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FULL RESEARCH PAPER
Prevention in practice

Vascular health after quitting smoking or switching to e-cigarette use: a systematic review of prospective studies with GRADE assessment

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Aims This systematic review aims to evaluate the effects of smoking cessation or switching to exclusive electronic cigarette (EC) use on vascular function in adult smokers, using prospective evidence from clinical studies.

Methods and results A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and Embase on 13 October 2025. Eligible studies included randomized controlled trials (RCTs), quasi-experimental designs, and prospective cohort studies reporting quantitative or narrative data on vascular outcomes [i.e. pulse wave velocity (PWV), augmentation index (AIx), and flow-mediated dilation (FMD)], after smoking cessation or switching to ECs. Risk of bias was assessed using the Joanna Briggs Institute tools. Results were synthesized qualitatively. Certainty of the evidence was determined using Grading of Recommendations, Assessment, Development, and Evaluation (GRADE). Twenty-three studies involving a total of 11 702 participants were included: 14 cohort studies, 5 quasi-experimental, and 4 RCTs. Overall, smoking cessation was consistently associated with improvements in PWV, AIx, and FMD, with some effects observable within 1 month and sustained up to 24 months. The overall certainty of evidence was very low, except for a moderate level of certainty derived from RCTs investigating FMD. Improvements were seen across different cessation methods, including pharmacotherapy and ECs. RCTs on ECs reported significant improvements in FMD irrespective of nicotine content, suggesting that combustion rather than nicotine may be the primary driver of vascular impairment. Sensitivity analyses excluding lower-quality RCTs confirmed the primary findings.

Conclusion Smoking cessation appears to improve vascular function, as reflected by early favourable changes in endothelial and arterial stiffness markers; however, the overall certainty varies from moderate to very low, according to the outcome. These findings are consistent with the biological plausibility of cardiovascular benefit from sustained smoking abstinence.

Lay summary Most studies reported that quitting smoking improved vascular function; however, the certainty of the overall evidence was very low, except for moderate certainty in RCTs assessing FMD.

- This systematic review found signals of improvement in how blood vessels function after smoking cessation, such as better elasticity and reduced stiffness, which are important for heart health. However, these findings come mainly from observational and non-randomized studies.
- The use of e-cigarettes as a smoking cessation aid was also linked to possible improvements in vascular function, but the available evidence is limited, and the long-term effects remain uncertain.

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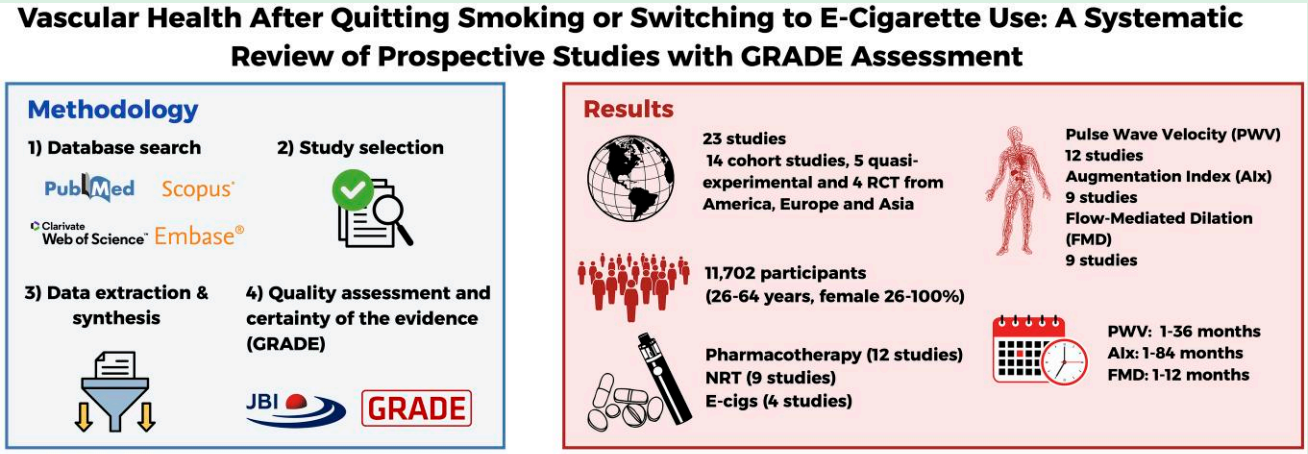
- Overall, while the results are encouraging, more robust and long-term studies are needed to confirm these early observations.

Graphical Abstract



Outcome	Smoking Cessation	Studies	Switching to E-Cigarettes	Studies
PWV	Reduction in PWV, more significant with pharmacotherapy.	1 RCT, 2 Quasi-Experimental, 6 Cohort	PWV decreases, suggesting improved arterial flexibility.	1 RCT, 1 Quasi-Experimental, 1 Cohort
AIx	Reduction in AIx, indicating less arterial stiffness.	1 RCT, 1 Quasi-Experimental, 6 Cohort	No significant data reported.	1 Quasi-Experimental
FMD	Improvement in FMD, irrespective of intervention type.	2 RCT, 1 Quasi-Experimental, 5 Cohort	Improvement in FMD, regardless of nicotine content.	2 RCT

Keywords Pulse wave velocity • Augmentation index • Flow-mediated dilation • e-cigarettes • Nicotine replacement therapy • Smoking cessation

Introduction

Despite global efforts, tobacco smoking remains a leading cause of preventable death, responsible for over 7 million deaths annually.[1] Chronic smoking substantially harms the cardiovascular system by promoting atherosclerosis, impairing vascular function, and increasing the risk of cardiovascular disease (CVD) and sudden cardiac death.[2] Consequently, smoking cessation is a cornerstone of CVD prevention, with clinical guidelines strongly recommending it to reduce cardiovascular risk.[3] Its effectiveness improves when behavioural counselling is combined with pharmacological therapies such as varenicline,[4] cytisine,[5] bupropion,[6] or nicotine replacement therapy (NRT).[7]

In recent years, electronic cigarettes (ECs) have emerged as a popular cessation aid, with systematic reviews supporting their effectiveness.[8] Regulatory bodies, including the US FDA and UK NICE, have recognized ECs as a less harmful alternative to combustible cigarettes for smokers unable or unwilling to quit.[9,10]

The cardiovascular benefits of cessation can be tracked non-invasively long before clinical events by measuring vascular biomarkers such as arterial stiffness and endothelial function. Carotid–femoral pulse wave velocity (PWV) is considered the gold standard for arterial stiffness[11] and is a strong predictor of cardiovascular outcomes; a 1 m/s increase corresponds to a 14% higher risk of events and a 15% higher risk of cardiovascular mortality.[12] The augmentation index (AIx), another marker of systemic stiffness and wave reflection, also predicts subclinical atherosclerosis and future events, with reductions from >30 to <20% associated with lower cardiovascular risk.[13–17] Endothelial dysfunction, assessed by brachial flow-mediated dilation (FMD), represents an early event in atherosclerosis. Impaired FMD is a robust predictor of cardiovascular events, with a 1% absolute increase associated with an 8–12% lower risk, while a one standard deviation decrease doubles cardiovascular risk.[18,19]

Given the strong prognostic value of vascular biomarkers, it is crucial to investigate how these parameters improve following smoking cessation, as tobacco smoking remains one of the most important modifiable risk factors for CVD. Non-invasive measures such as PWV, AIx, and FMD provide a sensitive window into the earliest vascular changes, allowing benefits of cessation to be captured long before the onset of clinical events. Understanding the extent and timing of these improvements is key for assessing the cardiovascular advantages of quitting. Thus, the aim of this systematic review is to synthesize evidence

from prospective studies on the impact of stopping smoking, with or without cessation aids (including ECs), on vascular health.

Materials and methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (see Supplementary material online, *Appendix S1*). The protocol was registered in PROSPERO (CRD420251016878) and has been accepted for publication in a peer-reviewed journal.[20]

Research question

Population (P): adults (≥18 years) who are regular smokers, with or without established cardiovascular risk factors (e.g. diabetes, hypertension, dyslipidaemia, and rheumatoid arthritis).

Intervention (I): smoking cessation achieved through any pharmacological aid or through exclusive switching to ECs.

Comparison (C): continued smoking or baseline (pre-cessation) values in within-subject designs.

Outcome (O): changes in vascular function indicators, including PWV, AIx, and FMD.

Study design (S): prospective clinical studies [i.e. randomized clinical trials (RCTs), non-randomized interventional (known as quasi-experimental) studies, and prospective cohort studies].

Regular smokers were defined according to the criteria adopted in the primary studies. Although definitions varied slightly across studies, regular smokers generally referred to participants with established daily smoking habits, most commonly reporting a consumption of ≥10 cigarettes per day and, where biochemical verification was available, an exhaled carbon monoxide level >10 ppm.

Search strategy

A comprehensive literature search was conducted on 13 October 2025, using the PubMed, Scopus, Web of Science, and Embase databases. Search strategies were tailored to each database, and the full search strings are presented in Supplementary material online, *Appendix S2*. To identify additional relevant studies, two reviewers (G.R.M.L.R. and R.P.) also screened the reference lists of all included articles. In addition, medical experts were consulted to minimize the risk of omitting recent or unpublished relevant literature. Relevant grey literature was also considered by reviewing the websites of leading medical and public health organizations in the fields of cardiovascular health and smoking cessation, including the World Heart Federation, American Heart Association, European Society of Cardiology, World Health Organization (WHO), and Centers for Disease Control and Prevention.

