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Articles selected and commented on by: **Prof. V. K. Vijayan**, Former Director, Vallabhbhai Patel Chest Institute, University of Delhi.



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It gives me great pleasure to conclude this year's series of **APSR Respiratory Updates** as Editor in chief.

I have been coordinating this **APSR Respiratory Updates** series since 2011. It has been a unique publication in highlighting the recent most important literature in respiratory medicine. I would like to take this chance to thank all previous expert authors over the past eight years for their great support to make this series happened. Editorial support from the Respiratory Editorial Office, especially Dr Christel Norman, is also imperative to the success of this series. My engagement in this coordination process for the series gave me great learning opportunities and updates on respiratory literature and I do hope this applies to our readers as well.

David C Lam, *Editor in chief*

A pragmatic trial of e-cigarettes, incentives, and drugs for smoking cessation.

Authors: Halpern S`D et al.

Reference: N Engl J Med 2018; 378: 2302-10.

URL: <https://www.nejm.org/doi/full/10.1056/NEJMsa1715757>

Comment: This study was conducted to know whether financial incentives, pharmacologic therapies, and electronic cigarettes (e-cigarettes) promote smoking cessation among unselected smokers. Smokers employed in 54 companies were randomly assigned to one of four smoking cessation interventions or to usual care. Usual care consisted of access to information regarding the benefits of smoking cessation and to a motivational text-messaging service. The four interventions consisted of usual care plus one of the following: free cessation aids (nicotine-replacement therapy or pharmacotherapy, with e-cigarettes if standard therapies failed); free e-cigarettes, without a requirement that standard therapies had been tried; free cessation aids plus \$600 in rewards for sustained abstinence; or free cessation aids plus \$600 in redeemable funds, deposited in a separate account for each participant, with money removed from the account if cessation milestones were not met. The primary outcome was sustained smoking abstinence for 6 months after the target quit date. Of the 6131 smokers enrolled for the study, 6006

underwent randomization. Sustained abstinence rates through 6 months were 0.1% in the usual care group, 0.5% in the free cessation aids group, 1.0% in the free e-cigarettes group, 2.0% in the rewards group, and 2.9% in the redeemable deposit group. With respect to sustained abstinence rates, redeemable deposits and rewards were superior to free cessation aids ($P < 0.001$ and $P = 0.006$, respectively, with significance levels adjusted for multiple comparisons). Redeemable deposits were superior to free e-cigarettes ($P = 0.008$). Free e-cigarettes were not superior to usual care ($P = 0.20$) or to free cessation aids ($P = 0.43$).

This pragmatic trial of smoking cessation has demonstrated that financial incentives added to free cessation aids resulted in a higher rate of sustained smoking abstinence than free cessation aids alone. Among smokers who received usual care (information and motivational text messages), the addition of free cessation aids or e-cigarettes did not provide a benefit.

Smoking cessation, weight change, type 2 diabetes, and mortality.

Authors: Hu Y et al.

Reference: N Engl J Med 2018; 379:623-632

URL: <https://www.nejm.org/doi/full/10.1056/NEJMoa1803626>

Comments: Hu Y et al planned the study to know whether weight gain after smoking cessation attenuates the health benefits of quitting. The subjects selected for the study were from three cohort studies involving men and women in the United States and the Authors identified individuals who had reported quitting smoking and prospectively assessed changes in smoking status and body weight. The risks of type 2 diabetes, death from cardiovascular disease, and death from any cause among those who had reported quitting smoking, according to weight changes after smoking cessation was estimated. The risk of type 2 diabetes was higher among recent quitters (2 to 6 years since smoking cessation) than among current smokers (hazard ra-

tio, 1.22; 95% confidence interval [CI], 1.12 to 1.32). The risk peaked 5 to 7 years after quitting and then gradually decreased. The temporary increase in the risk of type 2 diabetes was directly proportional to weight gain, and the risk was not increased among quitters without weight gain ($P < 0.001$ for interaction). In contrast, quitters did not have a temporary increase in mortality, regardless of weight change after quitting. As compared with current smokers, the hazard ratios for death from cardiovascular disease were 0.69 (95% CI, 0.54 to 0.88) among recent quitters without weight gain; 0.47 (95% CI, 0.35 to 0.63) among those with weight gain of 0.1 to 5.0 kg; 0.25 (95% CI, 0.15 to 0.42) among those with weight gain of 5.1 to 10.0 kg; 0.33 (95% CI, 0.18 to 0.60) among those with weight gain of more than 10.0 kg, and 0.50 (95% CI, 0.46 to 0.55) among longer-term quitters (>6 years since smoking cessation). Similar associations were observed for death from any cause.

