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

INTRODUCTION

Quitlines are one of many intervention services now available to tobacco users who want to quit. Tobacco abstinence outcomes improve with quitline interventions compared to people trying to stop on their own (1). Although quitlines began as a service that provided only information and counseling to cigarette smokers these services have evolved in significant ways since the mid-1990's. State and provincial quitlines operate in a very dynamic environment and most are committed to providing tobacco intervention services aligned with the 2008 United States Public Health Service Clinical Guideline (USPHS), "Treating Tobacco Use and Dependence" (2). As their experience in treating tobacco dependence and their budgets have grown the majority of quitlines have supplemented their core information and counseling services with additional evidence-based services – most notably provision of medications. Medication use increases the likelihood of tobacco abstinence and is consistent with the USPHS Guideline recommendation that all tobacco users engaged in a quit attempt should be offered at least one medication as part of their quit attempt (3).

Between 2004 and 2008 the number of U.S. quitlines offering free tobacco cessation medications to callers tripled. According to the North American Quitline Consortium (NAQC) annual survey of state and provincial quitlines for fiscal year 2008, 36 states report offering Food and Drug Administration (FDA) approved medications, although two of these states offer only discounted medications to callers (4). This is a substantial increase from 2006, when only 24 states were providing free medication (5). By 2006 all U.S. quitlines that offered medications provided the nicotine patch to callers. Today 27 also offer nicotine gum and 17 offer nicotine lozenges (16 offer both). Four states provide bupropion (Zyban®, Wellbutrin SR®) and two quitlines provide varenicline (Chantix®) free to eligible callers. As will be discussed these numbers encompass a broad spectrum of approaches ranging from providing full courses of medication to any appropriate caller to short courses of medication for limited periods of time to specific sub-populations of callers. At this time none of the Canadian provinces are providing free medications to quitline callers on a consistent basis although they do provide education and decision support regarding medication use (4). We anticipate that use of medications and the information on medications provided to tobacco users by quitlines will continue to increase.

This paper was created in response to a request from NAQC members to assist in addressing the many issues surrounding provision and distribution of medications to the populations they serve. The objectives of the paper are the following:

1. Provide a brief synopsis of the three major models of how quitlines integrate tobacco cessation medication with their other services.
2. Review published studies of use of medications by quitlines and the effect medications have on quitline utilization and tobacco abstinence rates.

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3. Discuss the major factors that must be considered in deciding if medications should be offered as part of quitline services. This includes such topics as cost-effectiveness analysis, choice of medication, determination of quantity of medication to provide and the method of distribution of medications that will be used.
4. Identify the challenges to the integration of medications into quitline services and provide suggestions for overcoming these challenges based on evidence-based research and expert consensus.
5. Identify areas that need to be explored further through research and sharing of ideas within the NAQC community to optimize use of medications in this setting.
6. Provide recommendations on key issues related to integration of medications into quitline services.

With these objectives the intent is for this paper to serve as a major resource and a common platform of knowledge for the many different audiences which are involved with tobacco quitline operations. Program managers and service providers may use this as they evaluate their current program, design new programs or maintain their current program. It provides funders of quitline programs the rationale and justification for additional costs that may be incurred by providing medications or expanding medication offerings by the quitline.

The paper relies heavily on the 2008 USPHS Guideline to identify and document evidence-based recommendations regarding use of medications as part of the treatment of tobacco use and dependence. The authors strongly suggest readers of this paper also become familiar with that important document which can be downloaded for free at http://www.ahrq.gov/path/tobacco.htm.

Current Models of Tobacco Cessation Medication Integration

All state and provincial quitlines provide some form of behavioral counseling to callers interested in quitting tobacco. Not all quitline models include distribution of free medications. Quitlines that do provide medication show substantial variation in how much medication is provided and how it is distributed. Within this context three major models of how tobacco cessation medications are integrated into quitline service portfolios exist.

1. Medication information only. The quitline serves as a clearinghouse for information regarding the various FDA-approved medications. The counselor may discuss medications as part of the treatment plan but payment for and procurement of the medications remains the responsibility of the caller. The quitline may be part of a larger, more comprehensive tobacco control organization which has a separate program responsible for the distribution of medications. Or, the quitline may encourage callers to obtain medications by self-pay, through their health plan, employer, or through other government resources. Finally, some quitlines may simply not have sufficient revenue to support use of medications. As of January 2009, fourteen U.S. state quitlines and all of the Canadian provincial quitlines follow this model (4).

2. Limited medication distribution. The quitline infrastructure is used to distribute tobacco cessation medications to selected populations such as the uninsured, underinsured, or specific populations that have high prevalence of tobacco use but historically low utilization of the quitline. Some may provide limited courses of medication for brief periods of time as a promotional tool but not provide medication to any callers on a sustained basis. This allows improved access to a relatively inexpensive but effective intervention and may incentivize these populations to seek out tobacco intervention services. Limited budgets, large populations and the mission of reaching as many people as possible with a proven, effective intervention make this method more appealing than trying to provide medication to all callers. In this model telephonic counseling services remain available to all callers but may be optional. Experience demonstrates increased call volumes and increased abstinence rates compared to counseling alone as referenced below. Some quitlines require the caller to actively participate in telephonic coaching in order to receive medications. Even if counseling is not provided the individual's experience with tobacco cessation medication may increase the awareness of the benefits of these medications and the quitline for future quit attempts - especially for those who may have never used either intervention before (6).

3. Full medication distribution. Many quitlines view medications as an integral part of their mission to provide comprehensive tobacco intervention services. They see providing tobacco cessation medications as consistent with the U.S. National Action Plan for Tobacco Cessation which encourages provision of universal access to counseling and medications (7). This is based on substantial scientific evidence that medication use increases the likelihood of tobacco abstinence and the USPHS Guideline that all tobacco users should be offered at least one medication as part

of their quit attempt (3). Although 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 (8). Linking free tobacco cessation medications for all callers with counseling ensures more tobacco users will receive both types of interventions (9).

Provision of Medication Has a Positive Impact on Many Quitline Activities: A Literature Review

Published reports of quitline experience with medications to-date have demonstrated significant benefits to quitlines and the people they serve. Table 1 below provides details regarding studies involving use of medications by quitlines. To summarize:

1. Promotion of quitlines and their services. Provision of free medication 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 (10-12). This results in substantial increases in the number of callers to quitlines (6, 10, 12-19).
2. Increased tobacco abstinence rates compared to counseling without medication provision (6, 9-11, 14, 16, 19).
3. Increased 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 (16).
4. Increased number of subsequent contacts to monitor and provide additional medication and thus opportunities for additional counseling with each person who enrolls (9, 16, 19).

Table 1. Summary of published studies of the impact of tobacco cessation medications on the key outcome measures of call volume, quit rates and cost-effectiveness.

Study	Medications Offered	Increase In Calls	Quit Rates (%)	Cost-Effectiveness (cost/quit) [U.S. dollars]	Comments
An (13)	8 weeks Patch/Gum (mailed)	679/month (NRT) vs 155/month	**18.2** (NRT) vs **10.0** (@ 6 months; 30-day;ITT)	$1934 (NRT) vs $1362	Survey. Compared to historical outcomes
Bauer (6)	2 weeks Patch/Gum (voucher)	148/day (NRT) vs 6/day	**22** (NRT) vs **12** (@ 4-6 months; 7-day; RR)	+ $210 (vs no NRT)	Survey. Compared to historical outcomes
Bush (14)	2 weeks Patch (mailed)	2592/month (NRT) vs 257/month	**15.1** (NRT) vs **8.1** (@ 6 months; 30-day; ITT)	NA	Survey. Compared to historical outcomes
Cummings (12)	Patches 1 week 2 weeks 6 weeks (mailed) 2 weeks Patches/Gum (voucher)	7213/week (NRT) vs 552/week	**No NRT 12** **1-week 21** **2-week 24** **6-week 33** **Voucher 27** (@ 4 months; 7-day; RR)	1-week + $306 2-week + $347 6-week + $347 Voucher + $274 (vs no NRT)	Non-randomized, different populations in each arm. Compared to historical outcomes
Cummings (10)	6 weeks Patch (mailed)	34,090 calls	**33.2** (NRT) vs **23.1** (@12 months; 7-day; RR)	+ $420 (vs no NRT)	Survey. Random sample of participants receiving NRT vs No NRT

