NAQC Issue Paper

NAQC's Issue Papers aim to provide critical knowledge on important quitline topics and guidance for decision making.

Integration of Tobacco Cessation Medications in State and Provincial Quitlines:
A Review of the Evidence and the Practice with Recommendations (2014 Update)

FORWARD

In 2009, the North American Quitline Consortium (NAQC) published *Integration of Tobacco Cessation Medications in State and Provincial Quitlines: A Review of the Evidence and the Practice with Recommendations*. It was NAQC's third Quality Improvement Initiative (QII) Issue Paper, published in response to a request from members to assist in addressing the many issues surrounding the provision and distribution of medications to the populations served by quitlines throughout North America. Over the past five years, the paper has served as a critical resource for quitline service providers in evaluating current medication delivery programs and in the design of new programs. Quitline funders have found value in the review of the evidence and in the recommendations for practice as they work to provide rationale and justification for providing or expanding medication offerings by their quitline.

In a May, 2013 meeting of NAQC's Advisory Council, members were asked to prioritize needed updates to current QII Issue Papers so that the reviews of evidence and recommendations found in each paper reflect current knowledge and remain relevant to the field. Two papers were prioritized for updating in that discussion: *Integration of Tobacco Cessation Medications in State and Provincial Quitlines: A Review of the Evidence and the Practice with Recommendations* and *Measuring Quit Rates,* also published in 2009 and NAQC's very first QII Issue Paper. Council members believed that there had been significant additions to the evidence related to medications since 2008, significant increase in the number of states providing medications via their quitline, and significant changes in the health care landscape (e.g., new products and health care reform) to warrant an immediate focus on a 2014 update to *Integration of Tobacco Cessation Medications in State and Provincial Quitlines.*

The purpose of this NAQC Quality Improvement Initiative Issue Paper 2014 Update is to provide a review of tobacco cessation medication integration with quitline services that reflects additions to the evidence base and resulting improvements in practice since the 2009 publication with special emphasis on:

1. Trends in medication integration in quitlines;
2. Changes to over-the-counter (OTC) nicotine replacement therapy (NRT) labeling and the impact this may have on the application and utilization of cessation medications in quitline settings, including the use of combination NRT, extended use of NRT, and pre-quit use of NRT;
3. Increase of dual tobacco use and electronic cigarettes and the challenges this presents to cessation medications in quitline settings;
4. Published studies on the integration of cessation medications in quitlines and the effect on quitline utilization and abstinence rates;
5. Cost-effectiveness analysis, choice of medication, determination of quantity of medication to provide and the method of distribution of medications that will be used;
6. Needed research and rapid-cycle testing to optimize effectiveness of cessation medications in quitline settings; and
7. Recommendations on the integration of cessation medications in quitline settings.

The 2014 Update relies on a number of references, including the U.S. Department of Health and Human Services Clinical Practice Guideline, Treating Tobacco Use and Dependence, 2008 Update (USPHS Guideline), Cochrane Review and other peer-reviewed journal articles to identify and document evidence-based recommendations regarding use of medications in the treatment of tobacco use and dependence. While we are fortunate that there is a great deal of

scientific evidence on the use of cessation medications in quitline environments, in some cases the evidence is not specific to quitlines. Since quitlines were first launched in 1992, evidence generated in settings other than quitlines has been considered and evaluated to determine the degree to which a specific practice can be effectively and safely implemented in the quitline environment. Finally, there is a great body of clinical and operational experience that is relevant to the discussion of delivery of cessation medications via quitlines, and it is used throughout the paper to supplement the scientific evidence when appropriate.

INTRODUCTION

Tobacco Cessation Medications

There are currently seven cessation medications approved by the U.S. Food and Drug Administration (FDA). Three are OTC (nicotine patch, gum and lozenge) and four require a prescription (nicotine inhaler and nasal spray, bupropion SR and varenicline). Five medications contain nicotine and two do not. All cessation medications are intended to reduce nicotine withdrawal symptoms and cravings associated with quitting. The most recently FDA-approved medication is varenicline which became available by prescription in 2006. Since that time, there have been no additional medications approved by the FDA.

Table 1

Medication	OTC	Prescription	Contains Nicotine
Nicotine patch	X		X
Nicotine gum	X		X
Nicotine lozenge	X		X
Nicotine inhaler		X	X
Nicotine nasal spray		X	X
Bupropion SR		X	
Varenicline		X	

Source: http://www.fda.gov/forconsumers/consumerupdates/ucm198176.htm

Cytisine is a medication that has been available in Eastern Europe for over 50 years and works similarly to varenicline. While it is not FDA-approved, research has demonstrated significantly higher quit outcomes at 12 months for those randomly assigned to cytisine compared to placebo.[1,2]

While the use of combination NRT was addressed in the first Medications Issue Paper, at that time there were no published studies conducted in quitline settings. A quitline-based study was published in 2012 that demonstrated significantly improved quit outcomes compared to mono-therapy.[3] Additionally, in 2013 the FDA issued label changes to OTC NRT packaging and warnings about using more than one type of NRT simultaneously, as well as smoking while using NRT, were removed from package labeling. Similarly, the warning about use of NRT longer than 12 weeks was also removed, though indications for the use of NRT were not changed.[4] New evidence and changes to packaging and warning labels have resulted in greater exploration of combination NRT in this 2014 Update.

Tobacco Cessation Medications and Quitlines

Tobacco quitlines are currently available in all 10 provinces and two territories in Canada, Mexico, and all 50 states, Puerto Rico, Guam, and the District of Columbia[5] and have consistently proven effective in helping tobacco users quit[6]. The range of services offered by state and provincial quitlines varies, often depending on funding and priority populations identified by states and provinces. Quitlines in the U.S. began providing over-the-counter cessation medications in the late-1990's as they recognized improved quit outcomes and increased utilization of quitlines as a result of integrating pharmacological treatment with behavioral counseling, and became increasingly comfortable providing pharmacological assistance and support for those quitting tobacco.[6] No Canadian quitlines provide medications to tobacco users as part of their services. However, both Quebec and British Columbia make over-the-counter (OTC) nicotine replacement products available to all provincial residents.[5]

The percentage of state quitlines that provide cessation medications has increased since the first edition of *Integration*

of Tobacco Cessation Medications in State and Provincial Quitlines: A Review of the Evidence and the Practice with Recommendations from 70% in 2008 to 87% in 2012.[5] The median state medication budget was $310,024 (n=28) in 2008 but declined in 2012 to $212,251 (n=53).[5] As of May 2014, 42 states, one territory, and two Canadian provinces offer free cessation medications, while seven states offer discounted OTC or prescription cessation medications[7]. Among states that provide free cessation medications, the nicotine patch is most likely to be offered (n=44 states), followed by gum (n=35) and lozenge (n=24). Free prescription cessation medications include bupropion SR (n=3), varenicline (n=3), the nicotine inhaler (n=2) and nicotine nasal spray (n=2). A much smaller number of states offer some form of discounted medication.

Table 2: State and Provincial Quitlines Offering Free Cessation Medications

Free Medications							
	Patch	*Gum*	*Lozenge*	*Spray*	*Inhaler*	*Varenicline*	*Bupropion*
States	44	35	24	2	2	3	3
Provinces	0	0	0	0	0	0	0

Source: http://map.naquitline.org/reports/medication/

Table 3: State and Provincial Quitlines Offering Discounted Cessation Medications

Discounted Medications							
	Patch	*Gum*	*Lozenge*	*Spray*	*Inhaler*	*Varenicline*	*Bupropion*
States	4	4	4	2	2	5	4
Provinces	0	0	0	0	0	0	0

Source: http://map.naquitline.org/reports/medication/

Current Models of Tobacco Cessation Medication Integration and the Factors that Influence Them

Clearly there have been shifts in the practice of delivering cessation medications via quitlines over the past five years. While eligibility criteria, the types and durations of medications provided and funding may shift from year to year, or even within a given year, and the ability of a quitline to promote the availability of medications may fluctuate, the basic models that describe the various approaches to medication integration have remained nearly the same as those in 2008. It is also important to note that a state may shift between the four models described below during a given year, as funding allows.

1. Medication information only. As of May 2014, there are seven states and one territory that do not offer cessation medications,[7] down from 14 state quitlines following this model in January, 2009.[8] In these cases, the quitline serves as a critical clearinghouse for information on cessation medications. Quitline counselors provide decision-support to assist callers with making an informed choice on which types of medication may be right for them, though the caller is responsible for payment and procurement of medications. Given the strong evidence base for medication impact on quitline reach and effectiveness of services, quitlines adhering to this model most often lack an adequate budget to support their integration. Medication information and decision-support remain a vital activity of all quitlines and when it is the only medication-related activity of a quitline, represents the least intensive medication integration model. As the Patient Protection and Affordable Care Act (ACA) is implemented, more callers may have coverage for one or more forms of cessation medication through their health plan or employer. As a result, quitline counselors may play an expanding role in referring callers to their health plans for accessing medication benefits.

2. Limited medication distribution. Under this model, quitlines distribute cessation medications to selected "priority" populations that have high prevalence of tobacco use in hopes of increasing their utilization of the quitline. Other quitlines employ this model when providing limited courses of medication for only limited periods of time. Limited budgets, large populations and the mission of reaching as many people as possible with evidence-based services makes this model more appealing than trying to provide medication to all callers.[8] It is important to note that in this model, counseling remains available to all callers but may be optional, whereas most

quitlines require callers to actively participate in counseling in order to receive medications. An example of limiting provision of medications to priority populations is illustrated by Washington's quitline that at times has provided NRT only to specific callers including the uninsured, and those covered by Medicaid, Medicare, Indian Health Services and the Veterans Administration.

3. Full medication distribution. Some quitlines view medications as an integral part of their mission to provide comprehensive tobacco intervention services consistent with strength-of-evidence 'A' recommendations in *Treating Tobacco Use and Dependence, 2008 Update*.[6] While behavioral counseling alone and medication use alone are effective in increasing tobacco abstinence rates, there is a greater likelihood of tobacco abstinence when they are used in combination.[6] Under this model, select medications are provided to all eligible callers, though the type of medications and the dosage/duration may vary. In addition, there are states that require enrollment in quitline counseling in order to receive medication and some that do not.

4. Partnership distribution. While Canadian quitlines do not provide medications to quitline callers, there are formally established partnerships that link medication provision by a health care provider with quitline counseling in British Columbia (BC), Quebec and Yukon.[7] For example, in British Columbia (BC) 12-weeks of free nicotine gum and patch are available to callers by phoning 8-1-1. The operators at 8-1-1 can warm-transfer to QuitNow (BC's quitline), but it is not mandatory for them to do so. (Donna Czukar, personal communication, June 1, 2014) In the U.S., use of this model may grow as the ACA is implemented.

