

Should the threshold for expired-air carbon monoxide concentration as a means of verifying self-reported smoking abstinence be reduced in clinical treatment programmes? Evidence from a Malaysian smokers' clinic

Lei-Hum Wee^{1*}, Robert West², Jeevitha Mariapun³, Caryn Mei-Hsien Chan⁴, Awang Bulgiba³, Devi Peramalah³, and Swinder Jit⁵

*Correspondence: Lei-Hum Wee

Email: weeleihum@gmail.com

Mobile: +6012 302 1928

Fax: +603 2694 7621

Faculty of Health Sciences,
National University of Malaysia,
50300 Kuala Lumpur, Malaysia.

Author Details:

¹Faculty of Health Sciences, National University of Malaysia

²Cancer Research UK, University College London

³Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya

⁴Department of Medicine, Faculty of Medicine, University of Malaya.

⁵Tanglin Polyclinic, Federal Territory Health Department

Abstract

Background

It has been proposed that the expired-air carbon monoxide (CO) threshold for confirming smoking abstinence in clinical practice be reduced below 10ppm. Optimal thresholds may vary across regions. Data are needed to assess the impact of such a change on claimed success.

Methods

A total of 253 smokers who attended the Tanglin quit smoking clinic in Malaysia were followed-up 1, 3 and 6 months after the target quit date. All participants received a standard behavioural support programme and were prescribed either varenicline or nicotine replacement therapy. Expired-air CO was measured at every visit. Respondents' smoking status was assessed using a range of different CO thresholds (3, 5 and 10ppm) and the impact on quit rates was calculated. Predictors of success as defined using the different thresholds were assessed.

Results

The 6-month abstinence rates were: 1 month - 54.9% at 10ppm, 54.9% at 5ppm and 48.6% at 3ppm; 3 months - 36.0% at 10ppm, 35.2% at 5ppm and 30.4% at 3ppm; at 6 months - 24.1% at 10ppm, 24.1% at 5ppm and 20.6% at 3ppm. Older smokers were more likely to be recorded as abstinent at 6 months regardless of the threshold used.

Conclusions

Reducing the threshold for expired-air carbon monoxide concentrations to verify claimed smoking abstinence from 10ppm to 5ppm makes minimal difference to documented success rates in Malaysian smoker's clinic patients. Reducing to 3ppm decreases success rates slightly. Predictors of success at stopping appear to be unaffected by the threshold used.

Keywords

Smoking cessation; Carbon monoxide; Predictors for abstinence; Success rates.

Introduction

Despite the health hazards, 23.1% of Malaysian adults aged 15 years or older smoke tobacco (43.6% of men and 1.0% of women) (National Institute of Health Malaysia, 2011; Global Adult Tobacco Survey, 2011). Almost half (48.6%) of adult smokers report that they have tried to quit smoking but only 9.5% of ever smokers have managed to do so (Global Adult Tobacco Survey, 2011). Smokers clinics, providing behavioural support plus stop-smoking medication such as nicotine replacement therapy, can dramatically improve rates of success at quitting (Cahill, Stevens, Perera, & Lancaster, 2013) and such services are now available in many countries (Raw, Regan, Rigotti, & McNeill, 2009). Many of them rely on expired-air carbon monoxide (CO) monitoring to verify self-reported abstinence. There has been debate about what is the optimum threshold is for this (Cropsey, Trent, Clark, Stevens, Lahti, & Hendricks, 2014; Al-Sheyab, Kheirallah, Mangnall, & Gallagher, 2015). This paper reports a study that aimed to address this issue.

The measurement of smokers' CO levels provides objective assessment of recent smoking (Sandberg, Skold, Grunewald, Eklund, & Wheelock, 2011; Society for Research on Nicotine & Tobacco, 2002). A threshold of 10 ppm is commonly used in clinical studies (Tonnesen, Nørregaard, Mikkelsen, Jorgensen, & Nilsson, 1993; Jorenby et al., 1995). Other studies have used values ranging from 5 to 8 ppm as the cut off (Sandberg et al., 2011; Kapusta et al., 2010; Low, Ong, & Tan 2004; Jarvis, Tunstall-Pedoe, Morabia, Bernstein, Curtin, & Berode, 2001; Middleton & Morice, 2000; Feyerabend, Vessey, & Salojee, 1987; Joumard, Chiron, Vidon, Maurin, & Rouzioux, 1981). Getting the right threshold is important because it could undermine motivation for a non-smoker to have his or claim of abstinence incorrectly queried and fail to detect those who have smoked so that remedial action can be taken. In addition, it is crucial for performance monitoring and clinical studies comparing success rates with different treatment options.

