); $I^2 = 70\%$											
Test for overall effect: $z = 4.68$ ($p < 0.00001$)											

Note: ORs are calculated using the equation: $OR = (\% \text{Quit}_{\text{treatment}} / (1 - \% \text{Quit}_{\text{treatment}})) / (\% \text{Quit}_{\text{control}} / (1 - \% \text{Quit}_{\text{control}}))$. NNT is calculated using the equation: $NNT = N_{\text{treatment}} / (\text{Quit}_{\text{treatment}} - \% \text{Quit}_{\text{control}} * N_{\text{treatment}})$. Cost per smoker is calculated by multiplying treatment costs in Table 1 by duration of treatment. Where individuals were offered choice in NRT, average monthly cost of NRT was used. Additional detailed assumptions used to develop costs in Table 1 are described in Appendix Table 5. Cost per quit is calculated by multiplying NNT by cost per smoker.

^aIndicates study used self-reported cessation outcomes. Pooled calculations include only studies where cessation outcomes are bio-chemically verified through saliva, urine, or exhaled cotinine levels.

^bIndicates studies with multiple treatment arms that have been pooled to estimate the overall effect of treatments versus control.

NRT, nicotine replacement therapy; RC: reduction counselling; MI: motivational interviewing; HE: health education; SNRTQ, smokers not ready to quit; M-H, Mantel-Haenszel method to estimate pooled ORs, assuming a fixed effects model; NNT, number needed to treat.

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Appendix Table 4. Sensitivity Analysis of Cessation Interventions for SNRTQ

Reference	Treatment details/ Actual use	Min cost assumptions	Max cost assumptions	Minimum cost per smoker	Maximum cost per smoker	Number needed to treat	Minimum cost per quit	Maximum cost per quit
Pharmacological								
Bollinger et al. 2000	Recommended 6 to 12 cartridges per day. Encouraged to decrease after 4 months, but allowed to continue for 18 months. Actual use: Average of 4.5 cartridges a day at 2 weeks and 2.6 a day at 18 months.	4 cartridges per day; 168 cartridges last approximately 6 weeks.	If 12 cartridges/day, then 168 cartridges will last 2 weeks.	\$3,731.31	\$11,193.94	50	\$186,565.67	\$559,697.00
Wennike et al. 2003	Subjects allowed to use gum freely, up to 12 months. Actual use: Mean daily gum usage at 2 weeks: 7.8 pieces (2 mg) and 9.8 pieces (4 mg), at 12 months: 10.8 pieces (2 mg) and 10.6 pieces (4 mg).	If 7 pieces/day; 100 pack will last approximately 2 weeks. 24 packs will be needed for 12 months.	If 10 pieces/day; 100 pack will last approximately 10 days. Approximately 36 packs will be needed for 12 months.	\$697.44	\$1,046.16	17	\$11,880.96	\$17,821.43
Hatsukami et al. 2004	26 weeks bupropion or placebo (150 mg once for first 3 days; 150 mg, twice daily thereafter); each month, asked if willing to quit, if so enrolled into cessation arm, which includes 7 weeks of bupropion.	Approximately 3 months of Bupropion.	6.5 months of Bupropion.	\$663.06	\$1,436.62	70	\$46,416.54	\$100,569.16
Batra et al. 2005	Participants instructed to use as desired for up to 12 months, 6 to 24 pieces per day. Actual use: Mean daily usage at 2 weeks: 6.5 pieces; at 4 months: 6.5 pieces; at 12 months: 6.1 pieces.	If 6.5 pieces/day; 100 pack lasts ~2 weeks, so 2 packs/month.	If 10 pieces/day; 100 pack lasts 10 days. So 3 packs per month is 36 packs a year.	\$697.44	\$1,046.16	13	\$9,284.25	\$13,926.37
Rennard et al. 2006	Subjects allowed to use inhaler freely for up to 1 year, with a recommendation of 6 to 12 uses per day.	4 cartridges per day; 168 cartridges last approximately 6 weeks.	If 12 cartridges/day, then 168 cartridges will last 2 weeks.	\$2,487.54	\$7,462.63	15	\$38,239.83	\$114,719.50

