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Dr V K Vijayan, Former Director, Vallabhbhai Patel Chest Institute, University of Delhi, India
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Smoking and mortality- Beyond established causes

Authors: Carter BD et al.

Reference: NEJM 2015; 372: 631-40

URL: <http://www.nejm.org/doi/pdf/10.1056/NEJMsa1407211>

Comment: Mortality among current smokers is 2 to 3 times as high as that among persons who never smoked. Most of this excess mortality has been attributed to 21 common diseases that have been established as caused by cigarette smoking. It is possible that additional diseases can occur in smokers. In that scenario, the current mortality estimates may significantly underestimate the number of deaths attributable to smoking. In this study, the Authors pooled data from five contemporary U.S. cohort studies that included 421,378 men and 532,651 women 55 years of age or older. Participants were followed from 2000 to 2011, and relative risks and 95% confidence intervals were estimated with the use of Cox proportional-hazards models adjusted for age, race, educational level, daily alcohol consumption, and cohort. During the follow-up period, there were 181,377 deaths, including 16,475 among current smokers. Approximately 17% of the excess mortality among current smokers was due to associations with causes that are not currently established as attributable to smoking. These included associations between current smoking and deaths from renal failure (relative risk, 2.0; 95% confidence interval [CI], 1.7 to 2.3), intestinal ischemia (relative risk, 6.0; 95% CI, 4.5 to 8.1), hypertensive heart disease (relative risk, 2.4; 95% CI, 1.9 to 3.0), infections (relative risk, 2.3; 95% CI, 2.0 to 2.7), various respiratory diseases (relative risk, 2.0; 95% CI, 1.6 to 2.4), breast cancer (relative risk, 1.3; 95% CI, 1.2 to 1.5), and prostate cancer (relative risk, 1.4; 95% CI, 1.2 to 1.7). Among former smokers, the relative risk for each of these outcomes declined as the number of years since quitting increased. The Authors conclude that a substantial portion of the excess mortality among current smokers between 2000 and 2011 was due to associations with diseases that have not been formally established as caused by smoking. This study funded by the American Cancer Society underscores that systematic studies reveal occurrence of many diseases not reported earlier due to smoking, highlighting the importance of vigorously executing smoking cessation programs.

Randomized Trial of Four Financial-Incentive Programs for Smoking Cessation

Authors: Halpern SD et al.

Reference: NEJM 2015; 372: 2108-17

URL: <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1414293>

Comment: Though the financial incentives have been found to promote many health behaviors, the effective ways to deliver health incentives remain uncertain especially in smoking cessation programs. In order to find the most suitable financial incentive in smoking cessation, the Authors randomly assigned Caremark employees and their relatives and friends to one of four incentive programs or to usual care for smoking cessation. Two of the incentive programs targeted individuals, and two targeted groups of six participants. One of the individual-oriented programs and one of the group-oriented programs entailed rewards of approximately \$800 for smoking cessation; the others entailed refundable deposits of \$150 plus \$650 in reward payments for successful participants. Usual care included informational resources and free smoking cessation aids. 2538 participants were enrolled in the study. Of those assigned to reward-based programs, 90.0% accepted the assignment, as compared with 13.7% of those assigned to deposit-based programs ($P < 0.001$). In intention-to-treat analyses, rates of sustained abstinence from smoking through 6 months were higher with each of the four incentive programs (range, 9.4 to 16.0%) than with usual care (6.0%) ($P < 0.05$ for all comparisons); the superiority of reward-based programs was sustained through 12 months. Group-oriented and individual-oriented programs were associated with similar 6-month abstinence rates (13.7% and 12.1%, respectively; $P = 0.29$). Reward-based programs were associated with higher abstinence rates than deposit-based programs (15.7% vs. 10.2%, $P < 0.001$). The Authors conclude that reward-based programs were much more commonly accepted than deposit-based programs, leading to higher rates of sustained abstinence from smoking. Group oriented incentive programs were no more effective than individual-oriented programs. However the economic burden of reward-based smoking program will be huge especially in developing countries.

Cytisine versus Nicotine for Smoking Cessation

Authors: Walker N et al.

