A. SPECIFIC AIMS

Dental practices have advanced tobacco cessation by adopting a model of brief advice similar to that used by medical providers. We propose a randomized clinical trial designed to allow dental hygienists to provide additional tobacco cessation counseling with little additional marginal effort. This would be done using an internet-based referral to external resources. This system, termed "Refer2Quit", will allow hygienists to refer patients to a patient education website and accompanying Quitline, while the patient is still in the dental office. Our overall goal is to advance science related to internet use in health services delivery by targeting dental hygienists. The intervention will also support subsequent brief counseling by providing feedback on the activities of patients to the practice through a secure server.

We have these specific aims:

(1) To test the hypothesis that the proportion of patients **REFERRED** to self-management resource websites will be larger in intervention practices compared to control practices. We expect to observe a referral rate of 24% among intervention practices compared to the 12% observed from protocols similar to the control practices[1].

(2) To test the hypothesis that the proportion of patients referred who **GO** to the patient self-management website will be larger in intervention practices (40%) compared to control practices (20%).

(3) To test the hypothesis that the proportion of smokers who are referred who **QUIT** at six months will be larger among intervention (15%) compared to control (10%) because of the additional connectivity of the intervention.

This will done by randomizing 80 (40 per arm) community-based dental practices into a clinical trial that contrasts the intervention with a paper-based “information prescription”.

The intervention is a multi-component internet-delivered clinical microsystem intervention using: (1) "Refer2Quit", a point-of-care “patient referral portal” that hygienists can use to enroll patients into a self-management system; and (2) "Decide2Quit", a patient self-management portal organizing interactive, tailored, patient education and cessation planning links to other high-quality web (smokefree.gov) and offline resources (1-800-QUIT-NOW).

The control group would be randomized to a paper-based “information prescription” that hygienists would use to refer patients to a previously-developed patient self-management website that is not linked into the dental practice.

We anticipate that hygienists will be the primary drivers of this intervention (See figure 4). However, implementation of the intervention will vary from practice to practice and dentists may refer patients into the system at times. Below, we often refer to “providers” interacting with the system, to be inclusive of dentists and hygienists.

The significance of the proposed study is that it will be the first internet-delivered intervention targeted to dental hygienists that is specifically designed to increase smoking cessation through internet referrals. This study builds upon our previous NCI-funded successful R21 (Ford, PI), where we built our control self-management system for this study, and our previous successful Dental PBRN study (a NIDA/NIDCR-funded R01 entitled DentalTobaccoControl.Net, Houston, PI; R01-DA-17971) where dentists and hygienists were trained in face-to-face brief counseling using an internet-delivered continuing education system.

B. BACKGROUND AND SIGNIFICANCE

B.1. Smoking and Disease - Tobacco use has been called the number one behavioral health problem.[2-5] Among its innumerable morbidities, smoking is responsible for approximately one-third of all cancer deaths.[6] Regrettably, the decline in smoking has leveled and smoking rates in some southern states have been increasing.[7]

B.2. Self-Management for Smoking Cessation – Although considerably greater effects are seen with intensive smoking cessation counseling, easily disseminatable patient self-management interventions can potentially access much greater numbers of smokers.[8] Patient self-management interventions for smoking cessation include mass dissemination of tobacco cessation self-help materials, computer-tailored printouts, interactive voice response systems, and more recently, "Quitlines" and smoking cessation websites. [4, 9-16] Unfortunately, self-management interventions for smoking cessation have been under-utilized. Studies of quitlines note that as few as 3.5% of adult smokers call per year.[17] Because more than half of smokers see a dentist at least once per year,[18] hygienist referrals could greatly increase use of publicly available self-management interventions for smoking.

B.3. Computers, the Internet, and Smoking Cessation - Compared with general self-management materials, individually tailored self-help materials result in an additional benefit, with a pooled estimate of Odds Ratio 1.5 (95%CI 1.1-2.0).[9] Computers have been increasingly used to tailor information to individuals.[9-14] Computer-driven interventions for smoking cessation, such as automated telephone counseling and clinic-based expert computer system feedback, have been designed to assist smokers in deciding to quit.[9, 13, 19, 20] In a review of ten published trials of smoking cessation messages generated by expert systems, six showed significantly higher cessation rates or transitions in stage of change than comparison groups.[11] Access to the Internet continues to grow and the Internet is becoming a common source for health-related information.[21-25] The Internet has several characteristics that suggest it may be useful for improving health outcomes.[26] These include the ability to access interventions at any time, to provide confidential help, to tailor interventions, and to provide relatively low-cost interventions. Smokers appear to highly value these characteristics.[27]

Over 200 smoking cessation websites were in existence before 2005, [28] although the quality of these sites varies considerably.[29] A recent review[30] summarized the relatively positive evaluations to date,[31-39] but noted limitations in study design. One evaluation by Swartz noted cessation of 24% in the intervention group compared with 8% in the control in a per protocol analysis.[38] Another study of 1,501 users of QuitNet, a popular self-management website for smokers, found cessation rates of 7% at three months in an intent-to-treat analysis, but did not include a control group.[40] The generally positive, but usually modest effects are not surprising as these interventions have essentially packaged smoking cessation self-help programs previously proven effective when delivered through computer printouts, handouts, or voice response system and delivered them through a more interactive and accessible interface.

Most smoking cessation Internet sites have focused primarily on providing educational information to smokers.[31-36] Few Internet-based smoking interventions have been integrated with other smoking cessation efforts in a stepped-care approach.[30] In one study of the addition of Internet-delivered materials to nicotine replacement therapy, users of a tailored Internet-site had a cessation rate of 29%, compared with 23% in those using nicotine replacement and a non-tailored site.[35] However, none of these sites have focused on encouraging smokers to engage with health care professionals to help them quit smoking, which is associated with higher smoking cessation rates.[18, 41]

B.4. Clinical Interventions for Smoking Cessation - Brief clinical interventions, based on tobacco use screening and brief, structured, cessation advice from a provider, have been documented to improve patient cessation rates.[18, 42-44] The current USDHHS clinical practice guideline entitled "Treating Tobacco Use and Dependence" provides a summary of evidence-based recommendations.[18] The current guideline includes a framework for structured, brief clinical interventions using the "5As" of counseling: 1. ASK (Identify and document tobacco use status for every patient at every visit); 2. ADVISE (In a clear, strong, and personalized manner urge every tobacco user to quit); 3. ASSESS (Is the tobacco user willing to make a quit attempt at this time?); 4. ASSIST (Refer to resources, provide pharmacotherapy and counseling); and 5. ARRANGE (Schedule follow-up contact, preferably within the first week after the quit date).