Expired air CO has important limitations as a tool for verifying abstinence. The half-life of CO in the blood is around 2 to 4.5 hours (Society for Research on Nicotine & Tobacco, 2002; Sandberg et al., 2011) so it cannot detect smoking on the previous day. It also lacks specificity in areas of high pollution from burning fossil fuels, where ambient CO can produce readings as high as 10ppm and occasionally higher. It also

lacks sensitivity to be able to detect very light smoking. The original threshold of 10ppm was set at a time and under conditions where ambient CO was relatively high. Several researchers have proposed that under most current conditions thresholds of between 8 to 10 ppm are too high (Cropsey et al., 2014; Morabia et al., 2001; Middleton & Morice, 2000; Jarvis et al., 1987). They may incorrectly categorise as abstinent people who have in fact smoked, albeit at a low level (Perkins, Karelitz, & Jao, 2013).

Thresholds as low as 3-6 ppm have been proposed (Kapusta et al., 2010; Javors, Hatch, & Lamb, 2005; Low et al., 2004; Morabia et al., 2001; Middleton & Morice, 2000; Jarvis et al., 1987; Joumard et al., 1981). Some studies involving population surveys have supported this view (Cropsey et al., 2014; Javors et al., 2005). However, in smokers' clinics, the situation is somewhat different from that obtaining in population surveys. An important question is what happens in routine clinical practice.

In a large study involving the English stop smoking services, Brose, Tombor, Shahab, & West (2013) found that reducing the threshold to 5ppm made very little difference to recorded abstinence rates after 4 weeks and reducing it below that appeared to increase misclassification rate. This was one study in one country. Given that this is a global issue, it is important to assess how far this generalises. Malaysia has developed a national programme of stop smoking services somewhat similar, though with less coverage, to that found in the UK (Wee, Shahab, Bulgiba, & West, 2011a). However, it is a very different country with a different demographic profile. It therefore provides a potentially useful context to assess the generalizability of the UK findings. A previous study used a threshold of 10 ppm, but it is not known whether different results would have been achieved with different thresholds (Ng & Ann, 2012).

Unfortunately it is not possible to undertake a full sensitivity and specificity analysis using data from routine smokers' clinics because of the high rate of drop-out when people resume smoking. This means that two of the four cells needed for such an analysis (smoking/ high CO and smoking/ low CO) are subject to too great a degree of bias. Brose et al. (2013) used a different method. They examined, for those smokers who were reporting abstinence, what proportion of them would be classified as smokers under different thresholds. It may be expected that as the threshold is lowered, more would be classified as smokers. However, what they found was that it made very little difference down to a threshold of 5ppm. Below that figure, the

proportion classified as smokers rose markedly. They evaluated how far this was likely to be due to an increase in misclassification by examining whether known predictors of abstinence such as age and social grade predicted abstinence better or worse with the various thresholds. They found that under 5ppm the known predictors started to become less predictive. They argue that this suggested that under the very low thresholds there was an increase in the misclassification rate.

This study used a similar methodology to that used by Brose et al. (2013) in the Malaysian context. The aim was to assess:

1. At what point does reducing the threshold for CO verification of abstinence lead to a meaningful reduction in verified abstinence rates at 1, 3 and 6 months?
2. Do known predictors of abstinence show better or worse prediction of abstinence defined using different thresholds?

Methods

Design

This was a two year follow-up study where we collected data from 253 smokers who attended the Tanglin quit smoking clinic in the Federal Territory of Kuala Lumpur, Malaysia. The same sample was followed-up at 1-, 3- and 6-months.

Samples and Procedures

The Tanglin clinic is a quit smoking clinic under the jurisdiction of the Federal Territory Health Department in Kuala Lumpur, Malaysia. Respondents were prescribed either varenicline or nicotine replacement therapy (NRT), with expired-air CO measured at every visit. Only respondents who attended the quit smoking clinic for the first time were recruited (n=253). All received the standard behavioural intervention by the same qualified staff nurse throughout the quitting process. Respondents were largely from the urban population and were either self-referred, referred by friends and family members, or referred by their doctors. Breath CO monitoring was performed in the clinic using a Micro CO Meter.