PROVISION OF MEDICATION HAS A POSITIVE IMPACT ON MANY QUITLINE ACTIVITIES: A LITERATURE REVIEW

In addition to landmark studies noted in the 2009 publication,[8] published studies continue to demonstrate the positive impacts of integration of cessation medications with quitline services.

Positive Impacts on Reach

Provision of free medication by a quitline appears to motivate tobacco users who would not be as likely to access the quitline or try to stop tobacco use if free medications were not available, which in turn results in increased numbers of callers to quitlines.[8]

The Guide to Community Preventive Services[9] notes that "12 studies examined the effectiveness of offering free cessation medications (primarily nicotine replacement therapy) to callers to promote use of quitlines and enhance treatment options. Provision of medications was typically promoted through earned media activities such as press releases and announcements. Nine of the 12 studies evaluated changes in call volume and found a median relative increase of 396% (IQI: 134% to 1132%)."

The Smoking Treatment for Ontario Patients (STOP) offered free NRT with counseling communicated via media announcements and received over 7,500 calls in the first 24 hours.[10] Showing a more modest effect, in 2006 researchers in Minnesota demonstrated higher reach and quit outcomes with free NRT compared to no offer of NRT. Calls-per-month increased more than four-fold after the NRT offer, with over a three-fold increase in the percentage of callers who enrolled in multi-session counseling in order to access free NRT. The lead investigator reported that the NRT offer yielded increased participation and abstinence rates that resulted in an eight-fold increase in program impact.[11]

Building on results found by Tinkelman et al. in 2007,[12] in 2013, two quitlines demonstrated that call volumes can increase dramatically using paid-media promotion of free NRT. As a result of promoting eight weeks of NRT, Idaho increased call volume nearly seven-fold from 213 registered callers in December of 2013 to 1,433 registered callers the following month. Similarly, Georgia increased their call volume more than four-fold from 800 in October 2013 to over 2,600 in the following month. (Idaho Department of Health and Georgia Department of Health, personal communication, June 1, 2014)

Positive Impacts on Outcomes

Callers to quitlines who use cessation medications have increased tobacco abstinence rates compared to those callers who do not use medications.[13] This continues to be true despite the self-selection bias where those less dependent and more confident are more likely not to use medications in their quit attempts and those who are more nicotine dependent and less confident in their ability to quit are more likely to use cessation medications.[14]

Providing combination NRT (the nicotine patch plus nicotine gum) to quitline callers has further enhanced this treatment effect.[15] Quit outcomes for those randomized to either two-weeks or six-weeks of combined patch and gum were significantly higher for both of the combined-NRT cells than for two-weeks or six-weeks of the patch only. Furthermore, experience shows that callers receiving NRT delivered via mail in a split shipment, i.e., an NRT mailing occurs on two separate occasions during the course of the quit attempt, are more likely to complete more counseling calls those receiving their NRT in a single shipment.[13,16]

The Montana quitline offered callers the choice between varenicline and NRT to determine how the offer of different types of medications might influence utilization and outcomes. Those who selected varenicline were more likely to be older women, have 12 or more years of education, have health insurance, smoke cigarettes, have more than six-year duration of tobacco use, and have two or more lifetime cessation attempts than those selecting NRT. They completed more counseling calls and had improved quit outcomes at six months (17% versus 11%).[17]

Positive Impacts on Satisfaction

Medication delivery via quitlines increases satisfaction with the service provided which may increase the likelihood of improved adherence to call protocols as well as increase word-of-mouth referral to the quitline.[14,16]

Positive Impacts on Engagement

There is good evidence that if someone participates longer in a behavior changing program (i.e., engagement), they are more likely to succeed. Especially where the offer of medications increases the number of contacts with a caller to provide additional medication (e.g., split shipments), opportunities to provide additional counseling with each caller is also increased.[12,14,18]

Positive Impacts on Systems Change

In 2010, only 48.3% of those who had visited a healthcare provider in the past year received advice to quit smoking and 31.7% of smokers who tried to quit in the past two years used counseling and/or cessation medications.[19] Health care systems can effectively link patients with population-based treatment, such as quitlines, and recent efforts to promote the Ask-Advise-Refer model for health care providers is an example of quitlines as critical components of systems change initiatives to increase access to evidence-based cessation treatment. Access to evidence-based services that include counseling and access to free NRT also provides a feasible, cost-effective way to increase the reach of treatment after discharge from the hospital.[20]

Vermont smokers (n=884) were called by random digit dialing to determine past and future use of evidence-based cessation treatment. Among those who had recently attempted to quit, 61% had ever used a treatment, 21% had ever used a psychosocial treatment, and 57% had used a medication. Among those who planned to quit, 68% stated they would use a treatment, 35% would use a psychosocial treatment, and 62% would use a medication. The major predictors of past or future use of treatment were greater cigarettes per day, older age, being a woman, and seeing a health professional. This survey suggests that many smokers have used, or plan to use, a smoking cessation treatment, but less than 10% of Vermont smokers who try to quit use the state quitline, counseling, or free medication provision to do so.[21] Referral systems are one of three interventions deemed effective at increasing use of quitlines, according to the Community Preventive Services Task Force, which found that they increase both the use of quitline services and the number of patients who successfully quit using tobacco.[9]

Appendix A is a list of recent publications and peer-reviewed articles that address use of pharmacotherapy for smoking cessation. It should be noted that many of the studies were not conducted in quitline settings. Each article should be assessed for its relevance to the reader's needs and whether findings are applicable to the

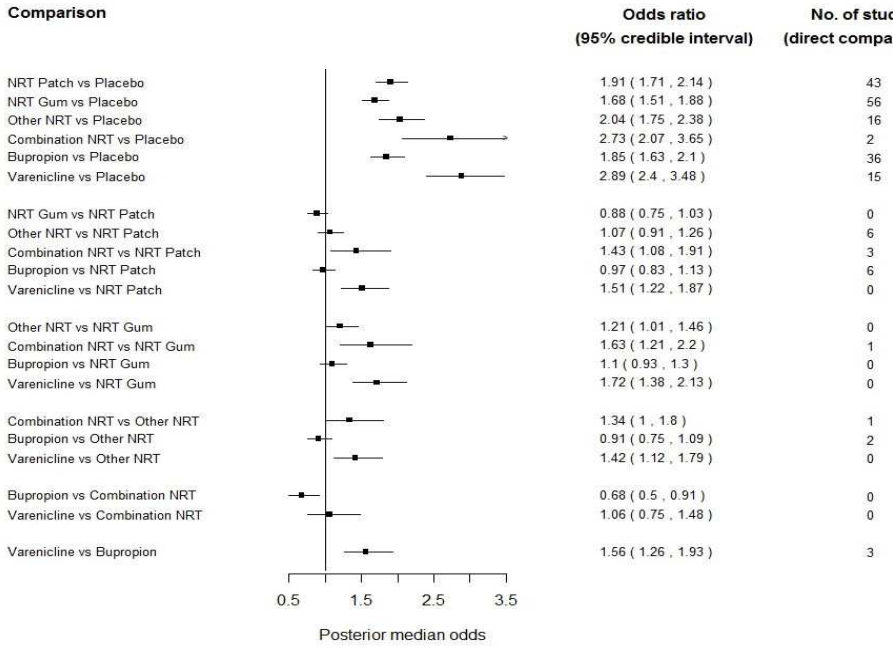
pharmacological treatments provided by their quitline.

Integration of Tobacco Cessation Medications into Quitline Services is Cost Effective

Pharmacologic interventions are proven to increase quitline abstinence rates. Single-therapy NRT has been shown to approximately double quit outcomes over placebo[6,22], while combined use of patch and gum has been shown to further increase quit outcomes over single-therapy NRT and be more cost effective than single modalities.[15] In a trial conducted by the Wisconsin Quitline, two-weeks of patch plus gum not only yielded a 48.2% quit rate at 26 weeks compared to 38.4% for patch-only, but also yielded a lower cost-per-quit of $442 per smoker versus $464.[15] Cost-per-quit is calculated by taking the cost of treatment services (program costs) and dividing it by the number of quitters for each type or combination of medications.

Absolute costs of providing quitline services rise with the addition of medications.[8] Quitlines need to determine if the value that medications bring across the entire spectrum of quitline services is worth these additional costs. Different medication types and durations of therapy will result in different quit outcomes (Table 4) and costs. Table 4 provides odds ratios for each medication and combination of medications (compared to placebo) that can be used to inform cost-effectiveness. Quit outcomes may also vary based on the population they are promoted and targeted to. Quitline promotions offering free medications may attract more dependent callers than are represented in the general population of smokers or compared to callers when no NRT is offered in a quitline setting. A Minnesota Helpline study found that 13% of callers reported using more than one tobacco product pre-NRT offer compared to 21% post NRT offer, suggesting a more nicotine-dependent group of callers.[11] In a Canadian study, the Ontario STOP Program found that callers to the quitline enrolling as a result of free NRT promotion were more likely to be daily smokers and score significantly higher on the Heaviness of Smoking Index (HSI) than the general population of smokers in Ontario.[10]

Table 4: Network meta-analysis of first-line cessation pharmacotherapies versus placebo and versus each other, with NRT by type



Adapted from Cahill, K. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Review;Issue 5. 2013.

**Credible Interval: CredI*

Implications of Table 4 for Practice

- Both NRT and bupropion perform similarly compared w[illegible] ratios (ORs) of 1.84 (95% CredI 1.71 to 1.99) and 1.82 (95% C[illegible]
- Different types of NRT are generally equally effective.
- Combinations of NRT outperform single formulations (v[illegible]1.91); versus gum: OR 1.63 (95% CredI1.21 to 2.20); versus 'c[illegible]

Adapted from Cahill, K. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Review;Issue 5. 2013.

**Credible Interval: CredI*

- NRT combined with nortriptyline or with bupropion is not shown to be more effective than NRT alone.
- Bupropion demonstrates no excess of neuropsychiatric events (RR 0.88 (95% CI 0.31 to 2.50)) or of cardiovascular events (RR 0.77 (95% CI 0.37 to 1.59)).

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- Varenicline is more effective than NRT or bupropion, when each is compared with placebo (varenicline vs placebo OR 2.88 (95% CredI 2.40 to 3.47)).
- Varenicline is superior to any single type of NRT, and is as effective as combinations of NRT (OR 1.06 (95% CredI 0.75 to 1.48)).
- Varenicline outperforms bupropion in head-to-head comparisons (OR 1.59 (95% CredI 1.29 to 1.96)).
- Varenicline demonstrates no excess of neuropsychiatric events (RR 0.53 (95% CI 0.17 to 1.67)), and a marginal but non-significant increase in cardiovascular events (RR 1.26 (95% CI 0.62 to 2.56)).

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- Nortriptyline approximately doubles the chances of quitting (RR 2.03 (95% CI 1.48 to 2.78)).

