Supplementary Material 3
Detailed description of the included studies

Supplementary Table 1a. Characteristics of randomized controlled trials measuring smoking cessation at 6 months or later Characteristics of randomized controlled trials measuring smoking cessation at 6 months or later

Bullen, 2013	
Methods	**Design**: 3 parallel groups RCT **Recruitment:** Participants were recruited via community newspapers, inviting people to call the study centre for eligibility pre-screening **Setting**: one single center in Auckland Australia **Inclusion criteria:** 18 years of age or older, smoked 10 or more cigarettes per day for the past year, and wanted to quit smoking. **Exclusion criteria:** Pregnant or breastfeeding women, people using smoking cessation drugs, those reporting heart attack, stroke, severe angina in the previous 2 weeks, and people with poorly controlled medical disorders allergies, or other chemical dependence were excluded
Participants	**Total N:** 657 smokers were included in this study, but we only extracted 584 participants for our review (2 of the 3 groups) as the e-cigarette placebo group did not fit our eligibility criteria. Most participants were women (62%), of a mean age > 40. Approximately one third were of Maori descent, and a little over half had completed grade 12 or above education level. The average daily number of cigarettes smoked at study onset was around 18, and mean Fagerström test result (0 to 10 scale) for cigarette dependence was > 5.
Interventions	**Randomization:** 4:4:1 ratio to nicotine e-cigarettes, nicotine patches and placebo e-cigarette group **Nicotine e-cigarette group** Participants were couriered a first-generation e-cigarette, spare battery and charger, as well as cartridges containing 10 to 16mg of nicotine per mL (although labelled to contain 16 mg), plus simple instructions to use the e-cigarettes as desired from 1 week before until 12 weeks after their chosen quit day. Participants received on average around 20% of the nicotine obtained from cigarette smoking. **Nicotine patch group** Participants were sent exchange cards in the mail redeemable for nicotine patches 21 mg from community pharmacies, with instructions to use the patches daily, from 1 week before until 12 weeks after their chosen quit day. Vouchers were also supplied to participants to cover dispensing costs. **Both groups**

	Participants in all groups were also referred to telephone-based behavioural support
Outcomes	Continuous abstinence at 6 months after quit day, defined as self-reported abstinence over the whole follow-up period allowing for 5 or less cigarettes in total, was self-reported, and verified with exhaled breath carbon monoxide of <10 ppm. Harms were both clinically assessed and self-reported, throughout the study period. Withdrawal symptoms were assessed at 1, 3, and 6 months. Reduction in daily cigarettes smoked was measured at 6 months, and acceptance of therapy was measured at 1 and 6 months.
Notes	Some of this study's authors reported ties to e-cigarette manufacturers, and smoking cessation drug companies
Hajek, 2019	
Methods	**Design:** 2 parallel groups RCT **Recruitment:** Participants were recruited through stop smoking services, which included trial information in their advertising. Participants were also recruited through social media, and leaflets advertising the trial were delivered to local households. **Setting:** 3 sites in the United Kingdom **Inclusion criteria**: Adults, with no strong preference towards e-cigarette or NRT, who were not using either type of product at the time of study enrolment **Exclusion criteria:** Pregnant women or breastfeeding women
Participants	**Total N:** 884 participants were included in this study Median age for both groups was 41, and women comprised 48% of participants. Most participants were White British, and the majority had post-secondary education. Median daily number of cigarettes smoked at study onset was 15, and mean Fagerström test result for cigarette dependence was 4.5 in the e-cigarette group and 4.6 in the NRT group.
Interventions	**Randomization:** nicotine-containing e-cigarettes of varying doses, and any choice of a list of NRT, in a 1:1 ratio **E-cigarette group** Participants were provided with a starter pack called One Kit, which included an atomizer, a battery, and one 30 mL bottle of Tobacco Royale flavor e-liquid. Participants were asked to purchase their future e-liquid online or from local vape shops and to buy a different e-cigarette device if the one supplied did not meet their needs. They were encouraged to experiment with e-liquids of different strengths and flavors. Those who were unable to obtain their own supply were provided with one further 10-ml bottle, but this was not offered proactively. Participants received oral and written information on how to operate the e-cigarette.