Measures

The questionnaire in the national language or Bahasa Malaysia was used during the interview at the first visit, prior to the quit attempt. The respondents' demographic details, smoking histories and current smoking habits assessed, including:

- a) Socio-demographic information: age, gender, ethnicity, education level and occupation;
- b) Past smoking history: age started smoking, previous quit attempts made, duration of previous abstinence;
- c) Current smoking habits: number of cigarettes smoked, time to first cigarette of the day, Fagerstrom Test for Nicotine Dependence (FTND) (Heatherton, Kozlowski, Frecher, & Fagerstrom, 1991);
- d) Current medical conditions.

Consistent with the Russell Standard (West, 2005), respondents who did not attend scheduled follow-up appointments were assumed to be smoking. Abstinence was defined as self report of no smoking since the quit date and a CO reading of less than a) 10pp, b) 5ppm and c) 3ppm. These figures were chosen to span the range that had been suggested as thresholds in previous research.

The FTND is commonly used in Malaysian quit smoking clinics and it has been validated in previous studies in this population (Wee, West, Bulgiba, & Shahab, 2011b; Wee et al., 2011a; Ng & Ann, 2012; Robson, Bond, & Wolff, 2013). Ethical approval was obtained from the Medical Review & Ethics Committee of the Ministry of Health Malaysia.

Statistical Analyses

Continuous variables were described as mean \pm SD. Categorical variables were described by numbers (percentages). The association between successful quitting and socio-demographic variables was analysed using backward elimination multiple logistic regression. The variables included initially were: age, age of starting smoking, cigarettes per day, race, occupation, educational level, and FTND. Logistic regression was carried out using a backward elimination model to assess the most parsimonious predictive model of quitting at each threshold. All analyses were performed using STATA 12.0.

Results

There were a total of 253 respondents with an average age of 38 years (SD±11.9). The sample consisted of both adolescents and adults from the age of 14 to 73. The respondents were predominantly male (97.2%) and of Malay ethnicity (77.9%). The majority (86.9%) had at least secondary level education with a smoking initiation mean age of 17 years. The average Fagerstrom Test for Nicotine Dependence (FTND) score was 4.9. Approximately one third of participants reported having a cigarette in the first 5 minutes of waking up (32%). The median cigarette consumption was 10 with an IQR of 10 to 20. Approximately 20% were diagnosed with at least one type of medical condition (Table 1).

(Insert Table 1 here)

Table 2 shows the percentages of smokers designated as abstinent using the three thresholds at each follow up point. It is clear that at 6 months there was no difference

in the percentage deemed as abstinence using a threshold of 5ppm versus 10ppm. There was a small reduction when the threshold was reduced to 3ppm.

Similarly, at 1 month, there was no difference at the threshold level of 10ppm and 5ppm in terms of the percentage of participants (54.9%) who were abstinent. The percentage reduced slightly to 48.6% at the threshold level of 3ppm or lower. At 3 months, the abstinence rate reduced from 36.0% at the threshold level of 10ppm, to 35.2% at 5ppm and to 30.4% at 3ppm.

(Insert Table 2 here)

Results from the logistic regressions indicated that the predictors of abstinence were similar across all CO cut-offs at 1 month, 3 months and 6 months (Table 3). The only difference was at 6 months, at 3 CO ppm, the average number of cigarettes smoked per day was also found to be a predictor of abstinence apart from age.

(Insert Table 3 here)

Discussion and conclusions

It made very little difference to success rates whether a CO-threshold of 10ppm or 5ppm was used to verify abstinence. Success rates were slightly lower at the 3ppm threshold. Age was a consistent predictor of success across the different CO thresholds at 1-, 3- and 6-months follow-up. The current findings confirm the findings of Brose et al. (2013) in suggesting that a threshold of 10ppm is acceptable in clinical situations.