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	Actual use: Mean inhaler use at 4 months was 6.4 uses per day, at 12 months was 5.8 uses per day.								
Ebbert et al. 2015	Subjects were given Varenicline, 1 mg twice daily for 6 months.	Varenicline, 1 pack per month, for 6 months.	Varenicline, 1 pack per month, for 6 months.	\$1,650.05	\$1,650.05	6	\$9,645.47	\$9,645.47	
Hughes et al. 2011	Subjects were given Varenicline, 1 mg twice daily for 2 months.	Varenicline, 1 pack per month, for 2 months.	Varenicline, 1 pack per month, for 2 months.	\$550.02	\$550.02	15	\$8,074.86	\$8,074.86	
Etter et al. 2004 ^a	Participants could choose between patch, gum, and inhaler and could switch between products or use multiple products. Products were available for 6 months.	6-month supply of patches.	6-month supply of inhalers.	\$254.64	\$1,722.14	42	\$10,590.44	\$71,623.73	
Carpenter et al. 2011 ^a	Subjects were given 2 boxes of NRT lozenges	2 boxes of NRT lozenges.	2 boxes of NRT lozenges.	\$64.56	\$64.56	56	\$3,615.36	\$3,615.36	
Jardin et al. 2014 ^a	Subjects were given both a 2-week supply of both 14 mg NRT patch and 4 mg lozenge.	2-week supply of NRT patch + 2-week supply of NRT lozenges.	2-week supply of NRT patch + 2-week supply of NRT lozenges.	\$85.78	\$85.78	11	\$931.18	\$931.18	
Pooled pharmacological				\$1,642.78	\$2,982.17	10	\$16,427.82	\$29,821.69	
Behavioral									
Glasgow et al. 2009	4 phone counseling sessions + 4 tailored newsletters + 1 targeted newsletter	Lowest-cost 4 phone sessions + printed mailings	From estimated marginal cost/patient in Glasgow et al. 2009.	\$104.25	\$795.44	45	\$4,695.65	\$35,828.41	
Davis et al. 2011	One 15-minute interview	One 15-minute counseling/MI session from study reporting lowest cost.	One 15-minute counseling/MI session from study reporting highest cost.	\$41.70	\$134.82	–	–	–	
Catley et al. 2016 ^b	Individual MI/counseling, 4 sessions, approximately 20 minutes each (2 sessions in person, 2 sessions telephone).	4 In-person/telephone Counseling/MI sessions from study reporting lowest cost.	4 In-person/telephone Counseling/MI sessions from study reporting highest cost.	\$83.40	\$795.44	19	\$1,584.60	\$15,113.36	

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Huang et al. 2016	Four 20-minute individual MI sessions.	4 In-person counseling/MI sessions from study reporting lowest cost.	4 In-person counseling/MI sessions from study reporting highest cost.	\$165.26	\$385.00	36	\$5,949.50	\$13,860.00
Danan et al. 2016 ^a	Pro-active mailing and one telephone call.	Cost of mailing + taking calls only.	Cost of mailing, taking calls + cost of one phone session from study reporting highest cost.	\$20.85	\$155.67	61	\$1,263.13	\$9,430.74
Klemperer et al. 2016 ^{a,b}	Three telephone sessions, each 10–15 minutes duration.	4 phone counseling/MI sessions from study reporting lowest cost.	4 phone counseling/MI sessions from study reporting highest cost.	\$83.40	\$795.44	24	\$2,001.60	\$19,090.56
Pooled behavioral Combination				\$95.69	\$669.88	47	\$4,497.30	\$31,484.33
Carpenter et al. 2003	5 in-person individual sessions (15–20 minutes) on reduction + NRT 24 weeks.	4 In-person counseling/MI sessions from study reporting lowest cost + lowest cost NRT for 6 months.	4 In-person counseling/MI sessions from study reporting highest cost + highest cost NRT for 6 months.	\$419.90	\$2,107.14	25	\$10,688.47	\$53,636.41
Carpenter et al. 2004 ^b	Reduction intervention: three 15-minute reduction counseling calls + 6 weeks of NRT gum or patches Motivation intervention: three 15-minute calls of reduction MI. (No NRT)	4 Telephone counseling/MI sessions from study reporting lowest cost. No NRT.	4 Telephone counseling/MI sessions from study reporting highest cost + NRT gum for 2.5 months.	\$83.40	\$882.62	6	\$500.40	\$5,295.72
Chan et al. 2011 ^b	3 face-to-face counseling sessions + 8 weeks NRT (either gum or patch)	4 In-person counseling/MI sessions from study reporting lowest cost + 2	4 In-person counseling/MI sessions from study reporting highest cost + 2	\$250.14	\$559.36	28	\$7,047.58	\$15,759.46

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Joseph et al. 2008	5 In-person sessions + 5 phone sessions + NRT (either 4 mg gum, 6 pieces/day or switch to patches if >6 pieces of gum/day)	months NRT patch. 4 In-person counseling/MI sessions from study reporting lowest cost + 4 Telephone counseling/MI sessions from study reporting lowest cost + NRT patches for 18 months.	months NRT gum. 4 In-person counseling/MI sessions from study reporting highest cost + 4 telephone counseling/MI sessions from study reporting highest cost + NRT gum for 18 months.	\$1,012.58	\$2,749.68	–	–	–
Pooled combination				\$394.66	\$1,269.07	16	\$6,158.89	\$19,804.52

Note: Additional intervention details and calculations of point estimates for NNT, ORs, cost per smoker, and cost per quit are described in Appendix Table 3. All cost estimates for interventions are based on values reported in Table 1, which are based on cost assumptions described in Appendix Table 5.