Fellows (15) *[See also Bush(14)]*	2 weeks Patch (mailed)	13,646/year (NRT) vs 6428/year	**15.7** (NRT) vs **8.2** (@6 months; 30-day;ITT)	$1050 (NRT) vs $3738	Survey. Compared to historical outcomes
Hawk (11)	2 weeks patch (voucher)	NA	**Q&W 29** **NRT 26** **Both 27** (@3-7months; 7day;RR)	$130 Quit & Win $179 NRT	Non-randomized. Three arms.
Study	**Medications Offered**	**Increase In Calls**	**Quit Rates (%)**	**Cost-Effectiveness (cost/quit) [U.S. dollars]**	**Comments**
Hollis (16)	8 weeks Patch (mailed)	NA	NRT vs None **17** vs **12** (brief) **20** vs **14** (mod.) **21** vs **14** (inten.) (@12 months, 30-day; ITT	vs Brief, no NRT $1912 (mod/-) $2640 (intense/-) $2467 (brief /+) $2109 (mod /+) $2112 (intense/+)	3x2 Randomized; Intensity of counseling +/- NRT
McAfee (17)	8 wk vs 2 wk patch (mailed)	NA	**19.6** (NRT) vs **14.3** (@6 months; 30 day;ITT)	$1405 (NRT) vs $1156	Randomized
Miller (18) *[see also Cummings (10)]*	6 weeks patch (mailed)	34,090 calls	NRT vs None **20** vs **2** NRT +/- Counseling call **38** vs **29** (@6 month; 7-day; ITT)	+ $464 vs no NRT	Survey Those receiving NRT vs those who did not
Swartz (9)	8 weeks Patch/Gum (voucher)	NA	**22.5%** (NRT) vs **12.3%** (@6 months; 30-day; ITT)	$1344 Per User NRT $275 No NRT $201	Survey. Sample of all callers, those receiving counseling + NRT vs those receiving only counseling
Tinkelman(19)	8 weeks patch (mailed) + counseling	3606/month (NRT) vs 2351/month	**14.9** (NRT) vs **10.3** (@ 6 months; 7-day; ITT)	NA	Survey. Randomized subset of participants before and after NRT available
Swan (20)	Bupropion SR	NA	**33.2** (mod + 300) **31.4** (mod +		Randomized. Four arms comparing brief and moderate intensity counseling and two doses medication

	300 mg/day 150 mg/day		150) **25.7** (brf + 300) **23.6** (brf + 150) (@12 months; 7-day; ITT)	NA	

NA=Not Analyzed within the publication RR=Responder Rate
NRT=Nicotine Replacement Therapy ITT=Intent to Treat Analysis

Integration of Tobacco Cessation Medications into Quitline Services is Cost Effective

A major factor impacting tobacco medication integration is the cost-effectiveness of adding free medication to the quitline services. That is, what is the incremental benefit to the quitline and its callers in relation to the increase in expense to add the costs of medication, its distribution and its monitoring? Pharmacologic interventions are additive to quitline counseling abstinence rates as documented above. However decision makers should be presented with a rigorous cost analysis of adding these medications to the program before a financial commitment is made. Absolute costs of providing services do rise with the addition of medications. Quitlines need to determine if the value they bring across the entire spectrum of quitline services is worth the additional costs. The information in this section is intended to help quitlines better assess the value of medications in their intervention efforts from a more scientific economic approach.

Cost-effectiveness is a form of economic analysis that compares the relative expenditure (costs) and outcomes (effects) of one or various options. Unfortunately the analysis of these two factors is not always straightforward. In determining the true cost of an intervention an attempt should be made to consider all the costs to deliver the intervention. There may be many "hidden" costs that are not readily apparent. For instance there are usually administrative costs to the provision of medications beyond the obvious costs of the medications and their shipping (e.g. time spent to reconcile orders or creation of software pathways to track the medications).

Interpretation of outcomes can also be complicated by many variables besides the intervention being studied. Ideally the outcome of the intervention that is measured should be as directly related to that intervention as possible. In measuring the cost-effectiveness of providing a prescription medication the increase in quit rates obtained compared to not providing the medication would seem straightforward. However the influence on the quit rate of just having to see a physician for the prescription and perhaps receiving positive reinforcement for their decision to stop smoking may be totally overlooked. It may not be possible to recognize or assess all of the outside factors that may be associated with an intervention and the measured outcome, but careful attention to as many of them as possible is critical to accurately defining the cost-effectiveness of an intervention.

Many aspects of the tobacco intervention process have defined costs and thus provide opportunities to determine the cost effectiveness of modifications to specific steps in the process. For example, one of the primary outcomes of the tobacco intervention process is to make people aware enough of the value of quitline services to take action and access the quitline to use those services. There are many forms of promotion that can be used; for example: public service announcements, paid advertisements, processes that encourage referrals from physicians, and offering of free medication. Some of these are obviously more costly than others but the higher cost may be justified if it results in increased utilization of the quitline compared to less costly promotions. Thus an analysis might be the cost of various forms of promotion and the number of people who call the quitline in response to that type of promotion. The number of calls to the quitline, combined with assessment of how each caller heard about the quitline and a careful determination of the total costs for each of these promotional approaches can then be used to calculate the **cost per call** of each form of promotion. This can permit an assessment of which type of promotion is more cost effective than the other in encouraging people to contact the quitline. Use of free medications as a promotional tool has been shown to reduce the **promotional cost per call** to quitlines (6, 11, 13, 15, 19). If the abstinence outcomes (e.g. quit rates) are measured and the total cost to deliver the intervention can be determined then **cost per quit** can be calculated. If that intervention is tobacco cessation medication, the costs of providing that medication can be assessed to determine if the addition produces enough of an increase in the abstinence rate to justify the cost of the medication.

Example: Fellows and colleagues prepared a cost-effectiveness analysis of the Oregon quitline program providing a free 2-week supply of nicotine patches (15). They compared the costs of promotion and intervention services before a free

patch program to the costs for promotion and intervention services resulting from the free patch program. **Cost per call** and **cost per quit** could then be determined. Promotional costs prior to the free patch program were primarily TV and radio advertisements (although the Centers for Disease Control paid for the production costs, the quitline program costs included those for air time, talent fees paid to the actors, tagging of the ads with logos and phone numbers and duplication costs) and were an estimated total of $1,385,537 annually. The free patch program used no paid advertising. Instead media kits were distributed to the counties that included fact sheets, news releases and a "costs of smoking" chart. They also made contact with various other state and local agencies providing information about the program. Cost for this promotion was estimated to be $48,600. Intervention costs included a one 30-minute telephone counseling session at $91 and two weeks of the nicotine patch at $42.82 (price includes shipping).

Quit rates, using self-reported 30-day continuous abstinence, were determined of eligible callers contacted at six-months after the intervention. Those unable to be reached were considered to have continued smoking. Using number of calls during a six-month period to estimate annual volume to the quitline, as a result of the free patch program over twice as many callers registered as compared to the program prior (13,646 vs. 6428). **Promotional cost per registered caller** was $4/caller for the free patch program vs. $215/caller for the prior program. The quit rate was 15.7% for the free patch program vs. 8.2% prior. Thus the estimated number of quitters was 4502 for the free patch program and 527 for the prior program. The increased intervention costs due to the additional phone calls was $1, 241,160 more/year than the prior program so total program costs were $2,250,484 for the free patch program and $1,970,085 for the prior program (an increased estimated annual cost of $280,399). Because of the increase in number of people who registered for the program and the increased effectiveness of the program with the addition of the nicotine patches, the estimated **cost per quit** was only $1050 for the free patch program vs. $3738 for the prior program (a reduction of $2688/caller). The authors concluded that the addition of free nicotine patch to their quitline program and shifting promotion costs from expensive paid media advertising to unearned (unpaid) media was a highly cost-effective strategy to increase quitting of tobacco.

Although cost-effectiveness is defined primarily in financial terms there can be immeasurable benefits to integration of medication into the quitline. For instance, in a study performed in Ohio it was determined that adding nicotine patches increased the tobacco abstinence rate by 13.7%. This increase reduced the **cost per quit** by $341.26. The conclusion from this analysis therefore was that using nicotine patches was "cost-effective" over time. However what was not considered in the analysis was the added benefit of marketing that was achieved by giving away free NRT. The response (beyond number of calls to the quitline) far exceeded the traditional costly marketing efforts such as increased good will toward consumers and the medical community; building relationships and support from private health plans and employers; improved respectability of the program; and increased positive attention to the program from media, lawmakers etc. (21).

Guidelines for Determining Cost-Effectiveness

There is an additional cost for providing 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. For heavily addicted smokers medication is highly recommended to achieve a reasonable quit rate. For less addicted smokers the use of medication may not be as critical. Most quitlines tend to attract heavy smokers so the addition of medication to the treatment program is probably worthwhile. However a decision to add medications is often not easy to make since it adds expense to the overall program and may limit the number of smokers who can be serviced. Before making a final decision on medication integration create a checklist and consider the following:

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' published experiences. Will the addition of medications increase reach enough to allow you to reduce current marketing costs and by what amount? Subtract added costs from the current costs to determine the incremental cost of adding medication (see #2 below). Will the additional costs bring sufficient value to the quitline to make it a good business decision?

2. Define the costs of all processes involved with setting up and maintaining the provision of medications to participants. This includes the obvious cost of the medication and mailing of the medication or voucher and any software and personnel time to directly manage the distribution. Also, include other indirect costs such as the cost of increased coach time for training on medication counseling, costs of additional medical oversight to monitor medication recommendations and side-effect concerns, costs for additional calls from members regarding

medications and additional coaching calls (especially if receiving more medication is contingent on regular contact with the coach). It also includes the additional costs of materials related to medications sent to enrollees.