The current findings provide a fair degree of confidence that a threshold of 10ppm is appropriate internationally for determining predictors. Caution should be therefore be applied if a lower CO threshold is used, unless there are clear and specific grounds for selecting a lower threshold. CO is produced endogenously as well as being absorbed through the lungs and most smokers are probably exposed to significant pollution from burnt fossil fuels which would also raise expired air CO concentrations. Apart from maximising the accuracy of recording, one has to consider the cost of

falsely categorising someone who is attending a smokers' clinic as a smoker versus a non-smoker. For example, it could be demotivating for an individual attending a quit smoking clinic to be accused of misreporting abstinence. Great care should be taken to avoid this unless there is a high degree of confidence that this is the case.

There are considerable cultural and geographical differences between Malaysian and English smokers (Wee et al., 2011b). Clinic attendees in Malaysia tend to have higher educational levels comprising predominantly of males, reflecting the fact that many fewer women smoke in Malaysia compared with published characteristics of smokers attending a national network of stop smoking clinics, UK (National Health Service, 2012; Wee 2011a; Kotz, Brown, & West, 2009). The clinic under study is located in an urban area with a greater proportion of professionals of younger age compared to the UK (mean age is in the 40s) (West, 2010). Malaysian smokers had a higher FTND score of 4.9 compared to the UK average of 3.9 (West, 2010).

Baseline CO readings were relatively low compared with the standard cut-off for CO of less than 10ppm to differentiate smokers and non-smokers for the National Health Service (UK) (Health and Social Care Information Centre, 2011), as only about 30% of the respondents had a CO reading of more than or equal to 10ppm. As to whether the respondents had already refrained from smoking prior to registering at the clinic is not clear.

A major strength of the study was the multiple follow up to 6 months. Another was the involvement of a rarely studied population. The study had a number of limitations. It did not aim to assess the sensitivity or specificity of different CO thresholds. That would have required a 'gold standard' measure of abstinence (possibly saliva cotinine) that was not available and was not the purpose of the study. The sample size was modest compared with the English sample, but was sufficient to provide reasonable confidence intervals around the estimates.

The study confirmed the acceptability of 10ppm as a standard CO threshold for validating abstinence in clinical samples internationally unless there are specific reasons for choosing a lower one.

Authors' contributions

AB proposed for the study to be carried out. WLH wrote the first draft of the manuscript. DP, JM and CCMH managed the literature search and contributed to the first draft of the manuscript. SJ personally carried out the data collection. AB and JM undertook the statistical analysis. RW edited several drafts. All authors contributed to and have approved the final manuscript.

Acknowledgements

We thank the Director General of Health, Ministry of Health Malaysia for permission to publish this study as well as the Department of Health, Federal Territories for allowing this study to be carried out at their clinic.

References

- Al-Sheyab, N., Kheirallah, K. A., Mangnall, L. J. T., & Gallagher, R. (2015). Agreement between exhaled breath carbon monoxide threshold levels and self-reported cigarette smoking in a sample of male adolescents in Jordan. *International Journal of Environmental Research and Public Health*, *12*(1), 841–854.
- Bailey, S. R., Bryson, S. W., & Killen, J. D. (2011). Predicting successful 24-hr quit attempt in a smoking cessation intervention. *Nicotine & Tobacco Research*, *13*(11), 1092–1097.

