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Periodontal and Inflammatory Effects of Switching to Combustion-Free Nicotine Delivery Systems: A 12-Month Randomized Controlled Trial

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Abstract

Introduction: Tobacco smoking is a recognized risk factor for periodontal disease, contributing to inflammation and poor oral health. Combustion-free nicotine delivery systems (C-F NDS) have emerged as alternatives, yet their long-term clinical implications on periodontal health remain unclear.
Objective: This study aimed to assess the 12-month effects of switching from conventional smoking to C-F NDS on cigarette consumption, gingival inflammation, plaque accumulation, and exhaled carbon monoxide (CO) levels.
Methods: A randomized controlled trial was conducted with 40 adult smokers, allocated into two groups: one continued smoking conventional cigarettes, and the other transitioned to C-F NDS (IQOS™ or RELX™). Variables measured included cigarettes per day (CPD), Modified Gingival Index (MGI), plaque accumulation scores (R30, R120, Simple OH Score) using Quantitative Light Fluorescence (QLF) technology with Qraycam , and CO levels. Data were analyzed using parametric and non-parametric tests with significance at $p < 0.05$.
Results: The C-F NDS group showed a significant reduction in CPD ($p < 0.0001$), and lesser progression of gingival inflammation (MGI Δ: 0.94 vs. 1.25; $p = 0.041$). Reductions were also observed in early plaque (R30, $p = 0.046$) and oral hygiene scores (Simple OH Score, $p = 0.026$). CO levels declined in both groups, with a greater reduction among C-F NDS users (ΔCO: -5.65 ppm vs. -4.25 ppm), although not statistically significant ($p = 0.621$).
Conclusion: Switching to C-F NDS is associated with reduced cigarette use, improved periodontal markers, and decreased exposure to combustion-related toxins. These findings support the inclusion of C-F NDS in harm reduction strategies for tobacco users.

Keywords: *combustion-free nicotine delivery system; gingival inflammation; plaque accumulation; tobacco harm reduction; carbon monoxide; smoking cessation; periodontal health; randomized controlled trial*

Background

Periodontal diseases, including gingivitis and periodontitis, are chronic, non-communicable, preventable, and treatable inflammatory conditions. Gingivitis is a mild, reversible form of inflammation, while periodontitis causes irreversible damage to tooth-supporting tissues due to bacterial infection in plaque.[1,2] The WHO estimates that 10–15% of the global adult population is affected, totaling approximately 796 million cases, particularly among individuals with limited access to dental care, low socioeconomic status, and poor oral hygiene.[1,2] Tobacco smoking remains a global public health concern, particularly in low- and middle-income countries. According to WHO (2023), over 8 million tobacco-related deaths occur annually, including 1.3 million deaths

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due to secondhand smoke. About 22.3% of the global population uses tobacco, with a higher prevalence among men (36.7%) than women (7.8%). In Indonesia, smoking prevalence is notably high among individuals aged 18–59, with the highest rates observed in the 40–44 age group.[3]

Smoking is a major risk factor for periodontal tissue damage due to its extensive local and systemic inflammatory effects. Cigarettes per day (CPD) is a commonly used clinical indicator to measure cigarette consumption intensity. A reduction in CPD correlates with decreased exposure to toxic substances and inflammatory biomarkers, such as TNF-α, making it a key indicator in behavioral transition studies.[4,5] Abrams et al. support harm reduction strategies through gradual CPD reduction to mitigate smoking-related health risks.[5]

Gingival inflammation, one of the earliest clinical signs of smoking, is typically assessed using the Modified Gingival Index (MGI). While active smokers may exhibit masked inflammation due to nicotine-induced vasoconstriction, gingival inflammation tends to progress. Transitioning to Combustion-Free Nicotine Delivery Systems (C-F NDS), such as electronic cigarettes, has been shown to reduce MGI scores and normalize mucosal inflammatory responses, similar to those observed during recovery in ex-smokers.[6-9]

Plaque accumulation is another critical factor in the pathogenesis of periodontal disease. Research using QLF-D technology has shown that smokers exhibit significantly higher plaque scores than C-F NDS users or non-smokers. C-F NDS users tend to have lower plaque scores and oral hygiene profiles closer to non-smokers, suggesting that switching to C-F NDS may inhibit pathogenic biofilm formation.[10-13]

Exhaled carbon monoxide (CO) levels serve as physiological indicators to objectively verify smoking status. C-F NDS produces non-combusted aerosols that significantly reduce CO levels compared to traditional cigarettes. Lower CO levels are associated with decreased systemic inflammation and improved periodontal parameters such as bleeding on probing (BOP) and MGI.[14-16]

Given these considerations, it is important to assess, over a 12-month period, the impact of transitioning from conventional cigarettes to C-F NDS on CPD, gingival inflammation, plaque accumulation, and CO exposure. This evaluation holds both clinical value in periodontal care and relevance for informing tobacco harm reduction policies in Indonesia.

Methods

Study Design

This was an open-label randomized controlled trial (RCT) conducted as part of the international SMILE Study initiated by CoEHAR, University of Catania, Italy. The study received ethical approval from the Health Research Ethics Committee of Padjadjaran University (No. 643/UN6.KEP/EC/2021) and was registered in the UMIN Clinical Trial Registry (UMIN000051684).