3. Look carefully at all of the options available, many of which are discussed in this paper. For example: Direct mailing of medication or providing a voucher? Or provision of coupons for a discounted price on the medication? Offer medications only to populations with the greatest need rather than to everyone?

4. It can be helpful in the discussions of funding of medications to also include the savings from reduced healthcare 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 (22).

CONSIDERATIONS IN THE INTEGRATION OF TOBACCO CESSATION MEDICATIONS INTO QUITLINE SERVICES

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

Careful consideration should be given to the public health objectives and the clinical objectives of the quitline and how the integration of medications with other quitline services supports these objectives. This includes the role medications can play in increasing reach, increasing participation, increasing effectiveness (increasing quit attempts as well as increasing the numbers of people who stay quit), increasing cost-effectiveness, and improving satisfaction with quitline services as documented above.
Despite the demonstrated benefits of medications there are legitimate reasons why offering free medications may not align or actually may interfere with the strategic objectives of the quitline. Some of these reasons are discussed below.

The primary objective of a quitline may be to provide access to tobacco dependence intervention counseling, filling a substantial gap in our current health delivery system.
Promoting medications may create significant unintended consequences. For example, focusing on medication may distract callers so they do not avail themselves of the substantial benefits counseling can also provide. The response to free medication has been demonstrated to often generate such an increase in call volume that the quitlines are unable to respond to demand, creating budgetary and public relations problems. In addition, many quitlines are imbedded in comprehensive state or provincial tobacco control programs that are working to encourage Medicaid, health plans and employers to include tobacco cessation medications and intervention services as part of their benefit plans. Distribution of free medications could be seen as a service that may disincent these groups from providing tobacco cessation medications. Finally, most quitlines have limited financial resources and must use care in allocating these resources. If they choose to spend their resources by offering free medications this may reduce their ability to promote the quitline via mass media, provide other services or even reduce level of current services (i.e., increase effectiveness of interventions offered at the expense of decreasing number of people reached).

Thus, although provision of medications by quitlines has been of demonstrated benefit to quitlines that have integrated medications into their services it must first fit within the overall objectives of the individual quitline. Once that has been determined other considerations in the integration of medications can be entertained.

What determines which tobacco cessation medications our quitline should offer?

Cost

Nicotine patches 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 reduced cost but does require a prescription. Nicotine lozenge is an over-the-counter medication but generic formulations are not widely available currently. Varenicline, nicotine nasal spray and 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 (23) and individual medication package inserts. Cost of each medication varies widely depending on brand, geography, volume discounts, etc. Local pharmacies and national pharmacy benefit managers can provide more specific information.

Effectiveness in Achieving Tobacco Abstinence

The use of effective medications is obviously important. 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. There are very few studies that have compared the various medications to each other in terms of effectiveness in a given population. A meta-analysis of multiple studies was performed for the USPHS Guideline to provide an estimate of relative effectiveness compared to placebo (24). Using nicotine patch as the reference the USPHS Guideline also compared relative effectiveness of each medication to the patch (25). These comparisons are summarized in the table below. Caution should be used when interpreting this table.

1. Although meta-analysis attempts to adjust for such factors the studies compared used different populations of study participants 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 participants. These findings may not be entirely translatable to the uniqueness of the quitline service environment.

Table 2. Meta-analysis of various tobacco cessation medication effectiveness for tobacco cessation compared to placebo and nicotine patch.

Medications	Effectiveness Relative to Placebo at 6 months post-quit Estimated Odds Ratio (95% C.I.)	Effectiveness Relative to Nicotine Patch Estimated Odds Ratio (95% C. I.)
Nicotine Patch (>14 weeks) + Nicotine Gum	**3.6** (2.5-5.2)	**1.9** (1.3-2.7)
Varenicline 2 mg/day	**3.1** (2.5-3.8)	**1.6** (1.3-2.0)
Nicotine Lozenge (4 mg)	**2.8** (1.9-4.0)	Not Available
Nicotine Nasal Spray	**2.3** (1.7-3.0)	**1.2** (0.9-1.6)
Nicotine Patch (>25 mg/d)	**2.3** (1.7-3.0)	**1.2** (0.9-1.6)
Nicotine Gum (>14 weeks)	**2.2** (1.5-3.2)	**1.2** (0.8-1.5)
Nicotine Inhaler	**2.1** (1.5-2.9)	**1.1** (0.8-1.5)
Nicotine Lozenge (2 mg)	**2.0** (1.4-2.8)	Not Available
Bupropion SR	**2.0** (1.8-2.2)	**1.0** (0.9-1.6)
Nicotine Patch (6-14 weeks)	**1.9** (1.7-2.2)	**1.0**
Nicotine Gum (6-14 weeks)	**1.5** (1.2-1.7)	**0.8** (0.6-1.0)

Adapted from the USPHS Guideline (26).

It appears that varenicline and the combination of nicotine patch and nicotine gum may be the most effective tobacco cessation regimens available, resulting in a likelihood of tobacco abstinence that is more than three times that of placebo. [The 95% Confidence Intervals (C.I.) would indicate that the likelihood of improved abstinence is at least 2.5 times that of placebo and could be as high as 5.2 times greater with the nicotine patch and gum combination]. These two regimens also appear to be significantly more effective than the nicotine patch by itself. **All of the other medications listed appear to double the likelihood of abstinence compared to placebo and except for short duration use of nicotine gum, are comparable in effectiveness to the nicotine patch. Thus it is important to assess other attributes of the medications to assist in determining which may be most appropriate for the quitline to offer.**

Ease of Use

Effectiveness of any medication is dependent on the medication being taken as directed including at the recommended frequency and duration. (This is referred to as adherence). Medications that are administered once or twice a day are more likely to be taken as directed than medications that need to be taken multiple times each day. Complexity of administration can also affect adherence. For example, to maximize the effectiveness of the nicotine gum it must be chewed until the user feels a tingling or peppery taste in their mouth after which the gum is to be parked against the side of the mouth to allow absorption of the nicotine. Once the tingling has faded the user is to chew again and repeat the cycle until the tingling or peppery sensation no longer occurs, at which time a new piece of gum is taken. This is much more

complex than opening a packet of nicotine patch, removing the backing, and applying the patch to the skin once a day. If it is more difficult to adhere to a more complicated regimen reduced effectiveness of the medication is likely to result.

Ease of Distribution

Legal and procedural issues related to over-the-counter and prescription medications are usual 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, education and safety nets are often required to ensure the correct medications at the correct dosage are available to the caller when they want them.

Safety and Frequency of Side-Effects

Closely tied to adherence is the potential of the medication to cause adverse effects (unwanted side-effects). The type of side-effect, their frequency and their severity 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 improved adherence. As summarized in the USPHS Guideline, tobacco cessation medications are well tolerated and discontinuation for adverse events is low (23). Studies in people with respiratory and cardiac disease have also demonstrated a wide threshold of safety. In general prescription medications tend to have the potential for more serious side-effects than those medications available over the counter. Some of the quitline experience with medications and side-effects of medications is described below.

Nicotine Replacement Therapy (NRT)

Most quitlines providing medications are distributing the over-the-counter NRT medications nicotine patch, nicotine gum and nicotine lozenge. Almost all of the reported studies of medications and quitlines concern nicotine patches and/or nicotine gum. Proven effectiveness, generic medications at lowest cost, low side-effect profiles, ease of use and no requirement for a prescription make these medications most appealing in the quitline setting. Most callers, when given the choice, will choose to use the nicotine patch.

Ossip and colleagues recently published a study on adverse events from NRT used as part of the New York State Smokers' Quitline (27). Eligibility to receive the free NRT included: $\geq$ 18 years of age; currently smoking $\geq$ 10 cigarettes/day; willing to make a quit attempt within the next 2 weeks; no reported contraindications to NRT such as heart attack or stroke with past 2 weeks, history of arrhythmias; pacemaker; severe chest pains or angina in the last month, use of bupropion SR or varenicline, pregnant or breast feeding. They were also screened for allergy to adhesive tape, or dental work, teeth or jaw problems if considering nicotine gum. Smokers who had received free 2-week or 4-week quantities of NRT (over 96% receiving nicotine patches) were contacted by the quitline at 2 weeks and 3 months after being sent the medication and asked questions relating to adverse effects from the medications. At 2-weeks 25.6% of respondents reported adverse events from the patch, 20.3% of those who used the gum and 31.7% who used lozenges. However, only 4.4% reported adverse events as a reason they discontinued the medication. At 3 months, 41.7% of respondents who had used the NRT reported any adverse effects during NRT use. Vivid dreams (15%), skin rash (11.4%) and sleep disturbances (12.2%) were most common. Only 5.4% of participants reported stopped the medication because of an adverse event. The authors concluded that "the prevalence and type of adverse events reported was consistent with product labeling", and "distribution of over-the-counter NRT through quitlines is safe for whose who are screened adequately per the labeling instructions" (27).