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- Cytisine increases the chances of quitting compared with placebo, without significant adverse or serious adverse events (RR 3.98 (95% CI 2.01 to 7.87)).

The Guide to Community Preventive Services: *The Community Guide: What Works to Promote Health*[24] provides an economic assessment of:

- Cost-effectiveness of providing quitline counseling and cessation information;
- Cost-effectiveness of adding cessation medications to existing quitline services; and
- Cost-effectiveness of providing a combination of quitline counseling, nicotine replacement therapy (NRT), and media promotion.

More cost-effectiveness information can be found in NAQC's Assessing the Cost-Effectiveness of Quitline Programs and also in **Appendix B**.

Guidelines for Determining Cost-Effectiveness

There is an additional cost for providing cessation medications to tobacco intervention programs however, it may prove to be cost- effective so long as the quit rates are increased sufficiently to justify the added expense. In addition to improved quit outcomes, free medications can also increase reach.[10,11]

For heavily-addicted smokers, cessation medication improves quit rates.[23] For less addicted smokers, the use of medication may not be as critical. More dependent smokers are more likely to seek help with quitting.[24] As such, quitlines tend to attract highly-dependent smokers, so the addition of medication to the treatment program is worthwhile and cost effective.[25,26] Comparing data from the 2010 Behavioral Risk Factor Surveillance Survey (BRFSS) with data on those who call quitlines, callers to quitlines are less likely to be non-daily smokers than the general population of smokers (2.8% vs. 21.8%).[27] Comparing quitline callers with the general population of smokers, quitline callers also tend to smoke more cigarettes per day (18 vs. 15).[28] So while adding cessation medication is likely to improve quit outcomes, adding medications also increases cost and may limit the number of smokers who can be served. In the first Medication Issue Paper, Dale, et al suggested creating a checklist and considering the following before making a final decision on medication integration:[8]

1. Determine the existing cost to market the quitline and deliver the existing services to the population being targeted. Estimate the potential increased number of calls that will occur from promotion of medications based on other quitlines' experiences. Will the addition of medications increase reach enough to allow you to reduce current marketing costs and by what amount?

2. Define the costs of administrative processes involved with setting up and maintaining the provision of medications to callers. This includes the cost of purchasing the medication, mailing costs of the medication, costs associated with using a fulfillment vendor, and any software and personnel time to directly manage the distribution.

3. Look carefully at all of the options available, many of which are discussed in this paper. For example: Should medication be provided by direct mailing of medication or by providing a voucher? Should the quitline provide coupons for a discounted price on the medication? Should the quitline offer medications only to populations with the greatest need, such as the uninsured or under-insured, or to everyone?

4. It can be helpful to also include the savings from reduced health care costs that may be gained in the first year and subsequent years of tobacco abstinence to the governmental and health care organizations that may be funding the quitline. The USPHS Guideline provides a succinct review of cost-effectiveness and other economic outcomes of treating tobacco dependence.[6]

CONSIDERATIONS IN THE INTEGRATION OF TOBACCO CESSATION MEDICATIONS INTO QUITLINE SERVICES

Does provision of medication fit within our quitline's strategic objectives?

There are some important considerations that quitlines should consider in deciding whether or not to provide cessation medications. The first is to consider the primary goal of the quitline and how medications support that goal. Each quitline will need to decide whether their strategic vision is one of providing fewer callers with more comprehensive treatment, that is, both cessation medications and counseling, or providing a potentially larger number of callers with less comprehensive treatment (counseling only).[6] For some, the increase in successful quit outcomes and higher satisfaction rates among quitline callers may offset the fact that they are able to serve fewer callers for a given budget.

In practice, most quitlines have tried to strike a balance between the number of callers they serve and the effectiveness of the treatment they provide. Providing starter-kits of OTC NRT is likely to prompt smokers to call the quitline, whereas providing no NRT may cause the service to be under-utilized.[10,11] Quitlines that run short of funds during a fiscal year may decide to "turn off" the medication benefit in order to continue providing counseling services through the remainder of the funding cycle. Doing this can cause some disruption and confusion among callers, as well as frontline staff, making good communication between quitline funder and service provider essential.

Some state quitlines limit medication (and other services) to those who are uninsured or under-insured. Other quitlines provide a medication benefit to all callers who intend to quit, but may offer longer regimens to priority populations. Some quitlines require the caller to participate in the counseling program offered through the quitline or through other behavioral support resources in order to receive or continue to receive medication. A few quitlines have gone to a single-call model, and provide NRT to those who are ready to quit. Clearly, states are finding ways to ensure that the services they provide and who they are delivered to align with the strategic objectives of their quitline. For more detailed information on the medications provided by state quitlines see http://map.naquitline.org/reports/medication/.

Another consideration is somewhat philosophical but is also directly tied to the determination of each quitline's primary purpose and role: whether the quitline funder has concerns that providing free medications to all or some quitline callers might deter health plans and self-insured employers from providing medications themselves, putting further stress on limited public funding for quitline services. The question of "who pays for cessation?" has emerged most recently as the tobacco control community supports public and private health care systems' implementation of the ACA.

As a result of ACA, the responsibility for paying for state quitline services should shift from the public sector to a more evenly shared public-private model, though the shift will take a great deal of leadership from state tobacco control programs and other entities the fund quitlines. Ultimately, the cost of cessation services should be borne by the health plans responsible for covering the care of particular populations (as defined by the ACA).[28] However, the degree to which these entities will utilize the existing infrastructure of state quitlines versus creating their own cessation services

remains to be seen. It goes without saying, the state tobacco control program should continue to assure services for the uninsured and underinsured.[29]

Quitlines can certainly play a pivotal role in helping health plans and self-insured employers meet the ACA requirements that also results in moving toward a shared model of payment for services. For example, a state quitline might create partnerships with health plans whereby the quitline would provide counseling and cessation medications to everyone who calls and the health plans would reimburse the quitline (i.e., the state funder) for services provided to their enrollees. This approach would avoid duplicative cessation services across a state and would leverage the infrastructure created by quitlines nationwide. Another approach may be to use a coordination-of-services model to triage those who call the quitline to the most comprehensive services available to them. Under this model, callers are asked about their employment and / or health plan coverage. If information about coverage offered by the employer or health plan is in the quitline's database, the caller is enrolled to the program that offers the most comprehensive services at intake.

For more information on the development of cost-sharing partnerships, see NAQC's Public-Private Partnership webpage.

What determines which tobacco cessation medications our quitline should offer?

Cost

Nicotine patches, nicotine lozenges and nicotine gum are available in generic form and are among the least expensive medications available. Bupropion SR is also available as a generic at a very low cost, but does require a prescription. With implementation of the ACA, more and more quitline callers will have medical coverage. However, getting a prescription from a health care provider will likely have cost-related barriers due to office or tele-health visit deductibles and co-pays. Varenicline, nicotine nasal spray and the nicotine inhaler are only available by prescription and no generics are available, making them the most expensive medications. For a detailed description of each FDA-approved medication, including average cost, please refer to the USPHS Guideline[6] and individual medication package inserts. Local pharmacies and national pharmacy benefit managers can provide more specific information as well.

The cost of cessation medications is also affected by the regimen provided. Using two-week or four-week starter-kits of OTC NRT can minimize costs. Using the Wisconsin quitline, Stevens Smith demonstrated that two weeks of combination NRT (two weeks of patch and one box of gum) produced higher intent-to-treat (ITT) 7-day quit rates (48.2%) than either two weeks (38.4%) or six weeks of patch-only (46.2%), and had a lower cost-per-quit ($442) than all other regimens (two weeks patch, $464; six weeks patch, $505; and six weeks patch + one week gum, $675).[15]

While the evidence points to increased effectiveness of combination nicotine replacement therapy compared to mono-therapy based on clinical trials, there is still a need for studying combination therapy in a real-world setting like quitlines. A recent study by Krupski, et al., *Cost and Effectiveness of Combination Nicotine Replacement Therapy Among Heavy Smokers Contacting a Quitline,* found good adherence with combination therapy (patch + lozenge) and numerical, but not significant, quit rates at seven months, though subgroup analyses found that uninsured study participants using combo-therapy reported 7-day quit rates (27.4% vs 17.2%, $p<0.05$), and 30-day quit rates (24.6% vs. 14.4%, p , 0.05) that were significantly higher compared to uninsured participants using mono-therapy.[29] More research is needed to investigate the cost effectiveness of providing combination therapy to various quitline participants.

Effectiveness in Achieving Tobacco Abstinence

All of the FDA-approved medications have been shown to be effective in increasing smoking abstinence rates when used with some counseling, compared to placebo.[23] Meta-analysis tells us that some cessation medications can be more effective than others.[6] A few studies have compared various medications to each other in terms of effectiveness in a given population. For example, in two head-to-head trials, varenicline demonstrated significantly higher abstinence rates than bupropion SR.[30] Varenicline and combination NRT, such as patch plus gum, have similar

effectiveness.[23] There appears to be no increase in cessation outcomes for adding bupropion SR to NRT.[23] Different NRT products seem to be equally effective, while combination NRT is more effective than any single form of NRT.[23] Cytisine may prove to be a low-cost medication, but it is not FDA-approved.[1,2,23]

The 2013 Cochrane Review of Pharmacological Interventions for Smoking Cessation is the most recent meta-analysis of medication effectiveness. The odds ratios (OR) of all medications were compared against placebo. Meta-analyses are useful when looking at a group of studies, but care needs to be taken in applying the results to quitlines since many of the trials took place in clinical-care settings. In particular, the following factors need to be considered:

1. Although meta-analysis attempts to adjust for such factors, the studies compared used different populations of study callers varying by such factors as amount smoked, age, geography, counseling intervention used, duration of treatment and year performed.
2. All of the reported findings are from clinical research studies involving multiple face-to-face contacts, usually including behavioral counseling, with the callers. The number of these contacts sometimes greatly exceeds those offered by most quitlines.
3. Integrating prescription medications into a quitline setting can be more challenging than integrating OTC medications. Because there is always a medical prescriber in the loop, the quitline counselor will need to use caution to avoid contradicting advice given by the health care provider, more familiar with the caller's medical condition and medications, and thereby undermining the physician-patient relationship. Prescription medications usually have more potential serious side effects and drug interactions than OTC medications.[23] Each quitline must determine the degree to which medication support is provided by counselors.