The search was performed without any restriction on publication date, and only articles published in English were considered.

Study selection

Studies were eligible for inclusion if they investigated the impact of smoking cessation or switching to EC use on vascular function outcomes (e.g. PWV, AIx, and FMD), in adult populations (≥18 years) classified as regular smokers. Eligible designs included RCTs, quasi-experimental, and prospective cohort studies. Studies involving populations with established cardiovascular risk factors were also included. Studies had to report either quantitative or narrative data on vascular outcomes following smoking cessation. To ensure interpretability, we included only studies where exclusive use (e.g. of ECs) could be clearly distinguished from persistent dual use (defined as the concurrent use of ECs and combustible cigarettes). Where outcomes were stratified by biochemical verification (e.g. CO levels), subgroups were considered separately.

Exclusion criteria comprised preclinical studies, retrospective cohorts, cross-sectional studies, case reports or series, non-peer-reviewed publications, and trials with fewer than 30 participants without a justified sample size.[21] Studies lasting <1 week or involving smokeless tobacco products (e.g. snus) were also excluded. These thresholds were adopted to reduce the inclusion of very small or ultra-short studies, which are more prone to imprecision, lack of representativeness, and limited clinical interpretability.

A detailed description of the inclusion/exclusion criteria is provided in the protocol.

Two independent reviewers screened titles and abstracts using EndNote (Version 21, Clarivate) to remove duplicates and manage records. Articles judged potentially eligible, or those for which relevance could not be excluded based on title and abstract, were retrieved in full text and independently assessed for eligibility. Discrepancies were resolved through discussion and consensus. Only studies meeting all predefined inclusion criteria were retained for the final synthesis.

Data extraction

Data extraction was carried out using a standardized form as specified in the published protocol. Key study characteristics were collected, including bibliographic details, study design, population descriptors, exposure and comparator definitions, follow-up duration, and outcome measures. Findings related to the impact of smoking cessation on vascular outcomes were extracted quantitatively where available or summarized narratively. Study limitations and conclusions were also noted.

Data synthesis

Given the substantial heterogeneity observed across the included studies, in terms of study design, patient populations, outcome definitions, and length of follow-up, a meta-analysis was not considered appropriate. Instead, we systematically tabulated the key characteristics and findings of each study and conducted a structured narrative synthesis. This approach allowed us to integrate the evidence in a transparent way, while highlighting patterns and differences across studies without producing potentially misleading pooled estimates. Vascular outcomes were categorized by type (i.e. PWV, AIx, and FMD) to facilitate interpretation across studies.

Risk of bias (quality) assessment

The risk of bias for each included study was independently assessed by two reviewers (G.R.M.L.R. and G.G.) using the Joanna Briggs Institute (JBI) critical appraisal tools, selecting the checklist appropriate to each study design (https://jbi.global/critical-appraisal-tools). Full details on the tools and appraisal criteria are available in the protocol. Disagreements

were resolved through discussion or, when needed, by consulting a third reviewer (R.P.).

Results of the risk of bias assessment are presented in graphic format, accompanied by a narrative synthesis grouped by study design. To explore the influence of methodological quality on the overall findings, a sensitivity analysis was conducted by excluding studies with equal to or more than three domains rated as 'no' on the JBI checklist. The risk of bias assessment was used to inform the interpretation of the findings and to highlight areas of greater methodological strength or concern across the included evidence.

Certainty of the evidence

The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach was applied by two independent reviewers (G.R.M.L.R. and R.P.) to assess the certainty of evidence for the three main outcomes (i.e. PWV, AIx, and FMD), for which more than one study was available. According to the GRADE framework, RCTs start as high-certainty evidence, whereas observational studies start as low-certainty evidence. The assessment considered the following domains: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence was downgraded if relevant limitations were identified in one or more of these domains. Because no meta-analysis was performed and the data were synthesized narratively, we followed the guidance proposed by Murad *et al.*[22] to apply the GRADE approach in the context of narrative evidence synthesis.

Results

The results of the literature search are summarized in *Figure 1* (PRISMA flow diagram). Full-text publications excluded during the eligibility assessment, along with reasons for exclusion, are detailed in Supplementary material online, *Appendix S3*. Finally, 23 eligible studies were identified. No relevant grey literature was identified during the search process.

General characteristics

The general characteristics of the included studies are reported in *Table 1*.

Most studies were cohort studies ($n = 14$), with other types being quasi-experimental ($n = 5$) or RCTs ($n = 4$). Across all included studies, a total of 11 702 participants were enrolled. The sample size was variable, ranging from 60 to 6597 participants. The follow-up period ranged from 1 month to a maximum of 84 months.

Included studies cover a diverse range of countries, including the USA, Italy, China, Greece, Japan, Portugal, Canada, Israel, and Brazil. Notably, four of the nine studies investigating FMD were from Japan.

Population characteristics were also variable. Eight out of 12 studies investigating PWV included women, ranging from 26 to 100% female. Seven out of nine AIx studies included women, with female representation ranging from 27 to 56%. All FMD studies included a female population, ranging from 26 to 65% female. Average populations across all studies range from 26 to 64 years. Ten studies included populations with CV risk factors such as dyslipidaemia, hypertension, and diabetes.

In total, 12 studies used pharmacotherapy as an intervention/smoking cessation therapy, nine studies used NRT, and four studies used ECs. Most of the included studies biologically verified smoking abstinence, using measures such as exhaled carbon monoxide or urinary cotinine levels. No included study was funded by the tobacco industry.

Vascular outcomes

The included studies found that PWV, AIx, and FMD generally demonstrated improvement in vascular function following smoking cessation using NRT, pharmacotherapy (i.e. varenicline/bupropion/cytisinicline), or EC use.

Pulse wave velocity

Multiple studies have assessed the impact of smoking cessation on arterial stiffness, as shown in *Table 1*. We found significant heterogeneity in study design, comparators, PWV type (carotid–femoral, aorto–radial, brachial–ankle), follow-up duration, cessation aids/devices, and reporting measures of arterial stiffness.

However, the vast majority of studies demonstrate reduced arterial stiffness (denoted by a negative value or a smaller positive value) after smoking cessation, often detectable by 1 month and sustained up to 36 months.

Treatment effects vary by aid. One head-to-head study favoured varenicline over NRT by 0.3 m/s at 3 months.[26] In Zhang *et al.*[44], a 24-month comparison was conducted between participants with cardiovascular risk factors (i.e. hypertension, hyperlipidaemia, or diabetes mellitus) and healthy volunteers. Within each group, individuals were either current smokers or engaged in smoking cessation treatment with varenicline or bupropion. In the smoking cessation group, PWV decreased by 1.2 m/s in healthy volunteers and by 0.8 m/s in participants with cardiovascular comorbidities, suggesting larger improvements in healthy population. An earlier shorter follow-up (6 months) study using NRT by the same researchers[45] found a reduction in PWV of −0.49 m/s in healthy volunteers and of −0.20 m/s in those with CV comorbidities.

Three studies used ECs as the smoking cessation tool.[25,27,32] Two reported early and significant improvements in PWV when cigarette smokers switched to EC (−0.5 m/s at 1 month[25]; −0.8 m/s at 12 months[32]) while a third study[27] showed a numerically (but not statistically significant) increase of +0.2 m/s in EC users compared with cigarette smokers at 1 month. Notably, subjects who dual-used ECs and tobacco cigarettes exhibited PWV changes similar to those who continued to smoke (0.3 m/s).

Interestingly, although not in the scope of this review, this study found that a single acute exposure to EC of up to 7 min resulted in a lesser extent of vascular stiffness than a comparable period with a tobacco cigarette, in chronic tobacco smokers. The difficulty with single-exposure studies is that there is often too much 'noise' in a single time point, single exposure to be able to extrapolate results to long-term effects.[46]

Finally, a 2025 pilot study using the novel agent cytisinicline also demonstrated a rapid 1-month improvement in PWV from 10.36 ± 2.37 to 8.69 ± 1.94 m/s ($P = 0.019$) in the cytisinicline group and no change in the continued smoking control group (9.87 ± 1.96 m/s–10.02 ± 2.23 m/s; $P = 0.822$).[28]