Bupropion SR (Zyban®, Wellbutrin SR®)

According to recent survey data four state quitlines provide bupropion SR as a medication option to its callers (4). There is one published study of tobacco abstinence outcomes with the use of bupropion SR and quitline counseling conducted within a health plan setting (20). Physicians affiliated with the quitline were the prescribing physicians of record and an office visit with their primary care physician was not required if the caller passed an extensive phone interview that excluded certain medical conditions. Use of either 150 mg/day or 300 mg/day doses of bupropion SR resulted in substantial abstinence rates, with moderate to intensive telephone counseling enhancing the outcomes of both doses. (At one year, although there was no difference between 150 mg and 300 mg/day, the benefit of proactive telephone counseling was retained). Side effects were common, especially with the higher dose, but there were no serious adverse events (e.g. deaths or seizures). The conclusion from the study was that bupropion SR could be safely and effectively used in a quitline setting (20). The most common side effect is insomnia (trouble sleeping) 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 1/1000) which can be minimized further with careful screening of participants for contraindications to its use. This includes a history of: seizures, closed head trauma, brain surgery or strokes and the eating disorders of anorexia nervosa and bulimia. Recently the FDA has required a boxed warning regarding bupropion SR and its association with psychiatric symptoms with its use (see further discussion below) (28).

Varenicline (Chantix®)

Only two quitlines currently report offering varenicline as a medication option. Varenicline was approved by the FDA for use in 2006 and is available only by prescription with no generic equivalent available. Clinical trials have demonstrated increased efficacy for smoking cessation compared to placebo and bupropion (29, 30). There appear to be few drug interactions with varenicline and except for a dosage adjustment in the setting of renal failure, there do not appear to be any medical contraindications to its use. Nausea and sleep disturbances such as vivid dreams and insomnia are the most frequently reported side-effects. The FDA recently issued a boxed warning regarding use of varenicline and the risk of developing serious psychiatric problems (see further discussion below). In a recently published preliminary analysis of the use of varenicline in a quitline study 17% discontinued medication prematurely, about one-half due to side effects and other symptoms. However, those who received telephone counseling (compared to web-based support) were less likely to have discontinued their medication (31). Thus, there are more risk management issues with use of varenicline in a quitline setting than with other, more established medications.

The South Dakota quitline recently reported their early experience with Varenicline (32). To obtain varenicline the caller must call the quitline and enroll in the counseling program. They must also make contact with their healthcare provider (in person or by telephone) and request a prescription for varenicline. Their healthcare provider determines if varenicline is appropriate and safe for the caller and if so faxes a prescription to the Central Pharmacy. The quitline coach notifies the Central Pharmacy that the caller is enrolled and the medication is sent to the caller's home address. Only one month's supply is provided. If the caller wishes to receive additional medication the caller must remain engaged in the counseling program and the quitline coach notifies the Central Pharmacy of the caller's continued involvement at the 3rd and 5th calls which are scheduled to match monthly prescription requirements for refills for up to 3 months.

Positive outcomes have included: increased calls to the quitline; physician referrals to the quitline represent 44% of all referrals (up from 26% prior to starting varenicline program); Central Pharmacy is able to track amount of medication received by participant so does not exceed the 3-month supply. Quit rates are reported to have improved significantly. Challenges have been primarily related to caller and physician behaviors: provider faxes prescription, but the person never calls the quitline to begin counseling; the prescriptions are faxed to a local pharmacy rather than the Central pharmacy; no fax is sent by the provider; the prescriptions are signed but incomplete, illegible or the wrong dose has been prescribed.

Boxed Warnings for Bupropion SR and Varenicline (28)

The FDA can require "Boxed Warnings" be included in prescribing information when there is 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. They are usually based on adverse reactions reported by physicians, pharmacists and people who have used the medications. In July 2009, the FDA issued this warning because of increased reports of neuropsychiatric symptoms in people using these medications to stop smoking (28). The symptoms included changes in behavior, 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. With the boxed warning healthcare providers are to advise patients, family members and caregivers of the potential for these symptoms and if they develop to stop the medication immediately and contact their health care provider. Patients are to be also advised to use caution when driving, operating machinery or involved in other hazardous activities until they know how the medications affect them. As consideration is given regarding provision of these medications by quitlines, two important points should also be entertained:

1. Many of the symptoms described are symptoms typically seen in people who are trying to stop smoking and are experiencing nicotine withdrawal. This confounds the interpretation of the reports.

2. 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.

Simultaneous Use of More Than One Tobacco Cessation Medication

Certain combinations of medications have been shown to be more effective than use of one medication alone; e.g. nicotine patch and nicotine gum or nicotine patch and bupropion SR (33). The combinations tested have typically involved use of a long-acting medication (such as nicotine patch or bupropion SR) with a short-acting NRT (gum, lozenge, inhaler). A recently published study demonstrated the superiority of a combination of nicotine patch, bupropion and nicotine inhaler over nicotine patch alone (34). Although use of combinations of these medications is not yet FDA approved, the USPHS Guideline endorses this strategy as an option, for example, to people who have failed monotherapy in their past quit attempts. For a comprehensive discussion of the use of combination therapy see the recent article by Hurt, et.al (35). Quitlines contemplating provision of combination therapy need to recognize that combination therapy: requires close clinical monitoring and tight adherence to medication protocols because of the increased potential for side-effects; and careful consideration of the benefit of increasing the likelihood of quitting tobacco at the potential expense of reach, given limited resources.

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

The optimal duration to provide tobacco cessation medication is still undefined. The USPHS Guideline varies from no more than 8 weeks for nicotine patch (as longer duration of use has not been shown to be more effective in clinical trials) to up to 12 weeks for nicotine gum, nicotine lozenge, bupropion SR and varenicline (23). Prolonged use of nicotine patch in combination with nicotine gum or nicotine lozenge, however, does seem to increase abstinence rates significantly (33). The Centers for Disease Control and Prevention (CDC) recommends quitlines provide a minimum of two weeks for all callers and up to 8 weeks for those financially disadvantaged (36).

To date many of the studies performed to address this question have typically been non-randomized, observational or survey-based with low response rates and other weaknesses that limit their reliability. Nonetheless they have provided some information to help guide this decision. Some of the studies reporting effectiveness of NRT in increasing calls to quitlines and improving tobacco abstinence rates over counseling alone provided a 2 week supply of NRT (6, 11, 14, 15, 17). None of these studies involved randomization with a non-NRT comparison group. Others, some using randomization, used 6 weeks (10) or 8 weeks (9, 13, 16, 17, 19). As little as one week of free NRT increased calls to a quitline and increased tobacco abstinence rates compared to not providing NRT (12), however this was not randomized. Yet provision of longer durations NRT have been found to increase tobacco abstinence rates compared with shorter durations of NRT—at a greater absolute cost per caller, but only slightly higher cost per quit (10, 12, 17).

Adherence and the Issue of "Waste"

Surveys of people who were sent medication or vouchers for medication found that 80-95% of those responding reported using at least some of the medication (6, 9,12, 13, 16). One study found that the percentage of the amount used was the inverse of the amount provided (12). That is if a caller was given a 1- or 2-week supply of medication they were more likely to use a larger percentage of it than those given a 6-week supply (where only about 50% was used). Of those quitlines offering only a 1- or 2-week supply of NRT, 20-47% of callers responding to a survey reported buying more NRT themselves (6, 12, 14, 17). For quitlines providing up to 8 weeks of NRT in two shipments of 4 weeks each and requiring counseling to receive the second shipment, 25-66% asked for a second shipment (9, 16, 17). Provision of counseling support increased utilization of medication relative to those not receiving counseling.

In summary, providing 2 weeks of medication does result in increased telephone calls to the quitline and increased tobacco abstinence rates compared to periods of time when no NRT was provided. This allows a larger number of people to have access to NRT than if everyone was provided 6 or 8 weeks, if funds are limited. There may be less "waste" of medication when providing less NRT as those given less use a larger percentage of what is given them. Finally, a significant percentage were motivated enough to obtain additional NRT from other sources after receiving the initial supply, particularly if they received counseling encouraging this behavior. On the other hand longer duration of NRT resulted in significantly greater tobacco abstinence rates than those given a shorter duration. However other factors besides duration of NRT use may impact on abstinence rates. For example people have to participate longer (and potentially receive more counseling) in programs to get longer durations of NRT.

The majority of callers using the quitlines in most states are uninsured or underinsured and less likely to be able to obtain more medication on their own to sustain a longer duration of therapy. Proponents of longer duration therapy argue that not providing a sufficient duration of medication reduces the caller's likelihood of success with this quit attempt—and may end up costing the quitline more if more people call the quitline and receive medication that is inadequate for their needs.

The many real-world quitline effectiveness studies of different strengths and durations of medications have clearly demonstrated the benefit of providing medications in this setting. Additional well-designed trials will shed additional light on the pros and cons of each of these different approaches to tobacco cessation medication distribution. In the meantime each quitline needs to do a careful, thoughtful analysis to determine what duration of medication will add the most incremental value to their program for the cost.

Which Medication Distribution Model will be Best for Our Quitline?