Given significantly improved quit outcomes, combination NRT should be strongly considered when contemplating the nicotine patch, gum, or lozenge.[6,23] Combinations of a long-acting form of NRT (nicotine patch) along with a short-acting form of NRT (gum or lozenge) consistently out-perform single forms of NRT in reducing nicotine withdrawal symptoms and producing higher quit outcomes.[6,23] With the removal of the *"do not use more than one form of nicotine replacement product at a time"* warning from OTC NRT packaging, quitlines have greater leeway to provide combinations of OTC NRT products. It should be noted that the FDA has not specifically endorsed combined use of NRT or use of NRT while smoking; they have simply removed the "do not use if you continue to smoke, chew tobacco, use snuff, or use [a different NRT product]or other nicotine containing products'' warning from the labeling. In making this announcement, the FDA Notice stated, "Upon reviewing the published reports of these and other studies, we have determined that the concomitant use of OTC NRT products with cigarettes or with other nicotine-containing products does not raise significant safety concerns."[4]

Ease of Use

Effectiveness of any medication is dependent on the medication being used correctly, including at the recommended frequency and duration, otherwise known as adherence. Medications that are administered once or twice per day are more likely to be taken as directed than medications that need to be taken many times each day. Complexity of administration can also affect adherence. For example, to maximize the effectiveness of the nicotine gum it must be chewed several times, after which the gum is to be parked against the side of the mouth to allow absorption of the nicotine. After a few minutes the user is to chew again and repeat the cycle several times for 20 – 30 minutes, at which time the gum is discarded. This is more complex than applying one nicotine patch to the skin once a day. Reduced adherence to a more complicated regimen can result in reduced effectiveness of the medication, which in turn can result in poorer quit outcomes among some users.

When providing any cessation medication, quitlines should have protocols in place to advise callers on correct use in order to optimize medication adherence. Quitline callers may say they know how to use the medications and have used them before, but when asked to describe how they understand the medications are to be used, they often respond incorrectly. Even a nicotine patch that is applied once a day needs to be applied correctly – above the waist and below the neck, and rotated daily avoiding the same location for at least seven days. While it is important to provide detailed use instructions at the time of dosing, it is even more important to ask the caller during ongoing

calls to describe how they are using the medication, reinforcing proper use and offering corrective guidance to those who are using their medication incorrectly.

Ease of Distribution
Legal and procedural issues related to over-the-counter and prescription medications are key factors in determining how complex distribution of medication to callers will be. A process for distributing over-the-counter medications will be much simpler, as there is no need to add the steps necessary to engage a licensed provider to write a prescription. With prescription medications multiple steps with clear communication to the tobacco user and his or her physician are required.

Safety and Frequency of Side Effects
There is always the potential of the medication causing unwanted and unpleasant side effects. Prescription medications typically have more side effects than OTC NRT. The type, frequency, and severity of side effects can influence use of medication by the caller. Quitlines will want to consider these characteristics in choosing medication for distribution to minimize liability concerns over adverse events and maximize effectiveness of the medication through adherence. Quitline counselors should be knowledgeable and have available support resources to guide them in discussing the side effect profiles of medications, as well as common symptoms of nicotine withdrawal in order to know when to refer the caller to see their health care provider and when to normalize the symptom as common among those quitting tobacco. Minor symptoms may be addressed by suggesting changes to the dosage or helping the caller to use the medication correctly.

Nicotine Replacement Therapy (NRT)
There are currently five FDA-approved NRTs for cessation, including three OTCs (nicotine gum, nicotine patches and nicotine lozenges) and two that require a prescription (nicotine inhaler and nicotine nasal spray). Most quitlines providing medications are distributing over-the-counter NRT medications that include the nicotine patch, nicotine gum and nicotine lozenge, in single modalities or in some combination. Almost all of the reported studies of medications and quitlines concern nicotine patches and/or nicotine gum. Proven effectiveness, availability of generic products, low side effect profiles, ease of use and no requirement for a prescription make these three NRTs easiest to distribute in the quitline setting, and only two state quitlines make the two prescription NRTs available to callers.[7] Most smokers, when given the choice, will choose to use the nicotine patch.[31,32]

Non-nicotine Medications
There are two FDA-approved non-nicotine cessation medications that require a prescription: bupropion and varenicline.

Bupropion
According to the most recent NAQC Quitline Profile data,[7] three state quitlines provide free bupropion and four offer discounted bupropion as a medication option to callers. Since the first Medication Issue Paper was published in 2009, there have been no published trials of bupropion in quitline settings. The most common side effect associated with bupropion use is insomnia, which has been reported to occur in about one third of people who take the medication. Less common adverse effects include dry mouth, anxiety and hypertension. There is a slight risk of seizures (approximately 1/1,000), which can be minimized further with careful screening of callers for contraindications to its use, although meta-analysis has shown seizure occurrence of less than 1:1,500.[23] Contraindications for bupropion SR include a history of seizures, closed head trauma, brain surgery, strokes, and the eating disorders anorexia nervosa and bulimia.[33] The FDA has required a boxed warning regarding bupropion SR and its association with psychiatric symptoms with its use (see further discussion below).[34]

Varenicline
The most recent NAQC Quitline Profile data also shows that three quitlines currently offer varenicline as a free medication while five offer it as a discounted option.[7] Varenicline was approved by the FDA for use in 2006 and is available only by prescription with no generic equivalent available until the patent expires in 2018. Clinical trials have demonstrated increased efficacy for smoking cessation compared to placebo, single therapy NRT, and

bupropion.[23] There appear to be no drug interactions with varenicline and, except for a dosage adjustment for severe kidney disease, there do not appear to be any medical contraindications to its use. Varenicline is contraindicated for those who are pregnant or breastfeeding. Nausea and sleep disturbances such as vivid dreams and insomnia are the most frequently reported side effects. The safety of varenicline has been the subject of some controversy. Shortly after its release the FDA issued a boxed warning regarding use of varenicline and serious psychiatric problems (see additional discussion in section on boxed warnings below). Some quitlines may feel there are more risk management issues associated with use of varenicline in a quitline setting than with OTC NRT medications.[8]

Boxed Warnings for Bupropion SR and Varenicline

The FDA can require that "boxed warnings" be included in prescribing information when there is post-marketing surveillance evidence that use of the medication has been associated with serious adverse effects. This mechanism is meant to heighten the awareness that these effects could occur. It does **not** mean the medication should not be used for its intended purpose. Boxed warnings are usually based on adverse reactions reported by physicians, pharmacists and people who have used the medications. In July 2009, the FDA issued a warning on bupropion SR and varenicline because of increased reports of neuropsychiatric symptoms in people using these medications to stop smoking.[35] The symptoms included hostility, agitation, depressed mood, suicidal thoughts and behavior, attempted suicide and completed suicides. These could occur in people with or without a history of mental illness, and whether they had stopped smoking or not. This warning was later updated to include a statement that those using varenicline " should contact their health care professional if they experience new or worsening symptoms of cardiovascular disease, such as chest pain, shortness of breath, calf pain when walking, or sudden onset of weakness, numbness, or difficulty speaking."[35] With the boxed warning, health care providers are to advise patients, family members and caregivers of the potential for these symptoms and to instruct patients to stop using the medication immediately if these symptoms develop and contact their health care provider. Patients should also be advised to use caution when driving, operating machinery or engaging in other hazardous activities until they know how the medications affect them. In considering providing these medications, quitlines should keep three important points in mind:

1. The 2013 Cochrane Review of pharmacological treatments states that:
    - Bupropion demonstrated no excess of neuropsychiatric events (RR 0.88 (95% CI 0.31 to 2.50)) or of cardiovascular events (RR 0.77 (95% CI 0.37 to 1.59)).
    - Varenicline demonstrated no excess of neuropsychiatric events (RR 0.53 (95% CI 0.17 to 1.67)), and a marginal but non-significant increase in cardiovascular events (RR 1.26 (95% CI 0.62 to 2.56)).

2. Many of the neuropsychiatric symptoms described in the boxed warning are symptoms often seen in people who are trying to stop smoking and are experiencing nicotine withdrawal. These reports should also be interpreted in the context that the same incident can be reported by several different persons. Recently published studies have shown no significant differences in adverse events between use of bupropion SR and varenicline, or placebo.[35,36]

3. The possible risks of serious adverse events that might occur using either of these medications should also be weighed against the significant health benefits of quitting smoking and the known risks of continued smoking.

Simultaneous Use of More Than One Tobacco Cessation Medication

As stated earlier, certain combinations of medications have been shown to be more effective than use of one medication alone, such as nicotine patch and nicotine gum or adding the nicotine patch to bupropion SR.[6] The first published trial comparing combination patch and gum with patch only in a quitline setting showed combination NRT to be significantly more effective than patch-only.[3] However, findings from Krupski, et al, did not find that heavy smokers who contact a quitline and are provided with a two-week supply of combined NRT demonstrate significantly enhanced rates of cessation compared to monotherapy.[30]

While the USPHS Guideline gave combination NRT a strong recommendation, OTC NRT labeling was not updated

until 2013. Among other changes, the revised labeling eliminated the language warning against using more than one form of NRT simultaneously. As noted earlier, the FDA did not change the indications for OTC NRT, nor endorse combination NRT. The scientific evidence clearly and convincingly demonstrates improved quit outcomes for combination NRT with no significant increase in serious adverse reactions.

Some clinicians in face-to-face settings have been combining NRT with varenicline, and while both medications are FDA-approved for smoking cessation, and the two drugs appear to be well tolerated when taken together, to date there is no empirical evidence to demonstrate improved efficacy.[37] Use of multiple patches (i.e., high dose patch exceeding 21mg)[38] and use of three or more cessation medications have been used in clinical care, but such use in a quitline setting has not been tested.[39]

How Much of the Tobacco Cessation Medications Should Our Quitline Provide?

The optimal duration of courses of tobacco cessation medications that quitlines should provide is still undefined. While many tobacco users do very well with six to eight-week medication regimens, some seem to require extended use of NRT to achieve long-term abstinence from tobacco use. Labeling for OTC NRT, after changes implemented by the FDA in 2013, no longer advises users to stop treatment after a certain number of weeks. Labeling has been changed to state…"it is important to complete treatment. If you feel you need to use [the NRT product] for a longer period to keep from smoking, talk to your health care provider."[4] The USPHS Guideline cites six to 14 weeks as a usual duration for the nicotine patch (and gum), and more than 14 weeks for long duration regimens.[6] The odds ratio for both usual and long-duration courses of the patch is 1.9, or roughly a doubling when compared to placebo, while the odds ratio for nicotine gum improves to 2.2 for extended duration compared to 1.5 for usual duration.[6] At the time of publication, only one trial was available for the nicotine lozenge, and the Guideline did not address the duration of use for this medication. Bupropion SR is often prescribed for smoking cessation by health care providers for eight to 12 weeks and varenicline for 12 weeks.[40] Extended use of both bupropion SR and varenicline has proven effective, and long-term use of varenicline for up to one year has been shown to be safe and effective.[41]

Cessation Medication Starter-Kits

The evidence for cessation medication starter-kits can be traced to trials conducted by New York and Oregon.[33,42] In *Reach, Efficacy, and Cost-Effectiveness of Free Nicotine Medication Giveaway Programs,* authors tested different durations of medications and delivery methods, including mailing NRT directly to study callers and sending vouchers for two week of nicotine patch or gum. Durations of therapy included one-week (mailed), two-weeks (voucher and mailed) and six-weeks (mailed). Quit rates varied by the amount of NRT sent, with those sent six-weeks of NRT reporting the highest rates (35%) while those sent one-week reporting the lowest rates (21%). It should be noted that the quit rates were not reliably different between the durations of therapy.