Unfortunately, the 5A's brief clinical intervention is under-utilized by providers and not systematically implemented.[45-49] Due to diffusion of the current clinical practice guideline, rates of the first two "A's" ("Ask and Advise") have increased through system-based interventions (i.e.: as part of routine checkup) .[50] However, implementation of Assist and Arrange is lower.[50, 51]

One important component of "Assisting" patients mentioned in the guideline is to refer patients to community resources such as quitlines.[18] As quitlines and websites have proliferated "Refer," as part of the

Assist agenda, has been increasingly emphasized.[52] Our microsystem emphasizes **Refer** as a critical step in assisting patients to quit.

B.5. Research Encouraging Providers to "Refer" - Referring patients to resources is considered a key component of Assist. Providers do refer some patients to quitlines. In one study, 20% of quitline users were referred by providers.[53] Barriers to "Refer" include provider's lack of: 1) time, 2) awareness of referral resources, 3) prompts, 4) materials to facilitate referrals, and 5) feedback on referral's success.

One method of referral recently studied is the use of "information prescriptions" to refer patients to quitlines or websites for information. In 2004, the National Library of Medicine and the American College of Physicians Foundations initiated a pilot project giving 1,000 participating physicians prescription pads with links to Medline Plus. Forty-two percent of the participating providers in the pilot states -Georgia and Iowa - stated that the "information prescriptions" helped to explain difficult concepts to their patients.

A 2006 study assessed two methods of referral to a quitline: a passive brochure or a more active fax-referral system.[1] The fax-referral was a point-of-care referral where patient phone numbers were faxed at the time of visit to the quitline – and the quitline staff then directly called patients. Overall, 12% (1,838/15,662) of smokers were referred. Of patients given brochures, 19% (249/1,342) called the quitline. Of patients referred through the fax-referral system, 59% (292/496) were contacted successfully by the quitline. This study provides evidence that providers can refer patients to quitlines. Thus, follow-up was much better in the active fax-referral system. Our proposed intervention builds upon this previous research by using an active referral process, and implementing a comprehensive marketing scheme to encourage providers to increase referral of patients.

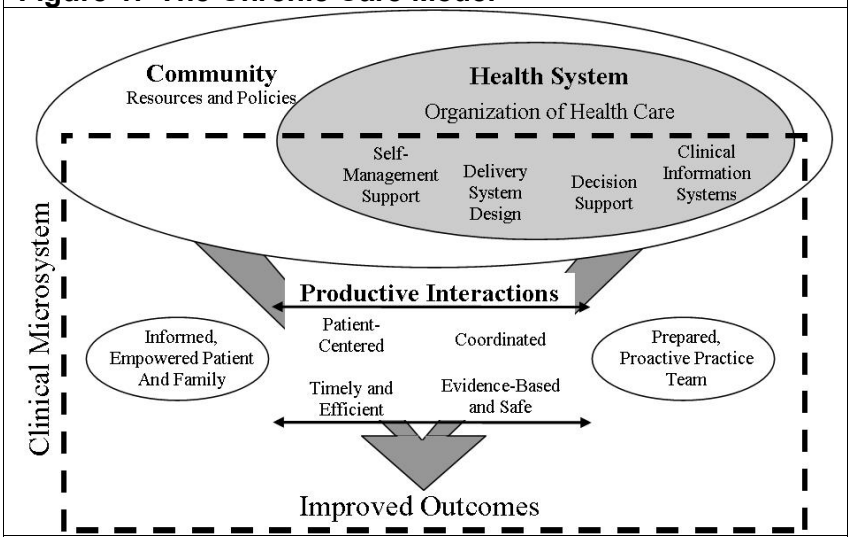
B.6. The Internet and Provider Interventions - There is an emerging consensus that there is not a "one best method" for improving clinical practice for all circumstances, but combination strategies are found to be more effective than single, episodic activities.[54-59] Strategies that actively recruit health care provider participation or individualize show more promise.[54, 55, 60, 61] Although traditional continuing education is not effective in changing practice, newer Internet-delivered interventions that train and motivate providers over time show great potential.[62-64] Our group has pioneered many of these Internet-delivered approaches and has evaluated methods for encouraging participation and engaging providers over time.[62, 65-69]

B.7. Theoretical Framework Underlying the Proposed Clinical Microsystem Intervention -

Clinical Microsystems are not simply healthcare teams; they are complex systems that include four "Ps" – Patients, Providers, Processes, and Patterns. Microsystem interventions are often targeted to enhance effective interactions between participants in the microsystem (patients,and providers) following Wagner's chronic care model (Figure 1).[70] This model has also been applied to improving smoking cessation[71, 72] and to dental practices.

Increasing standard protocols, data collection, and feedback between individuals in the microsystem can maximize patient-centered care.[73-75] Effective interventions help providers and their patients by identifying new ways that patients and providers can work together (Table 1; next page).[74]

Figure 1: The Chronic Care Model



* Adapted from Wagner (1998) Effective Clinical Practice[70]

From the provider and healthcare practice perspective, our goal is to develop an intervention that will be valuable to patients but also acceptable to providers. Thus, in crafting the intervention components, we will use concepts from Roger's Diffusion of Innovations Theory.[76] The evidence supporting this theory is based on extensive evidence from the field of sociology and supports the idea that key attributes of innovations explain

the variance in adoption rates. Specifically, interventions are more likely to be adopted if the have high perceived Relative Advantage, Compatibility, Trialability, Observability, and low Complexity.

Lack of compatability of innovations with practice microsystems is a common source of failure to implement and sustain. Thus, although we will encourage use of all components of the intervention, as with previous health promotion effectiveness studies, the integration of the system may vary from practice to practice. For example, we will ask hygienists to refer patients to the website during their dental visit. There are several potential ways that this could be implemented. First, the practice could have a hygienist enroll the patient through Refer2Quit at patient discharge. Second, hygienists could conduct brief counseling during visit intake (vital signs, etc) and if a patient is interested, use Refer2Quit while awaiting the provider. Part of our current provider website is a practice "Action Plan," an interactive module where providers can complete a plan (i.e.: Who does What?, and When?) for improvement in tobacco processes tailored to the needs of their practice.

Table 1: Translating care management to microsystem innovations

Older care-management view	**Microsystem rework**
Ambulatory care is visit-based	Care is designed to maximize self-management, in and outside of visit
"Demand" for services is patient driven, not in provider's control	Demand is more related to practice habits and efficiency can be increased
Have a designated case manager (Hygienist) to help patients	Develop "planned services" where all roles work towards a specific goal
Capacity to support care exists within the walls of the practice	External resources in the community should be tapped.

