# Pulmonary Disease and PWH

Joe Caperna, MD

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- HIV infection causes alteration in several lines of host defenses in the lung and respiratory tract that contribute to an increased risk for lung complications. These alterations include abnormalities in mucociliary function and soluble defense molecules, such as defensins within respiratory secretions. Within the lung parenchyma, innate and adaptive immune responses to pathogens may be impaired. For example, alveolar macrophages from HIV-infected individuals have been shown to be deficient in pathogen recognition. HIV also results in chronic stimulation and activation of inflammatory cells within the alveolar space. Although immunologic abnormalities are most marked in those who do not use ART, recent data demonstrate that, although ART restores immune function, inflammation and immunodeficiency may persist, particularly in patients who initiate ART at lower $CD4^+$ lymphocyte counts. (Proc Am Thorac Soc., 2011)

# Patients on ART

- In asymptomatic HIV-infected patients, immune responses and signaling pathways may be abnormal even among those on ART. Risk for premature comorbidities, such as cardiovascular disease, renal, and liver disease, has been associated with residual inflammation and immunodeficiency despite treatment with ART. A possible association of ART with airflow obstruction has been suggested, although ART has not been found to have direct toxic effects on the lungs. The consequences of persistently increased inflammation and the effects of ART on the pathogenesis of lung complications in HIV-infected persons are poorly understood. (Proc Am Thorac Soc., 2011)

# Lung Complications and PWH

- The spectrum of lung complications associated with HIV is broad, and many infectious and noninfectious complications have been recognized. These complications include diseases that are AIDS-defining or HIV-associated (e.g., *Pneumocystis* pneumonia [PCP], tuberculosis [TB], or bacterial pneumonia), disorders that are not classified as AIDS-defining but are more common in patients with HIV infection (e.g., lung cancer, pulmonary arterial hypertension, and chronic obstructive pulmonary disease), and conditions whose association with HIV is inconclusive or coincidental (e.g., sarcoidosis). In addition, lung complications can result from immune reconstitution inflammatory syndrome (also called immune reconstitution syndrome), which may occur after initiation of ART. (Proc Am Thorac Soc., 2011)

# Noninfectious Complications

- Because more people are living with HIV/AIDS and are living longer, noninfectious complications and comorbid illnesses have increased in frequency. In addition to an increased risk for infectious pulmonary diseases, HIV-infected persons appear to have an increased risk for several noninfectious pulmonary conditions, including chronic obstructive pulmonary disease (COPD), lung cancer, and pulmonary arterial hypertension. HIV infection has been associated with several different manifestations of COPD and airway abnormalities, including features of emphysema, chronic bronchitis, nonspecific airway abnormalities, and bronchial hyperresponsiveness. In one study of 114 HIV-infected persons compared with 44 age-, sex-, and smoking-matched HIV-uninfected control subjects, 15% of the HIV-infected persons had emphysema on CT scan, compared with only 2% of non–HIV-infected persons ($P = 0.025$). Another study found that HIV infection was associated with a 50 to 60% increased odds of COPD diagnosis. (Proc Am Thorac Soc., 2011)

# Flu Vaccine

- **Summary of Recommendations**
- For all adults and adolescents with HIV, administer age-appropriate inactivated influenza vaccine or recombinant influenza vaccine annually **(AI).**
- For pregnant people with HIV, administer inactivated influenza or recombinant vaccine at any time during pregnancy **(AI).**
- LAIV administered via nasal spray **is contraindicated** in people with HIV **(AIII).** Although a LAIV is available, it **is contraindicated** for people with HIV because of the paucity of safety data and the availability of alternative vaccines. Although unintentional administration of LAIV to adults with HIV has been well tolerated, **it is not recommended** for people with HIV.
- High-dose, recombinant, and adjuvanted influenza vaccines are recommended for people with HIV aged 65 years or older over standard-dose unadjuvanted inactivated vaccines **(AII).**[28]

