

# Evaluating effectiveness and safety toward electronic cigarette among Malaysian vapers: One-month observational study

Azizur Rahman, Mohamad Haniki Nik Mohamad, Shazia Jamshed

Department of Pharmacy Practice, International Islamic University of Malaysia, Pahang, Malaysia

## Address for correspondence:

Dr. Azizur Rahman,  
Department of Pharmacy Practice,  
International Islamic University of  
Malaysia, Kuantan Campus, 25200,  
Pahang, Malaysia.  
E-mail: aziznoor51@gmail.com

## ABSTRACT

**Objective:** Electronic cigarette (e-cig) is recently growing substitute for smoking. The attention and practice of e-cig among consumers is expanded globally, and Malaysia is not an exception to this, but the paucity of local data motivates us to do the current research.

**Methods:** A total of 220 e-cig vapers recruited for the study and divided into two categories based on smoking status as a single user and dual user. Both users observed for 1 month period to assess smoking cessation rate, adverse effects, withdrawal symptoms, and smoking-related diseases.

**Results:** A month follow-up showed still 28.44% ( $P \leq 0.001$ ) of the entire study population (62 of 218, intention to treat analysis) were abstained from tobacco smoking. However, a high number of single user shown more quit rate as compared to of dual users (72.9% [51] vs. 7.4% [11]; Odds ratio 33.43; 95% confidence interval: 0.102–3.410) and merely two persons (<1%) started e-cig by ever smokers. The key adverse effects and withdrawal symptoms that observed in dual users were coughing, breathing problems, and craving, whereas in single users high appetite cases documented; however, no cases of any diseases reported among both users during the whole study period.

**Conclusion:** A month follow-up showed a good smoking cessation rate among Malaysian vapers mainly in single users, whereas less number of quitters but the high reduction in tobacco cigarette consumption observed in dual users without any harmful effects. Furthermore, extended period studies are warranted to confirm its long-term safety and effectiveness among different Malaysian population.

**Key words:** Electronic cigarette, exhaled carbon monoxide, safety, smoking, vaping

## INTRODUCTION

An electronic cigarette (e-cig) is relatively newly emergent substitute for smoking. It is a battery powered device that available in various size and shapes but does not involve smoke, which enables users to inhale vaporized nicotine.<sup>[1]</sup> The main ingredients of e-cig liquids are with or without nicotine, propylene glycol,

glycerol, and some flavoring agents.<sup>[2,3]</sup> At present due to innovation of technology various categories of e-cig are available in the market such as 1<sup>st</sup> generations e-cig also called cigalike (means like conventional cigarette), 2<sup>nd</sup> generations (vape pens or e-go pens), and 3<sup>rd</sup> generations (also called advanced personal vaporizers [APVs] or modes). There is an upgrading

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from the 1<sup>st</sup> to 3<sup>rd</sup> generations, in features like enhanced in battery life, use of diverse atomizers with sufficient e-liquid filling capacities, innovative features such as variable voltage and/or variable wattage and temperature control. All these features for better vapor productions and to increase the number of puffs and to create vaping as pleasurable as smoking.<sup>[1]</sup>

Current research studies globally lack to expose the flawless effectiveness of e-cig as a smoking cessation aid. Some of the previously published studies suggest that e-cigs help smokers to quit or at least help in the reduction of tobacco smoking,<sup>[4-6]</sup> whereas the recent meta-analysis found that the use of e-cig does not reveal significant smoking quit rate among smokers.<sup>[7]</sup> Data from some countries suggested that e-cig use is doubled up from 2008 to 2014 in countries like North America, the European Union, and Republic of Korea and its use between smokers and ex-smoker is more compared to nonsmokers.<sup>[8-10]</sup> Consumer interest and practice of e-cig are growing rapidly all over the world and Malaysia is not an exception to this. As per Malaysian e-vaporizers and tobacco alternative association (MEVTA) currently in Malaysia there are 1 million e-cig users and vaping industry making some RM2 billion profits. MEVTA further claimed presently Malaysia is the second biggest market in the world after the US and have more than thousand vape shops and outlets that offering nearly four hundred local brands of e-liquid to consumers.<sup>[11]</sup> In view of this high consumption and further due to the paucity of local data toward e-cig use, encourage us to do the current research.

## METHODS

### Study design

The main objective of the study was to assess the safety and effectiveness of e-cig among Malaysian vapers (e-cig users) for the duration of 1 month. The inclusion criteria comprises of those vapers using e-cig alone or with tobacco cigarette (TCG) for last 1 month with the age of >18-65, possessing good health or agreed to sign consent form and commitment to follow the study procedure. Exclusion criteria were the participants who did used any anti-smoking drugs currently and for last 1 year like nicotine replacement therapy (NRT) or varenicline and with any history of drug dependence or alcohol use.

### Study questionnaire

An interview-administered questionnaire was developed after extensive reviewing previous studies

and consultation with expert academicians in related disciplines in English language.<sup>[6,12]</sup> Further questions related to safety and effectiveness of e-cig was added to cover study objective. In addition, a qualitative survey has done to discover attitude, behavior, and perception about Malaysian vapers toward e-cig so that to add any important missing questions connected with research title in study questionnaire.<sup>[13]</sup> The administered questionnaire consist of demographic characteristic of participants, reasons to initiate e-cig, questions related to evaluate effectiveness, and safety toward e-cig.