*adapted from Wasson (2003) Joint Commission Journal on Quality & Safety[74]

B.8. Significance

As noted, our overall goal is to advance science related to using the Internet in health services delivery and specifically for smoking cessation. Our proposed intervention is the first Internet-delivered intervention to target the dental microsystem for smoking cessation – providing access to hygienists and patients. The integrative potential of the Internet – to link intervention components together – will be co-opted to maximize the potential of active provider referrals to a patient self-management system. Notably, we will use dynamic web programming, and content management systems to minimize the upkeep of the system. Thus, this intervention will have low marginal costs and, if proven successful, can be easily disseminated.

Our proposed intervention is significant because of this disseminatability and its high potential to increase cessation rates. The impact of smoking cessation is great. For example, after a heart attack, the number of smokers needed to quit to save one life is thirteen, assuming a conservative 20% mortality in those continuing to smoke.[77] This number needed to treat estimate is more favorable than that for aspirin (67) or beta-blockers (26) in the treatment of heart attacks.[78, 79]

Also, this study is significant because it may be specifically appealing to younger smokers. Although Internet access is increasing in all demographic groups, including older adults and minorities, Internet access is very high in those less than 30. This is a specific at-risk group as recent data suggest that cigarette companies are targeting youth and younger adults, and rates of smoking among this group are increasing.

Our intervention has several innovations designed to maximize cessation rates. It is designed to create positive feedback loops for both providers and patients resulting in increases in referrals, increases in adherence to cessation advice, and, more generally, increases in all components of the 5A's.

Specific innovations designed to increase cessation include:

1. A Point-of-care Internet referral system (Refer2Quit). – This portal will be the first to allow hygienists to directly enroll patients in an Internet-delivered intervention during the clinical encounter. Active referral programs (such as fax-based referrals) produce greater patient participation compared with more passive brochures. We will take this concept to the next step - integrating the referral and enrollment into a single step. When patients arrive home after agreeing to be enrolled in the system, they will have a welcome email in their inbox from Decide2Quit and receive multiple reminders encouraging participation.

2. Increasing participation using email reminders and cues for providers and patients. Intervention "stickiness" is a computer programmer term that refers to maximizing engagement and repeated use of a

website. Participation is critical to the success of any Internet-delivered intervention. Thus, we have planned a series of marketing emails to increase participation. To overcome "fatigue" with these email reminders, we have found that content must be continuously updated so that each reminder is unique. In this project we will use "push" technology – such as email prompts to encourage providers to use Refer2Quit and encourage participation of enrolled patients in the Decide2Quit patient website.

3. Increasing observability of impact. Because the outcome (smoking cessation) is relatively rare, observing the impact of increased counseling activities is difficult. Therefore, we will overcome an important barrier to provider adoption of smoking counseling – low observability of impact. In Diffusion Theory, observability of impact is critical to adoption of new innovations.[76] Adoption of other preventive services, such as breast cancer screening, is quite high. However, the outcome, early detection and prevention of cancer mortality, is again rare. Although there are many differences between breast cancer screening and smoking counseling, one obvious difference is the presence of a *Proximal Outcome* in cancer screening – the mammography report. These mammography reports – mostly negative screenings – produce a feedback loop and allow for an "observable" impact. In our proposed intervention, we plan to *simulate* a mammography report – a Proximal Outcome – by creating "Provider Reports" within Refer2Quit (see Section D2 below) that detail 1) the numbers of patients referred, and 2) the number of referred patients actually participating. These rates will be compared with other participating providers. We hypothesize that this innovation will increase subsequent referrals by increasing observability of impact, and again, ultimately result in higher cessation rates.

Over the past seven years our multi-disciplinary team has consistently worked to develop direct-to-patient computer interventions and Internet-delivered interventions designed to provider's delivery of preventive services.[10, 21, 62, 69, 80-87] The DentalTobaccoControl.Net study (Houston, PI) has provided considerable preliminary data for this study. In addition to tobacco-related interventions, Drs. Houston and Ford have also conducted studies of the risks of tobacco[88-91] and tobacco control practices of providers.[45] We will use our expertise in usability assessment, web-use tracking, patient-reported outcomes, and health services research to conduct a detailed analysis of the impact of the system and how the system mediated the outcomes observed. This analysis design will significantly advance the science of Internet-delivered interventions and smoking cessation.

C. PREVIOUS WORK AND PRELIMINARY DATA

Our previous work documents a history of success in understanding Internet use and its social impacts, developing and disseminating patient and practice-level change interventions. Within this section, we provide two examples of successes from prior provider studies conducted by our group at the UAB Center for Outcomes and Effectiveness Research and Education that have been directly leveraged for the current study. In our preliminary data, we also highlight a *patient-level* intervention relevant to the current proposal.

1. Success in Provider Recruitment and Retention to Internet-delivered Interventions

Drs. Houston and Allison have developed a funded program in Internet-delivered interventions. Table 2 highlights our success in recruiting providers into these interventions. Dr. Allison is the director of the UAB Division of Continuing Medical Education. In developing and implementing these interventions, we work closely with the Internet Programming Lab within the Division. In conducting these prior studies, we have learned many lessons relevant to the current proposal including the fact that email reminders and updates can enhance participation and appropriate marketing and incentives are critical. [69]

Table 2: Recruitment success for recent Internet-based interventions evaluated by UAB Center for Outcomes and Effectiveness Research

Online Quality Improvement Intervention Title and Grant	Setting and Sample (Network Providers)	Ambulatory Practices (N)
Chlamydia Screening[62, 66, 68] (AHRQ U18HSO11124-03)	Aetna Primary Care Providers	191
MI-Plus (Myocardial Infarction Plus Comorbidities)[92, 93] (NHLBI R01HL70786-02)	Rural Physicians in Alabama	210
DentalTobaccoControl.Net [94] (NIDA 5R01DA017971)	Dentists and Hygienists	190
Rural Diabetes Online Care (NIDDK R18 DK065001)	Rural physicians	168 (still recruiting)

DentalTobaccoControl.Net was conducted as a Dental PBRN study and recruited from the Dental PBRN.