# Pneumonia Vaccine

- For all people with HIV without a history of pneumococcal vaccination or with unknown vaccine history:
- Administer either 20-valent pneumococcal conjugate vaccine (PCV20) or PCV15 **(AII).**
- If PCV15 is used, administer a dose of PPSV23 at least 8 weeks later **(AII).**No additional pneumococcal vaccine doses are recommended.
- For people with HIV who previously started or completed a pneumococcal vaccination series, there is no need to restart the series.
- People with HIV who received PCV13 and were 65 years or older when they received a dose of PPSV23 do not require further doses of PPSV23. Shared clinical decision-making is recommended regarding administration of PCV20 for adults aged ≥65 years who completed their vaccine series with both PCV13 and PPSV23. If a decision to administer PCV20 is made, a dose of PCV20 is recommended at least 5 years after the last pneumococcal vaccine dose **(CIII).**
- For people with HIV who received PCV13 and were younger than 65 when they received a dose of PPSV23, one dose of PCV20 administered at least 5 years after may be used to complete their pneumococcal vaccinations **(CIII)** or additional doses of PPSV23 are recommended as indicated below **(BIII).**
    - People with HIV who have received PCV13 and PPSV23 at age <65 should receive a second dose of PPSV23 at least 5 years after the first dose. If they are age 65 or older at the time of their second dose, they do not require additional doses of PPSV23.
    - If they were <65 at the time of the second dose, they should receive a third and final dose at or after age 65, at least 5 years after the second PPSV23 dose.
- People with HIV who have only received PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose to complete their pneumococcal vaccination series **(BIII).**
- People with HIV who previously received only the PCV13 should receive one dose of PCV20 at least 1 year later **or** receive PPSV23 at least 8 weeks later and then complete the PPSV23 series as recommended above **(BIII).**
- In June 2024, the ACIP recommended 21-valent PCV (PCV21) as an option for adults aged ≥19 years who are currently recommended to receive PCV15 or PCV20. Data and recommendations for PCV21 are currently under review in this guideline.

# RSV Vaccine

- In May 2023, the United States Food and **Drug** Administration approved the first two RSV vaccines for adults ≥60 years of age: RSVPreF3 (Arexvy) and RSVpreF (Abrysvo). Both vaccines target the prefusion F protein on the viral surface. mRNA-1345 (mRESVIA) is an mRNA-based RSV vaccine encoding the stabilized RSV prefusion F glycoprotein. In a trial of more than 35,000 participants 60 years and older, the vaccine demonstrated greater than 80% efficacy against RSV-related lower respiratory tract disease. Administration of a single respiratory syncytial vaccine (RSV) (Abrysvo, Arexvy, or mRESVIA) to all people with HIV ≥75 years old is recommended **(CIII).**
- Administration of a single RSV vaccine for people ages 60 to 74 with HIV and CD4 <200cells/$mm^3$ or with comorbid chronic conditions that increase risk for severe RSV disease is recommended..
- For pregnant people with HIV, administration of a single RSV vaccine (Abrysvo) between 32 and 36 weeks gestation with seasonal administration during September through January in most of the continental United States is recommended **(CIII).**
- No booster doses are currently recommended (**CIII).**

- Rates of lung cancer have been reported to be substantially increased among HIV-infected persons, even after controlling for the higher prevalence of smoking in this population. In one study, HIV infection was independently associated with a hazard ratio of 3.6 for lung cancer (95% confidence interval, 1.6–7.9). Similarly, in another study, HIV infection was associated with a standardized incidence ratio of 2.5 (95% confidence interval, 1.6–3.5) for lung cancer, adjusting for estimates of smoking prevalence.

- Our understanding of the prevalence, consequences, and mechanisms that account for the increased risk of noninfectious pulmonary conditions associated with HIV infection are not well understood. For example, studies have not addressed the role of screening (e.g., with pulmonary function testing to detect COPD or chest imaging to detect lung cancer), nor have they assessed treatment of these diseases in the setting of HIV. Little is known regarding the impact of chronic lung diseases on morbidity, including risk for lung infections and cardiac disease, as well as mortality and patient-centered outcomes such as quality of life. Effective methods to decrease smoking prevalence among HIV-infected populations are needed.

