

Smoking Cessation and Mental Health Populations—Speaker’s Notes

Updated March 2016

Slide 4: Smoking Rate by Psychiatric History in VA

Analysis of 2007 VHA Outpatient Survey of Healthcare Experiences of Patients, smoking rate has been updated to reflect data from the 2015 Survey of Veteran Enrollees

Slide 5: Tobacco Use by Smokers with Mental Health Disorders: Changes in Prevalence

Between 2004 and 2011, the decline in smoking among individuals with mental illness was significantly less than among those without mental illness. This suggests that tobacco control policies and cessation interventions targeting the general population have not worked as effectively for persons with mental illness.

Slide 6: Tobacco Use by Smokers with Mental Health Disorders: Percent of Cigarettes Smoked Past Month

On an average day, adults aged 18 or older smoked 588 million cigarettes. Adults with AMI or SUD represent 24.8 percent of adults. However, they used 39.6 percent of all cigarettes smoked by adults.

Slide 7: Tobacco Kills People with Mental Illness

On average, in the general population, female and male smokers die 13.2 & 14.5 years earlier than nonsmokers (*MMWR* 2002; 51:300).

A recent report from the US Center for Mental Health Services estimates that on average individuals with serious mental illness are dying 25 years prematurely, with major causes of death being chronic, tobacco-related diseases (Colton & Manderscheid, 2006). The mentally ill are at elevated risk for respiratory and cardiovascular diseases and cancer, compared to age-matched controls (Brown et al., 2000; Bruce et al., 1994; Dalton et al., 2002; Himelhoch et al., 2004; Lichtermann et al., 2001; Sokal et al., 2004).

Current tobacco use is predictive of future suicidal behavior, independent of depressive symptoms, prior suicidal acts, and other substance use (Breslau et al., 2005; Oquendo et al., 2004, Potkin et al., 2003).

Slide 8: Tobacco Use Complicates Psychiatric Treatment

Tobacco smoke may interact with medications through pharmacokinetic or pharmacodynamic mechanisms. **Pharmacokinetic interactions** affect the absorption, distribution, metabolism, or elimination of other drugs, potentially causing an altered response.

Polycyclic aromatic hydrocarbons (PAHs) in tobacco are responsible for induction of **cytochrome P450 enzymes** (CYP1A1, CYP1A2, and possibly CYP2E1 and CYP3A). The majority of drug interactions with

tobacco smoke are pharmacokinetic, resulting from the induction of drug-metabolizing enzymes (especially CYP1A2) by compounds in tobacco smoke. All of these drugs are metabolized via CYP1A2. Induction of CYP1A2 by PAHs in tobacco smoke will increase metabolism, resulting in potentially clinically significant decreased pharmacologic effects of the following drugs. **Following smoking cessation, a patient titrated on these medications may experience enhanced pharmacologic effects or toxicity:**

Bendamustine (Treanda): Bendamustine is metabolized by CYP1A2. Manufacturer recommends caution in using this drug in smokers as lower bendamustine concentrations may occur, with increased concentrations of its 2 active metabolites (Cephalon, Inc, 2008).

Caffeine: Clearance is increased by 56%. It is reasonable to advise patients to decrease their intake of caffeinated beverages when quitting smoking, because nicotine withdrawal effects might be enhanced by increased caffeine levels.

Clozapine (Clozaril): Studies have shown mixed results on the clinically significant changes in clozapine levels in smokers. However, upon cessation, a mean increase of 57.4% in clozapine levels has been demonstrated. Doses should be closely monitored upon smoking cessation to avoid high levels and increased toxicity (Meyer 2001).

Erlotinib (Tarceva): Clearance of this injectable antineoplastic agent used for pancreatic and non-small cell lung cancer is increased 24% with ~2-fold lower trough concentrations compared to nonsmokers (OSI Pharmaceuticals, 2007).

