EXHALED CARBON MONOXIDE LEVELS AMONG TOBACCO SMOKERS BY AGE

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Abstract. Measurement of exhaled carbon monoxide (ECO) has been used to confirm self-reported tobacco smoking. There is little data regarding ECO levels among Thai tobacco smokers by age. The objectives of this study were to determine ECO cutoff level to confirm tobacco smoking and to assess whether the cutoff level varies by age. During 2009 we evaluated 875 Thai volunteers aged 16-70 years, residing in Pathum Thani (central Thailand) and Khon Kaen (northeastern Thailand). Among the 875 volunteers, there were 584 non-smokers and 291 smokers. Each subject was interviewed and had their ECO level measured. The mean ECO level was 11.24 ppm among smokers and 2.25 ppm among non-smokers. The best ECO cutoff level to distinguish 291smokers from 584 non-smokers was 5 ppm (sensitivity 79.0%, specificity 89.9%).The optimal ECO cutoff level varied by age-group. For subjects aged 16-25 years, the best ECO cutoff level was 4 ppm (sensitivity 85.2%, specificity 77.5%) and for subject aged 26-70 years, the best ECO cutoff level was 5 ppm (sensitivity 79.4%, specificity 91.2%).These levels by age should be used among Thai subjects to determine smoking.

Keywords: exhaled carbon monoxide, cutoff level, tobacco smokers

INTRODUCTION

Measurement of exhaled carbon monoxide (ECO) levels can be used to determine smoking status; it is non-invasive, relatively inexpensive and portable (Jarvis *et al*, 1986; Irving *et al*, 1988). The ECO level has a good correlation with self-reported smoking (Brügger *et al*, 2014) and has been used in smoking control programs (Jarvis *et al*, 1986; 1987; Irving *et al*, 1988; Hung *et al*, 2006; Sejourne *et al*, 2010; Frei *et al*, 2012; Guan and Ann, 2012; Brügger *et al*, 2014). The ECO level is an accurate method for assessing current smoking in spite of high air pollution levels (Shafiq *et al*, 2008). ECO may be potentially useful as a non-invasive biomarker of airway inflammation and oxidative stress among non-smoking asthmatics (Zhang *et al*, 2010) and an early marker of acute exacerbation of chronic lung diseases (Abd *et al*, 2012). ECO may also be used to determine exposure to second hand smoke (Kumar *et al*, 2011), and as an indicator of indoor smoking (Gourgoulianis *et al*, 2002).

A number of studies have suggested different ECO cutoff levels for confirming self-reported smoking (Wald *et al*, 1981; Jarvis *et al*, 1987; Nakayama *et al*, 1998;

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Middleton and Morice, 2000; Jagoe *et al*, 2002; Deveci *et al*, 2004; Low *et al*, 2004; Christensen *et al*, 2004; Hung *et al*, 2006). ECO levels among Thai smokers have rarely been reported (Chatrchaiwiwatana and Ratanasiri, 2008). Studies have found different ECO cutoff levels among different populations (Pearce *et al*, 2005; Chatrchaiwiwatana and Ratanasiri, 2008) but this has rarely been studied among Thais. We had two objectives for this study: determine the ECO cutoff level to detect smoking among Thais and whether age affects that cutoff level among Thais.

MATERIALS AND METHODS

Study population

Eight hundred seventy-five people, aged 16-70 years, residing in sub-urban area of Pathum Thani (central) and Khon Kaen (northeastern), Thailand during the year 2009, volunteered to participate. Volunteers who were not able to speak or understand Thai and had respiratory diseases or systemic diseases of any kind were excluded from the study. Altogether 591 males and 284 females; 291 smokers and 584 non-smokers participated in the study. A smoker was defined as a person who had smoked at least one cigarette a day for a minimum of one year.

The required sample size was calculated based on the difference between mean (SD) of ECO among non-smokers (2.25±2.39 ppm) and the mean (SD) of ECO among smokers (11.24±8.72 ppm), with the alpha error 5% (2-tailed test). Based on the given sample size of 875 volunteers, the statistical power of the study was higher than 95%.

After obtaining informed consent from the subjects, they were each asked about their background characteristics, lifestyles and health habits, such as tobacco smoking and alcohol use. Then the ECO level was measured in each subject using a portable Micro CO Meter (Micro Medical, Kent, England).

The research protocol was approved by the Ethics Committee for Human Research at Khon Kaen University, Khon Kaen, Thailand (HE591188).

Exhaled carbon monoxide measurement

An ECO level was measured in each participant using a Micro CO Meter (Micro Medical, Chatham, Kent, England). ECO measurement was done in an open-air environment. The participants were asked to exhale completely, inhale fully, and then hold their breath for 15 seconds before exhaling rapidly into the disposable mouthpiece of the Micro CO Meter. Ambient CO levels were recorded before each breath. Ambient CO concentrations during the measurement were 0-2 ppm. The breath-hold should have been sufficient for equilibrium to take place. Since all participants held their breath for 15 seconds, the impact of ambient air CO on the test result was not expected (Deveci *et al*, 2004).

