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Are differences in guidelines for the treatment of nicotine dependence and non-nicotine dependence justified?

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Abstract

Despite the many similarities between nicotine dependence and other drug dependences, national guidelines for their treatment differ in several respects. The recent national guideline for the treatment of nicotine dependence has (i) less emphasis on detailed assessment; (ii) less emphasis on treatment of psychiatric comorbidity; (iii) less acceptance of reduction of use as an initial treatment goal; (iv) greater emphasis on pharmacological interventions; and (v) less emphasis on psychosocial treatment than national guidelines for non-nicotine dependences. These treatment differences may occur because (i) nicotine does not cause behavioral intoxication; (ii) psychiatric comorbidity is less problematic with nicotine dependence; (iii) psychosocial problems are less severe with nicotine dependence; and (iv) available pharmacotherapies for nicotine dependence are safer, more numerous and more easily available. However, it is unclear whether these treatment differences are, in fact, justifiable because of the scarcity of empirical tests. We suggest several possible empirical tests.

Keywords

Smoking; smoking cessation; substance-related disorders; therapy; treatment

Introduction

The US [1] and UK [2] national reports on nicotine dependence have described several lines of evidence that most smokers are dependent upon nicotine and that nicotine dependence shares the features of other substance dependences, e.g. impaired control over use of the

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Declarations of Interest

Dr Hughes is currently employed by the University of Vermont and Fletcher Allen Health Care. Since 2005, he has received research grants from the National Institute on Health, Pfizer and Sanofi-Aventis. During this time, he has accepted honoraria or consulting fees from Abbot Pharmaceuticals; Academy for Educational Development; Acrux DDS; Aradigm; American Academy of Addiction Psychiatry; American Psychiatric Association, Atrium, Cambridge Consulting, Celtic Pharmaceuticals; Cline, Davis and Mann; Constella Group; Concepts in Medicine; Consultants in Behavior Change; Cowen Inc; Cygnus; Edelman PR; EPI-Q, Evotec; Exchange Limited; Fagerstrom Consulting; Free and Clear; Health Learning Systems; Healthwise; Insyght; Invivodata; Johns Hopkins University; J. Reckner; Maine Medical Center; McNeil Pharmaceuticals; Nabi Pharmaceuticals; Novartis Pharmaceuticals; Oglivy Health PR, Pfizer Pharmaceuticals; Pinney Associates; Reuters; Shire Health London; Temple University of Health Sciences; United Biosource; University of Arkansas; University of Auckland; University of Cantabria; University of Greifswald; University of Kentucky; University of Madrid Medical School, US National Institutes on Health; Xenova and ZS Associates. Dr Weiss has received research funding from Eli Lilly and Company and has consulted to Titan Pharmaceuticals.

drug and withdrawal symptoms upon drug cessation. These commonalities would suggest that dependence on nicotine should be treated similarly to dependence on other drugs. Others have noted differences between nicotine and non-nicotine dependence disorders; e.g. nicotine dependence does not cause behavioral intoxication and rarely causes psychosocial problems [3]. These differences would suggest that different treatment approaches may be justified.

In fact, the content, format, intensity, intent and delivery of treatment differ for nicotine versus non-nicotine substance use disorders. For example, treatment of nicotine dependence usually consists of over-the-counter (OTC) medications with either no or very brief counseling via telephone [4,5], whereas treatment of other substance dependence disorders usually includes more intensive psychosocial treatments delivered via face-to-face counseling, without medications [6,7].

The recent publication of consensus treatment guidelines by national professional and governmental bodies for substance use disorders in general [8,9] and for tobacco dependence only [10] provide authoritative sources for the most well-accepted treatment strategies. The current commentary describes differences between the guidelines for treatments of the two types of disorder, and discusses whether differences are based on scientific evidence. This exercise may help clinicians and administrators to decide which treatment principles for alcohol and other drug dependence should and should not be applied to the treatment of nicotine dependence, and vice versa.

Our comments in this paper are not based upon a formal literature review, due in large part to the scarcity of empirical research. Instead they are based upon our subjective evaluation of the literature; thus, this paper is an editorial or commentary, not a systematic review.