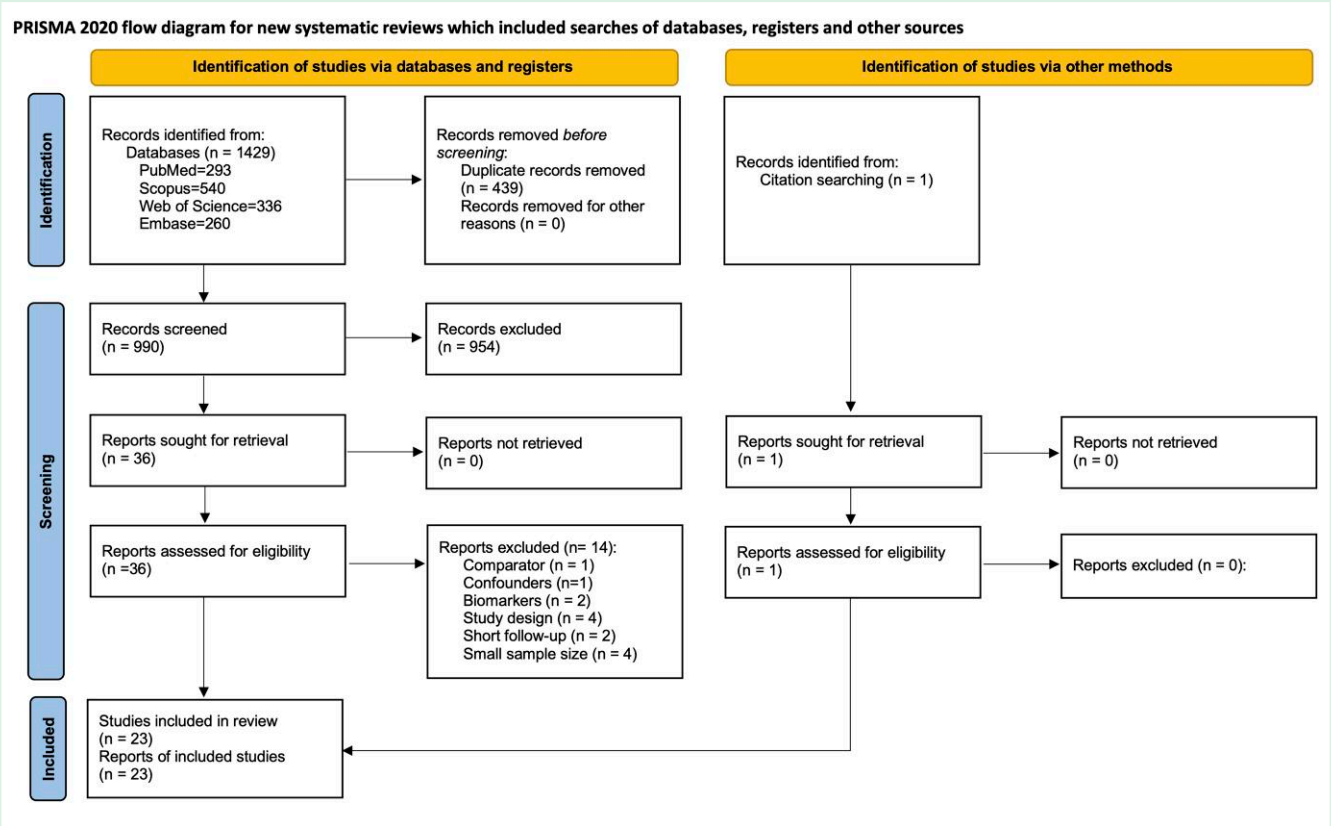


Figure 1 Flow chart of the review process.

In summary, there is a significant, early, and clinically relevant improvement in arterial stiffness as measured by PWV. The benefits are seen in studies that have used a variety of smoking cessation methods including varenicline and EC.

Augmentation index

Similar issues with regard to the wide heterogeneity of studies of PWV were also encountered with AIx. One study by Cooper *et al.*[23] that studied AIx change over 84 months in smoking cessation compared with healthy volunteers and smokers found an attenuated worsening in AIx over time after quitting smoking. The magnitude of benefit seen was approximately 4% lower AIx in the smoking cessation cohort compared with smokers. All other studies that met the criteria for this systematic review had a relatively short duration of follow-up from 1 to 24 months. This is reflected in the magnitude of AIx change seen. There are advantages and disadvantages to this shorter duration as numerous factors such as age, vasoactive medications, heart rate/physical fitness, and exercise can also affect AIx.[47] Unlike PWV, there was no advantage seen with varenicline over NRT in the study by Ikonomidis *et al.*[26]; however, AIx decreased among participants who achieved smoking cessation, suggesting that improvements were primarily related to abstinence from smoking rather than to the specific cessation pharmacotherapy.

Importantly, all studies showed a benefit in the smoking cessation arm in terms of reduced AIx (less stiffness) but the magnitude of AIx reduction varied significantly (*Table 1*) from <1% over 6 months[44,45] to a benefit of 12% reduction in AIx.[36] As would be expected in studies with a continued smoking arm,[27,36,37,39,42,44,45] AIx deteriorated but this was more marked in those with comorbidities.[44,45]

In summary, while all studies reported a reduction in AIx following smoking cessation, the magnitude of improvement varied considerably. This heterogeneity likely reflects differences in follow-up duration, participant characteristics, and concomitant factors influencing arterial stiffness. Despite these variations, the overall trend supports a beneficial effect of cessation on AIx.

Flow-mediated dilation

Multiple interventional studies reported changes in FMD following smoking cessation with pharmacological aids. Two RCTs specifically evaluated the effect of switching from combustible cigarettes to ECs. A study by George *et al.*[25] reported that chronic smokers who switched to ECs for 1 month showed a clinically significant improvement in FMD, irrespective of whether the EC contained nicotine or not. Klonizakis *et al.*[30] reported that over a 6-month period, FMD improved in participants who switched to either nicotine-containing or nicotine-free ECs, and a similar improvement was also observed in the NRT group of the same trial.

In studies where varenicline was used as cessation therapy, Okuyama *et al.*[35] and Kobayashi *et al.*[31] both reported an improvement in endothelial function after 5 months, although the former found benefits only in flow-mediated total dilation (FMTD), an index that incorporates low-flow-mediated

Table 1 General characteristics of the included studies

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
Cooper LL/2025/ ([23])	Cohort	NA	Non-smokers 52.7 ± 13.2 SC 60.4 ± 12.0 Smokers 52.2 ± 11.6	Non-smokers 56 SC 54 Smokers 52	6597	84	NA	(Change over time) Non-smokers 12.6 ± 0.3 SC 14.1 ± 0.4 Smokers 18.1 ± 0.5	NA
Fukumoto K/ 2021/([24])	Cohort	NRT	SC 64 ± 11 Smokers 61 ± 8	Smoking cessation 31 Smokers 14.3	79	4	NA	NA	SC 3.80 ± 2.24 to 4.60 ± 2.55 = +0.80 Smokers 4.41 ± 2.01 to 4.43 ± 2.26 = +0.02
George J/2019/ ([25])	RCT	EC (+nicotine) (Vapourlites Starter Kit with XR5 16 mg nicotine cartomizer); vs. EC (–nicotine)	EC nicotine free 48.4 (43.5–53.3) EC nicotine 48.0 (44.7–51.3) Smokers 44.2 (40.4–47.9);	65	114	1	Combined EC vs. smoking group –0.529; 95% CI: –0.946 to –0.112	NA	Change vs. smoking EC nicotine free 1.52 (0.90–2.15), EC nicotine 1.44 (0.78–2.09), all EC combined 1.49 (0.93–2.04)
Ikonomidis I/ 2017/([26])	RCT	Varenicline or NRT	50 ± 10	45	188	3	Varenicline 10.7 ± 0.2 to 10.5 ± 0.3 = –0.2 NRT 9.6 ± 0.4 to 9.7 ± 0.2 = +0.1	Varenicline 13.8 (5.8–36.8 IQR) to 9.1 (2.4–32.8) = –4.7 NRT 12.9 (6.2–33.2) to 8.8 (1.8–26.1) = –4.1	NA
Ikonomidis I/ 2018/([27])	Quasi-experimental	EC + nicotine [NOBACCO eGo Epsilon BDC 1100, eGo battery, 1100 mAh, 3.9 V, nicotine concentration 12 mg/mL (propylene glycol 74.3%, glycerin 20%, flavouring 4.5%, nicotine 1.2%)]	48 ± 5	56	70	1	EC 10.1 ± 0.4 to 10.3 ± 0.2 = +0.2 Dual use 10.1 ± 0.3 to 9.8 ± 0.2 = –0.3 Smokers 10.8 ± 0.6 to 10.7 ± 0.7 = –0.1	EC 28.9 ± 9 to 23.9 ± 7 = –5.0; Dual use 29.3 ± 8 to 25.6 ± 9 = –3.7; Smoking 34.9 ± 8 to 35.4 ± 9 = +0.5	NA
Ikonomidis I/ 2025/([28])	Cohort	Cytisinicline	50 ± 8	40	60	1	Cytisinicline 10.36 ± 2.37 to 8.69 ± 1.94 = –1.67	NA	Cytisinicline 7.51 ± 1.26 to 11.03 ± 2.27 = +3.52

Continued

Table 1 *Continued*

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
							Control 9.87 ± 1.96 to 10.02 ± 2.23 = +0.15		Control 7.36 ± 1.69 to 8.01 ± 1.25 = +0.65
Johnson HM/ 2010/([29])	RCT	NRT lozenge, NRT patch, SR bupropion, NRT patch + NRT lozenge, SR bupropion + NRT lozenge	44.7 ± 11.1	58.20	1504	12	NA	NA	SC 6.2 ± 4.4 to 7.2 ± 4.2 = +1.0 Smoking 6.48 ± 4.26 to 6.58 ± 4.05 = +0.1
Klonizakis M/ 2022/([30])	RCT	EC nicotine (10 mL bottle, Tornado V5, Totally Wicked, Blackburn, UK, up to 18 mg/mL nicotine), EC nicotine free, NRT	EC nicotine free 44 ± 13; EC nicotine 44 ± 14; NRT 44 ± 13	EC nicotine free 50; EC nicotine 45; NRT 56	248	6	NA	NA	EC nicotine free 5.6–8.1 = +2.5 EC nicotine 6.2–9.0= +2.8 NRT 6.7–9.5 = +2.8
Kobayashi M/ 2015/([31])	Cohort	Varenicline	57 ± 12	28.80	72	5	NA	NA	SC 4.0 (2.8–5.3) to 4.7 (3.0–6.1) = +0.7 Healthy volunteer 5.5 (3.5–8.2)—single time point only
Mandraffino G/ 2017/([32])	Cohort	None/EC allowed	27 ± 5	47	115	12	SC 7.3 ± 2 to 6.5 ± 1.9 = –0.8	NA	NA