There are two major mechanisms for distribution of medications: direct mail and voucher. Currently 33 quitlines provide direct mailing of medications and 1 provides medication via a voucher system. Seven quitlines use both depending on the medication dispensed (4). The table below summarizes characteristics of each system. However it must be noted that there have not been controlled trials comparing these two modes of distribution so some of the pros and cons are uncertain.

Table 3. Pros and cons of use of direct mail or vouchers in the disbursement of tobacco cessation medications.

Delivery Model	Costs	Pros	Cons

Direct Mail	• Cost of medication including procurement and storage
	• Cost of handling and distribution
	  ◦ Screening for eligibility/health conditions
	  ◦ Administrative costs related to medication shipping and handling, including costs of medication returns due to wrong addresses
		• Delivered directly to the caller, minimizing barriers to access
		• Control of specific medication distributed (brand name vs. variety of generics)
		• Central Pharmacy can track amount of medication sent to individual caller to limit excess medication delivery
			• Costs related to shipping errors and undelivered (or stolen) medication if not born by an external distributor
			• Waste of medications shipped but not used
			• May increase the responsibility of the quitline to provide complete information regarding medication usage and side-effects since local pharmacy involvement is eliminated.
			• Efficient communication structure required between central pharmacy and prescribing physician if prescriptions are incomplete or illegible

Voucher	• Cost of medication • Administrative costs related to pharmacy relations, education, follow-up, reimbursement • Cost of handling	• Avoids costs of maintaining in-house distribution system (procurement, storage and shipping of medications) or contracting and the logistics of working with third party to distribute medications • Avoids costs and waste of mailing medication to a wrong address	• Caller having to go somewhere to obtain the medication can be a significant barrier that prevents even those motivated to stop tobacco from obtaining the

	and distribution • Screening for eligibility/health conditions • Mailing of vouchers • Pharmacies may charge a processing fee	• By adding an additional step of having to go to a pharmacy in order to get the medication: may screen out those who are not as motivated to attempt a quit and who do not redeem the voucher, avoiding unused medication. • May be more appropriate for distribution of prescription medications since interaction with a pharmacist is more likely Keeps revenue within the state as working with local pharmacies than central distributor who may be out-of-state	medications • May require complex relationship management surrounding fulfillment and reporting with multiple local pharmacies • May decrease control of fulfillment, making it harder to manage refills especially if refills are tied to compliance with ongoing counseling.

Each quitline will need to assess these pros and cons as they determine which type of medication disbursement system to use. The use of a direct mail disbursement system allows more control over actual disbursement of the medication and maximizes the convenience by having it delivered to the caller's home. But costs to maintain an inventory of medication and to ship it may offset those benefits. A benefit of vouchers is as avoiding the cost of the mailing of medications. In addition, if the voucher is not redeemed because the caller has lost motivation to stop at that time, money is saved. However, the ability to conveniently access a participating pharmacy to redeem the voucher could be a significant barrier for some. Finally, although vouchers may be less expensive to distribute they require a more complex system to monitor disbursement of medications and reimbursement to participating pharmacies. In fact many large health-care systems that have both mail-order fulfillment and pharmacies encourage their members to use the mail-order system because it is cheaper than maintaining the in-person pharmacy infrastructure. Thus, for states contracting with service providers, the service provider may be able to negotiate volume discounts on medications and fulfillment. Use of both distribution systems could also be considered. For example, for home bound callers or those living in areas where access to a participating pharmacy is a problem, direct mailing of medications could be used. For callers in areas where access to a participating pharmacy is not a problem, the voucher system would appear to be a good option. In other scenarios, vouchers might work best when distributing prescription medications, retaining direct mail for over-the-counter NRT medications.

GUIDANCE FOR OVERCOMING QUITLINE CHALENGES TO PROVIDING MEDICATIONS

Legal/Liability Issues Related to Medication Distribution

Concerns about safety—risk of adverse outcomes in providing medications and liability issues related to adverse outcomes need to be addressed. Many of these issues reside at the state and provincial level and must be resolved by the individual quitlines. Quitline administrators and operators should seek guidance from a lawyer who practices in their state or province. The following are examples of how some quitlines have addressed liability issues:

- Limit provision of medications to only those that are available "Over the Counter (OTC)", that is, can be obtained by any adult without the requirement for a prescription. 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 coaches are consistent with packaged directions.
- Careful scripting of medication discussions to avoid providing diagnoses or being "prescriptive". Recommendations around medication use should be discussed in terms such as, "For people who smoke the amount you do, this is the dose of patch that is generally recommended", rather than the coach advising, "This is the dose of patch I want you to use." Discussions of medication should also include frequent reinforcement of the importance of checking with their health care provider to make sure this medication and dose is right for them and if they have questions or problems with use of the medication.
- Development of approved medication standing orders or strict guidelines on dosing recommendations coaching staff should follow. Close oversight of coaching recommendations and medication disbursement by experienced and licensed medical professionals is recommended. An efficient means for coaches to communicate with medical professionals if there are questions related to medication recommendations that fall outside of guidelines or standing orders should be in place.

- Review of the caller's eligibility and the coach's medication recommendations by a Registered Nurse or pharmacist under direct supervision of a physician prior to distribution of the medication provides an additional measure of safety.
- Active Medical Director (or other physician) oversight including regular review of medication guidelines or standing orders, audits of coaches' charts or calls for accuracy in medication discussions and accessibility to address staff questions and concerns regarding any of the tobacco cessation medications.
- If free or discounted prescription medications are offered through a quitline, systems should be in place to minimize any legal/liability issues for the quitline. This is covered in more detail below under the section, "Specific Guidelines for Provision of Prescription Medications".

Screening for Medication Eligibility

Eligibility criteria for distribution of medication varies between quitlines and is determined by funding and target population being served by the quitline, legal and liability concerns and FDA recommendations. These should be clearly enumerated and be required questions to be answered before medications are recommended.

- Age. Most quitlines will provide medication only to those $\geq$ 18 years of age, as many states define this as the age of adulthood when medications can be purchased without parental approval.
- Exclusionary medical conditions that might increase risk of series side-effects from use of the tobacco cessation medications. A partial list might include:
  - Recent (<2 weeks) myocardial infarction (for NRT products)
  - Generalized rash from previous use of a tobacco cessation medication use
  - Other allergic reaction from previous tobacco cessation medication use
  - Seizures (for bupropion SR)
  - Pregnancy or breast feeding (for all medications)
- The amount of tobacco used (cigarettes/day or tins/week). This eligibility criterion may be most applicable to those states that provide only one dose of NRT (for example, 21 mg patch). Limiting the medication to only those using more than a defined amount would reduce likelihood of nicotine toxicity.
- Insurance coverage eligibility will vary from state-to-state. Some states limit medication (and other services) to those who are uninsured or under-insured. Other states provide medication benefit to all callers.
- As noted above, some programs require the caller to participate in the counseling program offered through the quitline or from other resources in order to receive or continue to receive medication.
- Readiness to attempt to quit tobacco use within a specific period of time (usually 30 days). This is based on Prochaska and DiClemente's Stages of Change (37). People who acknowledge they plan to quit tobacco use and set a quit date within 30 days may be more likely to make a quit attempt and hence more likely to use the medication provided to them than people who say they may not be ready to quit within 30 days. Having this as an eligibility criterion may avoid sending medication that the caller never uses. However, some quitlines may choose to offer medications to any caller requesting them as having the medication available may lead to a quit attempt that otherwise would not have happened.

Special provision for distribution of medication for callers with eligibility exclusions can be considered under specific circumstances: e.g. if their primary physician provides written approval for use despite pregnancy or exclusionary medical condition. However, these exceptions require communication systems that can be time consuming and work best if there is readily accessible medical support built into the quitline infrastructure.

Communication of Medication Information

Content of call scripts, print and web materials that discuss use of Medications should include the following:

- Overall rationale for medication use in tobacco cessation as outlined in the USPHS Guideline (38).
- Emphasis on the benefits of active participation in the counseling components of the program in addition to medication use. As noted in the USPHS Guideline, the combination of medication with counseling has been demonstrated to increase the likelihood of tobacco cessation compared to either intervention by itself (8).
- Availability of information on all FDA approved medications (but emphasis on those specifically offered through the quitline). To make a truly informed choice about what medication may be right for them the caller should have access to information about all of the FDA approved medications (at least in the written and web materials).

Although the quitline may only be able to provide certain medications, the caller should know what others are available should they fail the one provided. If they have used the medications provided by the quitline in the past without success, this may be especially important information for them. The coach should be prepared to discuss any of the FDA approved medications.

- Encouragement to use the medication as directed and for as long as necessary to achieve abstinence and then maintain that abstinence.
- Specific directions (with telephone number) to call back to the quitline or contact their health care provider if questions or issues arise with the medication
- Provision of supplementary written materials on medications.