In the Oregon study, callers were randomized to receive either a two-week starter-kit or a full eight-weeks course of therapy. Outcomes showed that eight-weeks of NRT resulted in higher quit outcomes (19.6%) compared to two-weeks (14.3%). The length of use of NRT was longer among those receiving eight-weeks and quitline counseling call completion was higher (6.3 weeks and 2.0 calls respectively) than length of use and call completion among those receiving two-week starter-kits (4.3 weeks and 1.6 calls respectively). Of those provided starter-kits, 39.3% reported that they accessed additional NRT on their own.

The CDC recommends quitlines provide population-based cessation interventions, including counseling and medication.[43] In addition to proactive counseling calls, the CDC suggests that quitlines should consider including two weeks of OTC NRT for those interested in using medication.

Findings from a 2010 study by Cummings, et al. do not support the notion that sending more free nicotine patches to quitline callers will reliably increase quit rates. Five groups of smokers who called the New York State Smokers' Quitline (NYSSQL) between April 2003 and May 2006 were mailed two-, four-, six- or eight-week supplies of free nicotine patches. Callers were provided with one follow-up call and Medicaid callers were eligible to receive up to four follow-up calls. Authors did not find a clear cut dose response relationship between the number of free nicotine

patches sent to callers and quit rates measured a year later and suggest that it may not be cost-effective to send more than a starter kit of free medications.[44]

Adherence and the Issue of "Waste"

Experience has shown that some recipients of free NRT do not use the full regimen they receive. Unpublished data from the North Carolina (NC) Annual Quitline Evaluation Survey showed that among quitline callers who received a 2-week supply of patch, gum or lozenge in 2012, only 1% reported using none of it, while 67.2% reported using all or most of the NRT sent to them. Among reasons for not using all the medication, the most common were: started smoking again (19%); experienced side effects (16.8%); and successfully quitting and no longer needing NRT (12.9%). Among NC callers who were sent NRT, adherence data shows that among patch users, 81.2% used them every day and over 80% used them as advised by rotating the patch to different sites and applying them above the waist. As one would expect with medications that need to be used repeatedly throughout the day, gum and lozenge users were less compliant, with 72.1% and 70% reporting using the medication every day. Among these callers, 75.4% of gum users reported following the "chew / park" process and 92% of lozenge users allowed the lozenge to slowly dissolve. The biggest gap in adherence was that callers using gum and lozenge used only 4.8 and 4.4 pieces per day, rather than the manufacturer's recommended amount of 9 or more pieces per day.

Quitlines who provide free medications should take steps to encourage adherence. Callers should receive clear verbal use instructions followed by written instructions that meet health literacy standards (i.e., plain language). Quitline counselors can reference previous medication documentation in caller records to recognize those who have been sent medication and should provide these callers with follow-up adherence support. Smokers who are quitting will sometimes stop using a cessation medication because they feel they don't need it anymore due to low-urge severity. Callers may fail to realize that the reason their urge severity has decreased is because the medications have been doing their job. After discontinuing use of the cessation medication, they often find themselves struggling to stay quit. Quitline counseling staff has an opportunity to remind callers of the importance of using the full regimen of medication.

A large percentage of callers using quitlines in most states are uninsured or lack insurance coverage for tobacco cessation consistent with best practices, and are thus less likely to be able to obtain more medication on their own to sustain a longer duration of therapy.[5] Whether implementation of the ACA will provide coverage of OTC NRT remains to be seen. If health plans do cover these medications, provision and promotion of free two-week starter kits by quitlines may have an even greater impact than they currently do.

Finally, we know that free cessation medication increases calls to the quitline and improves quit outcomes compared to when no medications are offered. The question is not so much *whether* to offer medication but *how to structure the offer* to stretch woefully limited quitline budgets and to motivate callers to call the quitline.

Which Medication Distribution Process will be Best for Our Quitline?

Operational experience has shown that direct mail-order is likely the most efficient means to get OTC medications to quitline callers, as vouchers present an inherent barrier to access that requires the recipient to go to a pharmacy to source their medication. The California Smokers' Helpline switched to direct mail-order for some of its callers because they saw some of those receiving vouchers failing to make a quit attempt. They felt that switching to direct mail-order would increase quit attempts. (Gary Tedeschi, PhD, personal communication, June 1, 2014) One could reasonable argue that those who do not pick up their medication after receiving the voucher are not truly motivated to quit. Whether or not this is the case, the fact remains that the mail-order approach removes most barriers to medication access and increases the likelihood of making a quit attempt.

Mail-order fulfillment is most commonly handled by fulfillment vendors who store, pack and ship the NRT. Their services eliminate the need to store costly and bulky NRT on quitline premises or to lease costly warehouse space. Daily electronic feeds communicate dosages, regimens, names and addresses to the fulfillment vendor. Standard protocols include verifying the mailing address by the counselor before initiating shipment.

Each quitline will need to determine which type of medication distribution system to use. The use of a direct-mail system allows more control over actual fulfillment of the medication and maximizes the convenience by having it delivered to the caller's home. However, there are costs to maintain an inventory of medication and to ship it. One benefit of vouchers is avoiding the cost of mailing medications and lower costs if vouchers are not redeemed. Vouchers may be less expensive to distribute but they require a more complex system to monitor disbursement of medications and reimbursement to participating pharmacies.

GUIDANCE FOR OVERCOMING QUITLINE CHALLENGES TO PROVIDING MEDICATIONS

Legal/Liability Issues Related to Medication Distribution

There is some inherent liability associated with mailing OTC NRT to quitline callers. The FDA has deemed these medications safe and effective if used as directed without supervision of a physician. In general, this should limit quitline liability if recommendations given by quitline counseling staff are consistent with package directions. Recent FDA changes to OTC NRT labeling could potentially lessen liability concerns associated with combination NRT. However, the risk of adverse outcomes is possible, and risks can be minimized by seeking legal guidance for the state(s) in which the quitline operates. The following are examples of how some quitlines have addressed liability issues:

- Limit provision to OTC medications only.
- If the quitline decides to offer prescription medications, then ensure the following processes are in place:
    - Provide quality support for medication decision support processes to improve consistent delivery of information from the quitline counselor to the caller. Quitline counselors should be able to reference easily accessible NRT dosing algorithms while talking to callers.
    - Close oversight of coaching recommendations and medication disbursement by experienced professionals is recommended. An efficient means for coaches to consult with clinical or medical team members should be in place if there are questions related to medication fulfillment that fall outside of guidelines.
- Quitlines should provide annual ongoing training on medication protocols for counseling staff.

Screening for Medication Eligibility

There are no absolute contraindications for NRT, but there are medical conditions that may require supervision by a health care provider to assure patient safety. Eligibility criteria for distribution of medication vary between quitlines. Quitline counselors should follow a set of clearly worded questions that can be used to identify callers who should not be sent OTC NRT without permission from their health care provider. These include:

- Callers under 18 years of age, since OTC NRT is not approved for those under 18 years of age.
- Pregnant callers: Pregnant smokers should be advised to speak to their physician before using NRT or any other cessation medication.
- Callers with exclusionary medical conditions. However, these conditions are few for OTC NRT. Those that call for more physician oversight include:
    - Myocardial infarction or stroke within the past two weeks;
    - Generalized rash or other allergic reaction from previous use of a tobacco cessation medication; and
    - Unstable angina or severe arrhythmia.

There are some medical conditions that quitlines may consider not including as exclusionary criteria for OTC NRT, such as high blood pressure, breast feeding, or the intention to combine other cessation medications with NRT. Counselor protocols and support systems should prompt the counselor to advise these callers to let their doctor know about their intention to use NRT and to document that this information was provided in the caller's file.

The risks associated with use of these medications should be weighed against the known risks of continued smoking. Most quitlines that provide mail-order fulfillment of OTC NRT have processes in place to seek permission from the caller's physician before sending medication if the caller reports an exclusionary condition. This can be done by mail or fax. Integration with Electronic Health Records may make this process easier. NRT can be mailed once permission by the physician is received and the communication should be kept on file. Some quitlines have internal systems support built into the quitline infrastructure to facilitate medical overrides in special circumstances, such as callers who have exclusionary conditions, but who received NRT while hospitalized within the previous two weeks, or were released from the hospital with a prescription for NRT.

Each quitline will have to decide whether they want their phone counselors to ask exclusionary questions of callers who want to use prescription medications. One reason for doing this is to identify reasons why the caller's physician is unlikely to write a prescription and re-direct them to a medication that is more likely to be approved. For example, someone who wants to use bupropion SR but has a seizure disorder or is taking a monoamine oxidase inhibitor (MAOI) is unlikely to have their physician write them a prescription. By identifying these contraindications, the quitline counselor may be able to re-direct the caller to a medication that is better suited to them before they go to their physician only to be told no and then possibly decide that they will not quit. One reason for not screening for prescription medications is that it is the role of the health care provider to determine if a given prescription medication is medically appropriate for their patient and to assist their patient in making an informed choice whether or not to use a specific medication.

Some quitlines limit NRT availability to those who use a certain number of cigarettes per day or tins of spit tobacco per week. Others do not exclude light smokers, but take the approach of neither encouraging nor discouraging the use of NRT for lighter smokers. Very light smokers can be offered a low dose patch (7mg) or a form of NRT that allows the user to adjust dosage by increasing or decreasing how much is used per day based on their needs, similar to the gum or lozenge. In most cases the amount of nicotine being delivered to the smoker or chewer is less than the amount of nicotine delivered by their use of tobacco. Most quitlines base their NRT dosing algorithms on NRT package labeling, and the risk of nicotine toxicity is very low. Experience and research show that smokers tend to under-use their NRT medications, especially those that are designed to be taken repeatedly throughout the day, such as the nicotine gum and lozenge.[9] Quitline counselors should encourage those electing to use gum or lozenge to use enough per day to have a therapeutic effect, rather than cautioning against using too many pieces per day.

Communication of Medication Information

Quitline counselors should be able to communicate to quitline callers the rationale for using one or more cessation medications, provide a description of FDA approved medications, and help them make an informed decision whether to use a cessation medication. They should also be able to describe how each medication works to further help the caller select a suitable cessation medication. In the interest of treatment fidelity, medication adherence and risk management, it is optimal to provide some sort of readily accessible script or aid to support counselors in providing this information. This script or aid should address:

- Rationale for using cessation medication when quitting, including reducing nicotine withdrawal and making quitting easier;
- Medications that are FDA-approved for smoking cessation;
- Which medications are covered by the quitline or health plan, as experience shows coverage is the single greatest influence on what medications the caller will opt to use;
- Importance of using the medications correctly and at sufficient dosages to effectively manage urges;
- Encouragement to use the full recommended regimen of medication provided;
- Importance of taking subsequent counseling calls, including emphasizing that those who do take ongoing calls are more likely to successfully quit and stay quit;
- Encouragement to carefully review all written instructions on medication use provided to callers by the quitline, whether printed or online; and

- Specific directions to call the quitline or contact their health care provider if caller has questions or issues, including possible side effects.