	NRT group Participants were informed about the range of nicotine-replacement products (patch, gum, lozenge, nasal spray, inhalator, mouth spray, mouth strip, and microtabs) and selected their preferred product. Use of combinations was encouraged, typically the patch and a faster-acting oral product. Participants were also free to switch products.ps **Both groups** Participants in both groups were offered multisession behavioral support as per UK stop smoking service practice, involving weekly one on one session with local clinicians. Participants were also asked to sign a commitment to not use the unassigned treatment for 4 weeks
Outcomes	Continuous abstinence at 52 weeks after quit day, defined as self-reported abstinence over the whole follow-up period allowing for 5 or less cigarettes in total, was self-reported, and verified with exhaled breath carbon monoxide of <8 ppm. Harms were self-reported throughout the study period. Withdrawal symptoms were assessed at 1 and 4 weeks in abstainers. Reduction in daily cigarettes smoked was also measured at 52 weeks, as well as acceptance of e-cigarettes and NRT
Notes	Some of this study's authors reported ties to smoking cessation drug companies.
Lee SH, 2019	
Methods	**Design:** 2 parallel groups RCT **Recruitment:** Participants were recruited from a motor company in the Republic of Korea. **Setting:** One site in Cheonan, Republic of Korea **Inclusion criteria:** Participants were adults 18 years and above, male, who smoked at least 10 cigarettes per day in the preceding year, and who were motivated to stop smoking entirely or to reduce their cigarette consumption **Exclusion criteria:** Participants were excluded if they had a past medical history of serious clinical diseases or had attempted to stop smoking in the last 12 months by using other NRT.
Participants	**Total N:** 150 participants were included in the study Mean age was 42 years and all participants were men. Almost 40% had post-secondary education. Median daily number of cigarettes smoked at study onset was 1 pack per day, and mean Fagerström test result for cigarette dependence was 4.
Interventions	**Randomization:** nicotine-containing e-cigarettes, and nicotine gum in a 1:1 ratio **E-cigarette group**

	Participants received a 24-week supply of e-cigarettes eGo-C Ovale, Janty-Korea Co., Janty-Asia Co., Seoul, Republic of Korea, nicotine 0.01 mg/mL. **Nicotine gum group** Participants received a 24-week supply of nicotine gum Nicoman, Daewoog Pharmaceutical, Seongnam, Republic of Korea, 2 mg/tablet **Both groups** Participants in both groups were offered 55-minute education sessions on smoking cessation aids
Outcomes	Continuous abstinence was defined as abstinence from smoking from 9 to 24 weeks, validated with end-expiratory carbon monoxide (<10 ppm) and a negative urine cotinine result. Harms were self-reported throughout the study period. Reduction in daily cigarettes smoked was also measured at 24 weeks.
Notes	None of the study authors were found to have ties to industry.
Lee SM, 2018	
Methods	**Design:** 2 parallel groups RCT **Recruitment**: Participants were recruited from an anesthesia preoperative clinic for elective surgery. **Setting:** San Francisco Veterans' Affairs Medical Center, affiliated with the University of California in San Francisco United States of America **Inclusion criteria:** Participants were eligible if they presented to the clinic 3 or more days prior to elective surgery, smoked more than two cigarettes per day, and had smoked at least once in the last 7 days **Exclusion criteria**: Participants were excluded if they exclusively used other forms of tobacco (e.g. pipe tobacco) or marijuana only, were pregnant or breastfeeding, had an unstable condition, were using smoking cessation therapy at the time of study enrolment or were in another smoking cessation trial, or currently used e-cigarettes daily.
Participants	**Total N:** 30 participants were included in this study Most participants were men (90%) in their 50's. Some had comorbidities including diabetes, hypertension, heart disease, and chronic obstructive pulmonary disease. Most were Caucasians. The average daily number of cigarettes smoked at study onset was 15.3 in the e-cigarette group, and 10.8 in the NRT group, and the mean Fagerström test result for cigarette dependence was 3.7 in the e-cigarette group and 2.5 in the NRT group.
Interventions	**Randomization:** e-cigarettes and nicotine patches in a 2:1 ratio **E-cigarette group** Participants received a 6-week supply of NJOY e-cigarettes (Scottsdale, AZ, USA), a disposable first-generation e-cigarette that is available in shops and online. They were issued a number of e-cigarettes corresponding to

	the reported baseline cigarettes smoked per day, calculated assuming one NJOY e-cigarette was equivalent to 10 cigarettes. Participants were instructed to smoke bold (4.5%) e-cigarettes ad libitum for 3 weeks, then the Gold (2.4%) e-cigarettes ad libitum for 2 weeks, and then the Study (0%) e-cigarettes ad libitum for the final week. **Nicotine patch group** Participants randomized to the nicotine patches group were given a 6-week supply of Nicoderm CQ patches (5 weeks) and placebo patches (1 week) appropriate to baseline nicotine consumption. Those smoking an average of ten or more cigarettes per day were given a 21 mg/day patch for 3 weeks, a 14 mg/day patch for 1 week, a 7 mg/day patch for 1 week, and a 0 mg/day patch for 1 week. Participants who reported smoking an average of fewer than 10 cigarettes per day at baseline were given a 14 mg/day patch for 3 weeks, a 7 mg/day patch for 2 weeks, and a 0 mg/day patch for 1 week. **Both groups** Participants in both groups were given referral California Smokers' Helpline and were asked to refrain from the use of cigarettes during the study period.
Outcomes	Smoking cessation at 6 months was self-reported through 7-day point-prevalence abstinence and verified with exhaled breath carbon monoxide of <10 ppm. Harms and withdrawal symptoms were systematically collected at 8 weeks. Reduction in daily cigarettes smoked was also measured at 6 months, as well as acceptance of e-cigarettes and NRT.
Notes	None of the study authors were found to have ties to industry.