Continued

Table 1 *Continued*

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
Moreira RC/ 2024/([33])	Quasi-experimental	NRT	55.5** (IQR = 36.4–54.8)	27.83	117	3	NA	NA	SC 5.08 (IQR 3.53–7.69) to 6.72 (4.88–8.46) = +1.64 Smokers 6.96 (5.03–9.74) to 6.79 (4.69–9.06) = −0.17
Nielson CA/ 2014/([34])	Quasi-experimental	NRT patch	SC 26 ± 5 Smokers 28 ± 6	100	78	12	SC 14.26 ± 1.95 to 14.26 ± 1.96 = 0	NA	NA
Okuyama N/ 2024/([35])	Cohort	Varenicline	59 ± 11	27.10	118	5	NA	NA	SC 3.93 ± 1.91 to 4.89 ± 2.22 = +0.95 ± 2.28 Smokers 4.35 ± 2.62 to 4.38 ± 2.91 = +0.06 ± 2.81
Oren S/2006/([36])	Cohort	Bupropion	45 ± 11	50	60	6	NA	SC 63.1 ± 22 to 50.6 ± 17 = −12.5 Smokers 60.2 ± 20 to 61.3 ± 19 = +1.1	NA
Polonia J/2009/ ([37])	Cohort	Bupropion	SC 45.2 ± 1.9 Smokers 45.1 ± 1.4	28	71	6	SC 10.5 ± 0.3 to 10.2 ± 0.2 = −0.2 Smokers 10.4 ± 0.3 to 10.5 ± 0.3 = +0.1	SC 28.7 ± 1.9 to 19.5 ± 2.3 = −9.2 Smoking 27.8 ± 2.0 to 29.5 ± 1.9 = +1.7	NA
Schmidt KMT/ 2019 ([38])	Cohort	Nicotine patch/ varenicline/ combination NRT	49.3 ± 11.6	54	1417	36	Smokers 7.2 ± 1.7 to 7.5 ± 2.0 = +0.3 ± 1.5 SC 7.1 ± 1.5 to 7.2 ± 1.5 = +0.2 ± 1.2 m/s	NA	NA
Takami T/2011/ ([39])	Cohort	Varenicline	SC 51.3 ± 5.9, Smokers 53.5 ± 7.9	30	70	18	(Brachial–ankle PWV): SC 17.68 ± 0.54 to 15.64 ± 0.69 = −2.04 Smokers 18.02 ± 0.73 to 17.59 ± 0.85 = −0.43	SC 77.5 ± 3.4 to 71.1 ± 2.4 = −6.4 Smoking 77.9 ± 3.8 to 76.9 ± 4.1 = −1.0	NA
Umeda A/2013/ ([40])	Cohort	Varenicline	53.2 ± 13.6	21.30	74	3	NA	NA	SC 4.0 ± 1.8 to 5.5 ± 2.2 = +1.5
van den Berkmortel FW/2004/([41])	Cohort	NA	SC 43 ± 8 Smokers 47 ± 11 Non-smokers 46 ± 11	SC 45 Smokers 38 Non-smokers 48	138	24	NA	NA	NA
Xue C/2019/([42])	Quasi-experimental	NRT	SC 34.3 ± 8.2 Smokers 34.6 ± 5.5	0	100	12	NA	SC 18.73 ± 16.71 to 10.69 ± 10.68= −8.04 Smokers 17.54 ± 15.11 to 19.87 ± 17.42 = +2.33	NA

Continued

Table 1 *Continued*

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
Yu-Jie W/2012/ ([43])	Quasi-experimental	Varenicline and Bupropion SR	43.6 + 8.7	0	209	12	(Brachial–ankle PWV): Non-smokers 13.07 (12.98–13.11) to 13.27 (13.17–13.30) = +0.20 SC 15.14 (15.01–15.26) to 15.02 (14.95–15.11) = −0.12 Smokers 15.03 (14.94–15.10) to 15.24 (15.12–15.29) = +0.21	NA	NA

Continued

Table 1 *Continued*

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
Zhang P/2019/ ([44])	Cohort	Varenicline or Bupropion	41 ± 12	0	136	24	Healthy volunteers SC: Left 6.48 ± 0.79 to 5.21 ± 0.93 = −1.27 Right 6.50 ± 0.91 to 5.21 ± 1.06 = −1.29 Smokers Left 5.96 ± 2.14 to 5.77 ± 2.34 = −0.19 Right 6.02 ± 1.45 to 5.87 ± 1.25 = −0.15 Comorbidities: SC Left 7.02 ± 1.51 to 6.25 ± 1.25 = −0.77 Right 7.04 ± 1.58 to 6.23 ± 1.62 = −0.81 Smokers Left 6.11 ± 1.05 to 6.71 ± 1.08 = +0.6 Right 6.19 ± 1.09 to 6.65 ± 1.11 = +0.46	Healthy volunteers SC: Left 4.29 ± 11.99 to 3.73 ± 15.77 = −0.56 Right 4.26 ± 13.98 to 3.53 ± 12.4 = −0.73 Smokers: Left −6.49 ± 9.56 to −6.35 ± 10.86 = −0.14 Right −6.98 ± 9.53 to −6.56 ± 10.33 = −0.42 Comorbidities cohort: SC: Left 7.05 ± 16.98 to 6.65 ± 15.75 = −0.4 Right 7.89 ± 14.99 to 7.67 ± 12.83 = −0.22 Smokers Left 0.31 ± 11.21 to 0.69 ± 10.13 = +0.38 Right −0.52 ± 10.03 to −0.38 ± 9.91 = +0.14	NA

Continued

Table 1 *Continued*

First author/ year/(Ref)	Study design	Intervention/SC therapy	Age (mean ± SD/ **median)	% female	Sample size	Follow-up duration (month)	Quantitative findings (SD where available)		
							PWV (m/s)	AIx (%)	FMD (%)
Zhang P/2012/ ([45])	Cohort	NRT	40.5 ± 13.5	0	67	6	Healthy volunteers SC: 6.08 ± 1.19 to 5.59 ± 1.33 = −0.49 Smokers: 5.60 ± 1.22 to 5.53 ± 2.01 = −0.07 Comorbidities SC: 6.53 ± 1.48 to 6.33 ± 1.32 = −0.20 Smokers: 6.37 ± 1.42 to 6.22 ± 1.24 = −0.15	Healthy volunteers SC 3.75 ± 11.85 to 3.09 ± 14.17 = −0.66 Smokers −8.70 ± 8.11 to −8.46 ± 8.18 = +0.24 Comorbidities Cohort SC 6.72 ± 14.47 to 5.26 ± 14.63 = −1.46 Smokers −0.17 ± 9.83 to −0.74 ± 10.93 = +0.57	NA

AIx, augmentation index; EC, electronic cigarette; FMD, flow-mediated; IQR, interquartile range; NA, not applicable; NRT, nicotine replacement therapy; PWV, pulse wave velocity; SC, smoking cessation; SD, standard deviation; SR, sustained release.

Table 2 Summary of findings

Smoking cessation (with or without cessation aids, including exclusive e-cigarette use)			
Population: adults (≥18 years) who are regular smokers, with or without established cardiovascular risk factors			
Intervention: smoking cessation			
Comparison: continuous smoking			
Outcome	**Effect**	**Number of participants** **Studies**	**Certainty in the evidence**
Pulse wave velocity (PWV)	Most studies showed a reduction in arterial stiffness (PWV) following smoking cessation	302 2 RCTs	Very low[a,b] ⊕◯◯◯ (Due to serious risk of bias and very serious imprecision)
		2293 10 non-randomized (3 quasi-experimental, 7 cohort)	Very low[c] ⊕◯◯◯ (Due to study design and serious risk of bias)
Augmentation index (AIx)	All studies reported a reduction in AIx following smoking cessation	188 1 RCT	Very low[a,b] ⊕◯◯◯ (Due to serious risk of bias and very serious imprecision)
		7171 8 non-randomized (2 quasi-experimental, 6 cohort)	Very low[c] ⊕◯◯◯ (Due to study design and serious risk of bias)
Flow-mediated dilation (FMD)	Smoking cessation was consistently associated with improvements in FMD across the included studies	3 RCTs 1866	Moderate[d] ⊕⊕⊕◯ (Due to serious risk of bias)
		520 6 non-randomized (1 quasi-experimental, 5 cohort)	Very low[c] ⊕◯◯◯ (Due to study design and serious risk of bias)

[a]Serious risk of bias across studies because of unclear or inadequate randomization, blinding, and allocation concealment.
[b]Very serious risk of imprecision because of *N* of participants <400 and small or no effect (downgraded two levels).
[c]Serious risk of bias across studies because of insufficient strategies to control confounders or address incomplete follow-up in cohort studies.
[d]Serious risk of bias across studies because of unclear or inadequate randomization, blinding, allocation concealment, and incomplete follow-up.

constriction into the FMD measurement,[48] whereas no significant change was found in standard FMD. Umeda *et al.*[40] reported a statistically insignificant increase in FMD *during* varenicline use, but the improvement was statistically significant *after* completion of the varenicline treatment. For NRT, studies by Moreira *et al.*[33] and Fukumoto *et al.*[24] found that FMD improved at 3- and 4-month follow-ups, respectively. The former study was performed in people living with HIV/AIDS, a condition that is known to adversely affect endothelial function due to sustained viral replication, viral protein expression, chronic inflammation, and oxidative stress.[49]The 12-month RCT by Johnson *et al.*[29], which included five intervention arms and a placebo, found an overall improvement in FMD among all participants who achieved sustained abstinence, irrespective of the assigned treatment group. A recent pilot study using the novel agent cytisinicline demonstrated much larger gains in FMD compared with other interventions. Ikonomidis *et al.* demonstrated an improvement in FMD from 7.51 ± 1.26% to 11.03 ± 2.27% (P <0.001) within a month of smoking cessation (control 7.36 ± 1.69% to 8.01 ± 1.25%; P = 0.140).[28]

In summary, smoking cessation was consistently associated with improvements in FMD across intervention types, including ECs, NRT, and varenicline. Although the extent of improvement varied across studies and populations, the overall evidence supports a positive effect of cessation on endothelial function.