Statistical analysis

The data management and analysis were done using SPSS for Windows, version 15.0 (SPSS, Chicago, IL). Descriptive statistics, validity, bivariate and multivariable logistic regression analyses were calculated. The ROC curve, sensitivity, specificity, positive and negative predictive values, positive likelihood ratio (LR+), negative likelihood ratio (LR-), and odds ratio (OR) were calculated to assess validity of the ECO for predicting smoking status among all participants and by age-group. Bivariate analysis was conducted using nonparametric statistics. The Mann-Whitney *U* test was used to analyze the associations between

Table 1
Definition of terms used in the study.

1. ROC Curve = Reciever Operating Characteristic Curve.
2. CO3 = Exhaled carbon monoxide cutoff at 3 ppm.
3. CO4 = Exhaled carbon monoxide cutoff at 4 ppm.
4. CO5 = Exhaled carbon monoxide cutoff at 5 ppm.
5. CO6 = Exhaled carbon monoxide cutoff at 6 ppm.
6. CO7 = Exhaled carbon monoxide cutoff at 7 ppm.
7. CO8 = Exhaled carbon monoxide cutoff at 8 ppm.
8. CO9 = Exhaled carbon monoxide cutoff at 9 ppm.

Table 2
Validity of ECO cutoff levels for participants overall (n=875).

Test	CO3	CO4	CO5	CO6	CO7	CO8	CO9
ROC Curve							
Area under curve	0.764	0.835	0.844	0.831	0.817	0.79	0.79
(Significance)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Sensitivity (%)	89.7	85.9	79.0	71.7	66.6	60.0	52.1
Specificity (%)	63.1	81.1	89.9	94.5	96.7	97.9	98.3
Positive predictive (%)	54.7	69.4	79.5	86.7	91.0	93.5	93.8
Negative predictive (%)	92.5	92.0	89.6	87.0	85.3	83.1	80.5
Likelihood ratio+	2.43	4.55	7.80	13.07	20.42	29.15	30.36
Likelihood ratio-	0.16	0.17	0.23	0.30	0.35	0.41	0.49
Odds ratio	14.83	26.12	33.34	43.68	59.06	71.38	62.25

continuous variables and non-normally distributed variables, such as ECO level, age, and income. Differences between two proportions for all categorized variables were assessed using the chi-square test. A p-value < 0.05 was considered statistically significant. The best fitting multivariable logistic regression models were used to predict the association between smoking and ECO, adjusting for potential confounding factors among all participants and by age-group.

RESULTS

Table 1 shows the definition of terms used in the study. The validity of the different ECO cutoff levels for predicting smoking among all participants is shown in Table 2. An ECO ≥ 5 ppm gave the best sensitivity (79.0%) and specificity (89.9%) combination to distinguish smokers from non-smokers.

Tables 3 and 4 show the ECO levels varied by age. An ECO cutoff level of ≥ 4 ppm gave the best sensitivity (85.2%) and specificity (77.5%) for detecting smoking among subjects aged 16-25 years (Table 3). An ECO cutoff level of ≥ 5 ppm gave the best sensitivity (79.4%), and specificity (91.2%) for detecting smoking among subjects aged 26-70 years (Table 4).

The mean ECO level among smokers (11.24 ppm**)** was higher than among non-smokers (2.25 ppm**)** (Table 5). People who

Table 3
Validity of ECO cutoff levels for subjects aged 16-25 years (*n*=192).

Test	CO3	CO4	CO5	CO6	CO7	CO8	CO9
ROC Curve							
Area under curve	0.760	0.813	0.808	0.807	0.796	0.791	0.752
(Significance)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Sensitivity (%)	88.9	85.2	77.8	74.1	69.1	65.4	56.8
Specificity (%)	63.1	77.5	83.8	87.4	90.1	92.8	93.7
Positive predictive (%)	63.7	73.4	77.8	81.1	83.6	86.9	86.8
Negative predictive (%)	88.6	87.8	83.8	82.2	80.0	78.6	74.8
Likelihood ratio+	2.41	3.78	4.80	5.87	6.98	9.08	9.01
Likelihood ratio-	0.18	0.19	0.27	0.30	0.34	0.37	0.46
Odds ratio	13.66	19.78	18.08	19.80	20.36	24.37	19.53

Table 4
Validity of ECO cutoff levels for subjects aged 26-70 years (*n*=675).