Some quitlines have incorporated text messaging into their suite of services, and these text messages can be another important source of information and support for those using cessation medications. Similarly, some quitlines provide online information and support for cessation medications. Online functionality ranges from basic information about cessation medications, to being able to order OTC NRT medications to be mailed to the quitline caller and how to effectively and safely use each medication.

Minimizing the Cost of the Medication

While quitlines should always provide high quality medications, care should also be taken to source cessation medications at an affordable cost. Generic OTC NRT products are available that deliver identical amounts of nicotine and which most users will find suitable. To assure that medications reach the caller in a timely manner and are used as intended, the quitline can:

- Verify mailing addresses each time a medication shipment is initiated.
- Have a system in place to track shipped packages. Quitline callers frequently call to inquire about the status of their shipment. A system to track shipping is useful to inform them of the status of their shipment.
- Some quitlines provide two-week or four-week starter-kits of NRT. Others may choose to provide full regimens of medication. Regardless of how much product is sent, quitline callers should receive strong encouragement to use a full regimen of therapy. Those receiving starter-kits should be encouraged to:
    - Contact their health plan to inquire about additional NRT; or
    - Set aside money they would have used to buy cigarettes to purchase additional NRT if they are unable to obtain additional medication through their insurance provider.
- If an extended duration of medication is provided (e.g., more than four weeks), consider dividing distribution into at least two shipments. Relapse rates are highest in the first two weeks of quitting.[45] Sending a full six or eight-week regimen in a single shipment may result in a significant amount of unused medications. For example, if offering eight weeks of treatment, provide two shipments of four weeks each.
    - Use caution with two-week increments to avoid having callers run out of medications before they can receive the next shipment.
    - Consider conditioning additional shipments of medication from the quitline on ongoing engagement in counseling, which is proven to improve quit outcomes. Quitlines may want to get permission at the initial dosing call to leave a detailed phone message during subsequent outbound call attempts reminding the caller that they need to talk to a quitline counselor to receive their second shipment. This may help to avoid dissatisfied callers.

Specific Guidelines for Provision of Prescription Medications

Providing access to bupropion SR, varenicline, nicotine nasal spray or the nicotine inhaler in a quitline setting is complex. Aside from the obvious prescription processes, many quitline callers are uninsured and do not have access to a primary care physician (PCP), although implementation of the ACA (and the growing use of telehealth services to gain a doctor's prescription) may change this. Without a PCP, callers have very limited access to prescription medications. However, quitline counselors should be knowledgeable about these medications and be able to help callers make an informed choice about the seven FDA-approved cessation medications, including major contraindications for each one.

Callers can be referred to their health care provider to determine if the medication they want is medically appropriate for them. Smaller quitlines may determine that providing prescription medications is simply not worth the additional investment in infrastructure and training.

Quitlines should use caution when advising callers on how to use prescription medication, including recommending dosages. Depending on state law, doing so can be considered "medical care" and may be

considered beyond the scope of practice for a quitline counselor, regardless of their degree or certification. This includes addressing questions about specific symptoms or side effects reported by the caller. Reports of more serious symptoms such as suspected allergic reactions or thoughts of harming themselves or others should prompt the counselor to follow well-defined crisis protocols.

In order to avoid confusion or dissatisfied callers, it is important that clear directions are given on how the prescription is to be obtained. Prescription cessation medications are sometimes accessed differently than medications for other health concerns.

As both bupropion SR and varenicline now have FDA boxed warnings, discussion of these medications by the quitline counselors should include these alerts. It is recommended that counselors have a script to follow to assure the message is delivered accurately. Information should be provided neutrally by the counselor, and great care should be taken to avoid "scaring" the caller away from the use of these medications. It is important that the caller is advised to review the warnings and side effects with their primary care physician before using a medication. The goal is to help those interested in using varenicline or bupropion to make an informed decision about which cessation medication they want to use and what to do if they experience symptoms described in the alerts.

Providing Combinations of Medications

There now exists a large body of scientific evidence demonstrating improved quit outcomes for combination NRT.[6,23] The USPHS Guideline has given combined OTC NRT (patch and gum) a strength of evidence 'A' rating. The Cochrane Review has similarly reported evidence for the effectiveness of the practice.[46] The rationale for combination therapy is that it provides better management of nicotine withdrawal and improved urge-management. Furthermore, combination NRT is well-tolerated among smokers. For example, assuming the nicotine yield for each cigarette is somewhere between one milligram and three milligrams, a pack-a-day smoker is taking in somewhere between 20 and 60 milligrams of nicotine per day, depending on their smoking behavior. A 21mg patch is less likely to effectively manage their nicotine withdrawal than adding nicotine gum or nicotine lozenge to the patch, especially if their smoking patterns extract a higher amount of nicotine from each cigarette (i.e., more and deeper puffs). Using the combination NRT approach, the caller could be advised to use one 21 mg patch daily, and to use one piece of nicotine gum every one to two hours. As noted earlier, studies have shown no significant increase in serious adverse events among those using combination NRT.

For budgetary reasons, and due to the likelihood that mono-therapy provides sufficient nicotine replacement for very light smokers, this population may be excluded from receiving combination NRT at the time of initial dosing. However, a hard and fast rule here should be cautioned against. Some quitline callers may report smoking only five cigarettes per day, but upon further exploration the counselor finds they have tapered down from a much higher number of cigarettes in the week or two prior to calling. Each quitline will need to determine how they want to structure combination NRT protocols for these callers, as well as lighter smokers choosing to use mono-therapies who report they are struggling to stay quit during subsequent calls.

Each quitline will have to determine whether they want to implement combination therapy protocols and, if they do, how they will support them in a way that ensures quality and manages risk. Quality monitoring with clinical staff listening in on counseling calls is important in ensuring that protocols are followed. This holds true for combination NRT. As noted earlier, it is very important to ensure that callers receiving a single form of NRT know how to use it correctly, and this is even more important with callers receiving combination NRT. Counselors will have to be very explicit in explaining how the medications are to be used *together* to avoid sending the inadvertent message that the two medications are being sent so that the recipient can select *which* medication they want to use, thereby undermining the potential advantage of sending two types of NRT. As with mono-therapy, printed instructions that meet health literacy standards are important to include with combination NRT.

Regardless of whether the state quitline actually mails combination NRT, callers who meet eligibility criteria can still receive encouragement to add OTC gum or lozenge to the nicotine patch. The out-of-pocket cost for gum or lozenge will be less than that for two or four weeks of the patch, making it more likely that the caller will access it

on their own. They may also be able to access the other NRT from their health plan, if insured. If they are not insured, emphasizing that adding gum or lozenge to the patch will cost less per day than a pack of cigarettes may resonate among some callers.

Follow-up support during ongoing quitline counseling calls is critically important for those provided or intending to use combination NRT. All too often callers wait until they have a strong urge before using the short-acting medication (gum or lozenge). Given the slow onset of both medications, callers benefit from reminders to use the medications on a regular schedule to *prevent* strong cravings, rather than *responding* to strong cravings. Once a strong craving hits, the first thought a recently quit smoker has is typically to have a cigarette, not to use a piece of gum or a lozenge.

Other Tobacco Products

Smokeless (Spit) Tobacco

There are currently no FDA-approved cessation medications for those trying to stop smokeless tobacco (spit tobacco) use. Studies cited in the 2009 Medication Issue Paper showed little efficacy for improving cessation outcomes over that of placebo, but did show improved relief of withdrawal symptoms. These studies tested high-dose nicotine patch, nicotine lozenges, nicotine gum and bupropion SR. Spit tobacco can deliver very high doses of nicotine to heavier users. Some speculate that traditional dosages of mono-NRTs provide insufficient nicotine levels to improve outcomes over placebo.

Ebbert and Severson have published two trials using the four milligram nicotine lozenge with mixed results. The first study used the four milligram lozenge paired against a placebo that resulted in non-significant *biochemically* validated quit outcomes at 12-weeks (36% vs. 27.6%; p=0.138), but significant differences in *self-reported* 12-week outcomes (50.7% vs. 34.3%; p=0.013). The active lozenge produced significant withdrawal symptom relief and lower tobacco craving.[47] The second trial compared four milligram lozenge and tobacco-free snuff in multi-center clinical settings among spit tobacco users who were not ready to quit. There was no significant difference in abstinence outcomes between the two treatment approaches and no significant differences in withdrawal relief or tobacco craving were observed between the two treatments. At 26 weeks, biochemically-confirmed abstinence rates were similar between both groups (12% vs. 12%, p=.615).[48]

Use of NRT with spit tobacco users in quitline settings is common-place, despite lack of good efficacy data. Use of NRT products with this population, including combined patch plus gum or lozenge appears to be well tolerated. Use of combination nicotine patch and four milligram gum or lozenge for callers using two or more tins or pouches of spit tobacco weekly is sometimes used. High-dose patches have not been examined in quitline settings. While generally well tolerated in clinical settings, multiple patches provide a fixed nicotine dosage that may be difficult to adequately manage in a quitline setting.

Cigars, Pipes, other Forms of Tobacco and Concurrent Use of More Than one Form of Tobacco

Use of tobacco products other than cigarettes has increased over the past decade.[49] Between 5% and 17% of American adolescents report using hookah (water pipe) within the past 30 days.[50] Smoking of cigars, cigarillos and small cigars has increased among youth. One survey of 486 youth found that 76.7% reported ever-use of cigars, cigarillos and small cigars, while 40.7% had used them in the past 30 days.[51] Use of the cigar products was also strongly correlated with hookah use. Concurrent use of snus and cigarettes was illustrated in a survey of 5,000 adult smokers where 29.9% reported ever-use and 4.2% were current users.[52] Use of snus was non-existent among former or never-smokers. Almost all surveyed reported they were using snus to cut down on the number of cigarettes they smoked, but only 3.9% were using it to try and quit smoking entirely.