Other indices

There were three studies that met the inclusion criteria but assessed vascular function indices other than those mentioned above. Nielson *et al.*[34] also investigated vascular compliance and viscoelasticity. They found the former but not the latter, improved with smoking cessation, in young women. In addition to AIx, Xue *et al.*[42] also assessed reactive hyperaemia-peripheral arterial tonometry (RH-PAT) which assesses vascular function in the peripheral circulation at 12 months. At 12 months of follow-up, both endothelial function (RH-PAT and Aix) improved in participants who abstained from smoking (P < 0.001), while the above parameters deteriorated in continued smokers (P < 0.05). Lastly, van den Berkmortel *et al.*[41] investigated the impact

of smoking cessation on vessel wall intima–media thickness (IMT) in an observational study over 2 years and found that although IMT is thickened in chronic smokers, no difference in IMT progression could be shown after 2 years of smoking cessation when compared with results in persistent smokers and in non-smokers. Except for improvements in the IMT of the right common carotid artery, no significant differences in IMT progression elsewhere were seen between groups. The authors acknowledge that ageing over 2 years could have affected vascular compliance and that the risk reduction is more likely due to haemostatic or endothelial factors. They concluded 'smoking cessation should be recommended as it reduces cardiovascular risk rapidly after smoking cessation'.

Risk of bias assessment

The risk of bias assessment is presented in Supplementary material online, *Appendices S4–S6*, with studies grouped according to their design: RCTs, quasi-experimental studies, and cohort studies.

RCTs

Most RCTs demonstrated acceptable methodological quality across several domains, although some recurrent sources of bias were observed (see Supplementary material online, *Appendix S4*). Issues related to randomization and allocation (D1–D3) were noted in all studies, with procedures for random sequence generation and allocation concealment often inadequately described or entirely absent.

Blinding of participants and personnel (D4–D5) was generally not feasible due to the nature of the interventions.[26,30] For instance, in a study by Klonizakis *et al.*[30], those delivering the intervention were blinded only with respect to participants' allocation to the two EC groups, as the NRT group received support through the stop-smoking service. In a study by George *et al.*[25], randomization was applied exclusively to the comparison between nicotine-containing and nicotine-free EC groups; allocation to the smoking group was not randomized, as assigning participants who wished to quit smoking to continue smoking was considered ethically inappropriate.

Nevertheless, outcome assessment domains (D7–D9) were generally well addressed. Most studies used standardized and objective instruments to measure outcomes, and outcome assessors were blinded to group allocation, thereby minimizing the risk of detection bias despite the lack of participant blinding.

Attrition bias (D10) emerged in one study,[29] where loss to follow-up was neither adequately reported nor analytically accounted for.

Quasi-experimental studies

The quasi-experimental studies were generally well conducted across all assessed domains (see Supplementary material online, *Appendix S5*). Temporal sequencing between intervention and outcome (D1) was clearly established in all cases, and all studies incorporated appropriate comparison groups and ensured similarity between participants across groups (D2–D4). Outcome measurement domains (D5–D7) were also well addressed: all studies applied pre-/post-assessments using consistent procedures and validated tools, and outcomes were measured in a reliable way. The only identified limitation relates to participant retention (D8) in a study by Yu-Jie *et al.*[43], where follow-up was incomplete and not adequately described or analytically addressed.

Cohort studies

Most cohort studies included in the review exhibited a generally acceptable methodological profile, with participants typically recruited from comparable populations and exposure status (smoking vs. cessation) defined using consistent criteria (see Supplementary material online, *Appendix S6*). In five cohort studies, domain D1 was marked as not applicable, as these were single-cohort designs evaluating within-group changes before and after smoking cessation.[36,37,40,44,45] In two studies, exposure was not considered measured in a valid and reliable way, as smoking cessation was self-reported and not biochemically verified (e.g. no cotinine or CO levels were assessed), introducing a potential risk of misclassification due to inaccurate reporting of smoking behaviour.[23,32]

While confounding factors were often identified, they were not analytically controlled. Some studies relied solely on baseline comparability without employing multivariable adjustment, which limits causal inference.[28,36,37,39–41] Strategies to address incomplete follow-up were largely absent, with dropouts either not reported or excluded from the final analysis without further consideration.[23,32,37,38,40,41] Finally, in all studies, the domain assessing whether participants were free of the outcome at baseline was marked as not applicable, as the outcome of interest was defined as change over time in vascular function rather than the occurrence of a categorical event.

Sensitivity analysis

A sensitivity analysis was conducted for the RCTs by excluding studies with multiple methodological limitations as defined in the Materials and methods.[26,30] The remaining trials confirmed the primary findings, showing consistent results for FMD[25,29] and PWV.[25]

Certainty of the evidence

The results of the grading are reported in *Table 2*. Each outcome included a mix of study designs, with a limited number of RCTs and a predominance of non-randomized studies. Therefore, the certainty of evidence was assessed separately by study design. For non-randomized studies, the certainty started from a low level and was further downgraded to very low due to a serious risk of bias, mainly related to inadequate control of confounders and incomplete follow-up. For RCTs, the certainty started from a high level but was downgraded for risk of bias and imprecision, as most trials were small and characterized by unclear randomization, blinding, or allocation procedures. The certainty for RCTs assessing FMD was rated as moderate. A detailed assessment and justification for each GRADE domain and outcome are provided in Supplementary material online, *Appendix S7*.

Discussion

This systematic review synthesized prospective evidence on the effects of quitting smoking or switching to exclusive EC use on prognostically important markers of vascular health. Across all three evaluated outcomes (i.e. PWV, AIx, and FMD), the

available prospective studies suggest early improvements in vascular function following smoking cessation. However, the quality of evidence was rated as very low, with moderate certainty for RCTs on FMD. These findings are consistent with proposed mechanistic pathways underlying the reduction in cardiovascular risk observed after smoking cessation and suggest that early vascular markers may be informative for exploratory regulatory and harm-reduction research, pending confirmation in larger and longer-term studies.

The improvement in endothelial function, reflected by increased FMD, appears to be one of the earliest benefits. Studies consistently reported significant FMD recovery within 1–12 months of cessation.[28,29,33] This rapid response is biologically plausible, as the endothelium is directly exposed to the thousands of circulating toxins in cigarette smoke which acutely impair nitric oxide bioavailability. Removing this toxic insult allows for the restoration of normal endothelial signalling. The magnitude of FMD improvement observed falls within a range that, in other clinical contexts, has been associated with a lower risk of future cardiovascular events for each 1% absolute increase in FMD, particularly among patients with established disease but also in asymptomatic populations.[19,50]

Similarly, measures of arterial stiffness exhibited consistent improvement. Reductions in PWV were reported as early as 1 month and were sustained over follow-up periods of up to 2 years. The PWV reductions observed, such as the approximately −0.77 to −1.2 m/s decrease over 24 months reported by Zhang *et al.*[44], are particularly noteworthy. This magnitude of change falls within a range that has been associated with a reduction in cardiovascular mortality risk (~15%) in previous epidemiological studies.[12] Differences in PWV responses between healthy participants and those with comorbidities may reflect higher baseline arterial stiffness in higher-risk populations, as well as the influence of comorbidity-related factors such as systemic inflammation, renal impairment, and concomitant medications, which can independently affect PWV and the reliability of its measurement.

The magnitude of AIx reduction varied considerably across the included studies. For instance, reductions were modest in some cohorts, such as the <1% change observed in healthy volunteers in the studies by Zhang *et al.*[44,45], while others reported more substantial improvements of 9.2%[37] and 12.5%.[36] Interestingly, this heterogeneity is not simply related to the follow-up duration; the shorter-term Zhang *et al.*[45] study reported a greater AIx reduction in its comorbidity cohort than the longer-term study.[44] These data suggest that variability in patient profiles and in the type of cessation therapy employed (e.g. NRT vs. varenicline, cytisinicline, or bupropion) may have contributed to the heterogeneity of the observed results. Furthermore, many included studies did not adjust for key covariates such as medication use, diet, physical activity, or post-cessation weight gain. The unmeasured confounders may partly explain the observed improvements in vascular parameters.