Reference: NEJM 2014; 371: 2353-62

URL: <http://www.nejm.org/doi/pdf/10.1056/NEJMoa1407764>

Comment: Cytisine is a partial agonist that binds the nicotinic acetylcholine and placebo-controlled trials had indicated that it is useful for smoking cessation. The Authors conducted a study with the hypothesis that cytisine was at least as effective as nicotine-replacement therapy in helping smokers to quit. A pragmatic, open-label, non-inferiority trial was done in 1310 adult daily smokers who were motivated to quit and were randomly assigned in a 1:1 ratio to receive cytisine for 25 days or nicotine-replacement therapy for 8 weeks. Cytisine was provided by mail, free of charge, and nicotine-replacement therapy was provided through vouchers for low-cost patches along with gum or lozenges. Low-intensity, telephone-delivered behavioral support was provided to both groups through the quit line. The primary outcome was self-reported continuous abstinence at 1 month. Continuous abstinence from smoking was reported for 40% of participants receiving cytisine (264 of 655) and 31% of participants receiving nicotine replacement therapy (203 of 655) at one month. The effectiveness of cytisine for continuous abstinence was superior to that of nicotine-replacement therapy at 1 week, 2 months, and 6 months. In a pre-specified subgroup analysis of the primary outcome, cytisine was superior to nicotine-replacement therapy among women and non-inferior among men. Self-reported adverse events over 6 months occurred more frequently in the cytisine group (288 events among 204 participants) than in the group receiving nicotine-replacement therapy (174 events among 134 participants). Adverse events were primarily nausea and vomiting and sleep disorders. Authors conclude that combined with brief behavioral support, cytisine was found to be superior to nicotine-replacement therapy in helping smokers quit smoking, but it was associated with a higher frequency of self-reported adverse events.

Secondhand smoking is associated with vascular inflammation

Authors: Adams T et al.

Reference: Chest 2015; 148(1):112-119

URL: http://journal.publications.chestnet.org/data/Journals/CHEST/934177/chest_148_1_112.pdf

Comment: Secondhand smokers inhale a 100-fold lower dose than that is inhaled by active smokers. However, the relative risk for cardiovascular diseases in passive smokers is similar to

that of active smoker. The Authors undertook a study to investigate the vascular endothelial cell function in passive smokers to understand the mechanisms underlying the susceptibility of the vascular tissue to the toxins in secondhand smoke (SHS). The vascular endothelium for the study was obtained by endothelial biopsy in 23 healthy passive smokers, 25 healthy active smokers, and 23 healthy control subjects who had never smoked and had no regular exposure to SHS. Endothelial nitric oxide synthase (eNOS) function (expression of basal eNOS and activated eNOS [phosphorylated eNOS at serine1177 (P-eNOS)]) and expression of markers of inflammation (nuclear factor- κ B [NF- κ B]) and oxidative stress (nitrotyrosine) were assessed in freshly harvested venous endothelial cells by quantitative immunofluorescence. Vascular reactivity of the brachial artery was measured in the contralateral arm to the endothelial harvesting site by flow-mediated dilation (FMD). There was reduced expression of eNOS and P-eNOS and increased expression of NF- κ B in passive and active smokers compared with control subjects. The expression of nitrotyrosine was greater in active smokers than control subjects and similar in passive and active smokers. Brachial artery flow-mediated dilation was reduced in passive and active smokers compared with control subjects, consistent with reduced endothelial NO bioavailability. This study demonstrates that secondhand smoking increases vascular endothelial inflammation and reduces active eNOS to a similar extent as active cigarette smoking. This study is important due to the fact that it provides a clue for the possible mechanisms involved in the cardiovascular diseases in smokers and suggests that secondhand smoke has adverse effects on cardiovascular system similar to those seen in active smokers.

Estimates of the economic contributions of the bidi manufacturing industry in India.

Authors: Nandi A et al.