Participants

Subjects were recruited from the Periodontia Clinic at RSGM Padjadjaran University between September 2024 and March 2025. Participants were purposively selected based on the following inclusion criteria: aged 18–59 years, active tobacco smokers (defined as smoking at least 10 cigarettes per day for five or more years), generally healthy or diagnosed with mild gingivitis or periodontitis (CAL <2 mm), possessing at least 10 teeth with intact crowns and six anterior teeth in both the maxillary and mandibular arches, and willing to be randomly assigned to either continue smoking conventional cigarettes or switch to C-F NDS. Exclusion criteria included pregnancy or breastfeeding, a history of severe systemic disease, use of fixed orthodontic appliances or prostheses, recent consumption of antibiotics or anti-inflammatory medications within 14 days, or history of tooth loss due to periodontitis.

Variables

The independent variable in this study was the type of nicotine product used (conventional cigarettes versus C-F NDS). The dependent variables were Modified Gingival Index (MGI) scores, and plaque accumulation (R30, R120, Simple OH Score). Potential confounding variables included gender, diet, and adherence to the intervention protocol.

Operational Definitions

Combustion-Free Nicotine Delivery Systems (C-F NDS) refer to non-combustion nicotine products such as IQOS™ and RELX™. Gingival inflammation was assessed using the Modified Gingival Index (MGI), an ordinal scale ranging from 0 to 4. Plaque accumulation was measured using Quantitative Light Fluorescence (QLF) technology with Qraycam. Smoking status was verified using a MicroCO device, with a threshold of ≥7 ppm to confirm active smoking.

Procedures

Subjects underwent a multi-stage research procedure. During screening, participants completed medical and smoking history interviews, a lifestyle questionnaire, intraoral clinical examinations (including BOP and CAL), and CO verification. Those who qualified received prophylactic treatment involving scaling and root planing two weeks before baseline. Afterward, participants were randomized into either the control group (continuing to smoke conventional cigarettes) or the intervention group (switching to C-F NDS) using the Smile Study Randomization Tool. Interventions were conducted at four time points: baseline (day 0), day 90, day 180, and day 360. At each visit, periodontal examination (MGI), plaque accumulation measurement via QLF, and product distribution (IQOS or RELX starter kits and refills). Compliance was monitored through the Smile Study app, and any reported side effects were recorded and evaluated.

Data Analysis

Data were analyzed using standard statistical methods. Normality was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov tests. Parametric (independent or paired t-tests) or non-parametric (Mann-Whitney or Wilcoxon) tests were applied based on data distribution. Categorical data were analyzed using Chi-Square or Fisher's Exact tests as appropriate. A p-value of less than 0.05 was considered statistically significant.

Study Setting

This study was conducted at the Periodontia Clinic of RSGM Padjadjaran University Bandung, between March 2024 and March 2025. Data analysis was completed in April 2025.

Ethical Considerations

The study received prior approval from the relevant ethics committee. All participants provided informed consent and were covered by health insurance throughout the study. Adverse events were continuously monitored to ensure subject safety.

Results

Participant Characteristics

A total of 44 subjects were screened at baseline, and 40 met the inclusion criteria and were randomized. Of these, 16 participants continued smoking conventional cigarettes (control group), and 24 switched to C-F NDS (intervention group). The baseline demographic characteristics, including age, gender, BMI, and cigarettes per day (CPD), did not differ significantly between the groups ($p > 0.05$), indicating homogeneity and comparability.