Recent Guidelines

The most recent guideline for the treatment of tobacco dependence is the US Public Health Service's (USPHS) Treating Tobacco Use and Dependence[10]. This guideline was sponsored by governmental and non-profit organizations and authored by a group of 24 experts. The guideline focuses upon three audiences: primary care clinicians, smoking cessation experts and health-care systems. It provides an independent meta-analysis of the major questions and assigns strength of evidence ratings based on the quality and quantity of empirical support. The current paper focuses upon level A recommendations in the report, in which 'multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings'[10].

The most recent comprehensive guideline for the treatment of alcohol and other drug use disorders is the American Psychiatric Association's (APA) Practice Guideline For The Treatment of Patients with Drug Use Disorders[8]. The first edition had separate guidelines for the treatment of alcohol and illicit drugs [11] and for nicotine dependence [12]. The second edition, published in 2007, includes both in the same guideline. This edition was written by a group of 12 addiction psychiatrists and includes recommendations for alcohol, cocaine, marijuana, nicotine and opioid dependence. The guideline reviews the literature and assigns strength of evidence ratings to its recommendations evidence, but does not undertake formal meta-analyses. The guideline includes both generic and substance-specific recommendations and recognizes both similarities and differences across drugs. It states explicitly that 'not all principles are applicable to the treatment of every drug use disorder. This is particularly true for nicotine dependence treatment, as nicotine dependence rarely causes the behavioral or social harm seen with other drug dependencies'. The APA guideline makes several level I recommendations ('recommended with substantial clinical confidence') that will be the focus of this review.

Another well-respected guideline is the National Institute on Drug Abuse's (NIDA) Principles of Drug Addiction Treatment[9]. This guideline, published in 1999, gives 13 treatment principles that were developed during a scientific conference of a group of drug abuse experts. The exact methods of reaching consensus for the recommendations for this monograph are not stated and no 'levels of evidence' ratings are given. There are several references to nicotine dependence in the guideline. There are no statements on whether these principles vary across drugs.

For brevity, our commentary does not cite the many areas of agreement across the guidelines. Instead, we focus upon areas in which the guidelines appear to produce somewhat different conclusions. Before discussing these differences, readers should note that some of the differences could occur as a result of differences in the aims, methods and styles of the guidelines, rather than as a result of differences in the way that different drug dependence disorders should be treated. For example, the nicotine guideline appears to be more conservative, i.e. it relies more on the results of randomized controlled trials (RCTs) than the two non-nicotine drug guidelines, which also take into account non-RCT data via an evidence-based medicine approach [13,14]. The nicotine guideline includes primary care clinicians and health-care systems as part of its audience, and thus focuses upon both brief and intensive treatments. The non-nicotine guidelines focus more upon optimal intensive treatment recommendations delivered by treatment specialists.

Comparison of Guidelines

Our review of the three guidelines suggests five major areas of difference between the tobacco guideline and the two guidelines focusing upon alcohol and other drugs (Table 1). These are (i) perceived importance of assessment; (ii) emphasis on psychiatric comorbidity; (iii) treatment goals (i.e. total abstinence versus reduction of use); (iv) role of pharmacotherapy; and (v) role of psychosocial treatment.

Assessment

The APA and NIDA guidelines for non-nicotine disorders state that substantial assessment is 'essential' prior to and during treatment; the USPHS tobacco guideline states that treatment 'should be delivered even if specialized assessments are not used or available' (p. 79).

One possible reason that the non-nicotine guidelines recommend extensive assessment is that most treatment-seeking individuals who are dependent upon substances other than nicotine have problems in many aspects of their life, e.g. relationship, work, financial, legal or psychological areas [15]. The recommendation for assessment of these domains is based on the evidence (albeit limited) that treating these other problems improves overall outcomes and, to a lesser extent, drug use outcomes [16]. The importance of treating these associated problems is perhaps best exemplified by US federal licensure requirements for treatment for opioid dependence that require clinicians to provide psychosocial treatments for such ancillary problems when they prescribe medication (<http://buprenorphine.samhsa.gov>).