Reference: *Tob Control* 2015;**24**:369-375 doi:10.1136/tobaccocontrol-2013-051404

URL: <http://tobaccocontrol.bmj.com/content/24/4/369>

Comment: Bidis is the most common form of tobacco that is consumed in India and in South Asian countries. Bidis are largely untaxed and are subject to very few regulations to discourage their use. The reason put forth for not increasing the tax against bidis is the potential

for the loss of economic activity and employment in the bidi industry as a result of reduced consumption. The Authors conducted a nationally representative survey of unorganised bidi manufacturing firms (n=2841) in India to estimate the economic contribution of the industry. It has been observed that, of the 35 states and union territories of India, the bidi industry operated across 17 states, with over 95% of its production concentrated in 10 states. Bidi manufacturing firms contributed 0.50% of total sales and 0.6% of the gross value added by the manufacturing economy in 2005–2006. The industry employed approximately 3.4 million full-time workers, which comprise about 0.7% of employment in all sectors. A further 0.7 million were part-time workers. Bidi workers were also among the lowest paid employees in India. The industry offered only 0.09% of all compensation provided in the manufacturing sector (organised and unorganised). Authors conclude that there is only a small economic footprint of the bidi industry in India, and higher excise taxes and regulations on bidis are unlikely to disrupt economic growth at an aggregate level, or lead to mass unemployment and economic hardship among small bidi workers. Considering the large economic losses due to bidi related diseases and deaths compared to the small economic footprint of the bidi industry, higher taxes for bidis are justifiable.

Electronic cigarettes: human health effects.

Authors: Callahan-Lyon P.

Reference: Tob Control. 2014 May;23 Suppl 2:ii36-40. doi: 10.1136/tobaccocontrol-2013-051470.

URL: <http://www.ncbi.nlm.nih.gov/pubmed/25301815>

Comments There is a rapid increase globally in the use of electronic cigarettes that deliver a nicotine-containing vapor and these devices are marketed as a “healthier alternative” to conventional cigarettes. However, e-cigarette users and non-users are exposed to the aerosol and product constituents. However, there are no scientific data that have evaluated the safety of these devices and their efficacy in harm reduction and treatment of tobacco dependence. This is a review of published data using multiple electronic databases on the human health effects of exposure to e-cigarettes and their components. Forty-four articles are included in this analysis. E-cigarette aerosols may contain propylene glycol, glycerol, flavourings, other chemicals and, usually, nicotine. Aerosolised propylene glycol and glycerol produce mouth and throat irri-

tation and dry cough. No data on the effects of flavouring inhalation were identified. Data on short-term health effects are limited and there are no adequate data on long-term effects. Aerosol exposure may be associated with respiratory function impairment, and serum cotinine levels are similar to those in traditional cigarette smokers. The high nicotine concentrations of some products increase exposure risks for non-users, particularly children. The dangers of secondhand and thirdhand aerosol exposure have not been thoroughly evaluated. Though the levels of nicotine and toxins in e cigarettes are lower than in conventional cigarettes, the short-term health effects and the long-term carcinogenic and lung function effects of electronic cigarettes are not known. There are reports stating that electronic cigarettes may be effective in reducing conventional cigarette consumption, but the efficacy of electronic cigarettes as a tool to achieve smoking cessation has not been addressed in properly conducted scientifically valid studies. Till then electronic cigarettes cannot recommended for the treatment of tobacco dependence

Maternal smoking and the risk of still birth: systematic review and meta-analysis.

Authors: Marufu TC et al.

Reference: BMC Public Health. 2015 Mar 13;15:239. doi: 10.1186/s12889-015-1552-5.

URL: <http://www.biomedcentral.com/content/pdf/s12889-015-1552-5.pdf>

Comment: Smoking in pregnancy is known to be associated with a range of adverse pregnancy outcomes, yet there is a high prevalence of smoking among pregnant women in many countries, and it remains a major public health concern. The Authors have conducted a systematic review and meta-analysis to provide contemporary estimates of the association between maternal smoking in pregnancy and the risk of stillbirth. The Authors searched four databases namely MEDLINE, EMBASE, Psych Info and Web of Science for all relevant original studies published until 31st December 2012. Observational studies that measured the association between maternal smoking during pregnancy and the risk of stillbirth were included in the study. 1766 studies were screened for title analysis, of which 34 papers (21 cohorts, 8 case controls and 5 cross sectional studies) met the inclusion criteria. In meta-