Authors conclude that smoking cessation that was accompanied by substantial weight gain was associated with an increased short-term risk of type 2 diabetes but did not mitigate the benefits of quitting smoking on reducing cardiovascular and all-cause mortality. This study emphasises that the benefits of smoking cessation are not nullified by the short term risk of type 2 diabetes mellitus associated with weight gain.

Cardiovascular and neuropsychiatric events after varenicline use for smoking cessation.

Authors: Gershon AS et al.

Reference: Am J Respir Crit Care Med 2018; 197: 913–922.

URL: <https://www.atsjournals.org/doi/10.1164/rccm.201706-1204OC>

Comment: Varenicline has been reported to improve smoking cessation rates, but has also been associated with serious adverse events. A population-based, self-controlled risk interval study using linked universal health administrative data from the diverse, multicultural popu-

lation of Ontario, Canada, was conducted with the aim to determine the risks of cardiovascular and neuropsychiatric events after varenicline use in a real-world setting. New varenicline users from September 1, 2011 to February 15, 2014 were observed from 1 year before to 1 year after varenicline receipt. The relative incidences of cardiovascular and neuropsychiatric hospitalizations and emergency department visits in the 12 weeks after varenicline receipt (the risk interval) compared with the remaining observation period (the control interval) were estimated in two separate fixed-effect conditional Poisson regressions. There were 56,851 new varenicline users and among these, 6,317 cardiovascular and 10,041 neuropsychiatric hospitalizations and emergency department visits occurred from 1 year before to 1 year after receipt. The incidence of cardiovascular events was 34% higher in the risk interval compared with the control interval (relative incidence, 1.34; 95% confidence interval, 1.25–1.44). Findings were consistent in sensitivity analyses, most notably in those without any history of previous cardiovascular disease. The relative incidence of neuropsychiatric events was marginally significant in the primary (relative incidence, 1.06; 95% confidence interval, 1.00–1.13) but not all sensitivity analyses. There was only a 6% increase in the incidence of neuropsychiatric hospitalizations and emergency department visits which was of questionable robustness and clinical significance.

This study shows that varenicline use was associated with a significant increased risk of cardiovascular adverse events (even in people with no cardiovascular disease history) and no clear increase in neuropsychiatric adverse events. Physicians should look for cardiovascular adverse effects while prescribing varenicline for smoking cessation.



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The effects of smoking on treatment outcome in patients newly diagnosed with pulmonary tuberculosis.

Authors: Masjedi MR et al.

Reference: Int J Tuberc Lung Dis 2017; 21(3):351–356

URL: <http://dx.doi.org/10.5588/ijtld.16.0513>

Comment: The prevalence of tobacco use is high in countries with high prevalence of tuberculosis and smoking is an important risk factor for TB. Tobacco smoking has been reported to be associated with increased vulnerability to develop tuberculosis infection, recurrence and mortality. However, the effects of smoking cessation on sputum smear conversion and treatment success in TB are not studied adequately. This study was done to assess the effects of smoking and smoking cessation on treatment outcomes in patients newly diagnosed with TB in Iran. Newly diagnosed smear-positive TB patients were included in the study. All smokers participated in a smoking cessation programme. Sputum smear status was evaluated at the end of month 2, 5 and 6 of treatment, and smoking status was evaluated at the end of month 2. Differences in smear conversion rates were compared between the three groups, i.e., non-smokers, smokers and quitters. A total of 183 smokers and 151 non-smokers were included in the study. When smoking cessation was assessed after 2 months, 42.6% (78/183) of the smokers were found to have quit. The cure rate at the end of 6 months, precisely compatible with the conversion rate, was significantly higher among non-smokers ($p = 0.004$) and quitters at 2 months ($p = 0.049$) than among persisting smokers (83.4%, 80.8% and 67.6%, respectively).

This study revealed that cure rates in patients newly diagnosed with pulmonary TB were higher in non-smokers and quitters at 2 months than in smokers. Smoking cessation was found to reduce treatment failure rates compared to those who continued to smoke and a reduction in failure rate among quitters to that of non-smokers. This emphasises the need to include smoking cessation programmes in TB control plans.

Perception and current use of e-cigarettes among youth in China.

Author: Xiao L et al.