Fluvoxamine (Luvox): Clearance of this antidepressant is increased by 24%; plasma concentrations are decreased by 32%. Yoshimura et al. (2002) determined that plasma fluvoxamine concentrations were significantly lower in smokers (by 39%) compared with nonsmokers. Dosage modifications are not routinely recommended, but smokers might require higher dosages.

Inhaled insulin: The absorption of inhaled insulin (Exubera) was shown to be increased 2- to 5-fold in smokers when compared to non-smokers (Pfizer, 2006). While Exubera was removed from the market in 2007, future inhaled insulin products may be released so assessment of smoking status will be important before using an inhaled insulin.

Olanzapine (Zyprexa): Clearance of this atypical antipsychotic is increased by 40–98%. Gex-Fabry et al. (2003) showed that smokers had significantly lower concentrations (by 12%) compared with nonsmokers. Dosage modifications are not routinely recommended, but smokers might require higher dosages to achieve clinical response (Carrillo et al. 2003).

Ropinirole (Requip): Plasma concentrations may be reduced in smokers and dose increase may be required. In a study of patients with restless leg syndrome, C_{max} and AUC were reduced by 38% and 30% respectively in smokers compared to nonsmokers (GlaxoSmithKline, 2006).

Tacrine (Cognex): Clearance is substantially increased in smokers. The manufacturer states that mean plasma tacrine concentrations in smokers are threefold lower than those achieved in nonsmokers. The half-life of tacrine is decreased by 50%. Smokers might require higher dosages.

Theophylline: Clearance is increased by 58–100%; half-life is decreased by 63%. Closely monitor theophylline levels if smoking is initiated, discontinued, or changed. Maintenance doses are considerably higher in smokers. Within 7 days of smoking cessation, theophylline clearance might decrease by 35%. *Note:* A similar interaction occurs with aminophylline.

PAHs also induce the enzymes involved in glucuronic acid conjugation. Propranolol, mexiletine and codeine have been reported to have increased rates of glucuronidation in smokers. **Irinotecan (Camptosar):** Clearance of this antineoplastic agent for colorectal cancer is increased by 18%; lower levels of irinotecan and its active metabolite, SN-38 (~40% lower) occur mainly due to induction of the UGT1A1, which conjugates SN-38 and possibly CYP3A. Reduced systemic exposure of SN-38 results in lower toxicity (e.g., hematologic) and likely reduced efficacy; dose increases may be required (van der Bol 2007; Benowitz 2007).

Q&A with Dr. Neal Benowitz

1. What level of tobacco use is needed to have the drug interactions? Is it a dose response relationship?
 - Not much data about this. Without the data, the assumption is that any smoker is susceptible to the same degree of interaction.
2. Does nicotine have any drug interaction effects?
 - Nicotine should not affect drug metabolism. Nicotine, however, may interact via its stimulant effects and reduce the sedation caused by other drugs
3. How long does it take to see drug interaction effects with smoking tobacco?
 - Enzyme induction begins within a few days and peaks probably in a week or so. De-induction begins rapidly, but may also take a week or two to see full dissipation of effects.

Slide 9: Limited Integration of Smoking Cessation into MH and SUD Care

The Clinical Practice Guidelines (CPG) highlight explicitly state that smoking cessation should be addressed for smokers with psychiatric disorders in a manner similar to that of other smokers. Yet smoking is not consistently addressed in mental health settings, SUD treatment programs or by mental health providers. **One potential solution to providing tobacco cessation treatment to smokers with psychiatric disorders is to integrate treatment into mental health care settings and programs.**

Slide 10: Tobacco Use by People with Mental Illness is a Health Disparity

Groups with health disparities are referred to as vulnerable or priority populations. Mentally ill smokers meet the definition of a disparity group as they experience disproportionate tobacco consumption, disproportionate consequences or health burden from tobacco use, disproportionate economic burden

from tobacco use, and limited access to tobacco-related health care. Despite this situation major tobacco control organizations have not identified this population as a disparity group. However, future tobacco control efforts should prioritize smokers with mental illness, **as the largest provider of Mental Health care in the US the VA is well positioned to play such a role.**

Slides 11, 12 & 13: Barriers to Addressing Smoking: Myths About Tobacco Use and Mental Illness

These common beliefs regarding smoking among individuals with mental illness pose a significant barrier to addressing tobacco use in this population. As clearly addressed in the article by Prochaska, these myths are not based in reality and need to be countered to increase attention to smoking by individuals with psychiatric disorders.