- The World Health Organization estimates that smoking poses one of the greatest global health risks in the general population. After high blood pressure, smoking is ranked second among the 10 leading risk factors in the world causing death, and is ranked first in high-income countries. Smoking substantially increases the risk of death from lung and other cancers, heart disease, stroke and respiratory disease. Globally, smoking causes 71% of lung cancers, 42% of chronic respiratory disease, 10% of cardiovascular disease, and is responsible for 12% of male deaths and 6% of female deaths. (*AIDS Res Ther, 2018)*

- Rates of current smoking among people living with HIV (PLHIV) are 2–3 times that of the general population, which contributes to the higher incidence of non-AIDS-related morbidity and mortality in PLHIV. Given the benefit of smoking cessation, strategies to assist individuals who smoke to quit should be a primary focus in modern HIV care. Tobacco harm reduction focuses on reducing health risk without necessarily requiring abstinence. However, there remains uncertainty about the safety, policy and familiarity of specific approaches, particularly the use of vaporised nicotine products. Evidence suggests that vaporised nicotine products may help smokers stop smoking and are not associated with any serious side-effects. However, there is the need for further safety and efficacy data surrounding interventions to assist quitting in the general population, as well as in PLHIV specifically.

- In a study from Denmark, where antiretroviral therapy is free and HIV care is well organized, PLHIV who smoked lost more life-years to smoking than to HIV (12.3 years life lost associated with smoking versus 5.1 years life lost associated with HIV status). The excess mortality of smokers was tripled among those who were HIV-positive, compared to the background population and the population attributable risk of death associated with smoking was 61% among HIV positive patients compared with 34% among controls. Similar impacts on life expectancy among PLHIV have been reported from other European countries and North America. Importantly, those who quit smoking had a 40% lower risk of death compared with current smokers. (Clin Infect Dis, 2013)

- Cardiovascular disease and non-AIDS malignancies have become major causes of death among people living with HIV (PLHIV) [3]. The relative impact of HIV-related factors versus lifestyle factors, such as smoking, on these causes of death is often debated. Many cohort studies have reported higher rates of smoking among PLHIV than the general population. In a nationwide, population-based cohort study, all-cause and non-AIDS-related mortality was reported as higher among smoking compared with non-smoking PLHIV (mortality rate ratio 4.4, 95% confidence interval 3.0–6.7). (PLoS ONE, 2016) In addition PLHIV are at higher risk than non-smokers with HIV of developing bacterial pneumonia, *Pneumocystis jiroveci* pneumonia and COPD. (JAMA, 2013)

- Approximately 27% of cancers in PLHIV are attributable to smoking. (AIDS, 2015) In the absence of smoking, the risk of cancers unrelated to viral infections is not elevated and is similar to other morbidities, and the incidence for both infection- and non-infection-related malignancies increases with age. Unlike the early benefits seen for myocardial infarction risk after quitting smoking, the lung cancer risk remains elevated, with no decline in incidence observed over 7–8 years after stopping in a cohort study of PLHIV. However, in a microsimulation model-based analysis, quitting smoking did eventually impact the risk of lung cancer in people living with HIV, albeit over a lifetime. (JAMA, 2017)