Minimizing the Cost of the Medication

The actual cost to purchase the medications is obviously a major determinant of the overall cost to add tobacco cessation medications to existing quitline services. There are several strategies to minimize these costs as much as possible:

- Thoroughly explore all medication suppliers to determine product type and costs
- Provide generic medications whenever possible
- Limit the duration that medication is provided (and thus the amount provided) by the quitline. If additional medication is felt to be necessary processes should be in place that encourage individuals to obtain more medication on their own, through their insurance company or from other resources.
- If an extended duration of medication is provided consider dividing distribution into at least two shipments. In addition:
    - There is a significant relapse rate and subsequent drop-out from participation in the first few weeks, resulting in potential for significant amount of unused medications if the entire duration is sent at one time. For example, if offering 8 weeks of treatment, provide two shipments of 4 weeks each.
    - Require ongoing engagement in counseling in order to receive additional medication (which may also increase the effectiveness of the program, but also add counseling costs)
    - Realize each medication shipment has costs associated with processing and shipping and should be considered when determining overall cost savings
- Develop partnerships with health plans and employers to assist in covering the cost of medication (at least after the initial shipment) (14,19,40)

Specific Guidelines for Provision of Prescription Medications

Challenges to using bupropion SR and varenicline (or nicotine inhaler and/or nicotine nasal spray) in a quitline setting include: they require a prescriber's prescription in order to be dispensed; there are contraindications and/or dosage adjustments necessary with some co-morbid medical conditions; and —in rare instances—severe side effects. These challenges require additional processes to thoroughly screen callers for contraindications, increase training of coaching staff in addressing side-effects and/or engagement of prescribers in the procuring of medication and following-up on medication side-effects. Provision of prescription medications, then, requires clear delineation of responsibilities in which the quitline facilitates access to free prescription medications but the final screening, determination of appropriateness and the prescription are those of the licensed health care provider. Unfortunately, these restrictions may limit utilization of prescription medications as a significant percentage of many state quitlines' callers are uninsured and without access to a provider who can evaluate them and provide a prescription. Quitlines may also determine that the logistic complexity of supporting prescription medications is simply not worth the additional investment in infrastructure.

Quitlines could respond to these challenges in several ways:

- The quitline's primary focus may be only on providing decision support for the prescription medications, or providing only NRT that is OTC. The counseling staff is trained and has support materials that describe the pros and cons of the medication being discussed, how to use it correctly and specific details on how to obtain the medication. If the caller chooses to use a prescription medication, it is up to the caller to obtain the prescription from their health care provider and purchase the medication with whatever resources they have available to them (e.g. out of pocket or third party payer benefit plan).
- If prescription medications are offered through a quitline, systems should be in place to minimize any legal/liability issues for the quitline. Most of the responsibility for appropriate prescribing of these medications should reside with

the health care provider writing the prescription. It is their responsibility to determine if the prescription medication is appropriate (and safe) for the caller. Still, quitlines should have processes in place to:

- Provide adequate screening for contraindications to use of these medications. Prescribers may be unfamiliar with tobacco cessation medications and the coaches can serve as resources to prescribers and callers regarding appropriate medication use. Identifying contraindications to specific medications early in the assessment can also save time and refocus the session by discussing other medications and/or emphasizing additional cognitive and behavioral options to treatment of their dependence. If the quitline determines they cannot provide this level of screening and support, then they should either not include prescription medications, or ensure that the caller and their physician are clear that the determination of appropriateness is the responsibility of the healthcare provider and not the quitline.
- Procure a written prescription from a licensed prescriber, preferably one who has a relationship with the caller. Generally, the caller is responsible for contacting the prescriber and requesting the medication. Callers may be required to schedule an office visit with their health care provider in order to obtain a prescription; however, if their provider is familiar with the caller's medical condition(s), a visit may not be necessary. (As stated above, this may be an obstacle for the caller who does not have a relationship with a provider or cannot afford a visit to obtain the prescription). Some quitlines provide the caller with an automated letter that describes what, if any screening has been done by the quitline and what the recommended medication and dosing might be as guidance to the provider. The caller then provides this letter to their physician at the time of the prescription request.
- Clear directions on how the prescription is to be processed should also be provided to the caller and the physician. Options for fulfilling the prescription may be one of the following:
    - If the quitline has its own mail-order capacity or uses a central pharmacy, the prescription could be forwarded to the quitline (or the central pharmacy) by fax and the medication mailed directly to the caller.
    - If the quitline uses a Pharmacy Benefits Manager company, when the caller takes the prescription to the pharmacy, the pharmacy will fill the prescription and bill the Pharmacy Benefits Manager.
- Manage questions about medications appropriately. Questions clarifying dosing instructions or general information about side-effects can be managed by coaches. However, questions that are related to specific symptoms that the caller feels may be medication side-effects should be referred to the caller's physician or pharmacist. Although trained to recognize common side-effects of medication, for most coaches the level of training and lack of appropriate licensure does not permit them to diagnose a caller's specific symptom as related to the medication.
- As both bupropion SR and varenicline now have FDA boxed warnings, any discussion of these medications by the coaches should include these warnings.
- Establish policy and procedures for reviewing calls for quality assurance specifically addressing the accuracy of medication information provided by the coaches and their fidelity to the approved medication protocols.

Provision of Combinations of Medications

The USPHS Guideline has encouraged clinicians to consider using certain combinations of medications with their patients because they have been shown to be effective (33). The recommendation does not say that combination therapy should only be offered to people who meet a series of requirements such as failing properly dosed and complied single-dose therapy. However, a specific protocol may be reasonable for cost reasons when used within a quitline setting.

The example protocol detailed below for providing combinations of medications is designed assuming that it would be cost-prohibitive for many quitlines to provide this level of expenditure for medications to a large number of callers. Thus, to conserve financial resources when providing combinations of medications, it may be prudent to establish specific criteria for those eligible to receive combination therapy. An example of how this might be applied is as follows:

The caller is eligible for quitline benefit of combination of patch + gum or lozenge; bupropion SR + patch, gum or lozenge; varenicline + gum or lozenge. With this protocol however only ***one*** type of long acting medication (patch, bupropion SR or varenicline) would be provided in the initial shipment. Scripting to describe the rationale for combination therapy to the caller could be: "Some people find that the addition of a short acting NRT like the lozenge or gum is helpful to them if they have particularly strong urges or withdrawal symptoms not controlled by the nicotine patch (or bupropion SR or varenicline). Let's see how these first couple of weeks goes with this first medication by itself and if we think that a combination of medications might help you; we can discuss this at our next telephone call and send out a

short acting NRT with your next shipment if it seems appropriate at that time". If, at the next contact, the caller appears to be failing single therapy, the coach can request a second type of medication, document the rationale for doing so in the member's chart and obtain for approval and recommendations on type and dosing based on the coaches discussion with the caller.

IF the coach feels the caller should receive combination therapy at the ***first call***, prior approval of the medical director or supervisor would be obtained unless all four of the following criteria have been met and documented in the caller's chart:

- The member has tried to stop tobacco before
- AND, the member had received appropriate dosing of a tobacco cessation medication in the past
- AND, the member had used the appropriate dose of medications for at least two weeks
- AND, the member had failed to stop using tobacco during that time

If the caller does not meet all criteria, but the coach still feels the caller would benefit, an exemption request is completed and forwarded to the supervisor or medical director for consideration and recommendations. The information is reviewed and, if appropriate, approves the additional medication with dosing recommendations to the coach who then completes the fulfillment process. The caller is reminded to "visit with your health care provider before using this combination of medications to make sure it is safe for you to do so". If a prescription medication is recommended as part of this combination therapy, the caller is instructed to obtain the prescription from their provider.

Tobacco Cessation Medications for Pregnant or Breast Feeding Women

Significant controversy exists surrounding the safety of using tobacco cessation medication by women who are pregnant or breast feeding. The authors refer you the USPHS Guideline for a comprehensive discussion and bibliography related to this topic (40). Briefly, all of the FDA approved medications for tobacco cessation carry a FDA pregnancy category designation of "C" or "D"—not recommended for use by pregnant women (41). The evidence for these recommendations is based almost exclusively on animal studies in which nicotine was administered in doses and by mechanisms that may not be applicable to humans. However, these designations are not absolute contraindications to their use and do allow for use in life-threatening situations or when other treatment modalities have failed. Some clinicians (and their patients) may determine that the potential for fetal harm, including fetal death, is sufficiently high with continued smoking to warrant use of medication. The decision for use in these circumstances is to rest on the results of a careful, thorough, thoughtful discussion between the woman and her personal physician as to the risks of the medication balanced against the risks to her and the baby of continued smoking and the benefits to her and the baby of stopping.

As pointed out in the USPHS Guideline there are very few studies of tobacco cessation medication in pregnant women on which to make decisions. Many physicians feel that the risks of continued exposure to not only nicotine but 4000+ other chemicals in tobacco smoke is far greater than the risk of short term use of medicinal nicotine, and will prescribe tobacco cessation medication to their pregnant patient who wants to stop smoking and has been unsuccessful with other means. Many physicians are concerned about the safety and efficacy of these medications and will not prescribe them. In the end the ultimate decision is between the physician and the informed patient.

The same lack of studies on which to make an informed decision also applies to the use of tobacco cessation medications by women who are breast feeding. The greatest concern is for the nursing infant and exposure to nicotine or the other medications in the breast milk and the effect on development. No clear consensus exists on how these medications should be used, again relying on the woman and her personal physician to decide risks and benefits.