Slide 14: Readiness to Quit in Patients with Psychiatric Disorders

Recent studies of readiness to quit among individuals with mental illness indicate over 20% are intending to quit in the next 30 days (Preparation stage of change) and another 40% intend to quit in the next 6 months (Contemplation stage). These rates are comparable to those reported in the general population. Further, the studies have reported no relationship between severity of psychiatric symptoms and intention to quit smoking. **Thus, smokers with psychiatric disorders want to quit and are therefore amenable to intervention. The question becomes how best to assist and support their efforts to stop smoking.**

Slide 15: Quit Rates in Patients with Psychiatric Disorders

Smoking quit rate defined as proportion of lifetime smokers who were not current smokers, a commonly used approach in epidemiological studies of smoking. These data demonstrate clearly that although quit rates are lower among smokers with psychiatric disorders, they are able to and do quit smoking. **The question becomes how best to assist and support their efforts to stop smoking.**

Slide 16: Smoking and Substance Use Disorder

Among individuals treated for alcohol dependence, tobacco-related diseases were responsible for half of all deaths, greater than alcohol-related causes (Hurt & Offord 1996). In a 24-year study of long-term drug abusers, Hser et al. documented the death rate among cigarette smokers to be four times that of nonsmokers (Hser et al 2004, Hser et al 1994). The health consequences of tobacco and other drug use are synergistic and estimated to be 50% greater than the sum of each individually (Bien & Burge 1990).

Slide 17: Smoking Prevalence in Addiction Treatment 1987 — 2009

The correspondence of smoking with SUD's is clearly illustrated in this study that reviewed reports of smoking prevalence in addiction treatment settings.

The findings are sobering (pardon the pun)— although general population prevalence of smoking has declined significantly over this time period, **it looks as though prevalence in SUD treatment settings is the same as at was 25 years ago.**

This suggests that smokers with SUD's are not quitting at a rate comparable with the general population and also may reflect only limited progress in addressing tobacco use in the context of SUD intervention and treatment.

Slide 18: Smokers with SUD's Want to Quit

Evidence disputes the notion that SUD smokers are not motivated to quit. Studies find that the majority of smokers in SUD treatment would consider quitting, a study we did in San Diego found that almost half of veterans completing SUD treatment attempted to stop smoking in the 6 months after treatment. So clearly, a receptive audience exists among smokers treated for SUD.

Slide 19: Smoking Cessation Outcomes and SUD's

Active interventions show short term advantage, but outcomes same for treatment vs control in longer term. Evidence is better for long term effects for individuals who quit smoking during recovery (i.e., post treatment).

Slide 20: Smoking Cessation and Recovery

So, what do we know about the influence of smoking cessation or even trying to quit smoking, on recovery?

Of primary importance is that smoking cessation does not appear to compromise SUD treatment outcomes. There is no empirical basis for the notion that smokers with SUD's should wait to try and quit.

Participating in a tobacco intervention, REGARDLESS OF SMOKING OUTCOME, associated with better long term abstinence!

Slide 21: Summary: Tobacco Treatment for SUD Patients

The literature supports the value of addressing smoking cessation in the context of SUD treatment. Smoking cessation does not appear to impair substance use outcomes and in fact, participating in smoking cessation treatment, regardless of smoking outcome, is associated with better SUD outcomes.