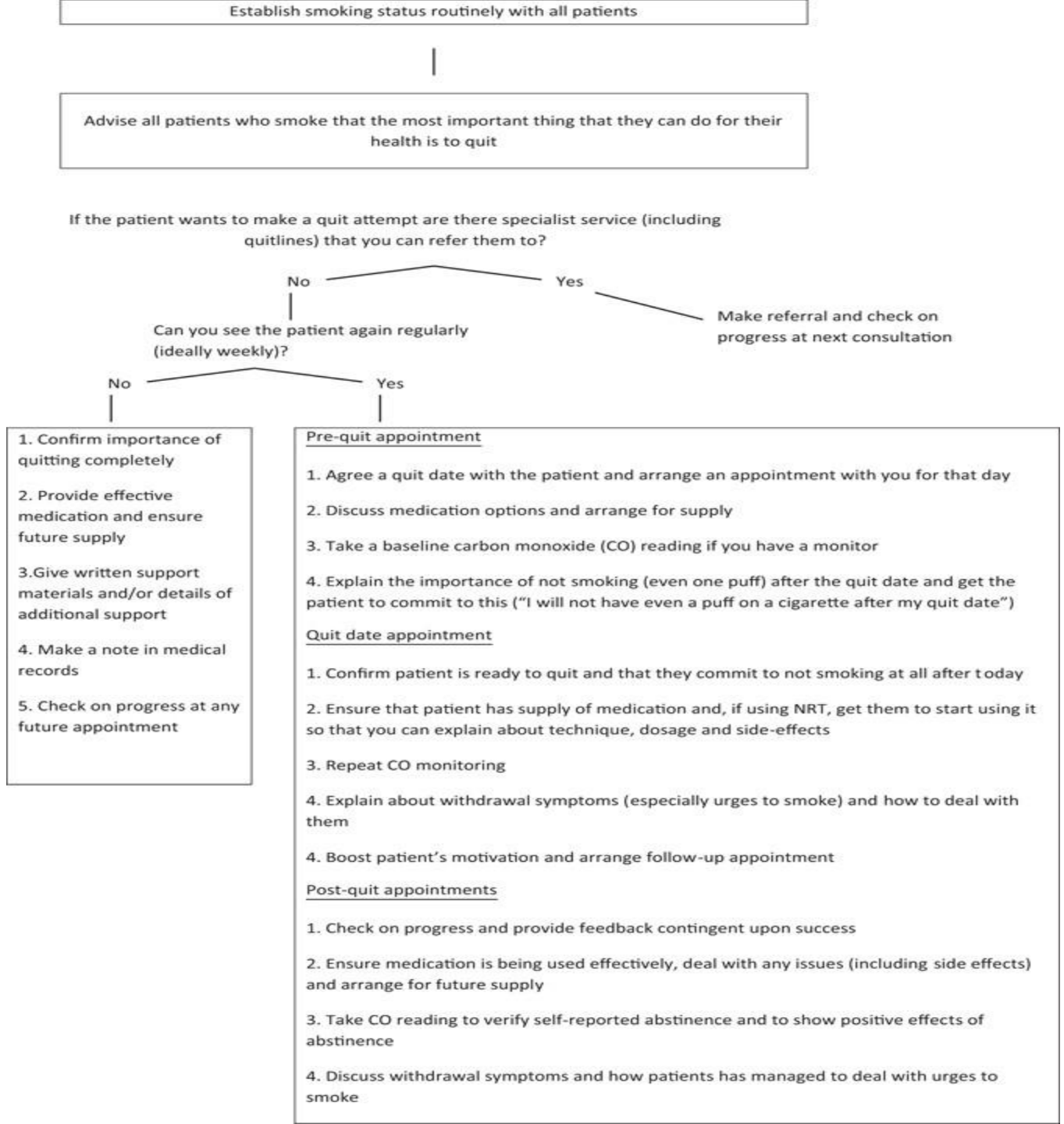
- Unfortunately, smoking is a difficult addiction to break with reports that 80% of smokers who attempt to quit on their own relapse within 1 month and only 5% achieve long-term abstinence. (Addiction, 2004) Tobacco harm reduction strategies are based on the utilization of innovative tobacco products, reduced tobacco consumption and pharmaceutical medication. In a systematic review published in 2016, there was evidence supporting nicotine replacement therapy (albeit assessed as low quality) but a lack of evidence for other harm reduction aids such as behavioral support. (Cochrane Database Rev, 2016)