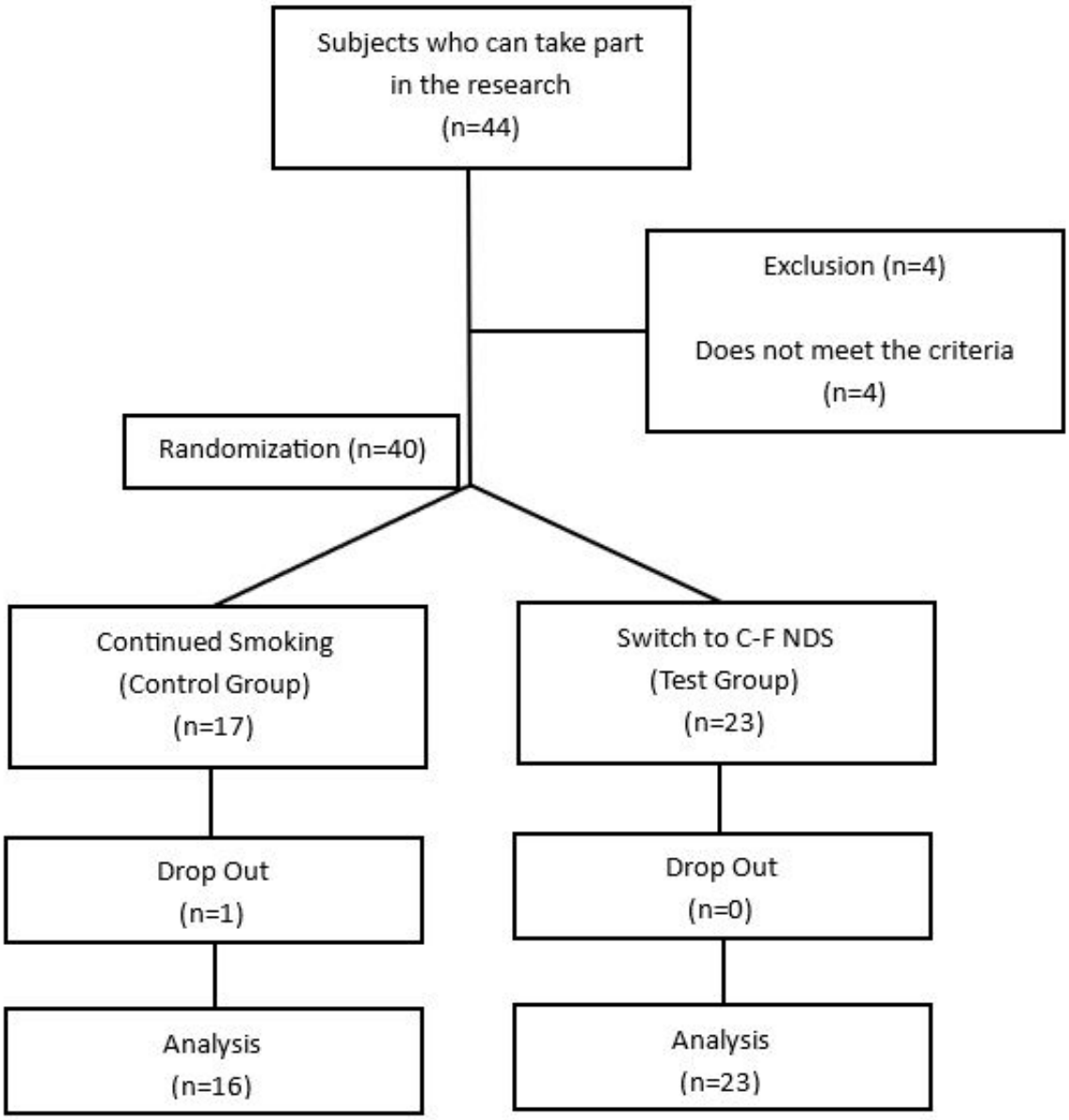


Chart 1 . Consort diagram

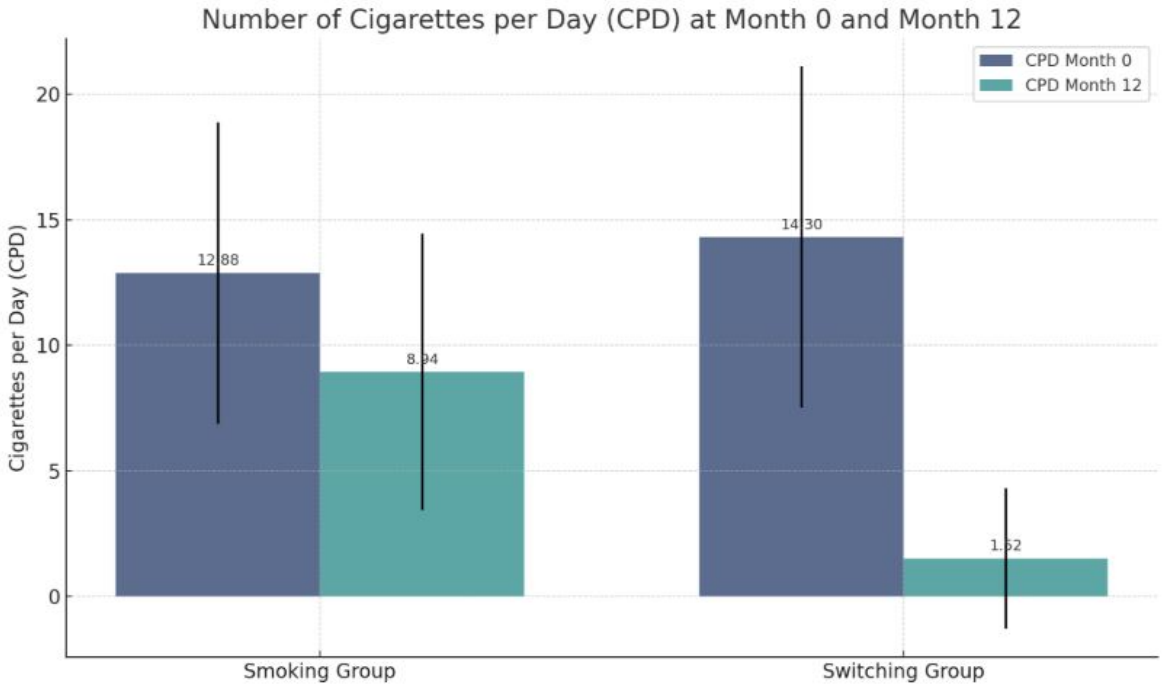
Cigarettes per Day (CPD)

There was a significant reduction in the number of cigarettes smoked per day among participants in the C-F NDS group over the 12-month period. The mean CPD in this group decreased from 14.30 ± 6.20 at baseline to 1.52 at month 12 ($p < 0.0001$). In contrast, the control group maintained a relatively stable smoking rate, with only a minor decrease from 12.88 ± 5.78 to 8.94 ± 6.10 CPD. The intergroup comparison confirmed the significant difference in smoking reduction ($p = 0.0001$), supporting the effectiveness of C-F NDS in reducing cigarette consumption.

Table 1 . Descriptive demographic and clinical characteristics by group

	Control Group (Smoking)	Test Group (Switch)	P
Age			
20-30 Years	7 (43.8%)	12(52.2%)	
31-40 Years	8(50.0%)	8(34.8%)	
41-50 Years	1(6.3%)	2(8.7%)	
51-60 Years	0(0.0%)	1(4.3%)	
Age			**0.631**
Mean±Std	32.31±5.805	33.35±7.049	
Median	31.50	30.00	
Range (min-max)	25.00-48.00	23.00-51.00	
Gender			**1.000**
Male	14(87.5%)	20(87.0%)	
Female	2(12.5%)	3(13.0%)	
BMI			**0.512**
Mean±Std	23.36±3.670	24.10±3.280	
Median	23.67	24.16	
Range (min-max)	18.08-30.04	18.26-29.40	
Cigarettes/day			**0.472**
Mean±Std	12.88±5.784	14.30±6.204	
Median	11.50	12.00	
Range (min-max)	6.00-24.00	5.00-28.00	