Slide 22: Smoking and Mental Illness– Impact on Functioning

Smoking has substantial and severe consequences for persons with serious mental illnesses, such as schizophrenia and bipolar disorder. Smoking negatively affects a range of domains of functioning, including symptomatology, cognitive functioning, quality of life and health. Persons with schizophrenia have multiple vulnerabilities to smoking, including poverty, limited education, unemployment, poor health behaviors, peer influences, impulsivity and stress. Smoking, even if it provides acute improvement to some aspects of functioning, in the long term serves to diminish the emotional, physical and financial quality of life. Despite this, smoking is often ignored by health care providers working with this population. The excess tobacco related morbidity and mortality for persons with schizophrenia highlights the urgency of addressing this disparity.

Slide 23: Tobacco Cessation Treatment for Smokers with PTSD

Historically, it is very rare to address tobacco dependence within mental health settings. This is unfortunate, not only because these settings are well placed to address tobacco use (mental health clinicians have the appropriate skills, safe setting, availability of useful treatments), but also because there is evidence that it may be more successful than referral treatment, even if the referral treatment is available in the same setting.

The largest study of this type was conducted by McFall et al. in 2010 with veterans with PTSD, comparing integrated care with usual care, which was referral to the local VA smoking cessation clinic.

The integrated care interventions offered smoking cessation pharmacotherapy to those who were interested but did not randomize patients to drugs versus placebo, so the effect of pharmacotherapy is unknown.

The results are promising. Bioverified point prevalence (by urine cotinine, a nicotine metabolite, measurement) may be lower than self-report since many patients have common environmental exposure to secondhand smoke (e.g., living with smokers, working in environment where exposed to secondhand smoke)

Beyond the VA integrated care study, only a few small pilot studies have examined smoking cessation for individuals with PTSD.

A randomized placebo controlled trial of smoking cessation with bupropion (n=15; Herzberg et al., 2001), found that the medication was well tolerated and associated with greater abstinence at 6 months (40% vs 20%) (level of significance not reported).

More recently, 22 smokers with PTSD received counseling, bupropion and NRT and were randomized to a contingency management intervention or a control group that received reinforcement independent of abstinence (Herzberg et al., 2013). At three months, abstinence rates were not significantly different (55% in the contingency management group v 18% in the control group). However, the lack of significance may reflect the small sample.

Finally, a recent pilot study examined the feasibility and utility of an ACT intervention in veterans with PTSD (Kelly et al., 2015). Results showed high retention rates (74%). Follow ups showed modest abstinence rates (16% at 3 months) and high rates of smoking reduction (47% reduction of smoking @ 3 month follow-up). PTSD symptoms decreased significantly over time.

Slide 24: Does Abstinence from Tobacco Exacerbate Depression or Schizophrenia?

An important part of treating smoking in these populations is the ongoing concern that smoking cessation may cause recurrence of the co-existing disorder. When anti-smoking regulations first came into effect in psychiatric institutions, there was concern that it would exacerbate the problems of inpatients. This was at a time when smoking was still considered only a 'bad' habit by many in the professions. We know now that is not the cause. Now, the questions are slightly different.

Initially, case studies suggesting recurrence of depression after quitting smoking. But depression is a chronic relapsing disorder, so really couldn't be argued that cessation was causative.

Two early studies suggested depression may be associated with quitting smoking. One showed greater recurrence of MDE in abstinent participants (Glassman et al. 2001), but the cell sizes were quite small and the study had differential loss to follow up. The second study (Tsoh et al., 2001) found no difference in MDE by smoking cessation outcome, but the overall incidence of depression in one year was high—14%—this is whether or not they had quit smoking. MDE occurrence did differ significantly by depression history, and was substantially higher among those with a history positive for MDD (24% recurrence) vs. those with no history of MDD (10%). The numbers were also quite small.

Since then additional studies have been conducted with findings indicating no differential risk for depression among those with a history of MDE. For example a large international study by Torres and colleagues (2010) of an online smoking cessation program offered in English and Spanish followed over 3,000 smokers after their quit date. Contrary to expectations, continued smoking, not abstinence, was related to reports of MDE 1 month following quit date. Although smokers with a history of MDE were more likely to report a depressive episode during follow-up, there was no interaction between history of MDE and abstinence. Thus, although smokers with depression may be more likely to report a depressive episode, this was not related to abstinence, reiterating that depression is a chronic relapsing disorder.