### Validity and reliability of instrument

The study questionnaire referred to three expert's academicians in the related field to discuss and judged the face and content validity of the final questionnaire. The questionnaire was revised several times until it is ready for pilot testing to evaluate the reliability of the questionnaire. Internal consistency reliability testing was conducted on 30 e-cig users and determines a Cronbach alpha value of 0.72 which reflect an acceptable reliability of the instrument. Further the reliability of this instrument was done by test-retest testing that conducted on twenty vapers of this subgroup after an interval of 2 weeks that revealed a satisfactory reading value of 0.730 with a Spearman's rank correlation coefficient ( $P < 0.05$ ) that specifies, there was no significant difference at two occasions and instrument is stable over time.

### Remodification of Fagerstrom Test for Nicotine Dependence and Glover-Nilsson Smoking Behavioral Questionnaire scales

The existing scales Fagerstrom Test for Nicotine Dependence (FTND) and Glover-Nilsson Smoking Behavioral Questionnaire (GNSBQ) determine the physical and behavioral dependence to smoking, respectively, but not for vaping, so we decided to re-modify these scales for physical and behavioral dependence to vaping, respectively.<sup>[14,15]</sup> Hence, we made slight changes and replaced some words from existing scale such as smoking with vaping and TCG with e-cig and renamed these scales as E-cig Modified FTND (ECG-MFTND) and E-cig Modified Glover-Nilsson Vaping Behavioral Questionnaire (ECG-MGNVBQ). The reliability testing for newly modified scales ECG-MFTND and ECG-MGNVBQ piloted on 30 e-cig users and determines Cronbach alpha values of 0.725 and 0.740, respectively, which reveal a satisfactory reliability of scales. Author permission has taken to use prevalidated scales (FTND and GNSBQ) and modified scales (ECG-MFTND and ECG-MGNVBQ) in our research.

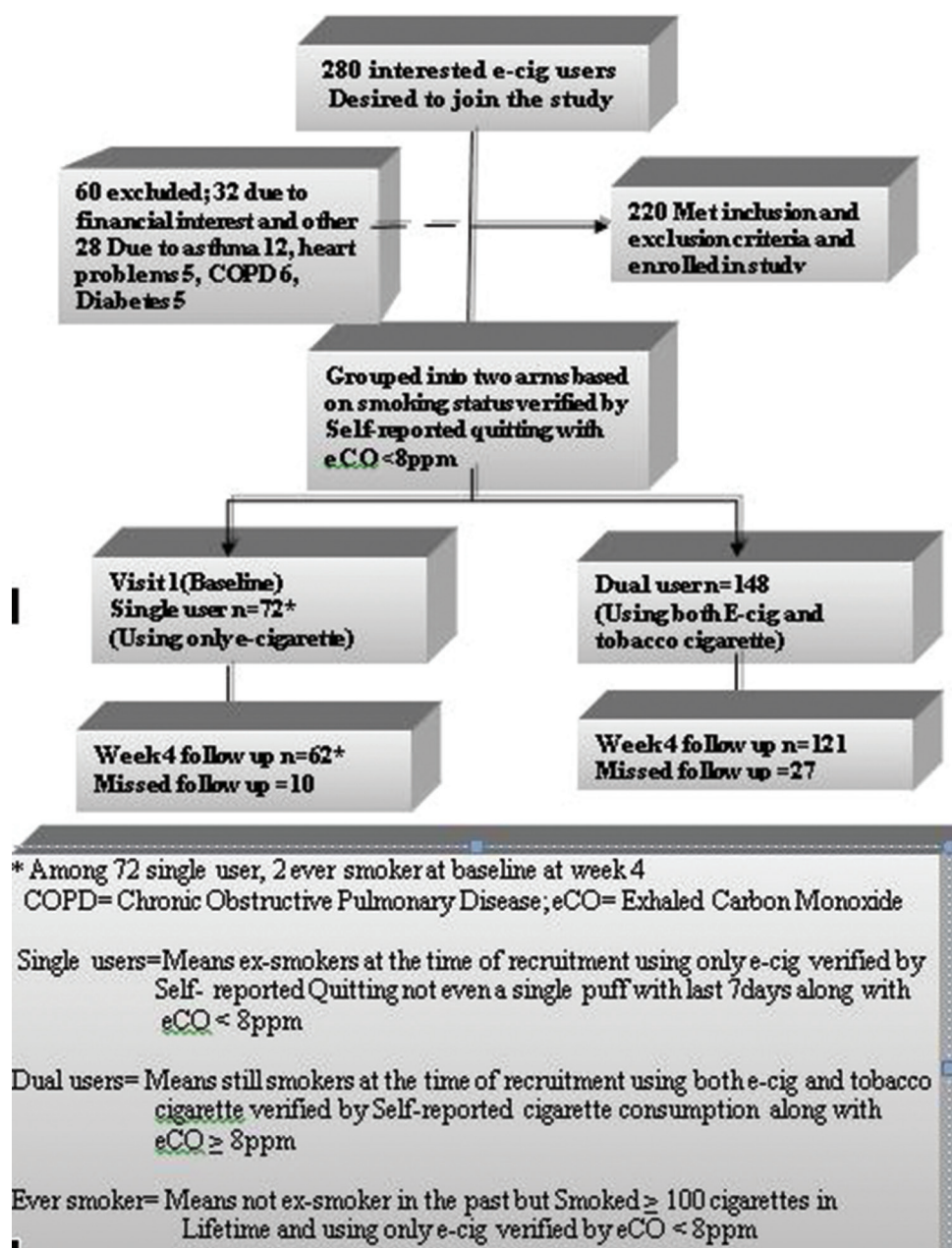
### Sample size

To observe 10% smoking abstinence rate in entire study population with 80% power, a sample of two hundred subjects were required for the study.<sup>[16,17]</sup> Moreover, some preceding trails on e-cig also designated comparable abstinence rate and sample size in their study populations.<sup>[4]</sup>

### Recruitment of participants

Participants enrolled in the study from Kuantan and Pekan Districts (Pahang state) of Malaysia from e-cig sales points and e-cigs vaping stations by contacting e-cig supplier. The basis of selection of the above-mentioned sites of Kuantan and Pekan signify the feasibility criteria

of research pertaining to constraint time and funding. It is justified more by the consideration of the availability of vapers in these cities. We informed subjects that there will be no incentives or encouragement to join the study; however, twenty ringgit will be given to each participant as a food and transportation expenses. Steps involved in the enrollment process were outline in Figure 1. Mostly, more than 90% of participants understand English questionnaire but for those participants who hard to understand English we used Bahasa Malay translator, who was fluent in both language English and Bahasa Malay by the same translator every time so that there should not be any bias and variability's in terms of reporting.