^aIndicates study used self-reported cessation outcomes. Pooled calculations include only studies where cessation outcomes are bio-chemically verified through saliva, urine, or exhaled cotinine levels; weights from Table 2 are used for all pooled estimates.

^bIndicates studies with multiple treatment arms which have been pooled to estimate the overall effect of treatments versus control.

SNRTQ, smokers not ready to quit; NRT, nicotine replacement therapy; MI, motivational interviewing; NNT, number needed to treat.

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Appendix Table 5. Detailed Costs of Behavioral Cessation Interventions for General Smokers

Interventions	Total cost/smoker (2016 \$)	Treatment details	References
Counseling or MI (In-person, about 4 sessions)	\$385.00	Five 1-hour group sessions	Barnett et al. 2014
	\$165.26	Four 30-minute individual, in-person sessions	Barnett et al. 2014
Average cost	\$275.13		
Counseling or MI (Telephone, 1 session)	\$84.42	One 15-minute session telephone motivational interviewing	Hollis et al. 2007
	\$134.82	One 30-minute call telephone motivational interviewing + One follow-up call	Hollis et al. 2007
	\$41.70	One single telephone counseling session	McAlister et al. 2004
Average cost	\$86.98		
Counseling or MI (Telephone, about 4 sessions)	\$166.32	Five 30-minute calls telephone motivational interviewing	Hollis et al. 2007
	\$88.14	Four sessions telephone counseling	Richter et al. 2015
	\$139.00	Two to six counseling sessions	McAlister et al. 2004
	\$83.40	Around four counseling sessions	McAlister et al. 2004
	\$795.44	Four telephone sessions + five newsletters	Glasgow et al. 2009
Average cost	\$254.46		
Mailings and follow-up calls only	\$20.85	Mailing printed materials and taking calls	McAlister et al. 2004
	\$7.18	Provider talks to patient about cessation and nicotine withdrawal	Ruger et al. 2008
Average cost	\$14.02		

Notes: All cost estimates have been standardized to 2016 U.S. dollars. Costs of behavioral interventions are averaged by intervention type for use in estimating cost per smoker calculations. Costs for in-person sessions from Barnett et al. 2013. Costs for telephone sessions from Hollis et al. 2007, McAlister et al. 2004, Richter et al. 2015 and Glasgow et al. 2009. Costs for printed materials from McAlister et al. 2004 and Ruger et al. 2009.

MI, motivational interviewing.

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Appendix Table 6. Summary of Effectiveness of Cessation Interventions for General Smokers

Intervention description	Control description	Follow-up	Control	Treatment	NNT	References
Pharmacological interventions						
NRT + limited behavioral support	Placebo/control	6–24 months	(40/1,000)	(64/1,000)	42	Stead et al., 2012
NRT + intensive behavioral support	Placebo/control	6–24 months	(150/1,000)	(240/1,000)	11	Stead et al., 2012
Bupropion	Placebo/control	6+ months	(115/1,000)	(187/1,000)	14	Hughes et al., 2014
Varenicline	Placebo/control	24+ weeks	(111/1,000)	(250/1,000)	7	Cahill et al., 2016
Behavioral interventions						
Telephone counseling – Callers to quitlines	Usual care	6+ months	(76/1,000)	(105/1,000)	34	Stead et al., 2013
Telephone counseling - Pro-active calls	Usual care	6+ months	(97/1,000)	(123/1,000)	38	Stead et al., 2013
In-person individual counseling	Usual care	6+ months	(305/3,922)	(431/3,933)	31	Lancaster and Stead, 2005
Motivational interviewing	Brief advice or usual care	6+ months	(104/1,000)	(131/1,000)	37	Lindson-Hawley et al., 2015
Combination interventions						
Combination of pharmacological and behavioral interventions	Control	6 months	(86/1,000)	(157/1,000)	14	Stead et al., 2016

Note: Summaries from most recent Cochrane reviews of different types of interventions for smoking cessation among a general population of smokers are presented. Each meta-analysis calculated treatment and control quits using the strictest definitions of abstinence available in each study reviewed. The authors calculate the number needed to treat (NNT) for each meta-analysis included here. Nicotine replacement therapy is denoted as NRT.