Graph 1. Number of cigarettes per day at month 0 and month 12



Source: data processed, 2025

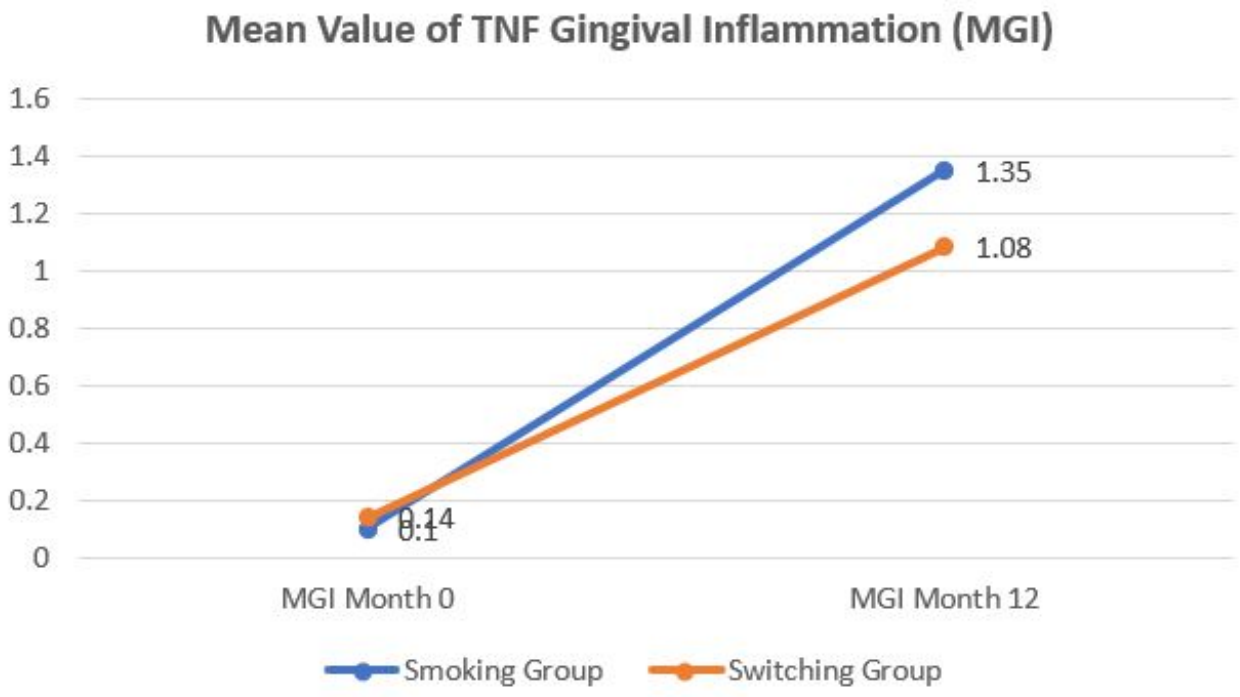
Gingival Inflammation (MGI)

The Modified Gingival Index (MGI) increased in both groups over the study period, indicating progression of inflammation. However, the increase was significantly lower in the C-F NDS group. At baseline, the mean MGI scores were similar between groups ($p = 0.789$), but at month 12, the C-F NDS group had a lower mean MGI (1.08 ± 0.36) compared to the smoking group (1.35 ± 0.54), with a borderline statistical significance ($p = 0.074$). Within-group analysis showed significant increases in MGI from baseline in both groups ($p < 0.0001$). The intergroup difference in change scores (mean ΔMGI = 1.25 for smokers vs. 0.94 for switchers) was statistically significant ($p = 0.041$), suggesting a protective effect of C-F NDS on gingival health.

Table 2. Mean Value of MGI in Conventional Smoking Group (Control) and C-F NDS (Test) Groups

Variable	Group		P value
	Smoking N=16	Switch N=23	
MGI Month 0			**0.789**
Mean±Std	0.10±0.080	0.14±0.180	
Median	0.07	0.08	
Range (min-max)	0.00-0.28	0.00-0.76	
MGI 12th Month			**0.074**
Mean±Std	1.35±0.542	1.08±0.356	
Median	1.37	1.10	
Range (min-max)	0.34-2.51	0.47-1.85	
P-value	**0.0001****	**0.0001****	

Graph 2. Graph of Mean Value of TNF Gingival Inflammation (MGI)



Source: data processed, 2025

Table 3. Comparison of MGI Difference in Conventional Smoking Group (Control) and C-F NDS Group (Test)

Variable	Group		P value
	Smoking N=16	Switch N=23	
Difference (0 vs 12) MGI			**0.041***
Mean±Std	1.25±0.542	0.94±0.374	
Median	1.23	0.95	
Range (min-max)	0.28-2.35	0.37-1.85	

Plaque Accumulation (R30, R120, Simple OH Score)

At month 12, participants in the C-F NDS group exhibited significant reductions in plaque accumulation compared to those who continued smoking. For initial plaque (R30), the C-F NDS group showed a mean reduction of -2.57%, while the smoking group experienced an increase of 1.69% (p = 0.046). For mature plaque (R120), the C-F NDS group showed a decrease (-2.96%), while the smoking group exhibited a slight increase (0.75%), although this difference did not reach statistical significance (p = 0.107).