Another reason for the recommendation for more intensive assessment of individuals with non-nicotine drug use disorders is to assess the degree of urgency of need for intervention. Often, patients with these disorders enter treatment because of an acute social consequence of drug use, e.g. abuse of one's spouse or children, driving while intoxicated or suicidal ideation [15]. Sometimes, these are sufficiently imminent that strong contingencies or a restrictive environment need to be prescribed (<http://www.asam.org/PatientPlacementCriteria.html>).

In contrast, tobacco use rarely causes such acute problems, for several reasons. The main reason is that nicotine in the doses used by smokers does not cause behavioral intoxication [17]. Reports of impulsive behavior, aggression, etc. among smokers due to increased smoking are extremely rare. Secondly, tobacco use is legal and thus does not require excessive risks to obtain. Thirdly, daily use of tobacco is relatively inexpensive compared to daily use of illicit drugs; thus, antisocial behaviors to obtain funds for drug acquisition are less likely. Fourthly, although tobacco use is somewhat stigmatized [18], this is less of an issue than it is for alcohol intoxication or illicit drug use.

Another potential reason for the difference in recommendations regarding the need for assessment is that all regular tobacco use is harmful, but regular use of alcohol or intermittent use of illicit drugs may not be. Thus, guidelines for alcohol and illicit drug use assume that not all alcohol/illicit drug users will require treatment and, thus, it is necessary to conduct an assessment to determine when treatment is, and is not, needed. In contrast, the tobacco guideline states explicitly that all users should receive treatment; thus assessment of need for treatment is unnecessary.

Treatment of Psychiatric Comorbidity

Both the APA and NIDA guidelines and the USPHS tobacco guideline recognize the high prevalence of psychiatric and psychological problems in nicotine, alcohol and drug users, and all three guidelines suggest that such comorbidity interferes with the likelihood of attaining abstinence. The APA and NIDA guidelines cite evidence that treating comorbidity along with the alcohol/illicit drug use disorder can improve outcomes, although the data on this are mixed [19]. The USPHS tobacco guideline, on the other hand, is silent on whether treatment of psychiatric problems, per se, increases the probability of smoking cessation.

One possible reason for the above differences is that the prevalence of comorbidity among those with non-nicotine dependence is greater than that among those with nicotine dependence. However, epidemiological studies that provide data on comorbidity with alcohol, illicit drug and non-nicotine drug dependence, using the same measures, have not shown prevalence differences [20,21]. Another possibility is that the comorbidity with alcohol and other drug dependence is more likely to interfere with attaining or maintaining abstinence than the comorbidities associated with nicotine dependence. We know of no data addressing this issue.

Another possible reason for the differential emphasis on psychiatric comorbidity is the fact that few tobacco treatment specialists have training in the detection or treatment of mental health problems [22]. Also, many, if not most, smoking cessation programs are not part of a medical or mental health program that could facilitate referrals for mental health treatment, if a psychiatric disorder were identified. Also, most cessation programs believe that their only responsibility to the smoker is to help with stopping tobacco, not to detect associated problems or ‘treat the whole person’. Addressing psychiatric problems, as well as other issues such as family problems or unemployment, also requires significant expertise and commitment of time and resources that are usually lacking in smoking cessation programs. Finally, it is unclear whether those who seek treatment for smoking want treatment of comorbidity, or whether they would see assessment of comorbidity as an unnecessary intrusion into their privacy.

Treatment Goals

The APA guideline states that for alcohol/drug users unwilling to agree to an abstinence goal, non-abstinence goals, such as reduced frequency of use and use of safer products or routes of administration, are acceptable intermediate goals. The guideline states, however,

that reduction goals should be accompanied by continuing advice that abstinence is the optimal outcome. The NIDA guideline does not comment on this issue. The USPHS tobacco guideline states that ‘the use of reduction strategies ... were not considered due to a lack of data and the fact that they are beyond the scope of a clinical practice guideline focused on treating tobacco use and dependence’ (p. 19).

The APA guideline recognizes that non-abstinence goals might undermine motivation to abstain, but then goes on to state that intermediate goals can lead to improvement in psychological, social and adaptive functioning and facilitate retention in treatment. The guideline postulates that increased self-efficacy, decreased severity of dependence and other beneficial effects from attaining intermediate goals could lead to an increased likelihood of eventual abstinence. The guideline also notes that agreeing to non-abstinence goals allows the patient to remain in treatment, giving the therapist more time to help to persuade the patient to set and achieve an abstinence goal. Unfortunately, while there are some data regarding the potential for alcohol-dependent individuals to achieve moderation of drinking [23,24] there are few empirical data, particularly from RCTs, on whether drug-dependent individuals can, in fact, control their use for a substantial period of time, or whether such reductions lead eventually to abstinence or resolution of problems from drug use.