Reference: Nicotine Tob Res 2018 July 20

URL: <https://doi.org/10.1093/ntr/nty145>

Comment: Authors conducted a study to provide nationally representative estimates of electronic cigarette (e-cigarette) use among youth in China and to explore the factors associated with awareness and use of e-cigarettes and the relationship between e-cigarette and conventional tobacco use. Data from the Global Youth Tobacco Survey, which was completed by 155 117 middle school students (51.8% boys and 48.2% girls) in China, and employed a multi-stage stratified cluster sampling design were analysed. SAS 9.3 complex survey procedures were used for data analysis and logistic regression was used to explore factors associated with e-cigarette use and the relationship between e-cigarette and conventional tobacco use. About 45.0% of middle school students had heard of e-cigarettes, but only 1.2% reported using e-cigarettes in the last 30 days. Among never-smokers, e-cigarette users were more likely to intend to use a tobacco product in the next 12 months than nonusers (adjusted odds ratio [OR] = 6.970, 95% confidence interval [CI] = 4.474% to 10.857%), and more likely to say that they would enjoy smoking a cigarette (adjusted OR = 14.633, 95% CI = 11.328% to 18.902%). E-cigarette use was associated with previous experimentation with cigarette smoking (OR = 3.2), having noticed tobacco advertising in the past 30 days (OR = 2.7), having close friends who smoke (OR = 1.4), and thinking tobacco helps people feel more comfortable in social situations (OR = 3.3) and makes young people look more attractive (OR = 1.3).

This study is the first nationally representative survey of e-cigarette use among youth in China. It found that among middle school students, prevalence of e-cigarette use is 1.2% and

prevalence of e-cigarette awareness is 45.0%. Chinese youths use e-cigarettes as a tobacco product rather than an aid to quitting. Among never-smokers, e-cigarette users were more likely to have intentions to use a tobacco product in the next 12 months, more likely to use a tobacco product offered by their best friends and enjoy smoking a cigarette than nonusers. Enhanced prevention efforts are therefore needed targeting e-cigarette use among youth.

Income disparities in smoking cessation and the diffusion of smoke-free homes among U.S. smokers: Results from two longitudinal surveys.

Authors: Maya Vijayaraghavan et al.

Reference: PLoS ONE 2018; 13(7): e0201467

URL: <https://doi.org/10.1371/journal.pone.0201467>

Comment: In this study, the Authors explored the role of smoke-free homes in cessation behaviour across income levels. Participants in the study included current smokers who were ≥ 18 years and who participated in the longitudinal 2002–2003 ($n = 2801$) or 2010–2011 ($n = 2723$) Tobacco Use Supplements to the Current Population Survey. Income was categorised as multiples of the federal poverty level (FPL) ($<300\%$ FPL versus $\geq 300\%$ FPL). The association of smoke-free homes with 1+day quit attempts and 30+days abstinence at 1-year follow-up was examined. A mediation analysis to examine the extent that smoke-free homes contributed to income disparities in 30+days' abstinence was conducted. Between the two surveys, heavy smoking (≥ 1 pack/day) declined by 17%, and smoking prevalence declined by 15% among those with higher-incomes ($>300\%$ FPL). Although similar in 2002, the prevalence of smoke-free homes was 33% lower among individuals living $<300\%$ FPL than those living $\geq 300\%$ FPL. Although the quit attempt rate was similar, the 30+days abstinence rate was higher in the 2010–11 cohort than in 2002–3 cohort (20.6% versus 15.5%, $p < 0.008$). Whereas smoking ≥ 1 pack/ day

was associated with lower odds of 30+days abstinence (Adjusted odds ratio [AOR] 0.7; 95% CI 0.5–0.9), having a higher income (AOR 1.9, 95% CI 1.4–2.6) and a smoke-free home (AOR 1.6, 95% CI 1.2–2.1) were associated with greater odds of 30+day abstinence. Differential changes in smoke-free homes across income groups between the two surveys contributed to 36% (95% CI 35.7–36.3) of the observed income disparity in 30+days' abstinence.

Authors conclude that increasing the diffusion of smoke-free homes among low-income populations may attenuate at least a third of the income disparities in smoking cessation. This highlights the need for interventions to increase adoption of smoke-free homes among low-income households.

Support for a point-of-sale cigarette display ban among smokers: findings from the international tobacco control (ITC) Netherlands survey.

Authors: van Mourik et al.