A crucial and novel aspect of this review is the evidence regarding switching to ECs, although it is based on a small number of studies. The available RCTs are consistent in the case of FMD, with measurable improvements reported in two studies.[25,30] These observations are consistent with the hypothesis that combustion-derived toxicants, rather than nicotine *per se*, may play a central role in smoking-related vascular impairment, as suggested by experimental work on human endothelium[51,52] and epidemiological studies on oral Swedish snus (i.e. snus has a high content of nicotine, but does not require combustion to deliver nicotine).[53,54] Our results differ from those of a recent systematic review suggesting that EC use increases arterial stiffness.[55] However, that analysis included three studies which measured the acute effects of ECs immediately post-use[56–58] and only one study measuring both acute and chronic effects, which was also included herein.[27] The prognostic value of arterial stiffness measurements applies only when assessments are conducted under strict resting conditions, with participants refraining from stimulant intake for several hours beforehand.[11] All acute-effect studies involve the administration of a stimulant (i.e. nicotine). There is no evidence that changes observed in these conditions have any prognostic value.[59] In fact, factors that are not associated with increased long-term cardiovascular risk, such as caffeine intake and NRTs, can acutely increase arterial stiffness.[60–62] Accordingly, non-nicotine ECs were not associated with acute adverse effects on arterial function in one previous study.[58] In contrast, smoking cessation with the use of NRTs has been associated with improvement in arterial function when measured at rest, even within 1 month and while still using NRTs.[62] Our findings are in agreement with a recent cohort study which showed that in smokers who underwent a percutaneous coronary intervention, smoking cessation or reduction with the use of ECs leads to the same reduction in future major cardiac adverse events as cessation without the use of any alternative product.[63]

Analysis of vascular endpoints across the studies included in our review suggests that switching from combustible cigarettes to ECs yields improvements that, in the limited available studies, fall within a similar range to those reported with standard smoking cessation pharmacotherapies, without implying equivalence in effectiveness. Within the current evidence, reductions in PWV (three studies) and AIx (one study), as well as gains in FMD (two studies), fall within a similar range to those reported in pharmacological cessation trials, supporting the hypothesis that the primary driver of benefit is the removal of combustion products rather than the specific cessation modality. Both the studies of George *et al.*[25] and Ikonomidis *et al.*[27] suggest that vascular benefits following EC use can emerge within a timeframe similar to that observed with pharmacotherapy-based cessation. However, further studies are needed to confirm these findings and better characterize the duration and extent of vascular improvements associated with switching to ECs, given the limited number of long-term EC-specific trials currently available and the heterogeneity derived from product and protocol use.

Although only one included study[27] provided data on dual use, its findings indicate that this behaviour should not be interpreted as being associated with significant vascular improvement. Yet, in that study, dual users exhibited a numerically favourable, albeit not clinically significant, change in PWV compared with exclusive EC users. This apparent paradox reflects the heterogeneity of dual use: 'strong switchers' vs. 'light switchers' differ substantially in cigarette reduction and toxicant exposure.[64] Previous studies document biomarker reductions among dual users[65,66] indicating that, under some patterns, dual use can yield partial harm reduction, a plausible explanation for our PWV findings. In any case, dual use—although it may represent a transitional phase from smoking to exclusive

e-cigarette use—should be avoided, with public health efforts directed towards achieving sustained smoking cessation.

The findings of this review, demonstrating a reversal of subclinical vascular damage, align with large-scale epidemiological data showing that smoking cessation leads to a substantial reduction in clinical cardiovascular events[67,68] although the rate of risk reduction varies between studies.[69–72] Our review is consistent with mechanistic hypotheses (i.e. the recovery of the arterial function) proposed to explain these clinical observations.

Studies with 30 or fewer participants were excluded due to concerns regarding imprecision and limited representativeness.[21] However, the exclusion of four studies with small sample sizes[73–76] did not alter the overall findings of the review. The results reported were consistent with the main body of evidence, supporting the robustness of the observed associations.

The overall quality of evidence was rated as very low, mainly due to the predominance of observational studies and methodological limitations such as incomplete follow-up and inadequate control of confounding factors. When considering RCTs separately, the certainty was also rated as very low for most outcomes, reflecting the small number and limited sample size of the available trials, except for FMD, for which the certainty of evidence was moderate. Across all study designs, smoking cessation was consistently associated with beneficial vascular effects, although the magnitude of improvement varied, likely reflecting differences in populations, interventions, and study designs.

This review's strengths include its focus on prospective studies and the use of objective, prognostically validated vascular outcomes that were measured in resting conditions. Blinding of participants to interventions like ECs vs. continued smoking is often not feasible, but the use of objective, blinded assessment using instrument-based outcomes mitigates the risk of detection bias. The sensitivity analysis, which confirmed the primary findings for FMD and PWV after excluding lower-quality trials, further strengthens our conclusions. In addition, the review is based on a rigorous methodology, with *a priori* registration on PROSPERO and protocol publication in a peer-reviewed journal.[20] Despite the strengths, there are some limitations in this review that need to be considered when interpreting the findings. First, the marked clinical and methodological heterogeneity across the included studies prevented quantitative synthesis and led us to adopt a qualitative approach. This heterogeneity was present in multiple domains. (i) Populations: the included studies encompassed healthy young volunteers,[32] middle-aged individuals with comorbidities,[44,45] and specific clinical populations such as people living with HIV,[33] with
substantial variation in sex composition across cohorts. The differences in vascular physiology and smoking-related cardiovascular risk are well documented between sexes, and such variability may have contributed to some of the heterogeneity observed across studies. (ii) Interventions: a wide variety of cessation aids were used, including different forms of NRT, varenicline, bupropion, cytisinicline and various types of ECs, making direct quantitative comparisons difficult. (iii) Outcome measures: although the three main outcomes were consistently assessed, the specific methodologies differed (e.g. brachial–ankle vs. carotid–femoral PWV), and these differences may influence the results. In addition, differences in cessation endpoint definitions (e.g. point prevalence abstinence vs. continuous) contributed to the observed heterogeneity.

Second, the methodological quality of the included studies varied, as detailed in the risk of bias assessment. Several RCTs did not adequately describe randomization or allocation concealment procedures. Some of the cohort studies relied on self-reported smoking cessation without biochemical verification (e.g. cotinine or CO levels), which introduces a risk of misclassification bias. Furthermore, many of these studies did not analytically control for potential confounding variables, such as concurrent changes in diet, physical activity, or medication use, which may also influence vascular health. Third, the follow-up duration of many included studies was relatively short. While benefits were seen as early as 1 month,[25,27,28] most studies had follow-up periods of 1 year or less. Arterial stiffening and atherosclerosis are chronic processes that develop over decades. Although these studies demonstrate early functional vascular improvement, they do not capture the long-term trajectory of vascular repair or sustained risk reduction, which requires longer follow-up. Fourth, as with many systematic reviews, this analysis is potentially subject to publication bias, where studies with statistically significant or 'positive' results are more likely to be published than those with null findings. We also restricted our search to articles published in English, which may have led to the omission of relevant studies published in other languages. Yet, the comprehensive search strategies adopted help to mitigate this risk. Finally, with specific reference to EC studies, the evidence included in this review does not fully capture the wide diversity of EC devices, nicotine concentrations, and flavouring agents currently available on the market. EC technology has evolved rapidly over the past decade, with substantial differences between early-generation products, pod-based systems, and more advanced devices in terms of nicotine delivery, aerosol composition, and user experience. As a result, the findings should be interpreted with caution when extrapolating to newer products, as their pharmacokinetic profiles and potential vascular effects may differ.

In conclusion, this systematic review shows that smoking cessation is associated with favourable changes in vascular health markers (i.e. PWV, AIx, and FMD). The certainty of the evidence ranges from moderate to very low across outcomes, yet the overall pattern consistently supports beneficial vascular effects following cessation. When considering RCTs separately, the certainty of evidence was very low for most outcomes due to the small number and limited size of available studies, but moderate for FMD. These findings suggest early functional improvements in endothelial function and arterial stiffness markers, offering a plausible mechanistic explanation for the reduction in cardiovascular risk observed after quitting smoking. While current evidence supports possible short-term improvements in vascular function with exclusive EC use compared with continued smoking, these findings remain highly uncertain due to the limited number of studies and substantial variability in device types, nicotine formulations, and study designs. The potential vascular benefits of EC use as a harm-reduction strategy should therefore be interpreted with caution and confirmed in adequately powered randomized trials.

There is a critical need for standardized and reproducible vascular health markers capable of detecting subtle functional changes. Such biomarkers would not only advance mechanistic research but also provide valuable tools for regulatory assessment of smoking cessation and harm-reduction products[77] . By capturing early subclinical effects, they could help clarify the impact of smoking cessation or switching to electronic

cigarettes on cardiovascular risk. Large, well-designed, long-term prospective studies are essential to validate these early findings and to inform future clinical practice, regulatory frameworks, and public health policies.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

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Author contribution

Jacob George (Conceptualization [equal]; Data curation [lead]; Formal analysis [lead]; Project administration [equal]; Resources [equal]; Supervision [lead]; Writing—original draft [equal]), Giusy Rita Maria La Rosa (Data curation [supporting]; Formal analysis [supporting]; Investigation [lead]; Methodology [lead]; Software [lead]; Writing—original draft [equal]), Jacqueline Yu (Investigation [supporting]; Validation [supporting]; Visualization [supporting]; Writing—original draft [supporting]), Davide Capodanno (Data curation [supporting]; Formal analysis [supporting]; Validation [supporting]; Writing—review & editing [supporting]), Giulio Geraci (Formal analysis [supporting]; Validation [supporting]; Visualization [supporting]; Writing—review & editing [supporting]), Takao Ohki (Validation [supporting]; Visualization [supporting]; Writing—review & editing [supporting]), Rohan Sequeira (Data curation [supporting]; Validation [supporting]; Visualization [supporting]; Writing—review & editing [supporting]), and Riccardo Polosa (Conceptualization [equal]; Funding acquisition [lead]; Investigation [supporting]; Project administration [equal]; Resources [equal]; Supervision [equal]; Writing—original draft [supporting]; Writing—review & editing [supporting])

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Data availability

All data are extracted from published original articles. The dataset is available from the corresponding author upon request.