2. Measuring Participation in Internet-delivered Provider Interventions

In prior projects we have developed new measures of provider engagement in Internet-delivered interventions (Table 3). In interventions with multiple components available longitudinally, measuring participation is complex and requires careful consideration. We have conceptualized participation in terms of volume of participation (e.g. number of pages), frequency, variety of participation (number of different functions used), and duration. These measures will again be used to evaluate the process of provider engagement in our proposed intervention. In addition, these aspects of participation can also be applied to patient participation and similar patient-level research has been published.[95]

Table 3: Participation Measures in MI-Plus Intervention Group

	NHLBI MI-Plus		VA MI-Plus
	Private Practice Physicians (n = 108)	VA Physicians (n = 125)	VA Physician Assistants (n = 68)
Participation Measures	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
A. Volume			
Number of Page Views Per Visit	16.4 (8.8)	15.6 (8.2)	15.6 (9.6)
B. Frequency			
Total number of Visits	3.8 (3.2)	6.7 (5.5)	5.9 (5.4)
Number of Visits Per Month	0.29 (0.22)	0.62 (0.52)	0.85 (1.5)
C. Variety			
Number of Components	2.3 (1.3)	2.8 (1.2)	2.7 (1.3)
Mean Percent of Cases completed	28%(27)	44% (32%)	40% (33%)
D. Duration			
Months from First to Last logon	7.9 (4.1)	7.0 (5.4)	6.2 (5.5)

PRELIMINARY DATA

In this section, we provide some preliminary data from an ongoing provider intervention that emphasizes the two principles above and other successes. This is followed by evidence from Dr. Ford's previous "Smoking Coach" patient intervention study.

Dental Tobacco Control.net (DTC.Net): Improving Practice (Houston, PI)

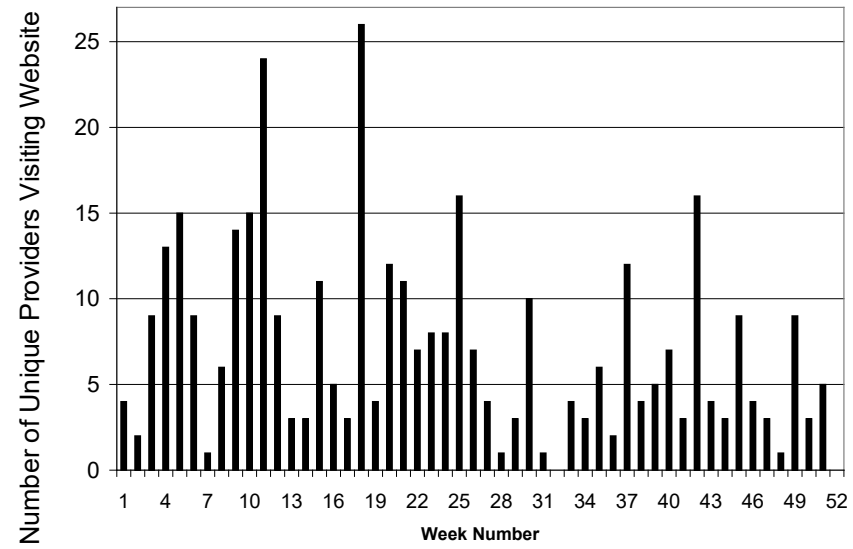
This NIDA-funded randomized trial (R01-DA-017971) is in its fourth year. We have developed an interactive Internet-delivered intervention designed to encourage dental providers to increase tobacco control activities in their practices. This study is directly relevant to the current proposal in that 1) we have developed a series of interactive provider education modules and a toolbox of useful materials that can be easily adapted as supplementary provider education for our proposed intervention (see Appendix A for screenshots), 2) we have demonstrated success in recruiting 190 practices to participate in the project, 3) we have demonstrated the ability to recruit patients at the time of their office visit in these practices, and 4) in preliminary analysis, we have demonstrated that the providers in the provider intervention have increased quit smoking advice rates.

Three hundred practices across four southern states, North Carolina, Georgia, Alabama and Florida, completed an initial interest survey. To blind participants to the specific tobacco control target, the intervention was described as an "Online Study Club for Oral Cancer Prevention." Interested practices were asked to complete a run-in phase where patient & practice data were collected and returned.

Success in recruiting practices - Of the 300 initial practices, 208 (69%) returned baseline data, and 95 intervention, 95 control were finally randomized. In DTC.Net, the 95 intervention practices were encouraged to logon and participate in the intervention. To date, 128 dentists and hygienists have logged onto the website. The total number of visits to the website since it was launched in June 2005 is 398 (28 visits per month).

Figure 2 displays the number of visits over time, with spikes that coincide with email marketing of new website content. This demonstrates our success in developing website "stickiness" or retention (See Appendix B).

Figure 2: Provider Visits to DTC.Net Intervention by Week



Recruiting patients to assess providers
We developed "patient exit cards" – brief surveys completed by patients at the end of their appointment – using principles of ecological momentary assessment.[96-98] The exit cards were designed to be completed in one to two minutes. The patient exit cards serve as our main outcome: a patient-reported performance measure of the provider's delivery of tobacco cessation advice. Of the 19,000 exit cards distributed by our 190 practices, 15,575 (82%) were returned with usable data at baseline. From these data, patients agreeing to a follow-up were part of a brief validity assessment at six of the practices. We contacted 161 patients by phone (1% sample) and found that patient's age, gender, and smoking status agreed in 98%.

Preliminary Analysis of Outcomes - To date we have entered follow-up data on 143 practices (76%), with a patient response rate similar to that at baseline (82% (9,498/11,600)).

The intervention has been successful at increasing advice (Table 4). At eight-months of follow-up, intervention practices increased cessation advice by 11%. When adjusting for patient age, gender, frequency of smoking, and clustering of patients within practices using generalized estimating equations, intervention patients were again more likely to receive quit tobacco advice (Adjusted Odds Ratio 1.6 (95% CI 1.3-1.9)). Using a group by time interaction term, we found that intervention practices significantly improved compared with control practices for ADVISE (p = 0.042).

Table 4: SMOKING CESSATION ADVICE

	Pre-Intervention	Post-Intervention
Intervention	**44% (710/1,611)**	**55% (748/1,361)**
Control	**42% (488/1,169)**	**45% (545/1,210)**

The practice-level intraclass correlation coefficient for ADVISE was 0.15, estimated using one-way ANOVA. This was very similar to an ICC reported for tobacco use screening by Eccles.[99] In DTC.Net, we have also estimated six-month patient tobacco-cessation rates using a telephone-based follow-up survey that can be used to estimate the intra-class correlation coefficient for tobacco–cessation rates within dental practices. One-way ANOVA analysis of this survey data estimated an ICC of 0.017 (95% CI 0.00-0.10) indicating that only 1.7% of the variance in cessation was accounted for by the dental practices.