Reference: BMC Public Health 2018; 18:740

URL: <https://doi.org/10.1186/s12889-018-5666-4>

Comment: One of the important marketing strategies adopted by the tobacco industry is displaying tobacco products at point-of-sale (PoS). The Authors designed a study to examine how support for a PoS cigarette display ban changed among smokers between 2010 and 2015 and to identify the variables that predict support among smokers for a PoS cigarette display ban. Longitudinal data were obtained from six annual surveys from the International Tobacco Control (ITC) Netherlands Survey. The sample consisted of between 1279 and 1800 smokers per year. Smokers were asked whether they supported a complete ban on displays of cigarettes inside shops and stores. Analysis of data showed that support for a PoS cigarette display ban increased from 28.9% in 2010 to 42.5% in 2015 (OR = 1.40, $p < 0.001$). A multiple logistic

regression analysis revealed that support for a PoS display ban of cigarettes was more likely among smokers who had more knowledge about the health risks of smoking (OR = 3.97, $p < 0.001$), believed smoking-related health risks to be severe (OR = 1.39, $p < 0.001$), had a more positive attitude towards quitting smoking (OR = 1.44, $p = 0.006$), reported stronger social norms to quit smoking (OR = 1.29, $p = 0.035$), had a higher self-efficacy for quitting smoking (OR = 1.31, $p = 0.001$), and had stronger intentions to quit smoking (OR = 1.23, $p = 0.006$).

The findings from the study reveal that support for a point-of-sale display ban of cigarettes increased among smokers over the years and support for display ban increased faster among highly educated smokers than among moderately educated smokers. Authors conclude that enhanced educational campaigns about the dangers of smoking may encourage smokers to quit smoking.

Tobacco Dependence Predicts Higher Lung Cancer and Mortality Rates and Lower Rates of Smoking Cessation in the National Lung Screening Trial.

Authors: Rojewski AM et al.

Reference: Chest 2018; 154(1): 110-118

URL: <https://doi.org/10.1016/j.chest.2018.04.016>

Comments: Based on the assumption that incorporating tobacco treatment within lung cancer screening programs has the potential to influence cessation in high-risk smokers, the Authors undertook a study to better understand the characteristics of smokers within a screening cohort, correlate those variables with downstream outcomes, and identify predictors of continued smoking. This study was a secondary analysis of the National Lung Screening Trial randomized clinical study. Tobacco dependence was evaluated by using the Fagerström Test for Nicotine Dependence, the Heaviness of Smoking Index, and time to first cigarette (TTFC); de-

scriptive statistics were performed. Clinical outcomes (smoking cessation, lung cancer, and mortality) were assessed with descriptive statistics and χ^2 tests stratified according to nicotine dependence. Logistic and Cox regression models were used to study the influence of dependence on smoking cessation and mortality, respectively. Patients with high dependence scores were less likely to quit smoking compared with low dependence smokers (TTFC OR, 0.50 [95% CI, 0.42-0.60]). Indicators of high dependence, as measured according to all three metrics, were associated with worsening clinical outcomes. TTFC showed that patients who smoked within 5 min of waking (indicating higher dependence) had higher rates of lung cancer (2.07% for > 60 min after waking vs. 5.92% \leq 5 min after waking; hazard ratio [HR], 2.56 [95% CI, 1.49-4.41]), all-cause mortality (5.38% for > 60 min vs. 11.21% \leq 5 min; HR, 2.19 [95% CI, 1.55-3.09]), and lung cancer-specific mortality (0.55% for > 60 min vs. 2.92% for \leq 5 min; HR, 4.46 [95% CI, 1.63-12.21]).

Authors have concluded that using time to first cigarette (TTFC); a one-question assessment of tobacco dependence, at the time of lung cancer screening has implications for personalizing tobacco treatment and improving risk assessment. Individuals with higher levels of nicotine dependence through the use of a single question assessment (TTFC) have the potential to influence tobacco treatment efforts and increase cessation success.

Acute effects of electronic and tobacco cigarettes on vascular and respiratory function in healthy volunteers: a cross-over study.

Author: Kerr DM et al.

Reference: J Hypertens 2018 Jul 30.

URL: [doi.10.1097/HJH.0000000000001890](https://doi.org/10.1097/HJH.0000000000001890)

Comment: The objectives of the study were to assess the acute effects of nicotine-

containing electronic cigarettes versus tobacco smoking on vascular and respiratory function and circulating microparticles, particularly platelet microparticles (PMPs), biomarker of haemostasis/thrombosis and endothelial microparticles (EMPs), biomarker of endothelial function. The study was conducted in 20 smokers immediately before and after electronic cigarettes use and tobacco smoking. The parameters assessed were heart rate (HR), blood pressure, reactive hyperaemia index (RHI, microvascular reactivity), augmentation index (arterial stiffness) and respiratory function. The number of microparticles was determined by flow cytometry using counting beads as a reference. Labelling with Annexin-V was used to detect the total microparticle fraction. EMPs were characterized as CD31+CD42- and PMPs as CD31+CD42+. HR increased after electronic cigarettes use and tobacco smoking ($P < 0.001$), whereas blood pressure remained unchanged ($P > 0.05$). RHI ($P = 0.006$), augmentation index ($P = 0.010$) but not augmentation index standardized to HR 75bpm ($P > 0.05$) increased with electronic cigarettes use but not with tobacco smoking. Following tobacco smoking, there was a significant increase in total microparticles ($P < 0.001$), EMPs ($P < 0.001$) and PMPs ($P < 0.001$). In contrast, electronic cigarettes were only associated with an increase in PMPs ($P < 0.001$), with no significant changes in the total microparticle fraction or EMPs (all $P > 0.05$). Peak expiratory flow significantly decreased following electronic cigarettes use ($P = 0.019$).