A study of smoking and depression in a sample of participants 50 years + in the English Longitudinal Study of Ageing examined changes in smoking and depression over 4 waves covering 6 years. Smoking at baseline predicted depression longitudinally and vice versa. However, when modeled concurrently, depression predicted continued smoking longitudinally but not the other way round irrespective of mental health history and adjusting for a range of covariates

A recent review (Ragg et al., 2013) found that the preponderance of evidence indicated no increased risk of a depressive episode for abstinent smokers with a history of major depression. Moreover, 2 of the studies found increased positive mood among abstinent smokers.

Although not conclusive, evidence to date does not support the initial concerns that quitting smoking may increase risk for a depressive episode and further supports the need for addressing tobacco use within mental health treatment settings.

Studies of smokers with schizophrenia have generally enrolled only those with stable symptoms. To date studies have found no detrimental effects of smoking cessation on cognitive functioning or mental health symptoms for smokers with schizophrenia. Bupropion and varenicline, two smoking cessation medications, may also serve to improve functioning in some domains. The findings support the value of smoking cessation for persons with schizophrenia. Overall, these findings support the value of smoking cessation in persons with schizophrenia.

Slide 25: Smoking Cessation and Mental Health Symptoms

More recently, investigators have conducted sophisticated analyses examining mental health symptoms and diagnoses and how these are influenced by quitting smoking. Taylor and her colleagues undertook a review and meta-analysis of 26 studies that included examination of mental health symptoms at baseline and following cessation. Included were smokers both with and without psychiatric diagnoses. Their findings were striking: Smoking cessation was associated with significant improvements in symptoms of depression and anxiety. Moreover, cessation was associated with improved positive mood, decreased stress and increased quality of life. Thus, quitting smoking can have far reaching positive consequences for smokers with and without mental illness. These effects were the same whether or not smokers had a psychiatric disorder. Of particular importance – the effect size found was equivalent to those observed for antidepressant medications.

A second study examined two waves of data from the NESARC (National Epidemiologic Survey on Alcohol and Related Conditions), with assessments conducted 3 years apart. The subsample included in the present analyses were individuals who met diagnostic criteria at Wave of mood/ anxiety disorder or substance use disorders Wave 1. Among smokers with current or lifetime history

Diagnosis of a mood or anxiety disorder at Wave 1, quitting smoking was associated with a decreased likelihood of recurrent/persistent mood/anxiety disorder (OR =0.6)

The above findings are particularly noteworthy given the common belief that smokers are self-medicating their depression and anxiety – it may in fact be that smoking exacerbates and/or maintains these symptoms. Moreover, these studies provide compelling evidence for mental health providers regarding the importance of addressing tobacco use in their patients.

Slide 26: Recommendations for Treating Patients in MH and SUD Care

Blank

Slide 27: Why Mental Health Providers?

Tobacco users expect to be encouraged to quit by health professionals. In a study examining whether health habit counseling affects patient satisfaction, Barzilai et al. (2001) determined that of 12 health habits examined (exercise, diet, alcohol history, alcohol counseling, tobacco history, tobacco counseling, passive tobacco exposure, contraception and condom use, substance use history, substance use counseling, STD prevention, and counseling about HIV testing or prevention), only tobacco history and tobacco counseling were significantly associated with full satisfaction with the clinician visit.

A clinician who does not address tobacco use during a clinical encounter tacitly implies that quitting is not important.

Mental health providers are particularly well positioned to address tobacco use with their clients because they are:

- Often the clinician for whom contact is the most frequent and who knows the patient best

- Able to combine psychopharmacological and behavioral/counseling treatment
- Trained in substance abuse *and/or behavior change* treatment
- Able to identify and address any changes in psychiatric symptoms during the quit attempt

Slide 28: What Can You Do?