Smoking Coach: An Internet–tailored Intervention (Ford, PI; Houston, co-PI)

In this NCI-funded R21 proposal, we designed and evaluated the "Smoking Coach" - an Internet-delivered, tailored, public health intervention for smoking cessation that not only included self-help strategies, but also encouraged seeking social support (Family Info) and help from health care providers (Doctor Info) (See Appendix C for screenshots). In this project, we began with a formative evaluation. Critical themes from focus groups included: make funding transparent (not affiliated with tobacco companies), provide at no cost to users, and improve the site name. The participants unanimously did not like the name "Smoking Coach" (too over-bearing). We then developed the site based on this formative research and using constructs from multiple behavioral theories including health belief model (HBM), [100] social cognitive theory (SCT),[101] and the transtheoretical model (TM). [102] Reviewers can access the website at www.free2quit.cme.uab.edu and login using the name: "reviewer." Although we cannot duplicate all the website content within the text of this

proposal, specific examples of how we used behavioral theory include: 1) using a personal story of a smoker for vicarious learning (SCT); 2) providing "How close am I to Quitting?" (Decisional Balance –TM) and "What do I need to overcome?" (Temptations – TM) calculators – interactive assessments with tailored feedback; 3) Risks to My Body (Perceived Susceptibility – HBM); and 4) supporting a smoke-free home around the time of quitting (Environment/Reciprocal Determinism – SCT). The components of the website work together to motivate those not quite ready to quit and to provide targeted strategies for those preparing to quit."

After initial development, two groups of current smokers were recruited using targeted advertisements on Google (May 2004 and February 2005). Smokers logged onto the website, consented to participate, and completed an introductory questionnaire that resulted in dynamic tailoring of the website. In Phase 1, we assessed usage patterns of 126 smokers. We noted that few participants used the family and doctor info (Table 5). After reviewing these statistics, we added an introductory page to the website with additional content encouraging use of all components. The introductory paragraph included actual data from previous users, encouraged users to use all components of the website, and was signed by the two physicians associated with the study.

Outcomes Assessment - In Phase 2, 212 smokers were randomized to a control website that was linked to other smoking information online (www.smokefree.gov) or to the intervention. Phase 2 trial participants (N = 212) were mostly female (68%), white (80%), and relatively young (63% less than 45). Time spent on the website and use of the family and doctor modules increased, compared with Phase 1 (Table 5).

Table 5: Use of the "Coach" Website Before and After Introductory Letter Added

	Phase 1 (n = 126)	**Phase 2** (n = 105)
	%	**%**
Used Specific Module		
Used Self-Help Strategies	58	69
Used Family Info Module*	29	50
Used Talking to your Doctor Module*	33	56
Time Spent on Website (Minutes) *		
Less than Three Minutes	31	24
Three to Ten Minutes	30	13
Over Ten to Twenty-five Minutes	15	31
Over Twenty-five Minutes	23	32
* $p < 0.001$ (comparing Phase 1 and Phase 2)		

Phase 2 smokers were then re-contacted by telephone in one month to assess smoking status. Sixty-four participants completed the one month follow-up assessment, and we found no differences in age, gender, education, or previous quit attempts among those with follow-up and those lost. In intent-to-treat analysis, 9% (9/105) of intervention participants quit smoking compared with 3% (3/107) of the control group ($p = 0.069$).[103] In an analysis based only on those who completed the follow-up assessment (n=64), a higher percentage of the intervention group reporting quitting (9/31=29%) compared to the control group (3/33=9%, Fisher's Exact $p = 0.055$). After adjustment for age, gender, and income, intervention users were still more likely to quit (Odds Ratio = 4.3 (95% CI 1.0 – 20.5)) compared with control. Because users varied in their intensity of using the website, we also looked for a *dose-response* effect. Compared with the control, low-level users (lowest quartile of use) had a small benefit (OR 2.5 (95% CI 0.2-30)), and higher level users were higher (4.44 (CI 1.04-18), p for trend = 0.04).

Among those who completed follow-up, 100% of the intervention group spoke with their family about quitting compared to 87% of the control group ($p = 0.045$), but no significant difference was seen in talking to a doctor (38% intervention versus 42% control, $p = 0.7$).[104] Overall, 36% of the 64 users who participated in follow-up used nicotine replacement and 10% used bupropion, with no differences by experimental group (intervention versus control $p > 0.5$ for both). Thus, although we demonstrated some modest success, the website was limited in that we were not successful in increasing treatment seeking among these patients. The manuscript for this study is currently under review.

These ***two studies*** highlight our expertise and prior success in demonstrating acceptability and feasibility of Internet-delivered smoking cessation interventions. They also identify the real boundaries to these prior experiments. **The current proposal does not represent a marginal improvement of this prior work, but a paradigm shift focusing on the clinical microsystem and using the automation and full integrative power of the Internet.** Our intervention can be defined as a complex intervention to improve health.[105] Following the framework for evaluation of complex interventions[105], this study is built on the previous exploratory trials, and designed as a definitive randomized trial in the real-world of clinical microsystems.

D. RESEARCH METHODS

D1. Overview, Task List, and Timeline

Our task list (Table 6) is organized into 6 categories: 1) intervention refinement and programming; 2) usability testing; 3) recruitment and retention of dental practices; 4) intervention maintenance; 5) data collection; and 6) analyses. As discussed is Section A, we evaluate the process of care.

The combination of the patient and hygienist internet interventions is entitled HI-QUIT (hygienists' internet quality improvement in tobacco cessation). HI-QUIT is conceptualized in two components: Refer2Quit and Decide2Quit (See Figures 4 and 5). Major innovations are the microsystem integration of the patient referral portal (Refer2Quit) and the hygienist education system. We will conduct a randomized controlled trial (RCT) to ascertain the efficacy of this multi-modal intervention in improving smoking cessation processes of care and patient outcomes. In relation to the smoking cessation impact of HI-QUIT, this trial is defined as a cessation-induction study – a test of treatment to prompt cessation among all smokers, including those who are not currently trying to quit.[106]

Studies of complex micosystem interventions are inherently complex and require detailed evaluations. In addition to our quantitative hypothesis-driven analysis, we will also conduct a secondary process analysis case-comparison of intervention practices with varying rates of adoption of HI-QUIT. The proposed intervention is designed to have a layered effect – changing hygienist performance (including advising smokers to quit and referring them to a self-management website) and also patient behavior (including going to use the website and ultimately quitting smoking). Thus, our analyses are designed to understand the intervention from each of these "layers" – from the patient and hygienist perspective.