analysis smoking during pregnancy was significantly associated with a 47% increase in the odds of stillbirth (OR 1.47, 95% CI 1.37, 1.57, $p < 0.0001$). In subgroup analysis, smoking 1-9 cig/day and ≥ 10 cig/day was associated with a 9% and 52% increase in the odds of stillbirth respectively. Subsequently, studies defining stillbirth at ≥ 20 weeks demonstrated a 43% increase in odds for smoking mothers compared to mothers who do not smoke, (OR 1.43, 95% CI 1.32, 1.54, $p < 0.0001$), whereas studies with stillbirth defined at ≥ 24 weeks and ≥ 28 weeks showed 58% and 33% increase in the odds of stillbirth respectively. This meta-analysis confirms a dose-response effect of maternal smoking in pregnancy on risk of stillbirth. Smoking cessation in pregnancy should be a public health priority to minimise the risk of stillbirth

A longitudinal study of electronic cigarette use among a population-based sample of adult smokers: association with smoking cessation and motivation to quit.

Authors: Biener L, Hargraves JL.

Reference: Nicotine Tob Res. 2015 Feb;17(2):127-33. doi: 10.1093/ntr/ntu200. Epub 2014 Oct 9.

URL: <http://www.ncbi.nlm.nih.gov/pubmed/25301815>

Comment There is a perception that the use of e-cigarettes may be a promising development to end cigarette smoking. However, there is no scientifically valid evidence that their use promotes cessation. The Authors investigated whether e-cigarette use increases smoking cessation and/or has a deleterious effect on quitting smoking and motivation to quit. Representative samples of adults in 2 US metropolitan areas were surveyed in 2011/2012 about their use of novel tobacco products. In 2014, follow-up interviews were conducted with 695 of the 1,374 baseline cigarette smokers who had agreed to be re-contacted (retention rate: 51%). The follow-up interview assessed their smoking status and history of electronic cigarette usage. Respondents were categorized as intensive users (used e-cigarettes daily for at least 1 month), intermittent users (used regularly, but not daily for more than 1 month), and non-users/ triers (used e-cigarettes at most once or twice). At follow-up, 23% were intensive users, 29% were intermittent users, 18% had used once or twice, and 30% had not tried e-cigarettes. Logistic regression controlling for demographics and tobacco dependence indicated that intensive

users of e-cigarettes were 6 times more likely than non-users/tryers to report that they quit smoking (OR: 6.07, 95% CI = 1.11, 33.2). No such relationship was seen for intermittent users. There was a negative association between intermittent e-cigarette use and 1 of 2 indicators of motivation to quit at follow-up. Though this study demonstrates daily use of electronic cigarettes for at least 1 month is strongly associated with quitting smoking at follow-up, further longitudinal studies are required in different geographical and socioeconomic groups to understand the role of e cigarettes in smoking cessation. Till then, it is not prudent to recommend e cigarettes for smoking cessation.

Association of Electronic Cigarette Use with Initiation of Combustible Tobacco Product Smoking in Early Adolescence

Authors: Leventhal AM et al

Reference: *JAMA*. 2015;314(7):700-707. doi:10.1001/jama.2015.8950.

URL: <http://jama.jamanetwork.com/article.aspx?articleid=2428954>

Comment The Authors undertook this study to evaluate whether e-cigarette use among 14-year-old adolescents who have never tried combustible tobacco is associated with risk of initiating use of three combustible tobacco products (ie, cigarettes, cigars, and hookah). This study was a longitudinal repeated assessment of a school-based cohort at baseline, at a 6-month follow-up and a 12-month follow-up. Participants were students who reported never using combustible tobacco at baseline and completed follow-up assessments at 6 or 12 months (N = 2530). At each time point, students completed self-report surveys during in-classroom data collections. Past 6-month use of any combustible tobacco product was more frequent in baseline e-cigarette ever users (n = 222) than never users (n = 2308) at the 6-month follow-up (30.7% vs 8.1%, respectively; difference between groups in prevalence rates, 22.7% [95% CI, 16.4%-28.9%]) and at the 12-month follow-up (25.2% vs 9.3%, respectively; difference between groups, 15.9% [95% CI, 10.0%-21.8%]). Baseline e-cigarette use was associated with greater likelihood of use of any combustible tobacco product averaged across the 2 follow-up periods in the unadjusted analyses (odds ratio [OR], 4.27 [95% CI, 3.19-5.71]) and in the analyses adjusted for socio demographic, environmental, and intrapersonal risk factors for smoking (OR, 2.73