- Brose L. S., Tombor I., Shahab L., & West, R. (2013). The effect of reducing the threshold for carbon monoxide validation of smoking abstinence: Evidence from the English stop smoking services. *Addictive Behaviours*, *38*, 2529–2531.
- Cahill, K., Stevens, S., Perera, R., & Lancaster, T. (2013). Pharmacological interventions for smoking cessation: An overview and network meta-analysis. *Cochrane Database of Systematic Reviews*, *5*:CD009329. doi: 10.1002/14651858.CD009329.pub2
- Cropsey, K. L., Trent, L. R., Clark, C. B., Stevens, E. N., Lahti, A. C., & Hendricks, P. S. (2014). How low should you go? Determining the optimal cutoff for exhaled carbon monoxide to confirm smoking abstinence using cotinine as reference. *Nicotine & Tobacco Research*, *16*(10), 1348–1355.
- Global Adult Tobacco Survey (2011). Global adult tobacco survey: Malaysia 2011. Retrieved from http://www.who.int/tobacco/surveillance/survey/gats/malaysia_country_report_2011.pdf
- Heatherton, T. F., Kozlowski, L. T., Frecher, R.C., & Fagerstrom, K. O. (1991). The Fagerstrom Test for Nicotine Dependence: A revision of Fagerstrom tolerance Questionnaire. *British Journal of Addiction*, *86*, 1119–1127.
- Jarvis, M. J., Tunstall-Pedoe, H., Feyerabend, C., Vessey, C., & Salojee, Y. (1987). Comparison of tests used to distinguish smokers from non-smokers. *American Journal of Public Health*, *77*, 1435–1438.
- Javors, M. A., Hatch, J. P., & Lamb, R. J. (2005). Cut-off levels for breath carbon monoxide as a marker for cigarette smoking. *Addiction*, *100*(2), 159–167.
- Jorenby, D. E., Smith, S. S., Fiore, M. C., Hurt, R. D., Offord, K. P., Croghan, I. T., ... Baker, T. B. (1995). Varying nicotine patch dose and type of smoking cessation counseling. *Journal of the American Medical Association*, *274*(17), 1347–1352.
- Joumard, R., Chiron, M., Vidon, R., Maurin, M., & Rouzioux, J. M. (1981). Mathematical models of the uptake of carbon monoxide on haemoglobin at low carbon monoxide levels. *Environmental Health Perspectives*, *41*, 277–289.
- Kapusta, N. D., Pietschig, J., Plener, P. L., Bluml, V., Lesch, O. M., & Walter, H. (2010). Does breath carbon monoxide measure nicotine dependence? *Journal of Addictive Diseases*, *29*(4), 493–499.

- Low, E. C. T., Ong, M. C. C., & Tan, M. (2004). Breath carbon monoxide as an indication of smoking habit in the military setting. *Singapore Medical Journal*, *45*, 578–582.
- Middleton, E. T., & Morice, A. H. (2000). Breath carbon monoxide as an indication of smoking habit. *Chest*, *117*, 758–763.
- Morabia, A., Bernstein, M. S., Curtin, F., & Berode, M. (2001). Validation of self-reported smoking status by simultaneous measurement of carbon monoxide and salivary thiocyanate. *Preventive Medicine*, *32*, 82–88.
- National Institute of Health Malaysia. (2011) *The 4th National Health & Morbidity Survey (NHMS-4) Report*. Kuala Lumpur, Malaysia: Ministry of Health Malaysia.
- Ng, C. G., & Ann, A. Y. (2012). Exhaled carbon monoxide levels among Malaysian male smokers with nicotine dependence. *Southeast Asian Journal of Tropical Medicine and Public Health*, *43*(1), 212–218.
- Perkins, K. A., Karelitz, J. L., Jao, N. C., Gur, R. C., & Lerman, C. (2013). Effects of bupropion on cognitive performance during initial tobacco abstinence. *Drug and Alcohol Dependence*, *133*(1), 283–286.
- Raw, M., Regan, S., Rigotti, N. A., & McNeill, A. (2009). A survey of tobacco dependence treatment services in 36 countries. *Addiction*, *104*(2), 279–287.
- Robson, N., Bond, A., & Wolff, K. (2013). A comparison of smoking behaviour characteristics between Caucasian smokers in the United Kingdom and Malay smokers in Malaysia. *Preventive Medicine*, *57*, S8–S10.
- Sandberg, A., Skold, C. M., Grunewald, J., Eklung, A., & Wheelock, A. (2011). Assessing recent status by measuring exhaled carbon monoxide levels. *PLOS One*, *6*, e28864.
- Society for Research on Nicotine & Tobacco. (2002). Biochemical verification of tobacco use and cessation. *Nicotine & Tobacco Research*, *4*(2), 149–159.
- Tonnesen, P., Nørregaard, J., Mikkelsen, K., Jorgensen, S., & Nilsson, F. (1993). A double-blind trial of a nicotine inhaler for smoking cessation. *Journal of the American Medical Association*, *269*(10), 1268–1271.
- Wee, L. H., Shahab, L., Bulgiba, A. & West, R. (2011a). Stop smoking clinics in Malaysia: Characteristics of attendees and predictors of success. *Addictive Behaviours*, *36*, 400–403.
- Wee, L. H., West, R., Bulgiba, A., & Shahab, L. (2011b). Predictors of 3-month abstinence in smokers attending stop-smoking clinics in Malaysia. *Nicotine & Tobacco Research*, *13*, 151–156.

West, R. (2005). Outcome criteria in smoking cessation trials: Proposal for the common standard. *Addiction*, 100, 299–303.