#	**Table 6:** Task List	Study Months	**1.**Intervention Refinement	**2.**Usability Testing	**3.**Recruitment - Retention	**4.**Intervention Maintenance	**5.**Data Collection	**6.**Analyses
1	Finalize recruitment plan and website plan	1-3	X	X				
2	Program Refer2Quit hygienist website	2-7	X					
3	Program Decide2Quit intervention patient website	2-7	X					
4	Conduct final usability testing by patients and hygienists	6-7		X				
5	Finalize website based on usability tests	7	X					
6	Develop and finalize investigators web "admin" portal	7	X	X	X			
7	**Activate HI-QUIT**	**7**				X		
8	Send mass mailing to identify interested providers	6-10			X			
9	**Enroll/randomize providers (Intervention Time 0 (I_0))**	6-10			X	X		
10	Collect baseline practice data online	7-23					X	
11	Complete practice run-in phase data (exit cards)	7-23					X	
12	Send repeated emails to dentist/hygienist for retention	7-23			X		X	X
13	Collect usage data from websites	7-23	X		X		X	X
14	**Have practice enroll patients through Refer2Quit**	7-23			X	X		
15	Send provider reports of patient enrollment	7-23				X	X	
16	Measure **Refer**ral Rates at baseline, 6 and 12 months after practice enrollment using patient exit card surveys (first cards collected in run-in phase)	7-12					X	**H1**
17	Measure number of referrals using Refer2Quit and Information prescriptions	7-23						**H1**
18	Measure rates of patients who **GO** to Decide2Quit	7-23					X	**H2**
19	Measure patient **QUIT** rates, quit attempts, and readiness to quit at 6 months (telephone follow-up)	10-30						**H3**
20	Validate 6-month quit with Cotinine*	10-30					X	**H3**
21	Test Hypotheses, prepare manuscripts	10-36						X

*Mailed salivary cotinine (Salimetrics); H1 = Hypothesis1; H2 = Hypothesis 2; H3 = Hypothesis 3 (See D5 for details of Measures)

To further clarify the flow of the development, intervention, and evaluation, Figure 3 below summarizes the planned timeline for accomplishing key tasks.

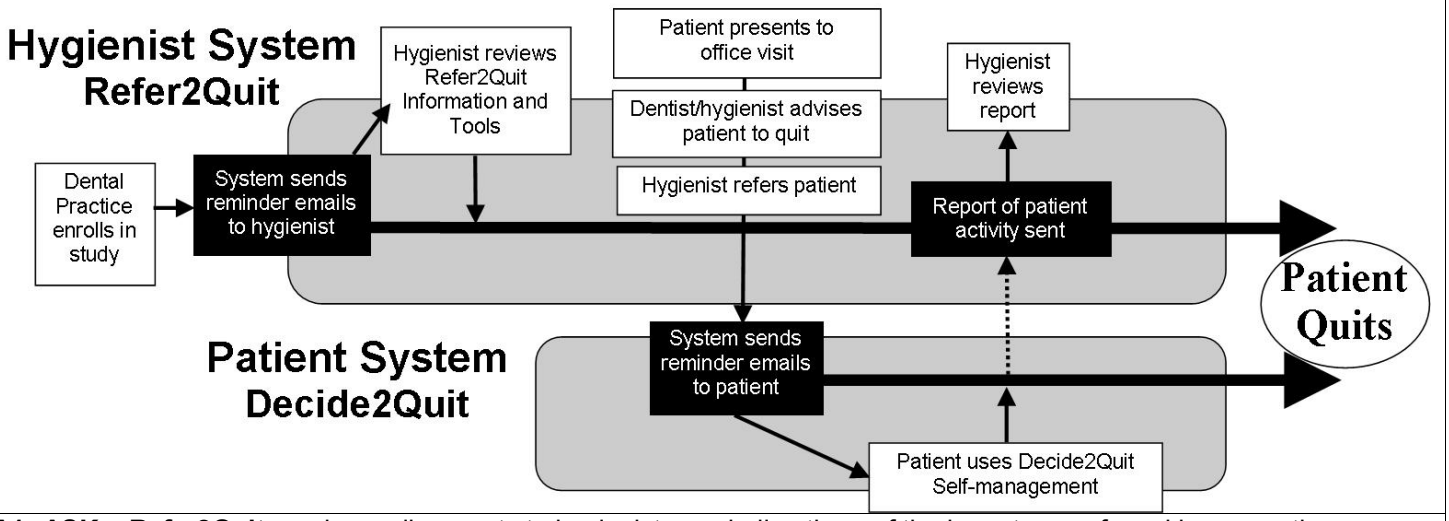
Figure 3: Timeline for Intervention Development, Implementation, and Evaluation

	Development	Intervention and Evaluation																											
	Year 1												Year 2												Year 3					
Study Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	26	28	30	32	34	36
Formative research																													
Develop Content																													
Program Website																													
Test Usability																													
Activate HI-QUIT							X																						
Enroll Practices																													
HI-QUIT Available*																													
Patient Exit Cards **(H1)** †																													
Web Activity (patient/provider) **(H2)**																													
Patient Telephone Follow-up **(H3)**‡																													
End of Project Surveys and Qualitative Interviews																													
Hypothesis Testing, Manuscripts																													

* Available for 21months for each practice, with monthly updates
† Patients recruited in 3 cohorts at Intervention Time 0 (I_0), I_0 + 6 months, I_0 + 12 months
‡ Telephone Follow-up: Tobacco users from website – cessation assessed at 6 months (with cotinine validation)

Although HI-QUIT is heavily focused on enhancing Refer, the intervention has the potential for impact across the 5As. To further clarify, Figure 4 depicts flow of a single example practice and patient over time.

Figure 4: How **HI-QUIT** will improve processes of care (5As) and increase smoking cessation – use of the clinical microsystem intervention over time by **One** example practice and **One** patient.



A1: ASK – **Refer2Quit** sends email prompts to hygienists reminding them of the importance of smoking cessation, hygienist downloads printable chart stickers, etc. to increase systematic screening.

A2: ADVISE – **Refer2Quit** materials provide additional knowledge to hygienist on strong advice, dentist/hygienist advises patient.