- Barriers identified to addressing smoking among PLHIV by health practitioners have included lack of confidence in nicotine replacement prescribing, competing priorities, lack of skills or knowledge, uncertainty around referral pathways and lack of confidence in the patient's ability to quit. (Drug Alcohol Depend, 2017) In addition to practitioner barriers, there are unique challenges faced by HIV-positive individuals that may impact on attempts to stop smoking such as engagement in HIV care, concurrent substance use and antiretroviral adherence. (AIDS Behav., 2017)

# From: Treating tobacco dependence: guidance for primary care on life-saving interventions. Position statement of the IPCRG

[a] Recommendations graded according to the Scottish Intercollegiate Guidelines Network system (described at http://www.bmj.com/cgi/content/full/323/7308/334 accessed January 2008)

| Recommendation | Grade[a] |
|---|---|
| Make your practice "smoke free" by banning smoking on the premises, displaying information on smoking cessation in the waiting room, asking every patient about smoking status, and promoting smoking cessation services | B |
| Opportunistically provide brief, clear advice to quit whenever appropriate (doctors) and offer available assistance with any quit attempt | A |
| Train practice nurses and other staff to encourage smokers to quit and offer assistance | C |
| Recommend a local telephone counselling service ("quit line"), where available, to all smokers who indicate interest in quitting | A |
| Consider prescribing drug treatment for tobacco dependence (e.g., nicotine replacement therapy, bupropion, varenicline) to people who smoke 10 or more cigarettes per day, after consideration of contraindications and comorbidity | A |
| Tailor your approach to smoking cessation advice or treatment to the individual's degree of readiness to quit | D |
| Use a non-judgemental communication style | C |
| Use motivational interviewing techniques[b] to help people understand their own attitudes to smoking and quitting, make their own decisions and solve problems encountered during a quit attempt | B |
| Provide or arrange intensive behavioural counselling, where resources permit | A |


Establish smoking status routinely with all patients
Advise all patients who smoke that the most important thing that they can do for their health is to quit
If the patient wants to make a quit attempt are there specialist service (including quitlines) that you can refer them to?
No
Yes
Make referral and check on progress at next consultation
Can you see the patient again regularly (ideally weekly)?
No
Yes
1. Confirm importance of quitting completely
2. Provide effective medication and ensure future supply
3.Give written support materials and/or details of additional support
4. Make a note in medical records
5. Check on progress at any future appointment
Pre-quit appointment
1. Agree a quit date with the patient and arrange an appointment with you for that day
2. Discuss medication options and arrange for supply
3. Take a baseline carbon monoxide (CO) reading if you have a monitor
4. Explain the importance of not smoking (even one puff) after the quit date and get the patient to commit to this ("I will not have even a puff on a cigarette after my quit date")
Quit date appointment
1. Confirm patient is ready to quit and that they commit to not smoking at all after today
2. Ensure that patient has supply of medication and, if using NRT, get them to start using it so that you can explain about technique, dosage and side-effects
3. Repeat CO monitoring
4. Explain about withdrawal symptoms (especially urges to smoke) and how to deal with them
4. Boost patient's motivation and arrange follow-up appointment
Post-quit appointments
1. Check on progress and provide feedback contingent upon success
2. Ensure medication is being used effectively, deal with any issues (including side effects) and arrange for future supply
3. Take CO reading to verify self-reported abstinence and to show positive effects of abstinence
4. Discuss withdrawal symptoms and how patients has managed to deal with urges to smoke

# Pharmacotherapy

- Prescribe drug treatment for tobacco dependence as indicated. Pharmacotherapy, particularly when accompanied by behavioral support, significantly improves long-term quit rates compared with no treatment or placebo. Pharmacotherapy should be offered to people who smoke 10 or more cigarettes per day or who smoke within 30–60 min of waking, after consideration of contraindications and comorbidity. (Tob Control, 2002) Selection of pharmacotherapy is based on clinical suitability, availability and patient choice.