**Figure 1:** Flow chart displaying recruitment and follow-up of e-cig users



## Randomization

Baseline data were collected from February 2015 to May 2015 and follow-up data after 1 month in July. At baseline, participants divided into two groups or arms based on smoking status and named as dual user (users who use e-cig along with TCGs) and single user (users who use e-cig only) assessed by self-reported quitting from tobacco smoking not even a puff in last 7 days together with exhaled carbon monoxide (eCO) value of  $<8$  ppm, measured by PiCO + Smokerlyzer®. Then, sociodemographic details, smoking and e-cig history, and reasons to initiate e-cig have been evaluated. Participant's safety verified at baseline and after week 4 by reporting adverse events, withdrawal symptoms and for smoking related diseases that may appear due to e-cig use. The severity of adverse events, withdrawal symptoms, and smoking-related diseases at both visits were based on subjects own experience and not according to investigator observation, that means, no physical examination was done to assess the severity of these effects and diseases. The subjects called in a batch of 2 to 3 and interviewed independently for 25–30 min to protect any confidentiality issues and not to reveal their answers with other subjects thus making recruitment process unprejudiced.

## Ethics approval

The study conducted as per ethics and the principles concerning human subjects. Study questionnaire, protocols, participant's information sheet, consent forms, and study related flyer to recruit participants were approved by the Research Ethics Committee of Kulliyah of Medicine, International Islamic University of Malaysia Kuantan on October 9, 2014, IREC no. 302.

## Data management and statistical analysis

The e-cig users were divided into two groups or arms as per their smoking status, namely single users and dual users at the time of enrollment in the study. Categorical variables were summarized as frequencies and percentages, whereas continuous variables were calculated as median because medians are less sensitive to extreme values. Cross tabulation and Chi-square were used to compare categorical variables, whereas Mann-Whitney U-test was used to compare continuous variables between both the groups. Wilcoxon signed ranks was used to compare nonparametric data within same groups such as ECG-MFTND with FTND, ECG-MGNVBQ with GNSBQ and cigarette consumption before and after using e-cig at baseline and post week 4 for dual users. Statistical methods were two-tailed, and  $P < 0.05$  was

considered significant. The analysis was performed by using Statistical Package for Social Sciences (IBM, SPSS Inc., Chicago, USA) for Windows version 21.

## RESULTS

At baseline, a total of 220 participants joined the study where 148 documented as dual users while 70 reported as single users and merely 2 (0.9  $<1\%$ ) participants reported as ever a smoker. A month follow-up shown still 28.44% subjects among both users (62 of 218, excluding 2 ever user) refrain from tobacco smoking; however, more number of single user 72.9% (51) was abstain from tobacco smoking as compared to 7.4% (11) of dual users (odds ratio [OR] 33.43; 95% confidence interval [95% CI]: 0.102–3.410). Moreover, single user was experienced less adverse effects and withdrawal symptoms as related to dual users at baseline visit 1 and post week 4.

### Baseline characteristic of participants

Table 1 displays baseline characteristic of each group. In both groups, the median age of participants was 23 years ( $P = 0.946$ ) and almost nearly 98% were male in both groups compare to female (1.4%;  $P = 1.000$ ). Marital status shows a significant difference between both groups ( $P = 0.041$ ), while more than 80% participants were single at the time of survey. There was no difference in race among dual and single users ( $P = 0.632$ ); however, 86% subjects were Malay as compare to Chinese (11.9%) and Indians (1.8%). Nearly 73% of both users reported either they were studying or holding diploma or degree ( $P = 0.902$ ). Occupation and income wise there was no statistical difference between both the groups, respectively, ( $P = 0.535$  and  $P = 0.468$ ). The physical and behavioral dependence to vaping measured for both groups by re-modified scales via ECG-MFTND and ECG-MGNVBQ, respectively, exhibited no statistical significant difference ( $P = 0.668$  and  $P = 0.625$ ), however, for dual users group comparison of physical and behavioral dependence to smoking assessed by FTND and GNSBQ, respectively, with physical and behavioral dependence to vaping that were measured by ECG-MFTND and ECG-MGNVBQ, respectively, showed a statistical significant difference ( $P \leq 0.001$  and  $P = 0.003$ ) indicates that dual user group at the time of survey they were more physical and behaviorally dependent to vaping rather than smoking.