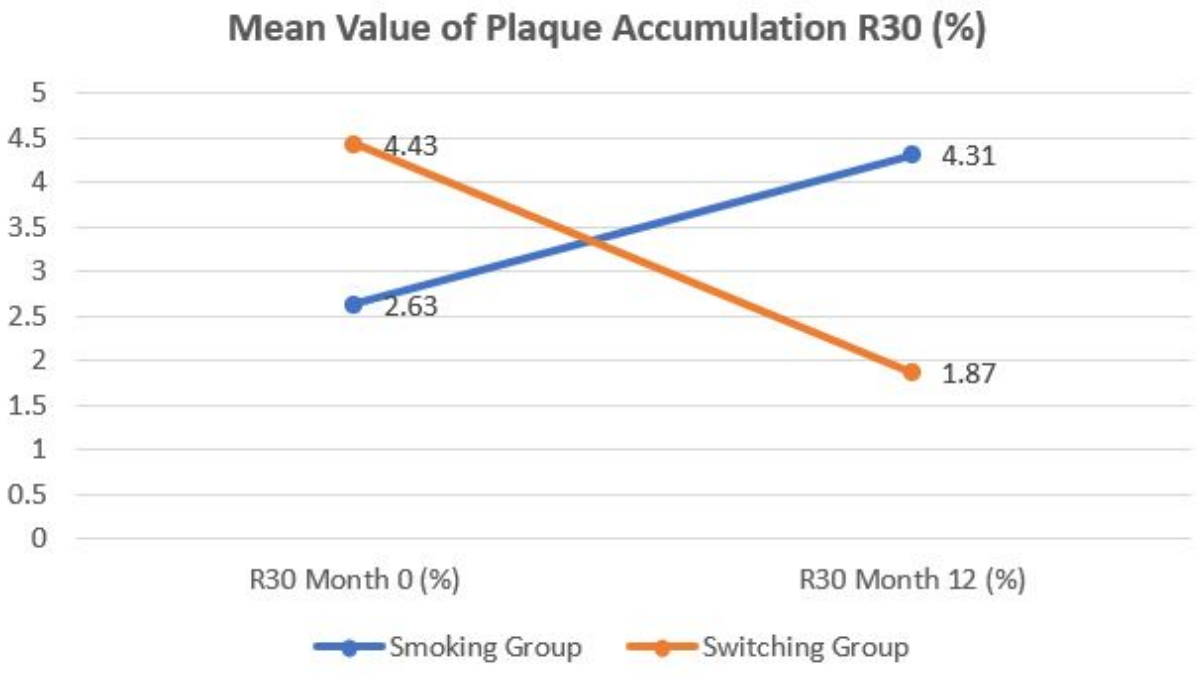
The Simple Oral Hygiene (OH) Score also showed favorable trends. The C-F NDS group had a mean reduction of -0.65, while the smoking group showed a mean increase of 1.00 (p = 0.026). These results suggest improved oral hygiene and reduced plaque accumulation among those who transitioned to C-F NDS.

Table 4. Mean Value of R30 in Conventional Smoking Group (Control) and C-F NDS (Test) Groups

Variable	Group		P value
	Smoking N=16	Switch N=23	
R30 Month 0 (%)			**0.251**
Mean±Std	2.63±3.964	4.43±6.294	
Median	0.50	1.00	
Range (min-max)	0.00-13.00	0.00-26.00	
R30 12th month (%)			**0.177**
Mean±Std	4.31±7.346	1.87±2.801	
Median	2.00	1.00	
Range (min-max)	0.00-29.00	0.00-12.00	
P-value	**0.422**	**0.073**	

Notes: For numerical data, the p value (side) is tested with an unpaired T test if the data is normally distributed with an alternative *Mann Whitney* test if the data is not normally distributed.

Graph 3. Graph of Mean Value of Plaque Accumulation R30 (%)



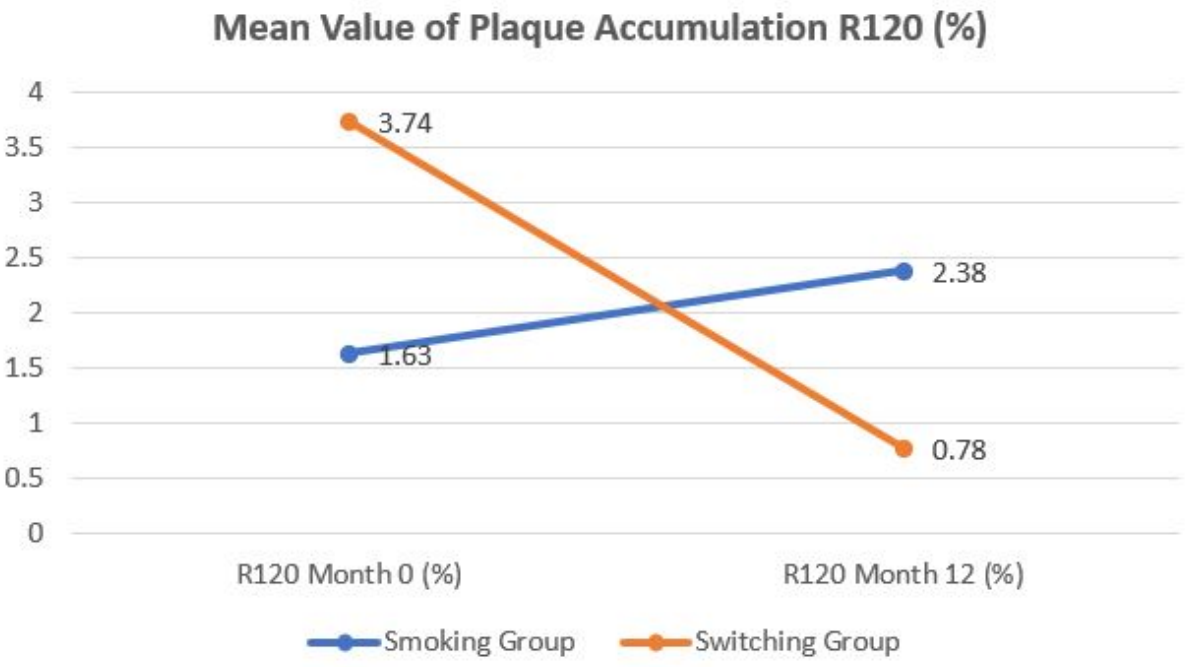
Source: processed data, 2025

Table 5. Mean Value of R120 in Conventional Smoking Group (Control C-F NDS (Test) Groups