These studies illustrate that use of more than one tobacco product, often called “dual use,” has increased over the last decade and a number of new products have contributed to dual use. Spit tobacco can be used by smokers in venues where smoking is prohibited. Dissolvable products, such as Camel Orbs, Strips or Stix, also provide an opportunity to

use tobacco in settings where smoking is not allowed. Alere Health enrollment data among state quitline callers shows a 7-fold increase in those reporting using two or more tobacco products in the past 12 years, ranging from 1.06% of tobacco users seeking assistance in 2002 to 7.45% in early 2014. (Alere Health, unpublished data, 2002-2014)

Alternative tobacco products like cigars, pipes, hookah, cigars, cigarillos, kreteks, bidis and small cigars vary widely in size, nicotine content and how they are used. Unlike manufactured cigarettes, it is difficult to develop cessation medication dosing algorithms for users of cigars, pipes, hookahs, bidis, kreteks, and electronic cigarettes. Given the range of nicotine content and nicotine yield in these products, and the lack of published studies to inform how to match NRT dosages to provide relief from nicotine withdrawal and cravings, each quitline has developed its own treatment approach. Short-acting forms of NRT such as gum, the lozenge, the inhaler and nasal spray provide some flexibility, and allow the user to adjust the frequency of use and the amount of nicotine they obtain from these products until they find therapeutic relief. However, short-acting NRT products may present challenges of under-utilization or incorrect use.

Electronic Cigarettes and Other Electronic Nicotine Delivery Systems (ENDS)

Use of e-cigarettes among smokers has doubled, from less than 10% in 2010 to more than 20% in 2011.[53] The increasing popularity of e-cigarettes and ENDS presents many challenges for quitlines. There are over two hundred different e-cigarette models containing varying amounts of nicotine with a range of flavors.

Currently there is insufficient scientific evidence that e-cigarettes are effective for cessation.[54] Results from two randomized studies indicated that e-cigarette use had cessation rates from 4-13% and other studies have had mixed results and design limitations.[55] Questions that need answering through scientific studies include:

- Do e-cigarettes help smokers quit?
- Do e-cigarettes help increase the population cessation rate?
- Do e-cigarettes reduce harm by either taking the place of, or partially taking the place of, cigarettes?
- Do e-cigarettes undermine cessation by displacing use of FDA-approved cessation therapies or encouraging smokers who otherwise might have quit to dual use e-cigarettes and cigarettes?[55]
- Are e-cigarettes a "gateway" to traditional tobacco products?
- Do e-cigarettes challenge environmental policy efforts to denormalize tobacco use and encourage cessation?

Tobacco dependence treatment professionals, including quitlines, are struggling with how to address e-cigarette use in the context of cessation. In the absence of established best practices, quitlines are creating treatment protocols for counseling and medications delivery. In the fall 2014, NAQC will publish an evidence synthesis on the topic to address these important questions.

Reduce to Quit

There is a body of evidence to support reducing cigarettes per day prior to the target quit date.[47] Structured, scheduled reduction has demonstrated superior outcomes compared to unstructured reduction.[55] There are a number of ways to reduce smoking prior to quitting, one of which is to reduce smoking frequency prior to the target quit date while supplementing with NRT. Recent FDA changes to OTC NRT labeling removed previous warnings against smoking while using OTC NRT products, but the FDA did not go so far as to endorse reduce-to-quit approaches using NRT. There is evidence to suggest that some smokers see reduction as an important first step to quitting.[56] A random sample of U.S. smokers indicated that approximately one-half would choose reduction over abrupt cessation.[57] One study showed that reduce-to-quit could be facilitated via phone intervention,[58] but did not include a pharmacological agent. Two studies have used OTC NRT to aid reduction.[22,59] Etter used four milligram nicotine gum, encouraging use of at least 10 pieces per day; Hughes tested two milligram and four milligram lozenge depending on time to first use after waking; and Riley incorporated a hand-held computer (LifeSign) with nicotine nasal spray.[60] None of these studies demonstrated improved quit outcomes over using no pharmacotherapy to aid reduction, and none reported any significant increase in adverse events.

The author of this paper concludes that while reduction-to-quit can be offered as a possible quit method, there appears to be little advantage in adding NRT to aid the process. On the other hand, if using NRT in this manner prompts smokers who would not otherwise make a quit attempt to do so, it may be money well spent. To be well-implemented, reduce-to-quit approaches require good oversight and it is unclear how quitline counselors would oversee such an approach given the limited number of contacts they have with callers.

SPECIFIC POPULATIONS

Tobacco Cessation Medications for Pregnant or Breast Feeding Women

Controversy continues to exist surrounding the safety of tobacco cessation medication use by pregnant smokers and nursing mothers. The USPHS Guideline cites inconclusive evidence for effectiveness and safety of NRT, bupropion SR and varenicline with pregnant smokers. Specific to NRT, it cites studies showing that the nicotine patch and gum have been shown to have small hemodynamic effects (blood flow) on the mother and fetus, but states these are less than the effect of cigarette smoking. It further acknowledges that cigarette smoking, unlike NRT, exposes the mother and fetus to thousands of harmful chemicals. More recently, the Cochrane Review cited insufficient evidence for safety and effectiveness of NRT with pregnant women.[61]

In a correlational study, researchers in the United Kingdom detected no effect for single forms of NRT with pregnant smokers, but did find an effect for use of the nicotine patch supplemented by a faster acting form of NRT.[62] The authors speculate that single forms of NRT may deliver insufficient amounts of nicotine due to the fact that pregnant women have higher metabolism, but call for a well-designed randomized control trial to confirm these findings.

As described in the section on Screening for Medication Eligibility, pregnancy is generally a use-exclusion for NRT. Some quitlines include breastfeeding as a use-exclusion as well, while others provide the medication and encourage the woman to inform her health care provider of her intent to use NRT. Pregnant women who have interest in using a cessation medication, or who are unable to quit without medication, should be advised to talk with their health care provider to discuss whether or not they should use a cessation medication. This decision should be made only after a thorough and thoughtful discussion between the woman and her personal physician, weighing the potential risks the medication poses to the woman and her baby against the known risks of continued smoking and the benefits of cessation.

If the caller wishes to use OTC NRT, the same physician override process can be employed as for any use exclusion where the physician approves the medication and the quitline sends it. If the woman's physician does not approve the use of a cessation medication, the quitline counselor can still support the woman in her effort to quit by focusing on cognitive, motivational and other behavioral strategies that will help facilitate the woman's quit attempt and increase the likelihood of tobacco abstinence without medication. Some quitlines have implemented more call-intensive programs for pregnant women, providing increased behavioral support for this important population.

Cessation Medication and Mental Illness

Persons with mental illness are estimated to be the single largest group of smokers, representing up to 44% of the tobacco market.[63] Depending on the diagnosis, smoking rates can be as high as 90%.

Table 5. Tobacco Use by Diagnosis

Schizophrenia	62-90%
Bipolar disorder	51-70%
	36-80%
Anxiety disorders	32-60%

Post-traumatic stress disorder	45-60%
Attention deficit/ hyperactivity disorder	38-42%
Alcohol abuse	34-80%
Other drug abuse	49-98%

Source: Morris C. Do Quitlines Have a Role in Serving the Tobacco Cessation Needs of Persons with Mental Illnesses and Substance Abuse Disorders? 2010

There is strong consensus among tobacco dependence treatment providers that persons with mental illness should be encouraged to quit and, in fact, want to quit. Persons with mental illness (including substance use disorders) benefit from the same interventions as the general population of tobacco users. A combination of counseling and cessation medications should be used, with special considerations for those with cognitive difficulties or current psychiatric symptoms.[64]

Questions about the ability of quitlines to adequately help smokers with mental illness quit have been raised, but smokers with mental illness make up a huge percentage of quitline callers. Data presented at SRNT in 2012 by Robert Vargas, Clinical Manager, Alere Health, showed that 46% of callers (n = 61, 670) who enrolled in quitline services between April and July, 2012 reported one or more mental health disorders. The most commonly reported conditions were depression (17%); generalized anxiety disorder (11%); and bipolar disorder (5%). According to the same data, those reporting a mental health disorder were more likely to smoke within five minutes of waking (85%) than those without disorders.[65]

Several quitline studies have found self-reported 7-day abstinence rates for persons with mental illnesses to be equivalent to general callers at the end of treatment and at six months.[66,67,68] Interestingly, California Smokers' Helpline callers reporting mental health issues received counseling and used NRT at higher rates (84% vs. 74% received as least one counseling call; 41.7% vs. 33.3% used NRT).[68] There was no difference in quit attempts (56.4% for mental health callers vs. 53.1% for non-mental health callers) or quitting success using 30–day point prevalence at two months (19% for mental health callers vs. 20.8 % for non-mental health callers).[69] Recent data from Colorado also found that persons with mental illnesses use the quitline and NRT at a greater rate than the general population, but also self-report that they have a lower chance of quitting. (Colorado Department of Public Health and Environment, unpublished data, 2009)

The USPHS Guideline indicates that the most effective cessation strategies for smokers with behavioral disorders are a combination of cessation medications and counseling. Studies indicate that smokers with mental illnesses and substance abuse disorders should be encouraged to use the full range of cessation medications unless contraindicated. Due to the fact that smokers with mental illness often present with high levels of nicotine dependence,[66] they may require higher dosages or combinations of cessation medications. Since combination NRT has been adopted by state tobacco quitlines only recently, it is possible that smokers with mental health conditions may have been under-treated with pharmacological interventions.

All smoking cessation medications appeared to be effective cessation aids among depressed smokers when used in combination with cognitive behavioral therapies.[6] Longer durations of treatment may be required and those receiving treatment should be monitored for mood changes.[69]

Treatment providers were cautious about using varenicline with smokers with mental illness after the FDA issued its boxed warning regarding neuropsychiatric symptoms that surfaced in post-marketing surveillance. Recent studies indicate that the medication is well-tolerated and effective in producing tobacco abstinence among those with depression, schizophrenia and other mental health disorders. Researchers re-analyzed data from 17 different

varenicline trials and found that it improves cessation outcomes 124% over placebo and 22% over bupropion SR, without increasing neuropsychiatric symptoms among those with and those without a recent history of psychiatric disorder.[70]

Use of varenicline with smokers with mental illness to sustain tobacco abstinence (maintenance) has been demonstrated as effective. One study explored varenicline combined with cognitive behavioral therapy (CBT) and produced improved outcomes compared to CBT alone.[71]

Many quitlines screen callers at enrollment for mental health conditions. Increased depression symptoms have been reported by those with a history of depression and who have tried to quit smoking in the past. These symptoms are commonly reported as a barrier to quitting among those who call quitlines for help. Common protocols include advising them to inform their health care provider of their intent to quit and seek their support during the quitting process.

Those taking medications for their disorder are commonly advised to have their dosages monitored after quitting tobacco. Dosages of mental health medications may need to be adjusted to compensate for changes in how the drugs are metabolized after quitting. Other than bupropion SR, which is contraindicated in those taking MAOI drugs, cessation medications do not seem to adversely affect mental health disorders.

The issue of quitline services for those with behavioral health issues has been a growing concern to the quitline and behavioral health communities. In 2010, the Quitline Behavioral Health Advisory Forum (BHAF), which includes a number of leading NAQC members and experts in behavioral health, produced a report in consultation with NAQC titled *"Do Quitlines Have a Role in Serving the Tobacco Cessation Needs of Persons with Mental Illnesses and Substance Abuse Disorders?"* The report made several observations regarding how quitlines are serving this population, and several recommendations regarding proposed steps to help quitlines address the needs of this population more effectively.