Blank

Slide 29: Clinical Case Discussion #1

1. What intervention approach/strategies would be appropriate for GT?
 - Motivational approach with goal of moving him from contemplation to determination (decision to quit).
 - Employ motivational techniques of open-ended questions, summary and reflection.
 - Have veteran generate his perceived pros and cons of quitting: what will be the consequences of quitting on his life? What are his perceived obstacles to quitting? How does his past experience with quitting influence his current desire to change?
 - Following examination of pros and cons, explore current intentions for change: What if any changes is he currently considering? Has he made any changes yet? What's the next step for him? At this point would be appropriate to assess perceived importance of quitting and confidence in being able to quit.
 - Once veteran demonstrates readiness to change, next step is to create quit plan; transition from why change to how to change. At this point it is appropriate to employ the following MI techniques: recapitulation (summarize current situation), Key questions (elicit from smoker, what is the next step?), Providing information and advice (upon veterans request or receiving permission to provide advice).
 - Final step is to elicit commitment to a change plan.
2. What are the key obstacles that might impede GT 's efforts at quitting smoking?
 - Reference to Clinical Guideline "variables associated with lower rates of abstinence" mental illness (PTSD, depression)
 - Smokers often perceive cigarettes as their primary coping strategy for managing negative affect; identifying adaptive ways for managing symptoms is critical to success. Education that quitting smoking leads to reductions in symptoms of depression and anxiety.
 - High nicotine dependence (FTND=7)
 - Medication will be important for helping to manage withdrawals and cravings (e.g., combination nicotine replacement: nicotine patch plus gum or lozenge)
 - High stress (disabled, presume limited income and resources)
 - As above, acknowledging perceived important of smoking for managing stress, identifying adaptive stress coping strategies.
 - Presence of smokers (neighbors smoke)

- Identifying strategies for addressing this temptation will be important, e.g., assertiveness skills: letting neighbors know he's quitting, asking them to not smoke around him and not to provide him cigarettes.
 - Coping strategies for managing this temptation (e.g., escaping the situation, identifying effective distraction techniques).
3. What level of intervention would be most appropriate for Mr. Smith?
- Given GT 's history (no prior quit attempts) and obstacles he is likely to require high intensity intervention including behavioral counseling and support along with medications. Long-term treatment may be required to facilitate successful quitting and support maintenance of change. Groups treatment may be the preferred modality as it can provide a source of social as well as practical support.

Slide 30: Clinical Case Discussion #2

1. What strategies would you use to engage DR in an active cessation attempt?
 - Motivational approach with goal of moving him from determination to action (initiating change efforts).
 - Employ motivational techniques of open-ended questions, summary and reflection.
 - Have veteran generate his perceived pros and cons of quitting: what will be the consequences of quitting on his life? What are his perceived obstacles to quitting? How does his past experience with quitting influence his current desire to change? If concerns regarding impact on his sobriety arise, with his permission, provide information regarding smoking cessation for individuals with substance use disorders si(no negative impact on sobriety, association of quitting smoking with better substance use outcomes).
 - Next, assess perceived importance of quitting and confidence in being able to quit. Elicit and reinforce change talk.
 - Move toward creating a quit plan; transition from why change to how to change.
2. What questions would you ask DR to help plan his quit attempt?
 - At this point it is appropriate to employ the following MI techniques: recapitulation (summarize current situation), Key questions (elicit from smoker, what is the next step?), Providing information and advice (upon veterans request or receiving permission to provide advice).
 - DR has previously quit for long periods of time, so identifying what he perceived as helpful and effective during prior attempts will be valuable(use of medications, behavioral strategies, sources of support, etc).
 - Help him identify obstacles in his current life and problem solve strategies for managing these (e.g., living in recovery home, stress associated with recovery process); identify specific triggers and elicit strategies for coping with these circumstances.
3. What level of intervention would be appropriate for DR? (brief counseling and medication)
 - Given his prior success quitting, lower intensity intervention may be sufficient. For example telephone counseling may be useful for providing him structure and reinforcement,

particularly while he's in the recovery home. Technology based cessation supports (app, texting program) may also be useful adjuncts.