Variable	Group		P value
	Smoking N=16	**Switch N=23**	
R120 Month 0 (%)			**0.239**
Mean±Std	1.63±3.096	3.74±6.290	
Median	0.00	1.00	
Range (min-max)	0.00-9.00	0.00-26.00	
R120 12th month (%)			**0.275**
Mean±Std	2.38±5.702	0.78±1.594	
Median	1.00	0.00	
Range (min-max)	0.00-23.00	0.00-7.00	
P-value	**0.878**	**0.027***	

Notes: For numerical data, the p value (side) is tested with an unpaired T test if the data is normally distributed with an alternative *Mann Whitney* test if the data is not normally distributed.

Graph 4. Graph of Mean Value of Plaque Accumulation R120 (%)



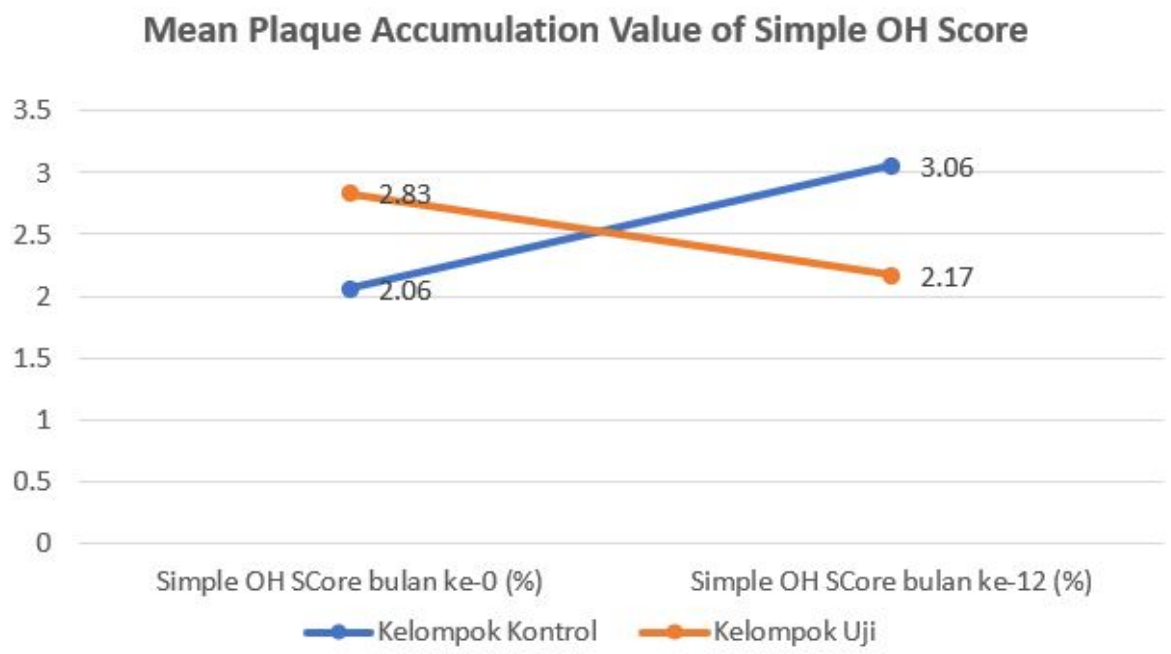
Source: data processed, 2025

Table 6. Mean simple OH score on Conventional Smoking Group (Control) and C-F NDS Group (Test)

Variable	Group		P value
	Smoking N=16	Switch N=23	
SIMPLE OH SCORE Month 0			**0.275**
Mean±Std	2.06±2.235	2.83±2.103	
Median	1.50	3.00	
Range (min-max)	0.00-5.00	0.00-5.00	
SIMPLE OH SCORE 12th month			**0.095**
Mean±Std	3.06±1.843	2.17±1.723	
Median	3.50	3.00	
Range (min-max)	0.00-5.00	0.00-5.00	
P-value	**0.065**	**0.065**	

Notes: For numerical data, the p value (side) is tested with an unpaired T test if the data is normally distributed with an alternative *Mann Whitney* test if the data is not normally distributed.