Although the USPHS tobacco guideline states that there is insufficient evidence regarding this issue in smokers, several quantitative and qualitative reviews have concluded that medication and behavioral treatments can assist in smoking reduction, and that reduction increases the likelihood of subsequent cessation [25,26]. In fact, nicotine medications are approved for reduction as an intermediary goal to cessation in several countries (Gunnar Gustavsson, personal communication, 10 July 2008).

Pharmacotherapy

The APA and NIDA guidelines for alcohol and drug use disorders indicate that medications are indicated for ‘selected’ or ‘many’ patients, implying that not all those seeking treatment need medications. The USPHS tobacco guideline states explicitly that all smokers should be encouraged to use medications unless they have contraindications.

The APA and NIDA guidelines may not recommend medications for all alcohol/illicit drug abusers in part because there are no Food and Drug Administration (FDA)-approved pharmacotherapies for several drug use disorders, e.g. cannabis and cocaine dependence [15]. However, sections of the APA guidelines for specific disorders in which efficacious medications are available (i.e. alcohol and opioid use disorders) suggest that medications are more useful in some subsets of patients than others. For example, the APA guideline discusses patient characteristics that could help a clinician to choose who is most likely to benefit from disulfiram for alcohol dependence (e.g. motivated, non-impulsive drinkers) and opioid agonists such as methadone and buprenorphine for opioid dependence (e.g. daily users). In fact, federal guidelines have codified that only a subset of opioid-dependent individuals should receive these medications (<http://www.buprenorphine.samsha.gov>). In contrast, the USPHS guideline states that all smokers wanting to quit should receive medication.

Perhaps one reason the USPHS tobacco guideline states that all smokers should use medications is because most medications for smoking cessation have been found beneficial in most subsets of smokers, e.g. even in light smokers and elderly smokers [10]. In addition, logical measures that have been used to try to select specific subgroups of nicotine-dependent patients to receive medications have not proved reliable for treatment matching [27]. Another important reason for the blanket encouragement to use medications is the benign adverse event profile of most anti-smoking medications [10]. In fact, the most widely

used medications are over-the-counter (OTC) medications [27]. This is in contrast to the medications used for other substance dependence, all of which are available by prescription only and most of which can produce clinically significant adverse events [15]. A final possible reason for encouraging pharmacotherapy in smokers is that 95% of formal treatment of nicotine dependence occurs currently in either primary care or public health settings [10]. In contrast, much treatment of other substance dependence occurs in specialized substance abuse or mental health counseling settings [15].

Interestingly, the APA guideline suggests that treatment of withdrawal symptoms is an acceptable goal in itself. However, the guideline does not view such treatment as increasing substantially the probability of recovery. The treatment of withdrawal is a goal in itself, because some withdrawal syndromes can be distressing and even life-threatening [10]. In contrast, the tobacco guideline does not recommend treatment of withdrawal per se, but cites withdrawal relief as a mechanism by which medications are effective. The lack of withdrawal as an indication is itself due probably to the fact that nicotine withdrawal is usually less painful than alcohol or opioid withdrawal [28]. On the other hand, several studies have shown that nicotine withdrawal can produce clinically significant distress and dysfunction [29].

Psychosocial Treatments

The APA and NIDA guidelines state explicitly that psychosocial treatment is ‘essential’ or ‘critical’ to treatment success. This makes sense, given that most of those who enter treatment for non-nicotine drug use have associated significant behavioral problems, e.g. relationship, legal, financial or occupational problems. Whether these problems preceded or are consequences of drug use is often not clear. However, even in the latter case, these problems do not disappear commonly with drug abstinence and thus require treatment attention [30].