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| Medication[a]: |
| Any patient smoking more than 10 cigarettes a day or who smoke within 30 -60 minutes of waking will suffer from withdrawal symptoms and should be offered pharmacological support once they set a quit date. Remember to offer psychological support during the first 3 months of the cessation attempt |
| Nicotine replacement therapy (*NRT*) |
| NRT should not be combined with smoking. Its main effect is to reduce abstinence and help the patient through the first couple of months of craving. Most patients use too low doses for too short a time. They should use a dose that takes away abstinence symptoms. Most people need a full dose for 2–3 months, then they might gradually reduce the use over some months. Added success has been shown if NRT is started 14 days prior to quit date |
| Dosage: It is often wise to combine two different NRTs—a patch to cover most of the day and gum or other types of NRT (e.g. spray) for craving situations during daytime |
| Patch: Comes in 14 mg/24 h or 10 mg/16 h for light smokers or in 21 mg/24 h—15 mg/16 h for more heavy smokers. Some patients need more than one patch a day to keep the symptoms low |
| Side effects: Skin rash, allergy, insomnia, wild dreams |
| Gum, inhalers, lozenges, sublingual tablets: To be administered every 1–2 h for relief of symptoms while awake. Since nicotine is absorbed through the mucosa in the mouth it is important to instruct the patient in the use of gum carefully. Chew a few times on the gum then "park" it in the mouth |
| Side effects: local-sore dry mouth, dyspepsia, nausea, headache, jaw ache. Often dose dependent |
| Contraindication: Pregnancy (in some countries) |
| Varenicline (©Champix, ©Chantix) |
| Varenicline is a nicotinic receptor partial agonist. In addition to blocking the receptor it also stimulates it thus reducing abstinence. It is the first drug designed for smoking cessation. Results are promising with quit rates up to 44% in some studies |
| Dosage: Start 1 week before quit date: 0.5 mg for 3 days, 0.5 mg bid for 4 days, then 1 mg bid from quit date for 12 weeks |
| Side effects: nausea and headache. There is no danger of seizures. Risk of psychiatric side effects is the same as for other smoking cessation medications |
| Contraindication: Pregnancy |
| Bupropion (©Zyban) |
| Bupropion is the first medication proven to reduce the craving |
| Dosage: twice daily starting with one tablet a day for a week two weeks prior to quit date, then regularly 150 mg bid from quit date for 7–12 weeks |
| Adverse effects: insomnia, headache, dry mouth, dizziness, anxiety |
| Contraindications: Seizures, pregnancy, major depression, schizophrenia, drugs for treating depression or schizophrenia |
| |

# Harm Reduction

- For people who do not want, or who feel unable, to stop smoking, it could be beneficial to try to reduce harm from continued tobacco use. Options include reducing the amount of tobacco used; cutting down only or prior to stopping smoking (“cutting down to quit”) and smoking reduction and temporary abstinence from smoking. There is some evidence that smokers who regularly engage in temporary abstinence with the use of NRT are more likely to stop smoking in the future and there is evidence to support use of nicotine replacement prior to smoking cessation. Smokers who use NRT for smoking reduction are approximately twice as likely to progress to quitting than those who do not. (NICE Guidelines, 2013)

# e-cigarettes

- Based on the concentrations of chemicals in e-cigarettes, vapor would be expected to be less harmful than smoking, though not free of risk. The Royal College of Physicians and Public Health England have estimated that the risk of long-term use of e-cigarettes is unlikely to exceed 5% of the harm done as a result of smoking tobacco. As the evidence accumulates recommendations may change but at present it is recommended that patients be advised to use methods of quitting with strong evidence for effectiveness where these are available. If patients ask about e-cigarettes, they should be informed that there is currently little hard evidence on the effectiveness of e-cigarettes in smoking cessation. They should also be told that while they are likely to be substantially safer than smoking, they probably do carry some risk and long-term use should be avoided if possible. On the basis of current evidence, they should also be told that use of an e-cigarette may impede their chances of quitting smoking at a later date. E-cigarettes should never be advised as a life-style choice. (NEJM, 2016)