Supplementary Table 1b. Characteristics of randomized controlled trial measuring smoking cessation earlier than 6 months

Hatsukami, 2019	
Methods	**Design:** 4 parallel groups RCT **Recruitment:** Participants were culled from two sets of studies, one of which also included two groups randomized to snus (spitless smokeless tobacco); one was complete substitution with snus, and the other was ad libitum use. Due to recruitment challenges, the two snus groups were dropped midway through the study, resulting in four experimental groups: ad libitum use of e-cigarettes (participants may smoke as many cigarettes as they like), complete substitution with e-cigarettes (aiming for smoking

	cessation), complete substitution with NRT, continued smoking with usual brand of cigarettes. Participants were recruited through various media outlets across three institutions. The advertisements stated that a study was recruiting smokers who were interested in trying a product that may reduce exposure to harmful tobacco smoke. **Settings:** 3 sites, University of Minnesota, Twin Cities (lead site); The Ohio State University, Columbus, OH; Roswell Park Cancer Center, Buffalo, NY United States of America **Inclusion criteria:** Participants were adults at least 18 years of age, smoked at least 5 cigarettes per day with a breath carbon monoxide test of at least 10 ppm or a NicAlert test = level 6, and in stable physical and mental health. **Exclusion criteria:** Participants were excluded if they had a serious quit attempt in the past 3 months, recent (<3 months) alcohol or drug abuse problems, regular use of other nicotine or tobacco products, were planning to quit smoking in the next 3 months, suffered from chronic conditions affecting results of biomarker analyses, were currently using NRT or other cessation medication, or if they were pregnant or planning to become pregnant, or breastfeeding
Participants	**Total N:** 264 participants were included in the study, but data for this review were only extracted from the complete substitution with e-cigarette group, and complete substitution with NRT group (152 participants), as the other two groups did not fit our eligibility criteria. Median age was 47 years, and women comprised 49% of participants. Most participants were White, and the majority had post-secondary education. The median daily number of cigarettes smoked at study onset was 15, and median Fagerström test result for cigarette dependence was 3.
Interventions	**Randomization:** e-cigarettes and nicotine gum or lozenges **E-cigarette group** Participants randomized to this group used Vuse Solo, manufactured by RJ Reynolds Inc as the primary e-cigarette. Early in the study, Blu e-cigarettes (cartridge-based system) and Fin (prefilled tanks system) were used, but Vuse attained the highest market share early on so the study switched exclusively to Vuse. E-cigarettes with a 4.8% nicotine concentration were provided to participants free of charge for 8 weeks, as well as 7 cartridges weekly, with the option of returning to the clinic to obtain additional cartridges if needed. Tobacco, menthol, mint, and berry flavors were available. **NRT group**

	Participants could choose between mint, cinnamon or fruit-flavored nicotine gum or nicotine lozenge, at a dose of 4 mg. If adverse effects were recorded, the dose was decreased to 2 mg. **Both groups** After randomization, participants were asked to complete daily diaries via interactive voice recording to chart the number of cigarettes smoked daily, as well as document assigned product use for the duration of the trial. Participants received a monetary bonus if they complied with the protocol; this included keeping an accurate record of product use, completing the daily diaries, and returning unused products. They also got a bonus payment if they had a carbon monoxide level $\leq$ 4 ppm at each visit. Participants also received a brief counseling session on how to avoid smoking.
Outcomes	Smoking cessation was determined by 7-day point prevalence at 8 weeks, mainly through biochemical verification but also by self-report Reduction in daily cigarettes smoked was also measured at 8 weeks, as well as acceptance of e-cigarettes and NRT. Harms were assessed systematically at 20 weeks, 12 weeks after the end of the study period. Withdrawal symptoms were assessed at weeks 1, 2, 4, 6, and 8.
Notes	One of the study authors is a member of the FDA Tobacco Products Scientific Advisory Committee and another one has served as an expert witness in tobacco company litigation.

Supplementary Table 1c. Characteristics of randomized controlled trial measuring other outcomes

Eisenhofer, 2015	
Methods	**Design:** 2 parallel groups RCT **Recruitment:** Not specified **Setting:** Not specified **Inclusion criteria:** Veterans who met criteria for tobacco disorder as per the DSM **Exclusion criteria:** Not specified
Participants	**Total N:** 11 participants were included Mean age was 52, and 82% were males. The vast majority of participants were African American. The average daily number of cigarettes smoked at study onset was 26.5, and the mean Fagerström test result for cigarette dependence was 7.5.
Intervention	**Randomization:** e-cigarettes and nicotine patches **E-cigarette group**

	Participants received nicotine-containing e-cigarettes with 16 mg of nicotine per cartridge **NRT group** Participants received nicotine patch 16 mg daily **Both groups** All participants were instructed to smoke ad libitum during week 1, and to smoke as little as possible during week 3.
Outcomes	Reduction in cigarettes smoked per day was self-reported at 3 weeks and compared to week 1. Withdrawal symptoms were compared between week 1 and week 3.
Notes	This study was available as an abstract only therefore limited details are available.