Although some quitlines have defined pregnancy as an absolute contraindication to provision of medications, other quitlines have taken the approach of respecting the decision reached by the caller and her physician about medication use. Since bupropion SR and varenicline are available by prescription only, the decision on their use may have already been made by the time the woman calls the quitline. If not, the coach should inform the caller regarding the unknown risks of using medication in pregnancy but the risks of continued smoking and benefits of quitting. If the caller wishes to use bupropion SR or varenicline, she is referred to her physician to obtain the prescription. If the caller wishes to use NRT she must obtain written signed documentation from her physician that they have discussed the use of medications during pregnancy (and/or breastfeeding) and both the caller and the physician agree with their use. This document is faxed or mailed to the quitline. Once documentation is received, the medication is provided. If the woman cannot obtain a physician's agreement, the coach should focus on cognitive and behavioral strategies that will facilitate the caller's quit attempt and increase the likelihood of tobacco abstinence without medication.

If NRT is used the following approach is recommended:

- Base initial dosing on the number of cigarettes/day and time to first cigarette as appropriate for non-pregnant smoker
- Use short-acting NRT such as nicotine gum, nicotine lozenge, or nicotine inhaler
- Use the least amount that will control withdrawal symptoms, minimize cravings and achieve and sustain abstinence
- If nicotine patches are required (intolerant of other forms of NRT, frequent dosing of short-acting NRT is required, or at caller request) their duration of use should be limited to 16 hours/day (removed at night)
- The NRT should be used as early in the pregnancy as possible and for the shortest duration as possible.

Special Situations

Smokeless Tobacco
There are no FDA-approved medications for those trying to stop smokeless tobacco use. Studies demonstrate little efficacy for improving abstinence for nicotine gum, nicotine patch or bupropion SR using the doses for smoking cessation interventions, but do show withdrawal symptom relief with these medications (42). Nicotine lozenges and higher doses of nicotine patch have been shown to be effective in small clinical trials (43-45). Published recommendations for dosing of nicotine patches for smokeless tobacco users do exist (46). See Appendix A for an example of recommendations regarding use of medications to treat smokeless tobacco users.

Cigars, Pipes, other Forms of Tobacco and Concurrent Use of More Than one Form of Tobacco
Because of the marked heterogeneity in the types of products available, and the amount and method they are used it is difficult to provide specific medication guidelines. For one quitline, counseling staff are directed to obtain specific information regarding the product, amount and frequency used including time to first use each day. This is discussed (electronically) with the Medical Director who then provides guidance as to type of medication and initial dosing to recommend. The caller is encouraged to review these recommendations with their health care provider before using.

THERE IS A NEED FOR RESEARCH

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

a) Increase quit rates
b) Are cost-effective
c) Are more effective when coupled with counseling
d) Deliver quit rates comparable to those seen in face-to-face settings

However there are many more "drill-down" questions that will require ongoing research to provide detailed answers. Just as the most effective use of quitlines is evolving so is the role medication plays in providing cost-effective tobacco cessation interventions. Some of the questions include:

- Counseling:
    i. Are there ways to more efficiently improve quit rates for callers with counseling, such as by varying call timing, triaging additional counseling based on predictors of success, or having briefer more focused calls? What is the population impact of different strategies for delivering counseling along with medication?
    ii. Would more frequent medication-focused contact with callers increase medication adherence? Would this improve outcomes? If so, is it cost-effective?
    iii. What is the best mechanism to communicate medication information and update medication use recommendations across NAQC?

- What role might Interactive Voice Response (IVR) and other technology (e.g. texting) have in lowering costs and promoting use of the medications provided to tobacco user?

- Medications:
    i. What is the optimal duration to provide medications?
    ii. Which, if any, medication adverse events should be systematically monitored?
    iii. How are interventions using combinations of medications integrated into quitline protocols?
- How does ordering medication online affect usage rates of the medication (i.e. likelihood of "waste")? Is there a difference in cessation effectiveness of medication provided by this mechanism compared to live telephonic intervention?

- What screening criteria for medication are most helpful and should be standardized? This includes, what screening criteria predict better outcomes; for example, does setting a quit date improve outcomes? Or what screening protocols may be beneficial in minimizing risks of medication side-effects?

- What should the content of the quitline intervention include related to medication that will increase effectiveness? More emphasis on using the medication as directed (adherence)?

- How should medication protocols be altered when working with specific populations of tobacco users? For example: light smokers; highly dependent tobacco users; those with mental illness; those attempting reduction of use with medications prior to stopping tobacco.

- How involved will quitlines be, and how much funding will they be able to provide as research identifies biomarkers which are predictive of which tobacco users benefit the most (and least) from the addition of medication, or that may help determine which medication may be most beneficial?

- What additional information would be helpful that should be included as part of the Minimum Data Set? For example:
    - Amount (in weeks) of medication received from the quitline (if any)
    - Amount (percentage) of medication used
        - If not 100%, why not—specifically, was early discontinuation related to a side-effect from the medication and what was that side-effect
    - If obtained more medication from sources other than quitline, what was that source?
    - If used more than one medication during their quit attempt, were those medications used in combination or sequentially?

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 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 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 without compromising reach. 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. At a minimum, quitlines should have protocols in place that will ensure callers have access to information about the benefits of medication and the characteristics of the specific FDA-approved medications, as well as the ability to expedite access to medications for callers through other sources (for example: personal physician, employer, Medical Assistance, non-governmental programs, out-of-pocket, etc.).

2. If medications are part of the services provided to all eligible callers, a minimum of a 2 week supply of medication should be provided to all callers and up to 8 weeks for those who are socio-economically disadvantaged, as recommended by the CDC (36). For other populations, the duration and type(s) of medication offered should be centered around the quitline's strategic objectives and on current scientific evidence and expert consensus.

3. Provision of medications as a promotional strategy should be considered as a means to increase the overall cost-effectiveness of medications and quitlines by reducing the need for more expensive promotional activities.

4. Careful consideration should be given to minimize unintended consequences of medication distribution, including diminution of the important role counseling plays in tobacco cessation, overwhelming resources with call volume beyond capacity, cost-shifting from other quitline services to medications and shifting responsibility for medication costs from health insurers to the quitline.

5. All callers should be strongly encouraged to use a full course of treatment as recommended by the USPHS Guideline (23). This may require the caller to purchase out of pocket or through reimbursement from their health plan. For economically disadvantaged callers, quitlines should strongly consider supplying this full course of treatment.

6. Quitline counseling staff should be trained and competent to discuss all of the FDA approved medications, and to provide detailed instructions on use for those offered by their quitline. This competency should include knowledge of contraindications, dosing and common side-effects and their management. The benefits of counseling, whether through the quitline or through other resources, should be strongly emphasized as well.

7. Quitlines should collaborate to seek additional funding to support the integration of medications with other quitline services, as well as for research on how to more effectively utilize tobacco cessation medications in the quitline environment.

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APPENDIX A

Medications for Smokeless Tobacco Treatment

Example of medication dosing guidelines for smokeless tobacco users:

- Dosing guidelines for the 24 hour nicotine patch (45):

  >3 cans or pouches/week = 42 mg/day
  2-3 cans or pouches/week = 21 mg/day
  <2 cans or pouches/week = 14 mg/day

  Adjust based on withdrawal symptoms, urges, and comfort. After 4-6 weeks of abstinence, taper every 2-4 weeks in 7-14 mg steps as tolerated

- For other medications, the following is suggested

  Nicotine lozenge or Nicotine gum

  4mg if > 3 tins/week or time to first use < 30 minutes
  2mg if ≤ 3 tins/week or time to first use > 30 minutes

  Nicotine inhaler and nicotine nasal spray are not recommended for use in ST users.

  Non-nicotine pharmacotherapy

  Neither bupropion SR nor varenicline are approved by the FDA for treatment of ST use. However, empiric evidence suggests that they may be of benefit in this population of tobacco users, using the dosing guidelines recommended for cigarette smokers (46).