Test	CO3	CO4	CO5	CO6	CO7	CO8	CO9
ROC Curve							
Area under curve	0.763	0.839	0.853	0.835	0.819	0.785	0.748
(Significance)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Sensitivity (%)	90	86.1	79.4	70.8	65.6	57.9	50.2
Specificity (%)	62.7	81.8	91.2	96.1	98.3	99.1	99.4
Positive predictive (%)	51.9	67.9	80.2	89.2	94.5	96.8	97.2
Negative predictive (%)	93.3	92.9	90.8	88.0	86.4	84.0	81.7
Likelihood ratio+	2.41	4.72	9.03	18.33	38.18	67.45	78.04
Likelihood ratio-	0.16	0.17	0.23	0.30	0.35	0.43	0.5
Odds ratio	15.02	27.82	40.02	60.39	108.93	158.81	155.82

smoked tended to be younger, male and have a lower income. Smokers were more likely to reside in or come from northeastern Thailand. Although the mean age of smokers in our study was younger, smokers tended to have lost more teeth than non-smokers.

The overall mean ECO level among subjects aged 16-25 years (7.59 ppm) was higher than among those aged 26-70 years (4.61 ppm) (Table 6). Although the subjects in the younger age group had a higher education, they smoked more and lost more teeth.

On multivariable logistic regression analysis, a history of smoking tobacco was associated with ECO level, age-group, gender and the interaction between ECO level and age-group. Smokers tended to be males and based on the significant interaction between ECO level and age-group, the ECO levels were different for the older and younger age groups (Table 7).

Findings from the best fitted multivariable logistic regression models by age-group revealed the ECO levels pre-

Table 5
Characteristics of study subjects by smoking status.

Variable	Tobacco smoking		
	No (n=584)	Yes (n=291)	p-value
ECO level (mean ± SD in ppm)	2.25 ± 2.39	11.24 ± 8.72	0.001[a]
Age (mean ± SD in year)	34.43 ± 11.06	33.45 ± 12.14	0.067
Income (mean ± SD in THB)	8,845 ± 6,258	7,396 ± 4,734	<0.001[a]
Age-group			0.001[b]
16-25 years	101 (17.9%)	80 (27.8%)	
26-70 years	464 (82.1%)	208 (72.2%)	
Gender			<0.001[b]
Male	304 (52.1%)	287 (98.6%)	
Female	280 (47.9%)	4 (1.4%)	
Region of residency			<0.001[b]
Not in northeast Thailand (urban)	201 (34.42%)	61 (21.0%)	
In northeast Thailand (sub-urban)	381 (65.24%)	230 (79.0%)	
In northeast Thailand (rural)	2 (0.34%)	0 (0.0%)	
Education			0.212
Up to lower secondary school	169 (29.0%)	100 (34.5%)	
Upper secondary school	202 (34.7%)	97 (33.4%)	
Vocational school	99 (17.0%)	32 (11.0%)	
University degree or higher	112 (19.3%)	61 (21.0%)	
Occupation			<0.001[b]
Not industrial employee	249 (42.6%)	162 (57.0%)	
Industrial employee	335 (57.4%)	122 (43.0%)	
Tooth loss			0.082
No	269 (46.1%)	116 (39.9%)	
Yes	315 (53.9%)	175 (60.1%)	

[a]Test of difference between mean ranks (Mann-Whitney U test), $p < 0.05$.
[b]Test of difference between proportions (chi-square test), $p < 0.05$.
THB, Thai Baht (1USD≃ 35THB).

dicted smoking status among both older and younger age groups, but was a better predictor in the older age group (Tables 8 and 9).

DISCUSSION

The mean ECO levels among smokers (11.24 ppm) and non-smokers (2.25 ppm) in our study were similar to previous studies among Thai adults (Chatrchaiwiwatana and Ratanasiri, 2008), but lower than those among Turkish smokers (21.17 ppm) and non-smokers (6.51 ppm) (Bahcebasi *et al*, 2011).

The ECO level of 11.24 ppm among smokers in our study is similar to that of 11.6 ppm from Singapore (Low *et al*, 2004), but lower than 13.6 ppm from India (Kumar *et al*, 2011), 17.13 ppm from Turkey (Deveci *et al*, 2004), 17.4 ppm from the UK (Middleton and Morice, 2000), 18.5 ppm from Japan (Yamaya *et al*, 1998), and 21.6 ppm from another study from Japan

Table 6
Characteristics of study subjects by age-group.