Graph 5. Graph of Mean Plaque Accumulation Value of Simple OH Score



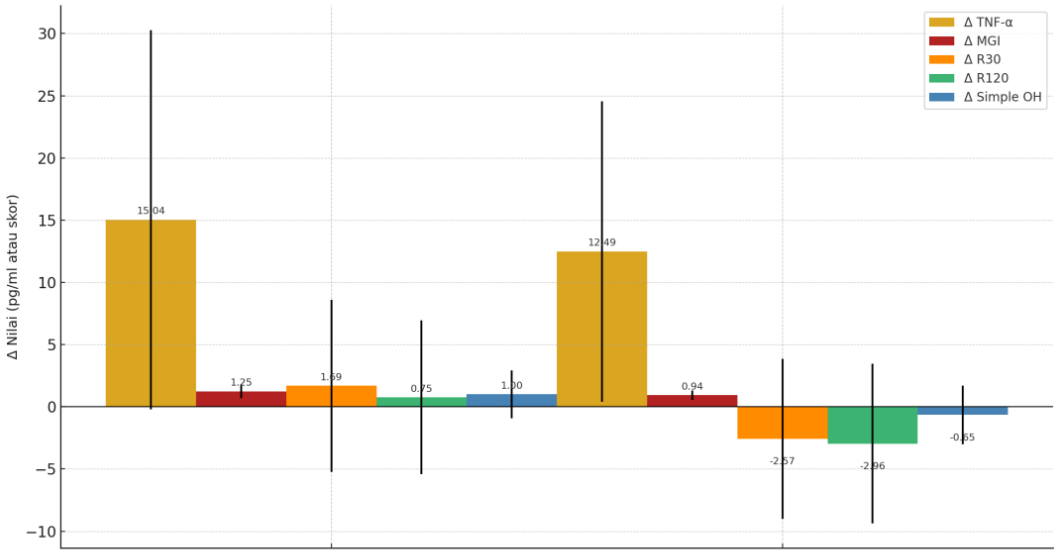
Source: data processed, 2025

Table 7. Comparison of Difference in Plaque Accumulation in Conventional Smoking Group (Control) and C-F NDS Group (Test)

Variable	Group		P value
	Smoking N=16	**Switch N=23**	
Difference (0 vs 12) R30			**0.046***
Mean±Std	1.69±6.926	-2.57±6.423	
Median	0.50	0.00	
Range (min-max)	-7.00-25.00	-26.00-5.00	
Difference (0 vs 12) R120			**0.107**
Mean±Std	0.75±6.181	-2.96±6.407	
Median	0.00	0.00	
Range (min-max)	-7.00-22.00	-26.00-3.00	
Difference (0 vs 12) *Simple OH score*			**0.026***
Mean±Std	1.00±1.932	-0.65±2.347	
Median	0.50	-1.00-	
Range (min-max)	-2.00-5.00	-5.00-3.00	

Notes: For numerical data, the p value is tested with an unpaired T test if the data is normally distributed with an alternative *Mann Whitney* test if the data is not normally distributed.

Graph 6. Graph of Mean Difference of TNF-α, Gingival Inflammation, Plaque Accumulation (R30, R120, Simple OHI Score)



Source: data processed, 2025

Carbon Monoxide (CO) Levels

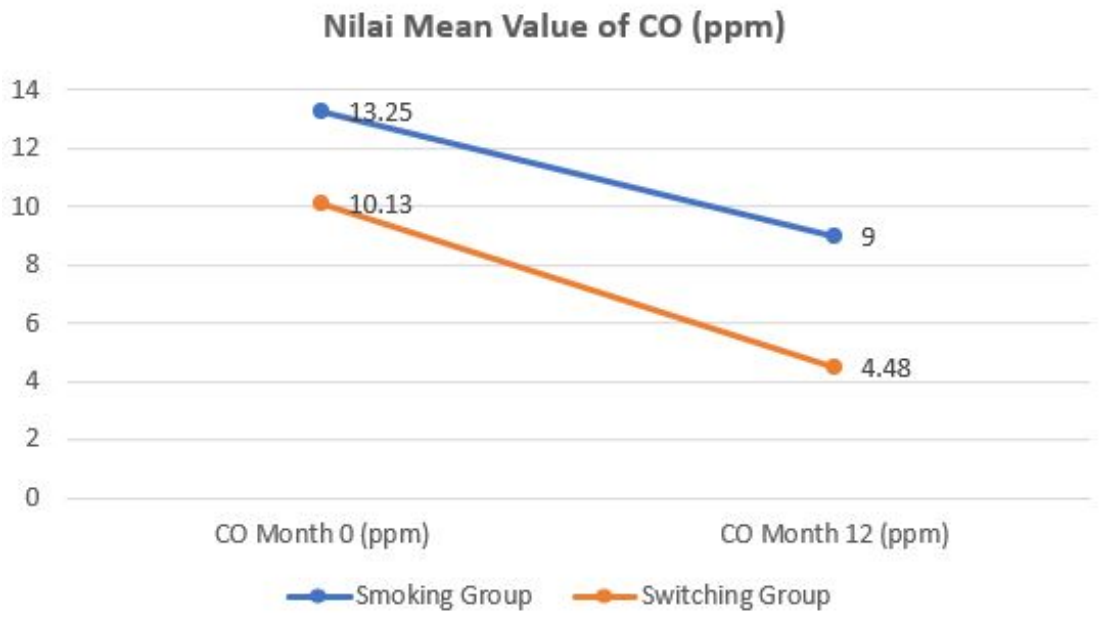
Exhaled CO levels decreased significantly in both groups over the study period, with a greater reduction observed in the C-F NDS group. The C-F NDS group showed a mean decrease from 10.13 ± 5.91 ppm at baseline to 4.48 ± 3.82 ppm at month 12 (p = 0.001). The control group showed a decrease from 13.25 ± 7.10 ppm to 9.00 ± 4.93 ppm (p = 0.018). Although the difference in the magnitude of change between groups (ΔCO: -5.65 vs. -4.25) was not statistically significant (p = 0.621), the downward trend in CO levels supports reduced exposure to combustion byproducts in C-F NDS users.