### Smoking history and electronic-cigarette status

Table 2 displays smoking and current status of e-cig between both users. In both the groups, nearly 95%

**Table 1: Baseline characteristics of participants**

Characteristics	Dual users (n=148)	Single user (n=70)	Total participants (n=218)	Statistic	P (two-tailed)
Age	23 (19-40)	23 (19-39)	23 (19-40)	U=5150.500	0.946*
Gender					
Male	145 (98)	69 (98.6)	214 (98.2)	-	1.0**
Female	3 (2)	1 (1.4)	4 (1.8)		
Marital status					
Married	22 (14.9)	19 (27.1)	41 (18.8)	-	0.041**
Single	126 (85.1)	51 (72.9)	177 (81.2)		
Race					
Malay	127 (85.8)	61 (87.1)	188 (86.2)	$\chi^2=0.918$	0.632
Chinese	19 (12.8)	7 (10)	26 (11.9)		
Indian	2 (1.4)	2 (2.9)	4 (1.8)		
Education					
Primary	-	-	-	$\chi^2=0.015$	0.902
Secondary	39 (26.4)	19 (27.1)	58 (26.6)		
Diploma/degree	109 (73.6)	51 (72.9)	160 (73.4)		
Occupation					
Private	70 (47.3)	38 (54.3)	108 (49.5)	$\chi^2=2.186$	0.535
Government	13 (8.8)	6 (8.6)	19 (8.7)		
Self-employment	15 (10.1)	9 (12.9)	24 (11)		
Student	50 (33.8)	17 (24.3)	67 (30.7)		
Income					
00 <sup>§</sup>	50 (33.8)	17 (24.3)	67 (30.7)	$\chi^2=2.541$	0.468
<2500 MYR <sup>#</sup>	2 (1.4)	2 (2.9)	4 (1.8)		
≥2500-5000 MYR	89 (60.1)	48 (68.6)	137 (62.8)		
>5000 MYR	7 (4.7)	3 (4.3)	10 (4.6)		
ECG-MFTND vaping	3 (1-7)	3 (1-7)	3 (1-7)	U=5000.000	0.668
FTND (dual user)	0 (0-9)			Z=-6.056	<0.001
ECG-MGNVBQ (vaping)	14 (3-22)	13 (3-24)	14 (3-24)	U=4972.500	0.625
GNSBQ (dual user)	10 (2-27)			Z=-3.006	0.003

For dual user physical and behavioral dependence to smoking were measured by FTND and GNSBQ, respectively, and compared with physical and behavioral dependence to vaping that were measured by re-modified scales ECG-MFTND and ECG-MGNVBQ, respectively, and *P* calculated by Wilcoxon signed rank test. \*Nonparametric data expressed as median and *P* calculated by Mann-Whitney U-test, \*\*Fischer exact test, <sup>§</sup>00=Student group, <sup>#</sup>MYR=Malaysian Ringgit, ECG-MFTND=E-cig Modified Fagerström test for Nicotine Dependence, FTND=Fagerström Test for Nicotine Dependence, ECG-MGNVBQ=E-cig Modified Glover-Nilsson Vaping Behavioral Questionnaire, GNSBQ=Glover-Nilsson Smoking Behavioral Questionnaire, e-cig=Electronic cigarette

of the participants never tried any therapy before to quit smoking while <5% used NRT (NRT, *P* = 0.585). The median starting age of smoking among both users was 15 (*P* = 0.125), whereas median pack/year of TCG was 7 in dual user compare to 5 for single user but not statistically significant (*P* = 0.114). The median e-cig use of single users was 8 months as compared to 4 months of the dual user, respectively, and it was statistical significant (*P* ≤ 0.001). More than 98% of both participants were using of e-cig on a daily basis, and merely 1.4% were occasional users (*P* = 1.000). Among both the groups mods or APVs type e-cigs were most broadly used (>95%) and <5% using e-go batteries type models (*P* = 1.000).

### E-liquid, nicotine, and puff intake during baseline visit 1 and at post week 4 visit 2

There was no statistical significant difference at both visits among both the users for consumptions of e-liquid (ml) per day, bottles per month, average puff

per day, and average puff to satisfy craving per day except high nicotine intake shown for dual users at after week 4 visit 2 compare to single user and it was statistically significant (V1 *P* = 0.407; V2 *P* = 0.034) [Table 3].

### Reasons to initiate electronic-cigarette use

Figure 2 exhibited the reasons to initiate e-cig use among both users. More than 90% participants in both groups started e-cig to quit smoking (*P* = 0.959), the second reason was to enjoy more flavors (27.5%, *P* = 0.747). The other important reasons, even though that was not statistical significant but reasons to start e-cig by both the groups were e-cig cheaper than tobacco smoking (24.3%, *P* = 0.870), due to health problems (18.3%, *P* = 0.515), family and friends advice to quit smoking (16.1%, *P* = 0.702), healthier alternative to smoking (10.1%, *P* = 0.633), and due to bad smell of TCG (7.8%, *P* = 0.825). Some statistical significant number of participants from single users