Appendix
Smoking Cessation for Smokers Not Ready to Quit: Meta-analysis and Cost-effectiveness Analysis
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Appendix Table 7. Subgroup Analysis: Estimates of Effectiveness and Cost-Effectiveness for Pharmacological Interventions for SNRTQ

Intervention	Treatment		Treatment		Control		Weight	ORo M-H fixed (95% CI)	NNT	Cost per smoker	Cost per quit
	Type	Duration	Quits	Total	Quits	Total					
NRT inhaler											
Bollinger 2000	NRT inhaler	18 months	21	200	17	200	84.60%	1.26 (0.65, 2.47)	50	\$5,166.43	\$258,321.69
Rennard 2006	NRT inhaler	12 months	17	215	3	214	15.40%	6.04 (1.74, 20.92)	15	\$3,444.29	\$51,664.34
Pooled NRT inhaler			38	415	20	414	100.00%	2.00 (1.14, 3.51)	37	\$4,901.22	\$180,280.41
Heterogeneity: $\chi^2=4.83$, $df=1$ ($p=0.03$); $I^2=79\%$											
Test for overall effect: $z=2.41$ ($p=0.02$)											
NRT gum											
Wennike 2003	NRT gum	12 months	19	205	7	206	47.10%	2.90 (1.19, 7.07)	17	\$1,046.16	\$17,784.72
Batra 2005	NRT gum	12 months	22	184	8	180	52.90%	2.92 (1.26, 6.74)	13	\$1,046.16	\$13,600.08
Pooled NRT gum			41	389	15	386	100.00%	2.91 (1.58, 5.36)	15	\$1,046.16	\$15,295.14
Heterogeneity: $\chi^2=0.00$, $df=1$ ($p=0.99$); $I^2=0\%$											
Test for overall effect: $z=3.44$ ($p=0.0006$)											
Varenicline											
Ebbert 2015	Varenicline	6 months	205	760	74	750	89.00%	3.37 (2.53, 4.50)	6	\$1,650.05	\$9,900.32
Hughes 2011	Varenicline	2 months	15	107	8	111	11.00%	2.10 (0.85, 5.18)	15	\$550.02	\$8,250.26
Pooled Varenicline			220	867	82	861	100.00%	3.23 (2.46, 4.25)	6	\$1,529.05	\$9,822.58
Heterogeneity: $\chi^2=0.96$, $df=1$ ($p=0.33$); $I^2=0\%$											
Test for overall effect: $z=8.38$ ($p<0.00001$)											

Note: ORs are calculated using the equation: $OR = (\%Quit_{treatment} / (1 - \%Quit_{treatment})) / (\%Quit_{control} / (1 - \%Quit_{control}))$. NNT is calculated using the equation: $NNT = N_{treatment} / (Quit_{treatment} - \%Quit_{control} * N_{treatment})$. Cost per smoker is calculated by multiplying treatment costs in Table 1 by duration of treatment. Where individuals were offered choice in NRT, average monthly cost of NRT was used. Additional detailed assumptions used to develop costs in Table 1 are described in Appendix Table 5. Cost per quit is calculated by multiplying NNT by cost per smoker.

Pooled NRT inhaler values come from Bolliger et al. 2000 and Rennard et al. 2006. Pooled NRT gum values come from Wennike et al. 2003 and Batra et al. 2005. Pooled varenicline values come from Ebbert et al. 2015 and Hughes et al. 2011.

SNRTQ, smokers not ready to quit; M-H, Mantel-Haenszel method to estimate pooled ORs, assuming a fixed effects model; NNT, number needed to treat; NRT, nicotine replacement therapy.

Appendix Table 8. PICO Statement

PICO Statement	
Population	Smokers not ready/willing to quit. This includes smokers who are not ready to quit at the time of the study, smokers who do not wish to quit but are willing to reduce, smokers who are not ready to quit within 30 days, smokers who are not ready to quit within 6 months.
Intervention	Pharmacological, behavioral, and combination interventions. This includes reduction interventions which include cessation as a secondary outcome.
Comparison	Placebo, usual care, or no treatment.
Outcome of interest	Smoking cessation, measured as 7-day point-prevalence 6 months after completion of treatment, biochemically verified through saliva or exhaled cotinine. Where this measure is not available, other measures of cessation are included, such as 1-day point-prevalence, continuous abstinence, cessation at longest point in time following conclusion of treatment, and self-reported cessation outcomes.

Note: I^2 test for heterogeneity and moderation analysis are conducted to assess how variation in PICO characteristics might influence the estimated pooled effect size.

Appendix Figure 1. Funnel plots for pharmacological, behavioral, and combination interventions.