NAQC has already taken action on the recommendation to include a screening question or questions in the NAQC Minimal Data Set as an optional question(s). A second recommendation from the 2010 BHAF report regarded training and supervision of quitline staff resulted in recommendations for broad training objectives and general supervision of quitline staff in this specific area. The report is available here.

THERE IS A NEED FOR RESEARCH

Much has been learned about use of medications in the quitline setting. We know that, when used in a real-world quitline setting, medications:

a) Increase quit rates, especially when used correctly;
b) Are safe and cost-effective;
c) Are more effective when coupled with counseling;
d) Are more effective when used in some combinations; and
e) Deliver quit rates comparable to those seen in face-to-face settings.

Some of the remaining unanswered questions about quitline use of medications include:

1. How can quitlines increase medication compliance / adherence? Specifically:
    a. How can quitlines improve correct use of medications, especially short-acting medications and use of combination NRT?
    b. How can quitlines encourage and assist callers to obtain additional NRT to supplement starter-kits?
    c. How can quitlines most effectively deploy text messaging or short messaging service (SMS) and mobile application technologies to deliver effective reminders to use cessation medications correctly, especially short-acting forms of NRT, and for a sufficient duration to prevent lapses and relapse?
2. What is the optimal course of medications for quitlines to provide?

3. What happens to medications that are sent but not used in their entirety? Are they "wasted" or do they prompt future quit attempts?
4. Are e-cigarettes an effective aid for smokers who are trying to quit? Should they be considered as an alternative for callers who have unsuccessfully tried to quit using several forms of NRT?
5. Should quitlines ever recommend a 'reduce-to-quit" approach using NRT and, if so, in what circumstances and what should the approach be?
6. How should medication protocols be altered when working with specific populations of callers, such as light smokers, callers who are highly dependent on nicotine, and those with mental illness?
7. What will be the impact of the ACA on the integration and delivery of medications by quitlines and the utilization of medications by callers?

In addition, trials/research on the following issues would be beneficial:

1. Tests of the feasibility delaying provision of medication until a caller completes two quitline counseling sessions.
2. Randomized controlled trials in quitline settings comparing varenicline with NRT (including single and combination formulations) to address current uncertainties about their respective efficacy and safety.
3. Long-term post-marketing surveillance of varenicline with regard to neuropsychiatric and cardiac events.
4. Large-scale trials exploring the potential of cytisine as an effective and affordable therapy.

RECOMMENDATIONS

Providing medications can be a cost-effective strategy to increase the reach and effectiveness of quitline services. There is not a "one size fits all" approach to the integration of medication benefits into other quitline services. The role medication plays will depend on such things as the available budget, partnerships with health plans, availability of medical and clinical support and the overall strategic objectives of a quitline.

1. All quitlines should carefully consider how best to integrate tobacco cessation medications as part of their services while balancing reach and effectiveness. This may limit the types of medication, the duration of medication and the populations to whom it is offered, but quitlines should strive to meet the recommended duration described below in Recommendation 2.

2. If medications are part of the services provided to all eligible callers, a minimum of a two-week supply of medication should be provided (as suggested by the CDC).[43] Longer durations of NRT can be provided based on funding and the strategic objectives of the quitline.

3. Quitlines should have protocols in place that will ensure that callers and users of their web-based services receive the necessary information to make an informed decision whether or not to use a medication, and which medication to use if they decide to include pharmacological treatment in their quit plan. Quitline counselors should have access to information about the benefits and characteristics of specific FDA-approved cessation medications, in order to provide instructions to callers on how to use them properly.

4. Quitlines that offer OTC NRT should explore the possibility of providing a combination of the nicotine patch and a short-active form of NRT (gum or lozenge), especially for those callers who are moderately to highly nicotine-dependent, have not had previous success quitting using a single modality of NRT, or who are struggling to stay quit during follow-up support calls.

5. Provision of free or discounted medications should be considered as a promotional strategy and therefore increasing the overall cost-effectiveness of medications and quitlines by reducing the need for more expensive promotional activities.

6. To appropriately share the cost of quitline services between the public and private sectors, especially in light of the ACA, states should engage in a process to develop cost-sharing and/or reimbursement agreements with

public and private entities (including the state Medicaid program, health plans, employers and others). States should determine the populations that the state quitline will cover at no cost and provide information about opportunities for public and private entities to contract with the state quitline or the quitline service provider for coverage.

7. The ACA has the potential to increase the availability of, and access to, evidence-based cessation treatment. State tobacco control programs and other agencies that fund quitlines should play a leadership role in assuring that high quality and coordinated cessation services that make cessation medications available to tobacco users exist within the state and are widely promoted to tobacco users.

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APPENDICES

APPENDIX A

The following is a list of recently published articles (since 2008) on tobacco cessation medications that have been included in the Cochrane Review of Pharmacological Treatment (2013). It does not represent all published literature on the subject since 2008.

Bupropion

Levine MD, Perkins KA, Kalarchian MA, Cheng Y, Houck PR, Slane JD, Marcus MD. Bupropion and cognitive behavioural therapy for weight-concerned women smokers. *Archives of Internal Medicine* 2010;170(6):543–550.

Planer D, Lev I, Elitzur Y, Sharon N, Ouzan E, Pugatsch T, et al. Bupropion for smoking cessation in patients with acute coronary syndrome. *Archives of Internal Medicine* 2011;171 (12):1055–60.

Combination Therapy

Mills EJ, Wu P, Lockhart I, Thorlund K, Puhan M, Ebbert JO. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. *Annals of Medicine* 2012;44(6): 588–97.

Cytisine

Hajek P, McRobbie H, Myers K. Efficacy of cytisine in helping smokers quit: systematic review and meta-analysis. Thorax 2013 February 12 [Epub ahead of print]. [DOI: 10.1136/thoraxjnl-2012-203035]

Special Populations

Coleman T, Chamberlain C, Davey M-A, Cooper SE, Leonardi-Bee J. Pharmacological interventions for promoting smoking cessation during pregnancy. *Cochrane Database of Systematic Reviews* 2012, Issue 9.

Lumley J, Chamberlain C, Dowswell T, Oliver S, Oakley L, Watson L. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database of Systematic Reviews* 2009, Issue 3.

Meyer TE, Taylor LG, Xie S, Graham DJ, Mosholder AD, Williams JR, et al. Neuropsychiatric events in varenicline and nicotine replacement patch users in the Military Health System. *Addiction* 2013;108(1):203–10.

Myung S-K, Ju W, Jung H-S, Park C-H, Oh S-W, Seo HG, et al. Efficacy and safety of pharmacotherapy for smoking cessation among pregnant smokers: a meta-analysis. *British Journal of Obstetrics and Gynaecology* 2012;119(9):1029–39.

Tsoi DT, Porwal M,Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. *Cochrane Database of Systematic Reviews* 2010, Issue 6.

van der Meer RM, Willemsen MC, Smit F, Cuijpers P. Smoking cessation interventions for smokers with current or past depression. *Cochrane Database of Systematic Reviews* 2009, Issue 1.

Varenicline

U. S. Food, Drug Administration. FDA drug safety communication: safety review update of Chantix (varenicline) and risk of neuropsychiatric adverse events.
http://www.fda.gov/Drugs/DrugSafety/ucm276737.html October 2011. Accessed January 19, 2012.

Gunnell D, Irvine D, Wise L, Davies C, Martin RM. Varenicline and suicidal behaviour: a cohort study based on data from the General Practice Research Database. *BMJ* 2009;339:b3805.

Harrison-Woolrych M, Ashton J. Psychiatric adverse events associated with varenicline: an intensive postmarketing prospective cohort study in New Zealand. *Drug Safety* 2011;34(9):763–72.

Harrison-Woolrych M, Maggo S, Tan M, Savage R, Ashton J. Cardiovascular events in patients taking varenicline: a case series from intensive postmarketing surveillance in New Zealand. *Drug Safety* 2012;35(1):33–43.

Kasliwal R, Wilton LV, Shakir SA. Safety and drug utilization profile of varenicline as used in general practice in

England: interim results from a prescription-event monitoring study. *Drug Safety* 2009;32(6):499–507.

Prochaska JJ, Hilton JF. Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis. *BMJ* 2012; 344:e2856.

Rigotti NA, Pipe AL, Benowitz NL, Arteaga C, Garza D, Tonstad S. Efficacy and safety of varenicline for smoking cessation in patients with cardiovascular disease. *Circulation* 2010;121(2):221–9. [: clinicaltrials.gov ID: NCT00282984]

Tonstad S, Davies S, Flammer M, Russ C, Hughes J. Psychiatric adverse events in randomized, double-blind, placebo-controlled clinical trials of varenicline: a pooled analysis. *Drug Safety* 2010;33(4):289–301.

Tønnesen P, LauriH, Perfekt R,Mann K, Batra A. Efficacy of a nicotine mouth spray in smoking cessation: a randomised, double blind trial. *European Respiratory Journal* 2012;40(3): 548–54. [DOI: 10.1183/09031936.00155811]

APPENDIX B

Cost-Effectiveness Economic Evidence (source: http://www.thecommunityguide.org/tobacco/quitlines.html)

Twenty-seven studies were included in the economic review. Twelve studies provided 13 estimates of cost-effectiveness measurements of different quitline services. All monetary values from studies are reported in 2010 U.S. dollars.

- Cost-effectiveness of providing quitline counseling and cessation information: median estimate of $2,012 per quality-adjusted life year (QALY) saved (range of values: $439/QALY to $2,627/QALY; 6 studies)
- Cost-effectiveness of adding cessation medications to existing quitline services: median estimate $795 per QALY saved (range of values: $272/QALY to $4,110/QALY; 6 studies)
- Cost-effectiveness of providing a combination of quitline counseling, nicotine replacement therapy (NRT), and media promotion: $7,813 per QALY saved (1 study)

Estimates of cost-effectiveness were assessed in comparison to a conservative threshold of $50,000 per QALY saved. Overall, the economic evidence indicates that quitline services are cost-effective across a range of different treatments and promotional approaches.

These results were based on a systematic review of all available studies, conducted on behalf of the Task Force by a team of specialists in systematic review methods, and in research, practice and policy related to tobacco use and secondhand smoke exposure.

- Quitline promotions offering free evidence-based tobacco cessation medications (primarily nicotine replacement therapy) to callers were evaluated in 12 studies.
    - Quitline call volume: median relative increase of 396% (IQI: 134% to 1132%; 9 studies)
    - Tobacco cessation rates among quitline callers: median absolute increase of 9.8 percentage points compared with callers who were not offered nicotine replacement therapy (IQI: 7.4 to 15.7 percentage points; 11 studies)

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