**Table 2: Smoking and electronic cigarette status**

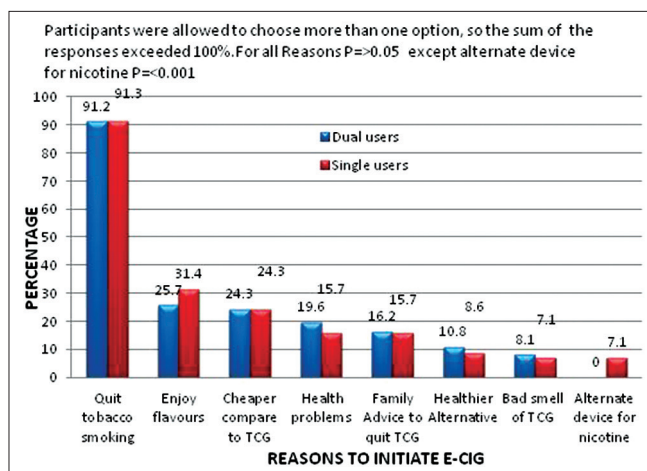
Characteristics	Dual users (n=148)	Single user (n=70)	Total participants (n=218)	Statistic	P (two-tailed)
Previous if any quit attempts in the past year?	0 (0-1)	0 (0-1)	0 (0-1)	$U=5094.000$	0.585**
Any therapy to quit smoking before					
Never attempted	142 (95.9)	66 (94.3)	208 (95.4)	-	0.730***
NRT*	6 (4.1)	4 (5.7)	10 (4.6)		
Smoking start age	15 (12-27)	16 (12-22)	15 (12-27)	$U=4521.000$	0.125**
Pack/year	7 (0.5-50)	4.75 (0.25-30)	6 (0.25-50)	$U=4494.500$	0.114**
E-cig use (months)	4 (2-24)	8 (6-24)	5 (2-24)	$U=1453.00$	<0.001
E-cig consumption					
Daily	145 (98)	69 (98.6)	214 (98.2)	-	1.000***
Occasionally	3 (2)	1 (1.4)	4 (1.8)		
E-cig shape					
2 <sup>nd</sup> generation (ego type)	6 (4.1)	3 (4.3)	9 (4.1)	-	1.000***
3 <sup>rd</sup> generations (mods)	142 (95.9)	67 (95.7)	209 (95.9)		
E-cig purchase					
Electronic shop	2 (1.4)	-	2 (0.9)	$\chi^2=1.757$	0.415
On internet	35 (23.6)	13 (18.6)	48 (22)		
E-cig shop	111 (75)	57 (81.4)	168 (77.1)		
E-cig liquid use					
Ready to use e-liquids	130 (87.8)	63 (90)	193 (88.5)	$\chi^2=0.219$	0.640
Do it yourself	18 (12.2)	7 (10)	25 (11.5)		

\*NRT=Nicotine replacement therapy, \*\*Nonparametric data expressed as median and *P* calculated by Mann-Whitney U-test, \*\*\*Fischer exact test, e-cig=Electronic cigarette

**Table 3: E-liquid, nicotine, and puff intake during baseline visit 1 and at post week 4 visit 2**

Visits	E-cig characteristics	Dual users (n=148)	Single user (n=70)	Total (n=218)	Statistic	P (two-tailed)
Baseline	E-liquid used per day (ml)	3 (1-8)	3 (2-6)	3 (1-8)	$U=4822.500$	0.380**
visit 1	E-liquid bottle per month (30 ml)	3 (1-8)	3 (2-6)	3 (1-8)	$U=4822.500$	0.380**
	Nicotine level in e-cig (mg/ml)	6 (6-24)	6 (6-12)	6 (6-24)	$U=4942.00$	0.407**
	Average puff per day on e-cig	200 (100-300)	200 (100-350)	200 (100-350)	$U=5128.500$	0.896**
	Average puff to satisfy craving/day	150 (100-250)	150 (100-250)	150 (100-250)	$U=4613.500$	0.113**
		Dual users (n=121)	Single user (n=60)	Total (n=181)		
At post week	E-liquid used per day (ml)	3 (2-6)	3 (2-5)	3 (2-6)	$U=3586.000$	0.876**
4 visit 2	E-liquid bottle per month (30 ml)	3 (2-6)	3 (2-5)	3 (2-6)	$U=3616.000$	0.960**
	Nicotine level in e-cig (mg/ml)	6 (6-24)	6 (3-12)	6 (3-24)	$U=3231.000$	0.034**
	Average puff per day one-cig	200 (150-300)	200 (150-300)	200 (150-300)	$U=3435.500$	0.502**
	Average puff to satisfy craving/day	150 (100-250)	150 (100-250)	150 (100-250)	$U=3489.500$	0.619**

\*\*Nonparametric data expressed as median and *P* calculated by Mann-Whitney U-test. e-cig=Electronic cigarette

**Figure 2: Reasons to initiate e-cig use**

group (7.1%,  $P = 0.001$ ) reported, they initiated e-cig to take nicotine in an alternate form.

### Measure of effectiveness

Table 4 displays the e-cig effectiveness to control smoking in both groups. The median usage of TCGs among both groups before starting e-cig was 20/day ( $P = 0.05$ ). While intake of TCG for dual users at baseline visit 1 and at week 4 was median of 5/day but in different ranges. There was statistically significant reduction in consumption of TCG before and after using e-cig at both the visits for dual users' ( $P \leq 0.001$ ) measured by Wilcoxon test. At visit 2, 181 subjects followed up, 121 dual users, and 60 single users. Among single users, nine

**Table 4: Measure of effectiveness**

TCG and eCO at baseline visit 1					
Characteristics	Dual users (n=148)	Single user (n=70)	Total participants (n=218)	Statistic	P (two-tailed)
TCG/day before using e-cig	20 (10-60)	20 (5-40)	10 (5-60)	$U=4412.000$	0.055
TCG/day before using e-cig versus TCG/day consumption at baseline visit 1 (for dual users)	5 (1-30)	-		$Z=-9.281$	<0.001
eCO	8 (1-59)	3 (1-6)	5 (1-59)	$U=1577.500$	<0.001
TCG and eCO at post week 4 visit 2					
Characteristics	Dual users (n=121)	Single user (n=60)	Total participants (n=181)	Statistic	P (two-tailed)
TCG/day consumption at baseline visit 1 versus TCG/day at week 4 (for dual user) TCG/day at post week 4	5 (1-30)	-	-	$Z=-5.190$	<0.001
eCO	5 (0-20)	0 (0-5)	5 (0-20)	$U=684.00$	<0.001
At post week 4	6 (2-20)	2 (1-7)	5 (1-20)	$U=1346.50$	<0.001
Measure of effectiveness (7 days point prevalence abstinence rate at post week 4, ITT analysis)					
At week 4 post e-cig use	7 days point prevalence abstinence rate at week 4 n (%)		OR (95% CI)		P (two-tailed)
Both users (n=218)	62 (28.44% of 218)		-		<0.001
Single user (n=70)	51 (72.9% of 70)		33.43 (0.102-3.410)		<0.001
Dual user (n=148)	11 (7.4% of 148)				