References

Slide 4: Duffy SA, Kilbourne AM, Austin KL, Dalack GW, Woltmann EM, Waxmonsky J, Noonan D. 2012. Risk of smoking and receipt of cessation services among Veterans with mental disorders. *Psychiatric Services*. 63 (4): 325-32.

Slide 6: SAMHSA, The NSDUH Report: Data Spotlight, March 20, 2013

Slide 7: Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Prev Chronic Dis*. Apr 2006;3(2):A42.

Carney CP, Jones LE. Medical comorbidity in women and men with bipolar disorders: a population-based controlled study. *Psychosom Med*. Sep-Oct 2006;68(5):684-691.

Dalton SO, Laursen TM, Mellekjaer L, Johansen C, Mortensen PB. Risk for cancer in parents of patients with schizophrenia. *Am J Psychiatry*. 2004;161:903-8.

Lichtermann D, Ekelund J, Pukkala E, Tanskanen A, Lonnqvist J. Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiatry*. Jun 2001;58(6):573-578.

Ruschena D, Mullen PE, Burgess P, et al. Sudden death in psychiatric patients. *Br J Psychiatry*. Apr 1998;172:331-336.

Bruce ML, Leaf PJ, Rozal GP, Florio L, Hoff RA. Psychiatric status and 9-year mortality data in the New Haven Epidemiologic Catchment Area Study. *Am J Psychiatry*. May 1994;151(5):716-721.

Goff DC, Sullivan LM, McEvoy JP, Meyer JM, Nasrallah HA, Daumit GL, et al. A comparison of ten-year cardiac risk estimates in schizophrenia patients from the CATIE study and matched controls. *Schizophr Res*. 2005;80:45-53.

Hurt RD, Offord KP, Croghan IT, et al. Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort. *JAMA*. Apr 10 1996;275(14):1097-1103.

Himelhoch S, Lehman A, Kreyenbuhl J, Daumit G, Brown C, Dixon L. Prevalence of chronic obstructive pulmonary disease among those with serious mental illness. *Am J Psychiatry*. 2004;161:2317-9.

Oquendo MA, Galfalvy H, Russo S, et al. Prospective study of clinical predictors of suicidal acts after a major depressive episode in patients with major depressive disorder or bipolar disorder. *Am J Psychiatry*. 2004 Aug;161(8):1433-41.

Breslau N, Schultz LR, Johnson EO, Peterson EL, Davis GC. Smoking and the risk of suicidal behavior: a prospective study of a community sample. *Arch Gen Psychiatry*. 2005 Mar;62(3):328-34.

Slide 8: Benowitz NL. (2007). Cigarette smoking and the personalization of irinotecan therapy. *J Clin Oncol* 25:2646–2647.

Carrillo JA, Herraiz AG, Ramos SI, Gervasini G, Vizcaino S, Benitez J. (2003). Role of the smoking-induced cytochrome P450 (CYP)1A2 and polymorphic CYP2D6 in steady-state concentration of olanzapine. *J Clin Psychopharmacol* 23:119–127.

Cephalon, Inc. (2008). Treanda Package Insert. Frazer, PA.

Gex-Fabry M, Balant-Gorgia AE, Balant LP. (2003). Therapeutic drug monitoring of olanzapine: The combined effect of age, gender, smoking and comedication. *Ther Drug Monit* 25:46–53.

GlaxoSmithKline. (2006). Requip Package Insert. Research Triangle Park, NC.

Meyer JM. (2001). Individual changes in clozapine levels after smoking cessation: results and a predictive model. *J of Clin Psychopharmacol* 21:569–574.

OSI Pharmaceuticals, Inc. and Genentech, Inc. (2007, May). Tarceva Package Insert. Melville, NY.

Pfizer, Inc. (2006, May). Exubera Package Insert. New York, NY.

van der Bol JM. (2007). Cigarette smoking and irinotecan treatment: pharmacokinetic interaction and effects on neutropenia. *J Clin Oncol* 25:2719–2726.