APPENDIX B

Tobacco Dependence Treatment Medication Summary

Description & Examples	Pros and Cons	Comments	Dosing Recommendations
Combination Therapy	**Pros** • Permits sustained levels of nicotine with rapid adjustment for acute needs • More efficacious than monotherapy **Cons** • May increase risk of nicotine toxicity • Cost	Providing two types of delivery system, one passive and one active, appears to be more efficacious. Should be considered for those who have failed single therapy in the past and those considered highly tobacco dependent. Not a FDA approved strategy.	Dose the patch, bupropion SR or varenicline as described. Prescribe 2mg gum, 2 mg lozenge, nicotine inhaler or nicotine nasal spray on an as needed basis when acute withdrawal symptoms and urges to use tobacco occur. If patch is used adjust dose of patch if frequent use of other NRT: goal is to minimize need for short-acting NRT dosing.
Nicotine Patch *(OTC)* **24 hour delivery system** 21, 14, 7 mg/24 hr (Generic available)	**Pros** • Achieve high levels of replacement • Easy to use • Only needs to be applied once a day • Few side effects **Cons** • Less flexible dosing • Slow onset of delivery • Mild skin rashes and irritation common	Patches may be placed anywhere on the upper body-including arms and back. Rotate the patch site each time a new patch is applied. **May purchase without a prescription**	> 10 cpd = 21 mg/day ≤ 10 cpd = 14 mg/day • Adjust based on withdrawal symptoms, urges, and comfort. After 4-6 weeks of abstinence, taper every 2-4 weeks in 7-14 mg steps as tolerated.
Nicotine Lozenge (OTC) Delivers nicotine through the lining of the mouth while the lozenge	**Pros** • Easy to use • Delivers about 25% more nicotine than nicotine gum **Cons** • Do not eat or drink 15	Use at least 8-9 lozenges/day initially. Efficacy and frequency of side-effects related to amount used.	Based on time to first cigarette of the day: <30 minutes = 4 mg ≥30 minutes = 2 mg Based on cigarettes/day (cpd)

dissolves. 2 mg, 4 mg Flavors: Multiple (Some generics available)	minutes before use or during use • Should not be chewed or swallowed • Nausea (12-15%)	**May purchase without a prescription**	>20 cpd: 4 mg ≤20 cpd: 2 mg Initial dosing is 1-2 lozenges every 1-2 hours (minimum of 9/day). Taper as tolerated
Nicotine Gum (OTC) 2mg, 4mg Flavors: Multiple The term "gum" is misleading. It is not chewed like regular gum but rather is chewed briefly and then "parked" between cheek and gum. The nicotine is absorbed through the lining of the mouth. (Generic Available)	**Pros** • Convenient/Flexible dosing • Faster delivery of nicotine than the patches **Cons** • Not for people with dental problems and those with temporomandibular joint (TMJ) syndrome • Should not eat or drink 15 minutes before use or during use • Frequent use during the day required to obtain adequate nicotine levels	Many people use this medication incorrectly. Review package directions carefully to maximize benefit of product **May purchase without a prescription**	Based on cigarettes/day (cpd) >20 cpd: 4 mg gum ≤20 cpd: 2 mg gum Based on time to first cigarette of the day: <30 minutes = 4 mg >30 minutes = 2 mg Initial dosing is 1-2 pieces every 1-2 hrs (10-12 pieces/day). Taper as tolerated.

Description & Examples	Pros & Cons	Comments	Dosing Recommendations
Nicotine Nasal Spray Delivers nicotine through the lining of the nose when sprayed directly into each nostril.	**Pros :** • Flexible dosing • Can be used in response to stress or urges to smoke • Fastest delivery of nicotine of currently available products but not as fast as cigarettes **Cons** • Nose and eye irritation is common, but usually disappears within one week. • Frequent use during the day required to obtain adequate nicotine levels	Unlike nasal sprays used to relieve allergy symptoms, the nicotine spray is not meant to be sniffed. Rather, it is sprayed against the lining of each nostril once or twice an hour (maximum of five times in one hour). **Prescription required for purchase**	1 spray in each nostril 1-2 times/hr (up to 5 times/hr or 40 times/day) Most average 14-15 doses/day initially Taper as tolerated
Nicotine Inhaler A plastic cylinder containing a cartridge that delivers nicotine when puffed. The inhaler delivers nicotine to the oral mucosa, not the lung, and enters the body much more slowly than the nicotine in cigarettes.	**Pros** • Flexible dosing • Mimics the hand-to-mouth behavior of smoking • Few side effects **Cons** • Frequent use during the day required to obtain adequate nicotine levels • May cause mouth or throat irritation	Puffing must be done frequently, far more often than with a cigarette. Each cartridge designed for 80 puffs over 20 minutes of use. Patient does not need to inhale deeply to achieve an effect. **Prescription required for purchase**	Minimum of 6 cartridges/day, up to 16/day Taper as tolerated
Non-nicotine medication ***Bupropion SR*** (Zyban, Wellbutrin SR)	**Pros** • Easy to use • Pill form • Few side effects • May be used in combination with NRT (nicotine patches, spray,	A slight risk of seizure (1:1000) with this medication. Seizure risk should be assessed. Risk of seizure is increased if: • Personal history of seizures • Significant head trauma/brain injury • Eating disorder history	**Take doses at least 8 hours apart** Start medication one week prior to the Target Quit Date (TQD) **150 mg once daily for 3 days, then** **150 mg twice daily for 4 days, then**

(Generic Available)	gum and inhaler)** **Cons** • Contraindicated with certain medical conditions and medications	• Concurrent use of medications that lower the seizure threshold **Prescription required for purchase**	**On TQD STOP SMOKING** Continue at 150 mg BID 12 weeks, or longer if necessary. No need to taper.
Non-nicotine medication ***Varenicline*** (Chantix)	**Pros** • Easy to use • Pill form • Generally well tolerated • No known drug interactions **Cons** • Nausea is common	• Nausea is common. Take with food and titrating the dose as directed will help • It appears that varenicline can be safely used in combination with bupropion and/or NRT. However, efficacy of these combinations has not been shown • Dose must be adjusted if kidney function is impaired **Prescription required for purchase**	**TAKE WITH FOOD** Start medication one week prior to the Target Quit Date (TQD) **0.5 mg once daily X 3 days, then** **0.5 mg twice daily X 4 days, then** **ON TQD STOP SMOKING AND** **Take 1.0 mg twice daily X 11 weeks** If not smoking at the end of twelve weeks, may continue at 1.0 mg twice daily for an additional 12 weeks No need to taper.

The most effective dose varies by individual. Some of the dosing recommendations are not contained in current product labeling information. Adapted from Hurt RD, et al.(35); Fiore MC, et.al.(23)

APPENDIX C

U.S. Quitlines: Free and Discounted Quitting Medications (Fiscal Year 2008)

Data provided from the 2008 NAQC Annual Survey.

	Free Quitting Madications							Discounted Quitting Medications						
States and Territories	**Patch**	**Gum**	**Lozenge**	**Zyban**	**Chantix**	**Nasal Spray**	**Inhaler**	**Patch**	**Gum**	**Lozenge**	**Zyban**	**Chantix**	**Nasal Spray**	**Inhaler**
Alabama	X													
Alaska	X													
Arizona	X	X	X	X	X			X	X	X	X	X		
Arkansas	X													
California														
Colorado	X	X												
Connecticut	X	X	X											
Delaware	X	X	X											
Florida	X	X	X											
Georgia	X	X	X											
Guam	X	X												
Hawaii	X	X												
Idaho														
Illinois														
Indiana	X	X	X											
Iowa	X	X												
Kansas														
Kentucky														
Louisiana														
Maine	X	X	X											
Maryland	X	X												
Massachusetts	X													
Michigan	X	X	X					X	X	X				
Minnesota	X	X	X											
Mississippi	X	X												

States and Territories	Patch	Gum	Lozenge	Zyban	Chantix	Nasal Spray	Inhaler	Patch	Gum	Lozenge	Zyban	Chantix	Nasal Spray	Inhaler
Montana	X	X	X									X		
Nebraska														
Nevada								X	X	X	X	X	X	X
New Jersey														
New Mexico	X	X	X											
New York	X	X	X											
New Hampshire														
North Carolina														
North Dakota	X	X	X											
Ohio	X													
Oklahoma	X	X												
Oregon	X	X												
Pennsylvania														
Puerto Rico	X													
Rhode Island														
South Carolina	X	X												
South Dakota	X	X		X	X									
Tennessee														
Texas	X	X	X	X										
Utah	X	X												
Virginia														
Vermont	X	X	X											
Washington	X	X												
Washington, DC	X		X											
West Virginia	X	X	X	X		X	X	X	X	X				
Wisconsin	X	X	X											
Wyoming								X	X	X	X	X	X	X
Total	**37**	**30**	**18**	**4**	**2**	**1**	**1**	**5**	**5**	**5**	**3**	**4**	**2**	**2**

States and territories have elegibility criteria for providing medications to quitline callers. To view elegibility criteria for each quitline, from the Map select the quitline of interest and view its profile. For questions about data presented here, contact NAQC at naqc@naquitline.org.

APPENDIX D

Canadian Quitlines: Free and Discounted Quitting Medications (Fiscal Year 2008)

Data provided from the 2008 NAQC Annual Survey.

	Free Quitting Madications							Discounted Quitting Medications						
Provinces	**Patch**	**Gum**	**Lozenge**	**Zyban**	**Chantix**	**Nasal Spray**	**Inhaler**	**Patch**	**Gum**	**Lozenge**	**Zyban**	**Chantix**	**Nasal Spray**	**Inhaler**
Alberta														
British Columbia	**X**	**X**						**X**	**X**					
Manitoba														
New Brunswick														
Newfoundland and Labrador														
Nova Scotia														
Ontatio														
Prince Edward Island														
Quebec														
Saskatchewan														
Total	**1**	**1**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**0**	**0**

Provinces have elegibility criteria for providing medications to quitline callers. To view elegibility criteria for each quitline, from the Map select the quitline of interest and view its profile. For questions about data presented here, contact NAQC at naqc@naquitline.org.