\*For dual user, Wilcoxon signed rank test was applied for comparing TCG/day, consumption before using e-cig versus baseline visit 1 and baseline versus at post week 4 visit 2. At post week 4, 181 subjects followed up 121 dual users and 60 single users. Among total 151 subjects followed up face to face and smoking status were confirmed by measuring eCO, whereas for remaining 31 subjects self-reported smoking status confirmed by calling telephone without any eCO validation. Anyhow all 31 subjects considered dual user. 7 days point prevalence abstinence rate calculated based on ITT analysis n=218. 2 ever smokers not included in analysis. ITT=Intention to treat, TCG=Tobacco cigarette, eCO=Exhaled carbon monoxide, CI=Confidence interval, OR=Odds ratio, e-cig=Electronic cigarette

relapsed to smoking and comparison with dual users for TCG per day consumption at week 4 indicates that still single users tobacco consumption per day was far behind compared to dual users ( $P < 0.001$ ). The median level of eCO at visits 1 and 2 for dual users was 8 and 6 ppm whereas for single users it was 3 and 2 ppm correspondingly, designated statistical significant outcomes at both stages (<0.001). A month follow-up revealed 28.44% subjects among both users (62 of 218, intention to treat analysis, excluding 2 ever user) refrain from tobacco smoking, however, 72.9% (51) of the single user were abstained from tobacco smoking as compared to 7.4% (11) of dual users (OR 33.43; 95% CI: 0.102-3.410).

## Measure of safety

### Measure of adverse effects

Table 5 explains the adverse effects experienced by all users at both the appointments. The strongest adverse effect experienced by more than 60% of the participants in both the group at two stages was dry mouth (V1  $P = 0.692$ ; V2  $P = 0.192$ ). The other visible adverse effects but not statistically significant were sore throat (V1  $P = 0.242$ ; V2  $P = 0.608$ ), anxiety (V1  $P = 0.321$ ; V2  $P = 0.321$ ), and stomach disturbances (V1  $P = 0.320$ ; V2  $P = 0.058$ ). The noticeable statistical significant adverse effects shown in dual users at both phases were cough (V1  $P \leq 0.001$ ; V2  $P = 0.019$ ) and breathing problem (V1  $P = 0.020$ ; V2  $P = 0.028$ )

compared to single users. In addition, more headache cases observed in dual users during visit 2 as compare to visit 1 (V1  $P = 0.938$ ; V2  $P = 0.028$ ). Whereas, vomiting (V1  $P = 0.035$ ; V2  $P = 0.123$ ) and fever (V1  $P = 0.040$ ; V2 = 0) cases were significant in single users during visit 1 but not in visit 2. At both the stages, for dual user's more adverse effects partially disappear overtime as compare to the single user (V1, V2 =  $P \leq 0.001$ ).

### Measure of withdrawal symptoms

The most commonly appeared withdrawal symptoms shown high in dual users as compared to the single user at two visits were craving for smoking (V1, V2 =  $P \leq 0.001$ ). Whereas, increase high appetite cases reported more by single users as corresponding to dual users (V1  $P = 0.013$ ; V2  $P \leq 0.001$ ). The other nonstatistically significant withdrawal symptoms recorded in both groups were depression (V1  $P = 0.553$ ; V2  $P = 0.826$ ), difficulty in concentration (V1 = no cases; V2  $P = 0.054$ ), bad temper (V1  $P = 0.321$ ; V2 = no cases), sleeplessness (V1  $P = 0.321$ ; V2  $P = 0.481$ ), sleepiness (V1  $P = 0.645$ ; V2  $P = 0.136$ ), frustration (V1  $P = 0.972$ ; V2  $P = 0.592$ ), anger (V1  $P = 0.660$ ; V2  $P = 0.318$ ), and awakening at night (V1  $P = 0.321$ ; V2  $P = 0.331$ ) [Table 6]. Completely disappearance of withdrawal symptoms shown greater in single user as compared to dual users at both stages V1  $P \leq 0.001$ ; V2  $P = 0.045$ . Both users also reported accidents