Variable	Age group (years)		
	16-25 (n=192)	26-70 (n=683)	p-value
ECO level (mean ± SD in ppm)	7.59 ± 9.82	4.61 ± 5.59	0.007[a]
Age (mean ± SD in year)	21.90 ± 2.41	37.56 ± 10.58	<0.001[a]
Income (mean ± SD in THB)	6,271 ± 4,683	8,952 ± 6,012	<0.001[a]
Gender			<0.001[b]
Male	155 (80.7%)	434 (64.1%)	
Female	37 (19.3%)	243 (35.9%)	
Region of residency			0.033[b]
Not in northeast Thailand	45 (23.4%)	212 (31.4%)	
In northeast Thailand	147 (76.6%)	463 (68.6%)	
Education			<0.001[b]
Up to lower secondary school	13 (6.8%)	255 (37.8%)	
Upper secondary school	69 (36.1%)	227 (33.6%)	
Vocational school	26 (13.6%)	104 (15.4%)	
University degree or higher	83 (43.5%)	89 (13.1%)	
Occupation			<0.001[b]
Not industrial employee	112 (60.5%)	299 (44.2%)	
Industrial employee	73 (39.5%)	378 (55.8%)	
Tobacco smoking			0.004[b]
No	111 (57.8%)	467 (69.0%)	
Yes	81 (42.2%)	210 (31.0%)	
Tooth loss			0.074
No	74 (38.5%)	310 (45.8%)	
Yes	118 (61.5%)	367 (54.2%)	

[a]Test of difference between mean ranks (Mann-Whitney U test), $p < 0.05$.
[b]Test of difference between proportions (chi-square test), $p < 0.05$.
THB, Thai Baht (1USD≃ 35THB).

(Zayasu *et al*, 1997), and higher than 9.4 ppm from Pakistan (Akhter *et al*, 2014).

The ECO level of 2.25 ppm among non-smokers in our study was slightly higher than 1.2 ppm from Japan (Yamaya *et al*, 1998), 1.5 ppm from another study from Japan (Zayasu *et al*, 1997) and 1.9 ppm from Singapore (Low *et al*, 2004) and lower than 3.6 ppm from Turkey (Deveci *et al*, 2004) and 4.2 ppm from Taiwan (Hung *et al*, 2006).

In our study, when we increased the ECO cutoff from 5 ppm to 9 ppm, the specificity increased to 98% but the sensitivity decreased to 52%. Our results suggest using a high ECO cutoff is not suitable for ECO in our study population. Other studies also found the same results with the ECO cutoff level was increased (Aranda Regules *et al*, 2008; Marrone *et al*, 2011; Cropsey *et al*, 2014).

Our finding that the ECO cutoff varied by age (4 ppm for those aged 16-25 years and 5 ppm for those aged 26-70 years) was also seen in a previous study (Chatrchaiwiwatana and Ratanasiri, 2008) but their

Table 7
Adjusted odds ratios and 95% CI for variables associated with tobacco smoking in the best fitting multivariable logistic regression model for all participants (*n*=875).

Variable	Adjusted odds ratio	95% Confidence limit		*p*-value
		Lower	Upper	
Exhaled carbon monoxide (ECO)	1.261	1.152	1.381	<0.001
Gender (female)	0.025	0.007	0.085	<0.001
Age-group (26-70 years)	0.284	0.131	0.616	0.001
ECO by age-group	1.401	1.213	1.618	<0.001

Nagelkerke R square = 69.0%, Model significant at $p<0.001$.

Table 8
Adjusted odds ratios and 95% CI for variables associated with tobacco smoking in the best fitting multivariable logistic regression model for the younger age-group (*n*=192).

Variable	Adjusted odds ratio	95% Confidence limit		*p*-value
		Lower	Upper	
Exhaled carbon monoxide (ECO)	1.313	1.198	1.44	<0.001

Nagelkerke R square = 49.1%, Model significant at $p<0.001$.

Table 9
Adjusted odds ratios and 95% CI for variables associated with tobacco smoking in the best fitting multivariable logistic regression model for the older age-group (*n*=677).

Variable	Adjusted odds ratio	95% Confidence limit		*p*-value
		Lower	Upper	
Exhaled carbon monoxide (ECO)	1.766	1.58	1.974	<0.001
Gender (female)	0.03	0.009	0.101	<0.001

Nagelkerke R square = 71.8%, Model significant at $p<0.001$.

cutoff levels were 7 ppm for those aged 16-25 years and 8 ppm for those aged 26-70 years. In our study gender was associated with smoking status, unlike that of a previous study from Thailand (Chatrchaiwiwatana and Ratanasiri, 2008). This suggests various factors may influence smoking status and ECO levels and these may vary by population studied. Cropsey *et al* (2006) found ECO levels varied by population; therefore, appropriate ECO cutoff values need to be determined for specific populations.

In conclusion, our findings among

these studied Thai adults show ECO levels can be used to distinguish smokers from non-smokers and cutoff levels varied by age.

ACKNOWLEDGEMENTS

The authors appreciate the co-operation of the participants and the people involved in the study. We also thank the Faculty of Dentistry, Khon Kaen University for partly funding this study.

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