References

1. GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the global burden of disease study 2015. *Lancet* 2017;**389**:1885–1906.
2. Yao Z, Tasdighi E, Dardari ZA, Jha KK, Osuji N, Rajan T, *et al.* Association between cigarette smoking and subclinical markers of cardiovascular harm. *J Am Coll Cardiol* 2025;**85**:1018–1034.
3. Cho JH, Shin SY, Kim H, Kim M, Byeon K, Jung M, *et al.* Smoking cessation and incident cardiovascular disease. *JAMA Netw Open* 2024;**7**:e2442639.
4. Livingstone-Banks J, Fanshawe TR, Thomas KH, Theodoulou A, Hajizadeh A, Hartman L, *et al.* Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev* 2023;**5**:CD006103.
5. Puljević C, Stjepanović D, Meciar I, Kang H, Chan G, Morphett K, *et al.* Systematic review and meta-analyses of cytisine to support tobacco cessation. *Addiction* 2024;**119**:1713–1725.
6. Hajizadeh A, Howes S, Theodoulou A, Klemperer E, Hartmann-Boyce J, Livingstone-Banks J, *et al.* Antidepressants for smoking cessation. *Cochrane Database Syst Rev* 2023;**5**:CD000031.
7. Meng Y, Xiang S, Qu L, Li Y. The efficacy and acceptability of pharmacological monotherapies and e-cigarette on smoking cessation: a systemic review and network meta-analysis. *Front Public Health* 2024;**12**:1361186.
8. O'Leary R, La Rosa GRM, Polosa R. Examining e-cigarettes as a smoking cessation treatment: a critical umbrella review analysis. *Drug Alcohol Depend* 2025;**266**:112520.
9. Food and Drug Administration (FDA). FDA authorizes marketing of tobacco- and menthol-flavored JUUL e-cigarette products. 2021. **https://www.fda.gov/tobacco-products/ctp-newsroom/fda-authorizes-marketing-tobacco-and-menthol-flavored-juul-e-cigarette-products (25 July 2025)**.
10. National Institute for Health and Care Excellence (NICE). Tobacco: preventing uptake, promoting quitting and treating dependence. 2021. **https://www.nice.org.uk/guidance/ng209 (25 July 2025)**.
11. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, *et al.* Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J* 2006;**27**:2588–2605.
12. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol* 2010;**55**:1318–1327.
13. Janner JH, Godtfredsen N S, Ladelund S, Vestbo J, Prescott E. The association between aortic augmentation index and cardiovascular risk factors in a large unselected population. *J Hum Hypertens* 2012;**26**:476–484.
14. Lekakis JP, Ikonomidis I, Protogerou AD, Papaioannou TG, Stamatelopoulos K, Papamichael CM, *et al.* Arterial wave reflection is associated with severity of

extracoronary atherosclerosis in patients with coronary artery disease. *Eur J Cardiovasc Prev Rehabil* 2006;**13**:236–242.
15. Nurnberger J, Keflioglu-Scheiber A, Opazo Saez AM, Wenzel RR, Philipp T, Schäfers RF. Augmentation index is associated with cardiovascular risk. *J Hypertens* 2002;**20**:2407–2414.
16. Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, *et al.* Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation* 2004;**109**:184–189.
17. Chirinos JA, Zambrano JP, Chakko S, Veerani A, Schob A, Willens HJ, *et al.* Aortic pressure augmentation predicts adverse cardiovascular events in patients with established coronary artery disease. *Hypertension* 2005;**45**: 980–985.
18. Pyke KE, Tschakovsky ME. The relationship between shear stress and flow-mediated dilatation: implications for the assessment of endothelial function. *J Physiol* 2005;**568**:357–369.
19. Matsuzawa Y, Kwon T-G, Lennon RJ, Lerman LO, Lerman A. Prognostic value of flow-mediated vasodilation in brachial artery and fingertip artery for cardiovascular events: a systematic review and meta-analysis. *J Am Heart Assoc* 2015;**4**:e002270.
20. La Rosa GRM, Yu J, Geraci G, Capodanno D, Ohki T, George J, *et al.* Vascular and cardiovascular outcomes of smoking cessation and switching to electronic cigarette use: protocol for a systematic review of prospective studies. *JMIR Res Protoc* 2025;**14**:e74949.
21. Corder GW, Foreman DI. *Nonparametric Statistics for Non-statisticians: a Step-by-Step Approach*. New Jersey: Wiley & Sons; 2009.
22. Murad MH, Mustafa RA, Schünemann HJ, Sultan S, Santesso N. Rating the certainty in evidence in the absence of a single estimate of effect. *Evid Based Med* 2017;**22**:85–87.
23. Cooper LL, Majid S, Wang N, Fetterman JL, Palmisano JN, Benjamin EJ, *et al.* Cross-sectional and longitudinal associations of smoking behaviour with central arterial haemodynamic measures: the Framingham Heart Study. *Eur J Prev Cardiol* 2025:zwaf012.
24. Fukumoto K, Takemoto Y, Norioka N, Takahashi K, Namikawa H, Tochino Y, *et al.* Predictors of the effects of smoking cessation on the endothelial function of conduit and digital vessels. *Hypertens Res* 2021;**44**:63–70.
25. George J, Hussain M, Vadiveloo T, Ireland S, Hopkinson P, Struthers AD, *et al.* Cardiovascular effects of switching from tobacco cigarettes to electronic cigarettes. *J Am Coll Cardiol* 2019;**74**:3112–3120.
26. Ikonomidis I, Marinou M, Vlastos D, Kourea K, Andreadou I, Liarakos N, *et al.* Effects of varenicline and nicotine replacement therapy on arterial elasticity, endothelial glycocalyx and oxidative stress during a 3-month smoking cessation program. *Atherosclerosis* 2017;**262**:123–130.
27. Ikonomidis I, Vlastos D, Kourea K, Kostelli G, Varoudi M, Pavlidis G, *et al.* Electronic cigarette smoking increases arterial stiffness and oxidative stress to a lesser extent than a single conventional cigarette: an acute and chronic study. *Circulation* 2018;**137**:303–306.
28. Ikonomidis I, Thymis J, Kostelli G, Katogiannis K, Vlastos D, Gatourtzidou E, *et al.* The effects of cytisinicline for smoking cessation on arterial stiffness, endothelial function, and myocardial performance: a pilot study. *Eur Heart J Imaging Methods Pract* 2025;**3**:qyaf062.
29. Johnson HM, Gossett LK, Piper ME, Aeschlimann SE, Korcarz CE, Baker TB, *et al.* Effects of smoking and smoking cessation on endothelial function: 1-year outcomes from a randomized clinical trial. *J Am Coll Cardiol* 2010;**55**: 1988–1995.
30. Klonizakis M, Gumber A, McIntosh E, Brose LS. Medium- and longer-term cardiovascular effects of e-cigarettes in adults making a stop-smoking attempt: a randomized controlled trial. *BMC Med* 2022;**20**:276.
31. Kobayashi M, Takemoto Y, Norioka N, Iguchi T, Shimada K, Maeda M, *et al.* Vascular functional and morphological alterations in smokers during varenicline therapy. *Osaka City Med J* 2015;**61**:19–30.
32. Mandraffino G, Aragona CO, Scuruchi M, Mamone F, D'Ascola A, Alibrandi A, *et al.* Biglycan expression, earlier vascular damage and pro-atherogenic profile improvement after smoke cessation in young people. *Atherosclerosis* 2017; **257**:109–115.
33. Moreira RC, Rodrigues A, Leonardo BM, Arabe D, Santos R, Cardoso SW, *et al.* Smoking cessation is associated with short-term improvement of vascular health in a cohort of people living with HIV in Rio de Janeiro, Brazil. *Am J Cardiol* 2024;**214**:157–166.
34. Nielson CA, Frances MF, Fitzgeorge L, Prapavessis H, Zamir M, Shoemaker JK. Impact of a smoking cessation lifestyle intervention on vascular mechanics in young women. *Appl Physiol Nutr Metab* 2014;**39**:572–580.
35. Okuyama N, Fukumoto K, Takemoto Y, Yamauchi T, Makuuchi A, Namikawa H, *et al.* Effects of smoking cessation on endothelial function as assessed by flow-mediated total dilation. *Cardiovasc Ultrasound* 2024;**22**:11.
36. Oren S, Isakov I, Golzman B, Kogan J, Turkot S, Peled R, *et al.* The influence of smoking cessation on hemodynamics and arterial compliance. *Angiology* 2006; **57**:564–568.
37. Polonia J, Barbosa L, Silva JA, Rosas M. Improvement of aortic reflection wave responses 6 months after stopping smoking: a prospective study. *Blood Press Monit* 2009;**14**:69–75.
38. Schmidt KMT, Hansen KM, Johnson AL, Gepner AD, Korcarz CE, Fiore MC, *et al.* Longitudinal effects of cigarette smoking and smoking cessation on aortic wave reflections, pulse wave velocity, and carotid artery distensibility. *J Am Heart Assoc* 2019;**8**:e013939.
39. Takami T, Saito Y. Effects of smoking cessation on central blood pressure and arterial stiffness. *Vasc Health Risk Manag* 2011;**7**:633–638.
40. Umeda A, Kato T, Yamane T, Yano H, Ieiri T, Miyagawa K, *et al.* Does smoking cessation with varenicline worsen vascular endothelial function? *BMJ Open* 2013;**3**:e003052.
41. van den Berkmortel FW, Wollersheim H, van Langen H, Smilde TJ, den Arend J, Thien T. Two years of smoking cessation does not reduce arterial wall thickness and stiffness. *Neth J Med* 2004;**62**:235–241.
42. Xue C, Chen QZ, Bian L, Yin ZF, Xu ZJ, Zhang AL, *et al.* Effects of smoking cessation with nicotine replacement therapy on vascular endothelial function, arterial stiffness, and inflammation response in healthy smokers. *Angiology* 2019; **70**:719–725.
43. Yu-Jie W, Hui-Liang L, Bing L, Lu Z, Zhi-Geng J. Impact of smoking and smoking cessation on arterial stiffness in healthy participants. *Angiology* 2013;**64**: 273–280.
44. Zhang P, Guo R, Wang C, Xiao D, Qin H, Zhang L, *et al.* Echo-tracking evaluation of changes in common carotid artery wall elasticity after smoking cessation. *J Clin Ultrasound* 2019;**47**:144–149.
45. Zhang P, Guo R, Xiao D, Chu S, Gong L, Zhang C, *et al.* Influence of smoking cessation on carotid artery wall elasticity evaluated by echo-tracking. *J Clin Ultrasound* 2012;**40**:352–356.
46. Hajat C, Stein E, Selya A, Polosa R; CoEHAR study group. Analysis of common methodological flaws in the highest cited e-cigarette epidemiology research. *Intern Emerg Med* 2022;**17**:887–909.
47. Kelly RP, Millasseau SC, Ritter JM, Chowienczyk PJ. Vasoactive drugs influence aortic augmentation index independently of pulse-wave velocity in healthy men. *Hypertension* 2001;**37**:1429–1433.
48. Harrison M, Parkhurst K, Tarumi T, Lin H-F, Tanaka H. Low flow-mediated constriction: prevalence, impact and physiological determinant. *Clin Physiol Funct Imaging* 2011;**31**:394–398.
49. Wei S, Evans PC, Strijdom H, Xu S. HIV infection, antiretroviral therapy and vascular dysfunction: effects, mechanisms and treatments. *Pharmacol Res* 2025;**217**:107812.
50. Ras RT, Streppel MT, Draijer R, Zock PL. Flow-mediated dilation and cardiovascular risk prediction: a systematic review with meta-analysis. *Int J Cardiol* 2013;**168**:344–351.
51. Caruso M, Emma R, Distefano A, Rust S, Poulas K, Giordano A, *et al.* Comparative assessment of electronic nicotine delivery systems aerosol and cigarette smoke on endothelial cell migration: the replica project. *Drug Test Anal* 2023;**15**:1164–1174.
52. Wölkart G, Kollau A, Russwurm M, Koesling D, Schrammel A, Mayer B. Varied effects of tobacco smoke and e-cigarette vapor suggest that nicotine does not affect endothelium-dependent relaxation and nitric oxide signaling. *Sci Rep* 2023;**13**:15833.
53. Hansson J, Galanti MR, Hergens M-P, Fredlund P, Ahlbom A, Alfredsson L, *et al.* Use of snus and acute myocardial infarction: pooled analysis of eight prospective observational studies. *Eur J Epidemiol* 2012;**27**:771–779.
54. Hansson J, Galanti MR, Hergens M-P, Fredlund P, Ahlbom A, Alfredsson L, *et al.* Snus (Swedish smokeless tobacco) use and risk of stroke: pooled analyses of incidence and survival. *J Intern Med* 2014;**276**:87–95.
55. Cheraghi M, Amiri M, Omidi F, Shahidi Bonjar AH, Bakhshi H, Vaezi A, *et al.* Acute cardiovascular effects of electronic cigarettes: a systematic review and meta-analysis. *Eur Heart J Open* 2024;**4**:oeae098.
56. Antoniewicz L, Brynedal A, Hedman L, Lundbäck M, Bosson JA. Acute effects of electronic cigarette inhalation on the vasculature and the conducting airways. *Cardiovasc Toxicol* 2019;**19**:441–450.
57. Caporale A, Langham MC, Guo W, Johncola A, Chatterjee S, Wehrli FW. Acute effects of electronic cigarette aerosol inhalation on vascular function detected at quantitative MRI. *Radiology* 2019;**293**:97–106.