**Table 5: Adverse events experienced by both groups at baseline visit 1 and post week 4 visit 2**

Adverse events	Adverse events experienced at baseline visit 1				Adverse events experienced at week 4 visit 2		
	Groups	Total n (%)	Statistic $\chi^2$	P (two-tailed)	Total n (%)	Statistic $\chi^2$	P (two-tailed)
Dry mouth	Dual user	93 (62.8)	2.239	0.692	76 (62.8)	1.705	0.192
	Single user	46 (65.7)			42 (70)		
Sore throat	Dual user	32 (21.6)	4.183	0.242	10 (8.3)	0.263	0.608
	Single user	9 (12.9)			7 (11.7)		
Cough	Dual user	53 (35.8)	25.294	<0.001	33 (27.3)	5.506	0.019
	Single user	03 (4.3)			6 (10)		
Anxiety	Dual user	0 (0)	-	0.321*	8 (6.6)	0.986	0.321
	Single user	1 (1.4)			2 (3.3)		
Stomach disturbances	Dual user	2 (1.4)	0.950	0.320	1 (0.8)	3.589	0.058
	Single user	0 (0)			3 (5)		
Nausea	Dual user	-	-	-	2 (1.7)	2.32	0.127
	Single user	-			3 (5)		
Vomiting	Dual user	0 (0)	8.615	0.035	3 (3.3)	2.382	0.123
	Single user	4 (5.7)			4 (8.3)		
Headache	Dual user	14 (9.5)	0.128	0.938	15 (12.4)	4.820	0.028
	Single user	6 (9.2)			2 (3.5)		
Breathing problem	Dual user	27 (18.8)	9.867	0.020	15 (12.4)	4.80	0.028
	Single user	2 (2.8)			2 (3.5)		
Other (fever)	Dual user	0 (0)	6.431	0.040	-	-	-
	Single user	3 (4.3)			-		
	<b>Dual user</b>		<b>Single user</b>	<b>Total n (%)</b>	<b>Statistic <math>\chi^2</math></b>	<b>P (two-tailed)</b>	
Did the side effects disappear overtime at baseline visit 1?							
Not appear		3 (2)	6 (8.6)	9 (4.1)	18.931	<0.001	
Completely disappear		48 (32.4)	39 (55.7)	87 (39.9)			
Partially disappear		97 (65.5)	25 (35.7)	122 (56)			
Not disappear		-	-	-			
Did the side effects disappear overtime at week 4 visit 2?							
Not appear		2 (1.7)	9 (15)	11 (6.1)	21.149	<0.001	
Completely disappear		47 (38.8)	33 (55)	80 (44.2)			
Partially disappear		72 (59.5)	18 (30)	90 (49.7)			
Not disappear		-	-	-			

\*Fischer exact test. Scale: 4=Severe, 3=Moderate, 2=Mild, 1=Slight, 0=Absent

and technical problems connected with e-cigs use. Users from both groups informed no bad incidents occurred with the e-cigs use; however, some fewer than 6% subjects' stated liquid leak out technical problem happened with them. Higher number of dual users' participants informed they plan to use e-cig for  $\geq 2$  years (77 vs. 62.9) compare to single users, however, for  $>1$  year reported it is vice versa (34.3 vs. 23). The results were statistically significant ( $P = 0.013$ ) [Table 6].

#### Measure of diseases

Measure of the safety, furthermore done through by observing for diseases that mostly caused by smoking like chronic obstructive pulmonary diseases, asthma, any heart disease, stroke, hypertension, diabetes, thyroid disease, cataract, or any other. At baseline visit, we recruited only healthy subjects and any participants reporting of above mention conditions

excluded from the study. No cases of any diseases recognized among both users during the whole study period.

## DISCUSSION

This was the first observational study about e-cig which was not previously reported on Malaysian vapers with satisfactory number of participants. After 1 month follow-up more than quarter of the total study population abstain from tobacco smoking; however, the smoking quit rate detected high among single users as compared to dual users (OR 33.43; 95% CI: 0.102–3.410) and merely two persons (<1%) started e-cig by ever smokers. The other studies also reported the lone regular e-cig use for 1 month not along with TCG shown a significant quit rate as compared to dual use.<sup>[9,13]</sup> However, the smoking quit rate in our study found high as compared to other clinical trials.<sup>[4,5]</sup> The



**Table 6: Withdrawal symptoms experienced by both groups at baseline visit 1 and post week 4 visit 2**

Withdrawal symptoms	Groups	Withdrawal symptoms experienced at baseline visit 1			Withdrawal symptoms experienced at post week 4 visit 2		
		Total n (%)	Statistic $\chi^2$	P (two-tailed)	Total n (%)	Statistic $\chi^2$	P (two-tailed)
Craving for smoking	Dual user	139 (93.9)	101.601	<0.001	76 (62.8)	33.601	<0.001
	Single user	22 (31.4)			8 (13.3)		
Depression	Dual user	3 (2)	-	0.553*	1 (0.8)	0.048	0.826
	Single user	0 (0)			1 (1.7)		
Increase appetite	Dual user	9 (6.1)	6.144	0.013	7 (5.8)	33.090	<0.001
	Single user	11 (15.7)			19 (31.7)		
Difficulty in concentration	Dual user	-	-	-	4 (6.6)	3.698	0.054
	Single user	-			0 (0)		
Bad temper	Dual user	0 (0)	-	0.321*	-	-	-
	Single user	1 (1.4)			-		
Sleeplessness (insomnia)	Dual user	0 (0)	-	0.321*	1 (0.8)	0.496	0.481
	Single user	1 (1.4)			0 (0)		
Sleepiness	Dual user	11 (7.4)	0.213	0.645	8 (6.6)	2.227	0.136
	Single user	10 (14.3)			1 (1.7)		
Frustration	Dual user	1 (.7)	0.001	0.972	3 (2.5)	0.283	0.595
	Single user	1 (1.4)			1 (1.7)		
Anger	Dual user	3 (2)	0.194	0.660	2 (1.7)	0.997	0.318
	Single user	2 (2.9)			0 (0)		
Awakening at night	Dual user	0 (0)	-	0.321*	0 (0)	2.017	0.331*
	Single user	1 (1.4)			1 (1.7)		
		Dual user	Single user	Total n (%)	Statistic $\chi^2$	P (two-tailed)	
Did the withdrawal symptoms disappear overtime at baseline visit 1?							
Not appear		1 (0.7)	23 (32.9)	24 (11)	174.35	<0.001	
Completely disappear		2 (1.4)	40 (57.1)	42 (19.3)			
Partially disappear		134 (90.5)	7 (10)	141 (64.7)			
Not disappear		11 (7.4)	-	11 (5)			
Did the withdrawal symptoms disappear overtime at week 4 visit 2?							
Not appear		39 (32.2)	30 (50)	69 (38.1)	4.007	0.045	
Completely disappear		37 (30.6)	14 (23.3)	51 (28.2)			
Partially disappear		44 (36.4)	15 (25)	59 (32.6)			
Not disappear		1 (0.8)	1 (1.7)	2 (1.1)			
Have faced any technical problem with e-cig?							
No		143 (96.6)	63 (90)	206 (94.5)	-	0.058*	
Liquid leaked out		5 (3.4)	7 (10)	12 (5.5)			
Have faced any bad incidents with e-cig?							
No		148 (100)	70 (100)	218 (100)	-	-	
How long do you plan to use e-cig?							
<1 year		0 (0)	2 (2.9)	2 (0.9)	6.181	0.013	
>1 year		34 (23)	24 (34.3)	58 (26.6)			
≥2 year		114 (77)	44 (62.9)	158 (72.5)			