The USPHS tobacco guideline states that intensive psychosocial treatments should be used ‘whenever possible’ or ‘if feasible’. These statements could be interpreted to indicate that the tobacco guidelines place less emphasis on psychosocial treatment than the APA and NIDA guidelines. As stated above, this could be reasonable because those with nicotine dependence are less likely to have current, clinically significant behavioral problems. In addition, as stated above, smokers seeking help with stopping smoking may see an offer of treatment for other problems as irrelevant or intrusive.

Summary

This commentary has focused upon the differences in the treatment of nicotine dependence versus other forms of drug dependence. However, readers should not ignore the many commonalities between the two treatments. Both see dependence as a chronic relapsing disorder, view abstinence as the optimal goal and recommend combined psychosocial and medication therapy.

In the above sections, we have suggested possible reasons for the differences in the way in which nicotine dependence and other substance dependences are treated by comparing guidelines. Some of the differences in the guidelines are due to their different audiences; the tobacco guideline focuses both upon primary care providers and specialists, whereas the non-nicotine guidelines focus more upon specialists. In addition, the two guidelines differ somewhat in their reliance on evidence other than that gleaned from randomized clinical trials. However, we believe that some reasons for the differences in treatment recommendations are independent of the above structural differences in the guidelines.

First, other substance dependence, but not nicotine dependence, often produces behavioral intoxication and behavioral problems that require greater assessment and immediate attention. Secondly, the notion that co-occurring psychiatric disorders interfere with abstinence is accepted more widely for non-nicotine than nicotine dependence. As a corollary to this, the belief that treatment of the comorbidity aids abstinence and is thus integral to treatment is accepted more widely for substances other than nicotine. Thirdly, treatment of non-nicotine dependence is more accepting of non-abstinence intermediary goals than nicotine dependence. Fourthly, many of the medications used to treat nicotine dependence are available OTC and have fewer significant adverse events, and are thus encouraged for all patients. Fifthly, because of the behavioral intoxication from non-nicotine dependence and other reasons, those with non-nicotine dependence are more likely to have pressing and significant psychosocial problems that require psychosocial treatment than those seeking help only for smoking cessation.

We have conjectured logical reasons for these differences. We do not believe we can offer any firm conclusions about whether these differences are justifiable, given the scarcity of empirical research on this subject. We believe such research is needed, and Table 2 illustrates several questions that could be addressed by empirical research.

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Table 1

Selected differences in the treatment of non-nicotine drug versus nicotine dependence.

	APA guideline	NIDA principles	USPHS tobacco guideline
Assessment	'A comprehensive ... evaluation is essential ...' (p. 9)	'Treatment and services plan must be assessed continually' (#4)	'Treatment should be delivered even if specialized assessments are not used or available' (p. 79)
Comorbidity	'Specific treatment of comorbid disorders should be provided' (p. 12)	'Treatment must address ... psychological problems' (#3)	No statements about treating comorbid conditions per se
Treatment goals	'The goals of treatment ... may vary' (p. 10)	No statements about treatment goals	'The use of exposure reduction strategies were not considered due to a lack of data' (p. 19)
Pharmacotherapy	'Pharmacological treatments are beneficial for selected patients ...' (p. 10)	'Medications are ... important ... for many patients' (#7)	'Clinicians should encourage all patients ... to use effective medications ... except where contraindicated' (p. 106)
Psychosocial treatment	Psychosocial treatments are essential components ...' (p. 10)	'Counseling and other behavioral therapies are critical' (#6)	'Intensive interventions ... should be used whenever possible or if feasible' (p. 83)

APA: American Psychiatric Association; NIDA: National Institute on Drug Abuse; USPHS: United States Public Health Service.

Table 2

Research questions about the treatment of smoking.

Would a fuller assessment with tailoring of treatments increase smoking cessation outcomes?
Would treatment of co-occurring psychiatric disorders improve smoking cessation outcomes?
Would psychosocial treatments to improve employment, relationships, etc. increase smoking cessation?
Will future smokers have more non-nicotine psychosocial and psychiatric problems?
Are smokers who are seeking treatment for smoking receptive to treatment for non-smoking problems?
Is treatment more essential to recovery for non-nicotine drug than nicotine dependence?
Do some smokers have clinically significant nicotine withdrawal (e.g. that interferes with work or prompts medication use), and can medications decrease this to non-significant levels?