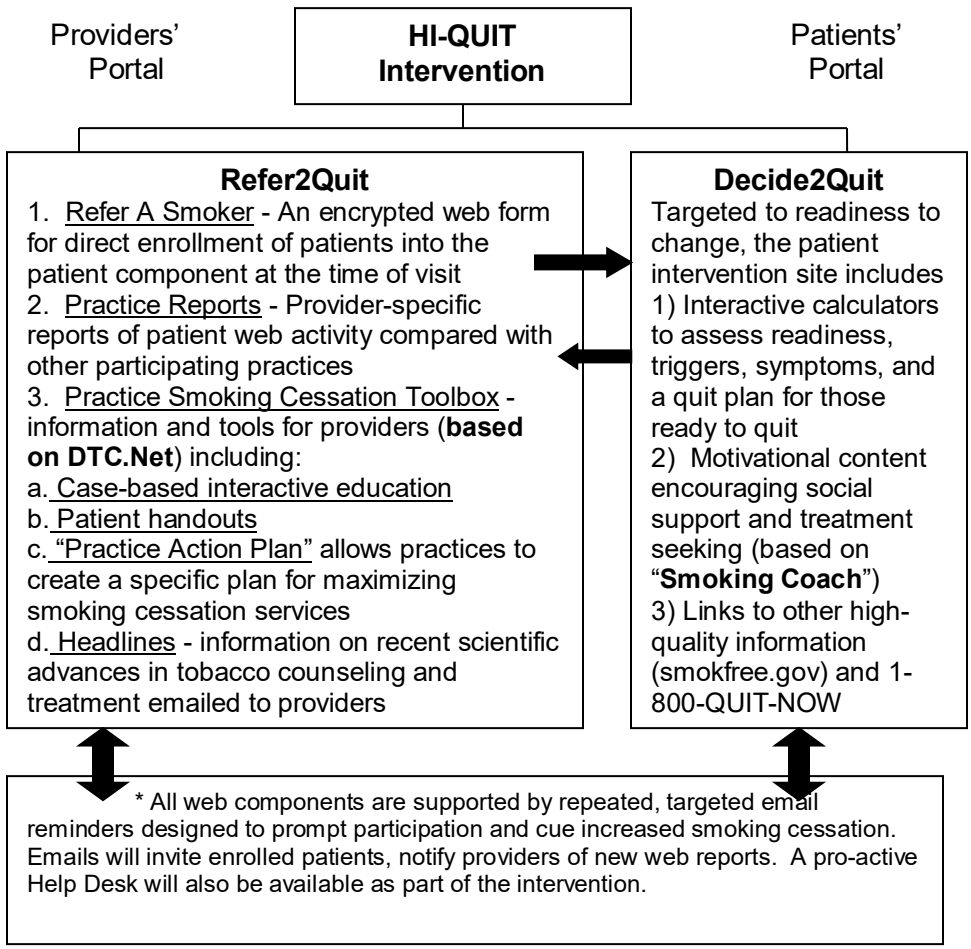
A3: ASSESS – Hygienist explains content of Decide2Quit and assesses willingness of patient to use system, and to Quit.

A4: ASSIST – Patient agrees to be recruited and hygienist uses **Refer2Quit** to directly refer. **Decide2Quit** sends email reminders to the patient. Patient uses system and talks to family because of the motivational messages.

D2. The Intervention – HI-QUIT

The intervention for HI-QUIT will be accessed through two portals: Refer2Quit designed for hygienists and Decide2Quit designed for patients. The components of HI-QUIT are described in Figure 5 below (supporting detail is provided in Appendices). We will work with the Internet Programming Lab in the UAB Division of Continuing Medical Education to program these components. This lab is responsible for the programming for Dr. Houston and Allison's prior web-delivered Interventions including DTC.Net. The Lab has also programmed the "Smoking Coach" patient website. The linking of these components is the major innovation of this study. The goal is to close the loop within the clinical micrsosystem between the patient, provider and processes. By developing components that have 1) active prompts to continued use (email reminders) and 2) are simple to use and thus easily integrated with other processes of care, we hypothesize that the use of both the patient and provider components will be multiplied by integration.

Figure 5: Major Components* of HI-QUIT



1. Hygienists' Portal - Refer2Quit: The core of the Refer2Quit hygienist portal is a Secure Sockets Layer (SSL) encrypted web form where providers can enter patient's emails into the system if they agree to be referred. Although we anticipate that hygienists will drive this intervention, dentists will also be able to access the intervention website. The form will be designed to be easily completed by hygienists or front office staff as the patient is discharged from the visit. The Refer2Quit component is targeted to providers. To maximize the use of Refer2Quit, we will supplement the component with supportive sub-modules designed to prompt providers to use the system and maximize their smoking cessation activities.

The Practice Toolbox is patterned after a series of successful Internet-delivered provider interventions including Dr. Allison's previous Chlamydia Screening intervention[62], and more so, the current DTC.Net intervention (see Appendix A). Reviewers can access this current website at www.oralcancerprevention.org. To login, you will be asked to enter a first and last name, use firstname = nih and lastname = reviewer.

2. Patients' Portal - Decide2Quit: The Decide2Quit patient intervention website will include previous self-management content developed and evaluated for "Smoking Coach" (current HI-QUIT control website) and will also undergo considerable augmentation to be integrated into the microsystem. The major augmentation to transform the "Smoking Coach" into Decide2Quit is the database linkages with Refer2Quit (provider portal), the automated email messaging, the administrative portal for content management. We will also add new content including the latest pharmacotherapies, new "How to Talk to Your Provider" content, and additional risk

calculators. We envision Decide2Quit as a portal to smoking cessation information. Thus, we will add links to other high-quality web-based information on smoking cessation such as **smokefree.gov**, and will provide links to community resources, heavily emphasizing the additional benefit of quitlines (1-800-Quit-Now).

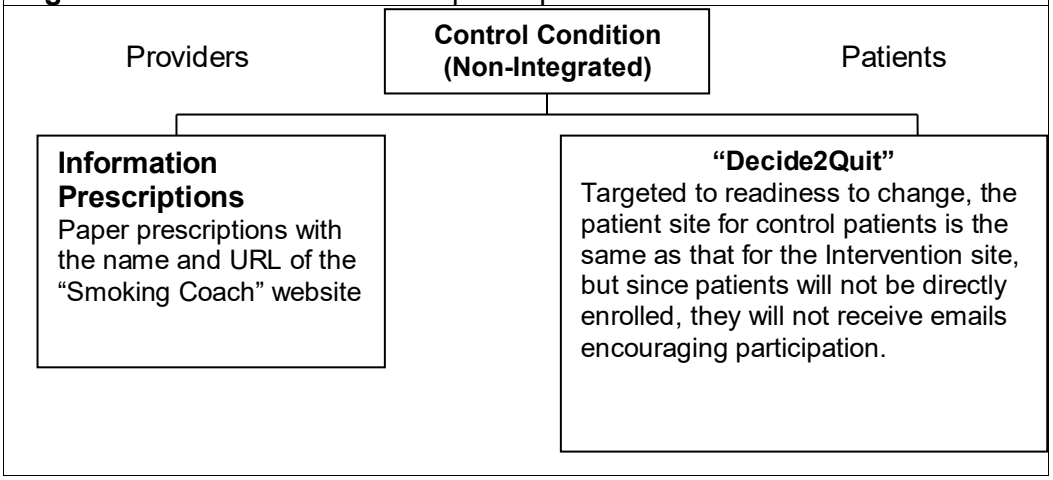
Help Desk: In addition to the technical aspects of the system, our recruitment and retention staff will serve as a "help desk." The help desk with respond to provider and patient questions, but will also be **pro-active**. Interventions that are easier to integrate into the processes of the clinical microsystem are more likely to be adopted. Top-Down, one-size-fits-all interventions often are not well integrated. We plan to be flexible and provide support to intervention microsystems in their implementation of HI-QUIT. Thus, we will work with offices to understand how each practice can best implement active referrals.