\*Fischer exact test. Scale: 4=Severe, 3=Moderate, 2=Mild, 1=Slight, 0=Absent. e-cig=Electronic cigarette

reason for this may be in such type of observational studies the participants who perceived favorable effects from e-cig inspired to join more as compare to those who confronted undesirable effects from vaping. Therefore, the results should be explained with care and cannot be generalized to other population.

The prime important reason to initiate e-cig among both the group participants was to quit smoking. Majority of the participants thought that e-cig is a better option to

quit smoking or at least to reduce consumption of TCGs. Earlier studies also revealed e-cigs helped smokers to abstain from smoking and reduction in intake of TCGs,<sup>[4-6]</sup> although existing proofs are far away to ascertain flawless efficiency of e-cigs in smoking termination compare to other conventional Food and Drug Administration approved therapies.<sup>[4,5]</sup> At present, it is a challenging issue for researchers, so more research is needed to conclusively establish the status of e-cig as a smoking cessation agent compared to other conventional therapies.

A significant majority of single users indicated that they began e-cig as an alternative device to take nicotine. Moreover, all the participants in our survey used nicotine. This specifies that nicotine plays a vital role in the success of e-cig as smoking aid.<sup>[18,19]</sup> The former studies done on other population also denoted similar results.<sup>[19-21]</sup> A more than quarter of our survey population (majority of diploma and graduate student) reported that they initiated e-cig to quit the smoking with the pleasant way by enjoying different flavors of e-liquids, although they were all smokers before starting e-cig. Some of the previous studies reported that due to these features of e-cigs, more adults usually teenagers and nonsmokers inclined toward vaping.<sup>[22,23]</sup> Nevertheless, the above factors focused toward a misleading image of e-cigs in smoking cessation control. Hence, there is a probability that vaping may promote nicotine addiction, especially among youths due to various flavors and could renormalize smoking habit for ex-smokers and interrupt smoker's passion to quit smoking. Advance research is needed to discover indisputably, about the attractiveness of nicotine and without nicotine. E-cig between smokers and ex-smokers and regulatory laws should be implemented on its use so that it should not be misused by nonsmokers and adolescents.

Nearly 2/3<sup>rd</sup> of subjects experienced at least one side effect at both stages among both users. The strongest adverse effect experienced in both the group was dry mouth, followed by sore throat, anxiety, nausea, stomach disturbances, whereas the highest noticeable withdrawal symptom among both groups was craving for smoking but chiefly noted in dual users. The above side effects confronted by our subjects reported by some previous studies as well.<sup>[4-6,24,25]</sup> The appearance of adverse effects and withdrawal symptoms detected less in single users and disappeared overtime more swiftly compared to dual users at both times. This could be the reasons for more smokers to transferring to vaping as e-cig managed well the withdrawal symptoms appeared due to smoking<sup>[24,25]</sup> except increased appetite symptoms that leads to weight gain problem. Hence, further studies are warranted in different population for a long period to testify that will the appearance of more appetite cases and the disappearance of withdrawal symptoms is either temporary or permanent, as most of the smokers relapse to smoking and only 3-6% abstinent from smoking after a period of 6 months due to withdrawal symptoms related problems.<sup>[26]</sup>

In our study, merely two participants (<1%) reported they were ever smoker before initiation of e-cig. They might start vaping as a curiosity to experience this and to enjoy flavors. Earlier studies also reported a minor population of nonsmoker group also practicing vaping.<sup>[6]</sup> As mentioned before, constant inspection and controlling laws should be applied so that it should not be misused by nonsmokers and youngsters.

### Limitations of study

There were some limitations of our study because our study population was mostly middle-aged Malay males with less number of Chinese and Indians from Kuantan and Pekan districts of Malaysia with short 1 month period. Thus, findings may not be generalized to other population of e-cig users and moreover in such studies subjects were recruited from those who were inspired and enthusiastically to quit smoking, which limit the generalization. But still our observational study shows a real understanding, benefits, and undesirable effects among Malaysian vapers in short time period. Moreover, in this study we used two re-modified scales via ECG-MFTND and ECG-MGNVBQ that evaluate and indicate the physical and behavioral dependence to vaping, respectively, that never done before on vapers' community.

## CONCLUSION

A month followed up shown good smoking cessation rate among Malaysian vapers with mostly in single users, whereas less number of quitters but substantial reduction in TCG consumption observed in dual users. The major adverse effects and withdrawal symptoms that mainly observed in dual users were coughing, breathing problems, and craving, whereas in single users, high appetite cases documented, however, no cases of any diseases reported among both users during whole study period. Moreover, single user was experienced less adverse effects and withdrawal symptoms as compare to dual users. Nevertheless, further more conventional and extended period studies are warranted to confirm its long-term safety and effectiveness among different Malaysian population.

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## Conflicts of interest

There are no conflicts of interest.

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