Yoshimura R, Ueda N, Nakamura J, Eto S, Matsushita M. (2002). Interaction between fluvoxamine and cotinine or caffeine. *Neuropsychobiology* 45:32–35.

Slides 11, 12 & 13: Prochaska JJ. 2011. Smoking and mental illness – Breaking the link. *NEJM*. 365 (3): 196-8.

Slide 14: General Psychiatry Outpatients: Acton et al. (2001). Depression and stages of change for smoking in psychiatric outpatients. *Addictive Behaviors*. 26(5):621-31.

Depressed Outpatients: Prochaska et al. (2004). Depressed smokers and stage of change: implications for treatment interventions. *Drug Alc Dep*. 76(2):143-51.

Psychiatric Inpatients: Prochaska et al. (2006). Return to smoking following a smoke-free psychiatric hospitalization. *Am J Addiction*. 15(1):15-22.

Methadone Clients: Nahvi et al. (2006) Cigarette smoking and interest in quitting in methadone maintenance patients. *Addictive Behaviors*. 31(11):2127-34

Slide 15: Schroeder SA and Morris CD. (2010) Confronting a neglected epidemic: tobacco cessation for persons with mental illness and substance abuse problems. *Ann Rev Public Health*. 31: 297-314.

Slide 16: Bien TH, Burge R. 1990. Smoking and drinking: a review of the literature. *Int. J. Addict*. 25: 1429-54

Hurt RD, Offord KP, Croghan IT, et al. Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort. *JAMA*. Apr 10 1996;275(14):1097-1103.

Hser YI, Gelbert L, Hoffman V, Grella CE, McCarthy W, Anglin MD. 2004. Health conditions among aging narcotics addicts: Medical Examination Results. *J. Behav. Med*. 27: 607-22

Hser YI, McCarthy WJ, Anglin MD. 1994. Tobacco use as a distal predictor of mortality among long-term narcotics addicts. *Prev. Med*. 23: 61-9

Castellsague, X., Munoz, N., De Stefani, E., Victora, C.G., Catelletto, R., Rolon, P.A., Quintana, M.J., 1999. Independent and joint effects of tobacco smoking and alcohol drinking on the risk of esophageal cancer in men and women. *Internat J Cancer*, 82, 657–664.

Pelucchi, C., Gallus, S., Garavello, W., Bosetti, C., La Vecchia, C., 2006. Cancer risk associated with alcohol and tobacco use: Focus on upper aero-digestive tract and liver. *Alcohol Res Health*, 29, 193–198.

Slide 23: McFall M, Saxon AJ, Thompson CE, Yoshimoto D, Malte C, et al. 2005. Improving the rates of quitting smoking for veterans with posttraumatic stress disorder. *Am. J. Psychiatry* 162:1311–19

McFall M, Saxon AJ, Malte C, Chow B, Bailey S, Baker DG, Beckham JC, Boardman KD, Carmody TP, Joseph AM, Smith MW, Shih M, Lu Y, Holodniy M, Lavori PW. 2010. Integrating tobacco cessation into mental health care for posttraumatic stress disorder. *JAMA*. 304 (22): 2485-93.

Slide 24: Ragg et al., 2013. The impact of smoking cessation on schizophrenia and major depression. *Australas Psychiatry*, 21 (3), 238-45.

Torres et al., 2010. Quitting smoking does not increase the risk of major depressive episodes among users of Internet smoking cessation interventions. *Psychological Medicine*, 40 (3,) pp 441-449

Tsoh et al., 2001. Development of major depression after treatment for smoking cessation. *Am J Psychiatry*;157(3):368-74.

Slide 26: Schroeder SA and Morris CD. (2010) Confronting a neglected epidemic: tobacco cessation for persons with mental illness and substance abuse problems. *Ann Rev Public Health*. 31: 297-314.

Slide 27: Barzilai DA, Goodwin MA, Zyzanski SJ, Stange KC. (2001). Does health habit counseling affect patient satisfaction? *Prev Med* 33:595–599.