[95% CI, 2.00-3.73]). Product-specific analyses showed that baseline e-cigarette use was positively associated with combustible cigarette (OR, 2.65 [95% CI, 1.73-4.05]), cigar (OR, 4.85 [95% CI, 3.38-6.96]), and hookah (OR, 3.25 [95% CI, 2.29-4.62]) use and with the number of different combustible products used (OR, 4.26 [95% CI, 3.16-5.74]) averaged across the 2 follow-up periods. This study suggests that use of e-cigarettes is prospectively associated with initiation of combustible tobacco product use among teen agers. This has great public health importance as e cigarette use may promote initiation of conventional cigarette smoking especially in children.

Association of Smoking Status with Angina and Health-Related Quality of Life after Acute Myocardial Infarction

Authors: Buchanan DM et al.

Reference: Circ Cardiovasc Qual Outcomes. 2015;8:00-00. DOI: 10.1161/ Circoutcomes.114.001545.

URL: <http://circoutcomes.ahajournals.org>

Comment: Though it is known that smoking cessation after acute myocardial infarction (AMI) decreases the risk of recurrent AMI and mortality by 30% to 50%, many patients continue to smoke after AMI. The Authors undertook a study to know the association of smoking with angina and health-related quality of life (HRQOL) after AMI. Patients in 2 US multicenter AMI registries (n=4003) were assessed for smoking and HRQOL at admission and 1, 6, and 12 months after AMI. Angina and HRQOL were measured with the Seattle Angina Questionnaire and Short Form-12 Physical and Mental Component Scales. At admission, 29% never had smoked, 34% were former smokers (quit before AMI), and 37% were active smokers, of whom 46% quit by 1 year (recent quitters). In hierarchical, multivariable, regression models that adjusted for socio-demographic, clinical and treatment factors, never and former smokers had similar and the best HRQOL in all domains. Recent quitters had intermediate HRQOL levels, with angina and Short Form-12 Mental Component Scale scores similar to never smokers. Persistent smokers had worse HRQOL in all domains compared with never smokers and worse Short Form-12 Mental Component Scale scores than recent quitters. The Authors conclude that

smoking after AMI is associated with more angina and worse HRQOL in all domains, whereas smokers who quit after AMI have similar angina levels and mental health as never smokers. This study further emphasizes the need for all patients who had suffered acute myocardial infarction should quit smoking.

Effects of quitting cannabis on respiratory symptoms.

Authors: Hancox RJ et al.

Reference: Eur Respir J 2015; 46: 80–87 | DOI: 10.1183/09031936.00228914.

URL: <http://www.ncbi.nlm.nih.gov/pubmed/25837035>

Comment: Studies had indicated that smoking cannabis can cause symptoms of bronchitis independently of tobacco. It is also known that prolonged tobacco smoking can cause irreversible airway obstruction and the cessation of tobacco smoking often leads to the resolution of respiratory symptoms within months of quitting. However, there are not many studies that had addressed whether quitting cannabis leads to a similar resolution of symptoms. The Authors assessed associations between changes in cannabis use and respiratory symptoms in a population-based cohort of 1037 young adults. The participants were asked about cannabis and tobacco use at ages 18, 21, 26, 32 and 38 years. Symptoms of morning cough, sputum production, wheeze, dyspnoea on exertion and asthma diagnoses were ascertained at the same ages. Frequent cannabis use was defined as ≥ 52 occasions over the previous year. Associations between frequent cannabis use and respiratory symptoms were analysed using generalized estimating equations with adjustments for tobacco smoking, asthma, sex and age. Frequent cannabis use was associated with morning cough (OR 1.97, $p < 0.001$), sputum production (OR 2.31, $p < 0.001$) and wheeze (OR 1.55, $p < 0.001$). Reducing or quitting cannabis use was associated with reductions in the prevalence of cough, sputum and wheeze to levels similar to nonusers. This study demonstrates that frequent cannabis use is associated with symptoms of bronchitis in young adults and reducing cannabis use often leads to a resolution of these symptoms. However studies are required to know whether airway obstruction occurs in cannabis users and quitting cannabis use is associated with resolution of airway obstruction (if present) along with resolution of respiratory symptoms.