58. Chaumont M, de Becker B, Zaher W, Culié A, Deprez G, Mélot C, *et al.* Differential effects of e-cigarette on microvascular endothelial function, arterial stiffness and oxidative stress: a randomized crossover trial. *Sci Rep* 2018;**8**: 10378.
59. Farsalinos KE. Acute vs. Chronic effects of e-cigarettes on vascular function. *Eur Heart J* 2020;**41**:1525.
60. Ioakeimidis N, Tzifos V, Vlachopoulos C, Terentes-Printzios D, Georgakopoulos C, Tousoulis D. Acute effect of coffee on aortic stiffness and wave reflections in healthy individuals: differential effect according to habitual consumption. *Int J Food Sci Nutr* 2018;**69**:870–881.
61. Mahmud A, Feely J. Acute effect of caffeine on arterial stiffness and aortic pressure waveform. *Hypertension* 2001;**38**:227–231.
62. Adamopoulos D, Argacha J-F, Gujic M, Preumont N, Degaute J-P, Van De Borne P. Acute effects of nicotine on arterial stiffness and wave reflection in healthy young non-smokers. *Clin Exp Pharmacol Physiol* 2009;**36**: 784–789.
63. Kang D, Choi KH, Kim H, Park H, Heo J, Park TK, *et al.* Prognosis after switching to electronic cigarettes following percutaneous coronary intervention: a Korean nationwide study. *Eur Heart J* 2025;**46**:84–95.
64. Sutton SK, Brandon KO, Harrell PT, Martínez Ú, Simmons VN, Gore LR, *et al.* Identifying prospective subpopulations of combustible and electronic cigarette dual users in the United States via finite mixture modeling. *Addiction* 2022;**117**:2493–2503.
65. McRobbie H, Phillips A, Goniewicz ML, Smith KM, Knight-West O, Przulj D, *et al.* Effects of switching to electronic cigarettes with and without concurrent smoking on exposure to nicotine, carbon monoxide, and acrolein. *Cancer Prev Res (Phila)* 2015;**8**:873–878.
66. Arnold MJ, Nollen NL, Mayo MS, Ahluwalia JS, Leavens EL, Zhang G, *et al.* Harm reduction associated with dual use of cigarettes and e-cigarettes in black and Latino smokers: secondary analyses from a randomized controlled e-cigarette switching trial. *Nicotine Tob Res* 2021;**23**:1972–1976.
67. Jeong S-M, Jeon KH, Shin DW, Han K, Kim D, Park SH, *et al.* Smoking cessation, but not reduction, reduces cardiovascular disease incidence. *Eur Heart J* 2021;**42**:4141–4153.
68. Godtfredsen NS. Smoking reduction, smoking cessation, and mortality: a 16-year follow-up of 19,732 men and women from The Copenhagen Centre for Prospective Population Studies. *Am J Epidemiol* 2002;**156**:994–1001.
69. Rosenberg L, Palmer JR, Shapiro S. Decline in the risk of myocardial infarction among women who stop smoking. *N Engl J Med* 1990;**322**:213–217.
70. Dobson AJ, Alexander HM, Heller RF, Lloyd DM. How soon after quitting smoking does risk of heart attack decline? *J Clin Epidemiol* 1991;**44**: 1247–1253.
71. Negri E, La Vecchia C, D'Avanzo B, Nobili A, La Malfa RG. Acute myocardial infarction: association with time since stopping smoking in Italy. GISSI-EFRIM investigators. Gruppo Italiano per lo studio della sopravvivenza nell'infarto. Epidemiologia dei fattori di rischio dell'infarto miocardico. *J Epidemiol Community Health* 1994;**48**:129–133.
72. Duncan MS, Freiberg MS, Greevy RA, Kundu S, Vasan RS, Tindle HA. Association of smoking cessation with subsequent risk of cardiovascular disease. *JAMA* 2019;**322**:642–650.
73. Roux A, Motreff P, Perriot J, Pereira B, Lusson J-R, Duale C, *et al.* Early improvement in peripheral vascular tone following smoking cessation using nicotine replacement therapy: aortic wave reflection analysis. *Cardiology* 2010; **117**:37–43.
74. Kato T, Umeda A, Miyagawa K, Takeda H, Adachi T, Toyoda S, *et al.* Varenicline-assisted smoking cessation decreases oxidative stress and restores endothelial function. *Hypertens Res* 2014;**37**:655–658.
75. Rehill N, Beck CR, Yeo KR, Yeo WW. The effect of chronic tobacco smoking on arterial stiffness. *Br J Clin Pharmacol* 2006;**61**:767–773.
76. Sugiura T, Dohi Y, Hirowatari Y, Yamashita S, Ohte N, Kimura G, *et al.* Cigarette smoking induces vascular damage and persistent elevation of plasma serotonin unresponsive to 8 weeks of smoking cessation. *Int J Cardiol* 2013;**166**: 748–749.
77. Polosa R. Examining the evidence for the health impact of combustion-free products: progress and prospects for tobacco harm reversal and reduction. *Intern Emerg Med* 2021;**16**:2043–2046.