The results from the study demonstrate that acute exposure to tobacco smoking as well as electronic cigarettes influences vascular and respiratory functions. Tobacco smoking significantly increased microparticle formation indicating possible endothelial injury and electronic cigarettes use induced vasoreactivity and decreased peak expiratory flow. These findings suggest that both electronic cigarettes and tobacco smoking negatively impact vascular function.

Global economic cost of smoking-attributable diseases.

Authors: Goodchild M, et al.

Reference: Tob Control 2018; 27: 58-64.

URL: <http://dx.doi.org/10.1136/tobaccocontrol-2016-053305>

Comment: Numerous studies conducted mostly in high income countries have documented the detrimental impact of smoking on health and quantified the economic cost that smoking imposes on society. However, there are only few studies from developing countries documenting the economic cost of smoking. The aim of this study was to measure the economic cost of smoking-attributable diseases in countries throughout the world, including in low- and middle-income settings. The Cost of Illness approach was used to estimate the economic cost of smoking attributable diseases in 2012. Under this approach, economic costs were defined as either 'direct costs' such as hospital fees or 'indirect costs' representing the productivity loss from morbidity and mortality. The same method was applied to 152 countries, which had all the necessary data, representing 97% of the world's smokers. The amount of healthcare expenditure due to smoking-attributable diseases totalled purchasing power parity (PPP) \$467 billion (US\$422 billion) in 2012, or 5.7% of global health expenditure. The total economic cost of smoking (from health expenditures and productivity losses together) totalled PPP \$1852 billion (US\$1436 billion) in 2012, equivalent in magnitude to 1.8% of the world's annual gross domestic product (GDP). Almost 40% of this cost occurred in developing countries, highlighting the substantial burden these countries suffer. The limitations of the study as pointed out by the Authors are the estimates do not include the harm from second-hand smoke or smokeless forms of tobacco. Economic costs would have been substantially high if these were also included in the analysis.

This study brings out the fact that smoking imposes a heavy economic burden throughout the world and highlights the urgent need for countries to implement stronger tobacco control measures to address these costs.

Analysis of Article 6 (tax and price measures to reduce the demand for tobacco products) of the WHO's Framework Convention on Tobacco Control.

Authors: van Walbeek C and Filby S

Reference: Tob Control 2018 Jul 25. pii: tobaccocontrol-2018-054462.

URL: <http://dx.doi.org/10.1136/tobaccocontrol-2018-054462>

Comment: This study analysed the extent to which parties to the WHO Framework Convention on Tobacco Control (FCTC) have implemented Article 6 since the convention's entry into force. The WHO FCTC Article 6 deals with price and tax measures to reduce the demand for tobacco. Compliance was measured using nine indicators, derived from the 2016 version of the FCTC's reporting instrument's core questionnaire, and the WHO's MPOWER cigarette affordability measure. Data were collected from WHO country profiles, and the 12 country mission reports by the Impact Assessment Expert Group. The number of parties reporting any type of excise tax increased from 87% (134/154) in 2008 to 92% (160/174) in 2016. Specific excise tax systems were implemented by 36% (63/174) of FCTC ratifying countries in 2016, up from 32% (49/154) in 2008. The proportion of parties with mixed tax structures has increased from 25% (39/154) in 2008 to 32% (56/174) in 2016. The proportion of parties that levy the tax as a fully ad valorem tax has decreased from 29% (45/154) in 2008 to 24% (42/174) in 2016. Cigarettes have become less affordable in 46% (78/168), more affordable in 13% (21/168) and unchanged in terms of affordability in 41% (69/168) of parties between 2008 and 2016. The number of parties that earmark tobacco tax revenues for public health increased from 13 in 2008 to 30 in

2016. Many finance ministries are hesitant to increase the excise tax, mainly due to illicit trade concerns.

This analysis has shown that there has been some improvement in tobacco tax policy over time. However, parties should adopt stronger tax measures, despite industry opposition and threats about illicit trade.



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