Do smokers support smoke-free laws to help themselves quit smoking? Findings from a longitudinal study

Authors: Nagelhout GE et al.

Reference: *Tob Control* 2015;**24**:233-237 doi:10.1136/tobaccocontrol-2013-051255

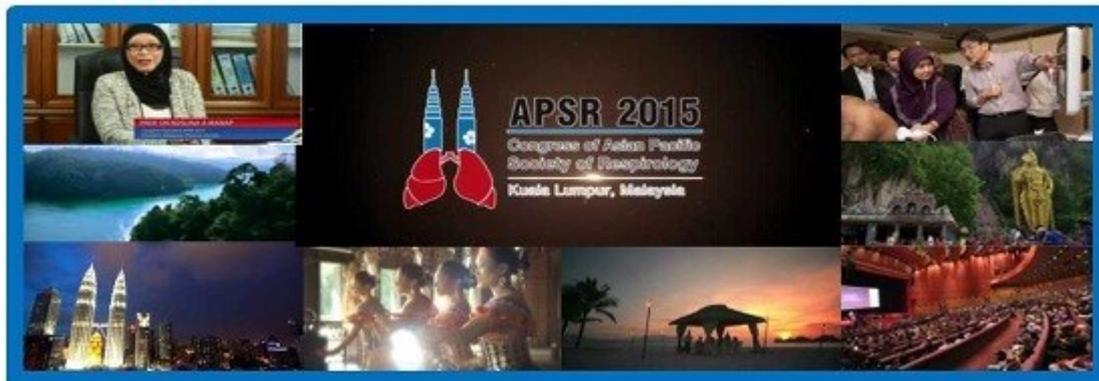
URL: <http://tobaccocontrol.bmj.com/content/24/3/233.full.pdf>

Comment A large number of smokers support smoke-free laws. One possible explanation for why smokers support laws that would restrict their own behavior is the theory of self-control. The laws could serve as a self-control device for smokers who are trying to quit. The Authors planned a study to test the hypothesis that support for smoke-free laws predicts smoking cessation. Longitudinal data (1999–2000) from a US national sample of adult smokers (n=6415) from the Current Population Survey, Tobacco Use Supplements were analysed for the study. At baseline, smokers were asked whether they made a quit attempt in the past year. They were also asked whether they thought smoking should not be allowed in hospitals, indoor sporting events, indoor shopping malls, indoor work areas, restaurants, or bars and cocktail lounges. At 1-year follow-up, smokers were asked whether they had quit smoking. The study has demonstrated that smokers who supported smoke-free laws were more likely to have made a recent quit attempt. At 1-year follow-up, those who supported smoke-free laws in 4–6 venues were more likely to have quit smoking (14.8%) than smokers who supported smoke-free laws in 1–3 venues (10.6%) or smokers who supported smoke-free laws in none of the venues (8.0%). These differences were statistically significant in multivariate analyses controlling for demographics. This study demonstrates that smoke free laws may help smokers to quit smoking if such individuals have a desire to quit smoking.

More on this topic in Respiriology:

[Daube, M., Eastwood, P., Mishima, M. and Peters, M. \(2015\), Tobacco plain packaging: The Australian experience. *Respirology*, 20: 1001–1003. doi: 10.1111/resp.12621](#)

[Lam, D. C.L., Nana, A., Eastwood, P. R. and Asian-Pacific Society of Respiriology \(APSR\) \(2014\), Electronic cigarettes: 'Vaping' has unproven benefits and potential harm. *Respirology*, 19: 945–947. doi: 10.1111/resp.12374](#)

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