Table 8. Mean CO Values in the Conventional Smoking Group (Control) and C-F NDS Group (Test)

Variable	Group		P value
	Smoking N=16	**Switch N=23**	
CO Month 0			**0.251**
Mean±Std	13.25±7.095	10.13±5.911	
Median	10.50	8.00	
Range (min-max)	7.00-27.00	3.00-30.00	
CO 12th Month			**0.001***
Mean±Std	9.00±4.926	4.48±3.824	
Median	8.50	3.00	
Range (min-max)	3.00-19.00	2.00-20.00	
P-value	**0.018***	**0.001***	

Notes: For numerical data, the p value (side) is tested with an unpaired T test if the data is

Graph 7. Graph of Mean Value of CO



Source: data processed, 2025

Table 9. Comparison of CO Difference in Conventional Smoking Group (Control) and C-F NDS Group (Test)

Variable	Group		P value
	Smoking N=16	Switch N=23	
Difference (0 vs 12) CO			**0.621**
Mean±Std	-4.25±5.580	-5.65±6.644	
Median	-4.00	-5.00	
Range (min-max)	-16.00-5.00	-27.00-8.00	

Overall, participants who switched to C-F NDS demonstrated significant reductions in CPD, gingival inflammation progression, plaque accumulation, and CO exposure. These findings support the potential of C-F NDS as a harm reduction tool with beneficial effects on periodontal and oral health outcomes over a 12-month period.

Discussion

A significant reduction in daily cigarette consumption (CPD) was observed in participants who switched to C-F NDS, decreasing from more than 10 cigarettes/day to an average of 1.52 over 12 months (p = 0.0001) (5,19). This result underscores the effectiveness of C-F NDS in reducing active tobacco exposure and confirms its role as a viable component of harm reduction strategies.[6] The reduced CPD was also associated with decreased levels of inflammatory biomarkers and improvements in periodontal clinical parameters, highlighting the broader systemic benefits of switching to non-combustion alternatives.[20]

In terms of gingival inflammation, as measured by the Modified Gingival Index (MGI), both groups experienced increases, but the rise was significantly lower in the C-F NDS group (ΔMGI: 0.94 vs. 1.25; p = 0.041).[21] Unlike conventional cigarette use, which may mask clinical signs of inflammation due to nicotine-

induced vasoconstriction,[7,8] C-F NDS appears to allow for the restoration of normal inflammatory signaling, including physiological responses such as bleeding on probing.[9,10] Prior studies further support this observation, noting that switching to C-F NDS facilitates a normalization of mucosal vascular and immune responses, resembling the pattern seen in former smokers.[11,12]

Analysis of plaque accumulation revealed a significant decline in early plaque (R30: Δ -2.57%; p = 0.046) and improved oral hygiene (Simple OH Score: Δ -0.65; p = 0.026) among C-F NDS users, whereas participants who continued smoking showed increased plaque indices.[13] Although mature plaque (R120) did not show statistically significant reduction (p = 0.107), the direction of change remained favorable for C-F NDS users. These results are consistent with prior research employing QLF-D technology, which demonstrated greater reductions in anterior plaque following transitions to non-combustion nicotine products.[14-15] This suggests that C-F NDS may help prevent early biofilm formation, a crucial contributor to gingivitis and periodontitis.[15]

Carbon monoxide (CO) levels, a key biomarker of exposure to combustion, were also significantly reduced in both groups, with a greater decline in the C-F NDS group (ΔCO: -5.65 ppm vs. -4.25 ppm), though the difference was not statistically significant (p = 0.621).[21] The decline in CO reflects reduced systemic toxicant exposure and supports previous evidence linking combustion-free nicotine use to lower inflammation-related damage.[7,16] Additionally, CO reduction indicates better compliance with C-F NDS use and reinforces its potential role in decreasing the overall toxic burden associated with conventional smoking.

These findings enhance our understanding of C-F NDS as not only an alternative to conventional cigarettes but also a clinical intervention that provides measurable health benefits, both systemically and locally. Prior studies have shown that switching to C-F NDS leads to reduced TNF-α levels, a critical pro-inflammatory cytokine involved in periodontal disease.[19] This biological plausibility is further supported by Benowitz and St. Helen's framework, which describes how ENDS technologies reduce toxicant exposure while maintaining nicotine delivery.[21]

From a public health perspective, C-F NDS could offer an accessible and scalable harm reduction strategy, particularly in populations with high smoking prevalence and limited access to dental care, such as in Indonesia. The World Health Organization has emphasized the need for innovative approaches to reduce non-communicable disease burdens[2], and C-F NDS could be part of such frameworks. Nonetheless, it is crucial to communicate that while C-F NDS are less harmful than combustible tobacco products, they are not risk-free. Their adoption should be part of an integrated cessation strategy supported by healthcare providers.[3,16]

In conclusion, switching to C-F NDS has been associated with significant improvements in key periodontal health indicators, reductions in smoking behavior, and lower exposure to combustion-derived toxicants. These findings reinforce the role of C-F NDS within a broader tobacco harm reduction framework. Future studies should continue to investigate the long-term sustainability of these benefits across diverse populations and clinical settings.

Conclusion

This 12-month randomized controlled trial demonstrates that switching from conventional cigarettes to combustion-free nicotine delivery systems (C-F NDS) significantly reduces cigarette consumption, mitigates gingival inflammation, and improves plaque control and oral hygiene status. Although not all outcomes reached statistical significance, the observed trends consistently favored the C-F NDS group, particularly in reducing systemic exposure to carbon monoxide. These findings reinforce the role of C-F NDS in tobacco harm reduction strategies and highlight their potential contribution to improved periodontal and overall oral health. Further longitudinal studies are recommended to confirm these outcomes and evaluate long-term effects in broader populations.

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Author Contributions

All authors act as the guarantor of the manuscript, participated in the conception, data acquisition, data interpretation, writing of the study, data analysis, and statistical analysis of the study.

Conflict of Interest

None Declared

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