D3. The CONTROL – information prescriptions to refer to patients

1. Hygienist Control – Information Prescriptions

In planning this proposal, we considered several potential controls as suggested by the framework for evaluating complex interventions.[105] In DTC.Net, we are currently using a wait-list control group. Control providers will have access to the full intervention after data collection is complete. Thus, control hygienists are delivering "usual care." However, for this intervention, we felt that a wait-list control ignores other recent advances in provider referrals to self-management in smoking cessation (i.e.: information prescriptions).

Figure 6: Control - Information prescriptions to refer to control website



Also, although we have not had differential attrition in the wait-list control, compared with intervention, in DTC.Net, anecdotally, control providers have expressed concerns about having "nothing new" to provide to patients. We are concerned about the threat of long-term wait-listing to overall retention in the control group. Specifically, we want to test the uniqueness of the integration clinical microsystem intervention. After consideration, we have chosen a more active, symmetric control reflecting recent offline research into provider referrals. Thus, our control group provides parallel interventions – for providers and then patients – that are *not* integrated.

We have chosen an "information prescription" control. Providers in the control group will be provided preprinted pads of "information prescriptions" with their office information, motivational messages for patients, a space for the provider to sign, and the control website address.

The information prescription pads also have an important role in our analysis. The pads will have numbered leave-behind receipts used to tally the number of referrals issued. These pads will be collected from the control practices to obtain an accurate account of the number of patients referred. The control group will **not** have access to 1) HI-QUIT Help Desk, 2) Refer2Quit portal at the point of care; 2) Feedback Reports of patient activity; 4) automated email reminders for patients and providers; 5) HI-QUIT content updates and linking functions.

2. Patient Control

With the paper information prescriptions, control hygienists will refer patients to Decide2Quit website. Screen shots are included in Appendix C. The webserver will tally the number who "GO" to the website. Again, control group patients will **not** be referred electronically and they will **not** have access to: 1) HI-QUIT Help Desk; 2) automated email reminders for patients; 3) HI-QUIT linking functions.

D4. Maximizing the Intervention - Programming, and Usability Testing

As noted in our task list, the majority of the effort in this project will be devoted to the randomized trial, with recruitment, retention, data collection, and analyses being the major tasks. We have begun to develop conceptual mock-ups of the Refer2Quit portal. *The goal of the referral portal is to be used within the flow of dental care, so the portal must be highly accessible and require minimal data entry. Currently, we plan to only ask hygienists to log into the system and enter the patients email address; that is the only data entry and should take less than one minute.* However, implementing the Internet-delivered intervention will require some refinement of both the content and programming. As noted, content upgrades are critical to engagement and we plan to continuously improve both the patient and provider sites as the study progresses using the following phases:

1. Hardware and software for programming. The technological foundation of the intervention will be updated as the Internet evolves. Under the direction of Dr. Houston, the programming will be developed and maintained by the UAB Continuing Medical Education (UAB CME) web development lab. The UAB CME web lab has four graduate level computer science students at all times and two half-time graphic designers. Currently, our study team uses Windows NT server; Active Server Pages (ASP) server application; Ultra Dev 4; Adobe Photoshop; and Oracle databases for data collection. We will alpha-test the program using multiple web browsers and various bandwidths to avoid cross-platform issues in accessing the intervention. The encryption of content is critical and needs of HIPAA compliance will be carefully tested.

2. Usability Assessment. Volunteers recruited from dentist practices in the Birmingham area will perform beta-testing of the potential human-computer interface to confirm that the system is understandable and easily used. To avoid contamination, we will not recruit these pilot testers into the main RCT. We will beta-test the website with a series of individual patient and hygienist interviews while reviewing the modules. We will use "Think Aloud" protocols detailed by Kushniruk [107-109] as follows: while the participants are reviewing the content, the user will be asked to vocalize thoughts, feelings, and opinions while interacting with the program. Think Aloud allows you to understand how the user approaches the interface and what considerations the user keeps in mind when using the interface. Participants will complete a rating instrument including questions addressing the acceptability, accuracy, ease of use, and satisfaction with the program. We will use these data to refine the program.

D5. Recruitment and Randomization Phase 1: Dental Practices

To conduct the RCT, we will recruit dental practices. We plan to recruit 80 general dentistry practices (40 total practices per arm) from the *Dental PBRN* to participate using recruitment methods developed in DTC.Net and our other Internet-delivered trials (see Table 2) each of which have nearly 200 practices participating.

Inclusion Criteria: Our primary inclusion criteria are community-based practices with Internet access available in the office seeing an average of five or more smokers in a week. Because access to the Internet by health providers continues to increase, when this study is conducted, access to broadband Internet in dentist offices will be approaching universality. Based on our prior experience, enrollment of practices in these studies is complex and somewhat easier if the number of providers in the practice is lower. *We will exclude practices that have ongoing computer-based smoking cessation programs for patients.*

Recruitment and consent to cluster-randomized trials is often layered, especially if the intervention is delivered at several layers. Thus, based on prior methods, we have designed a stepped recruitment and consent procedure. **Provider Recruitment** will follow 5 steps:

1. Initial interest Survey	→	**2. Initial Practice consent**	→	**3. Provider Agreement to be Contacted**	→	**4. Run-in Data Collection**	→	**5. Provider consent and randomization**

In our current Dental PBRN study, DTC.Net, we recruited 190 practices from four states. In the NHLBI-funded MI-Plus study, we recruited 210 providers from Alabama and Mississippi. Using a combination of mass mailings with stepped follow-up and a run-in phase, we have been successful in recruiting and retaining large number of provider practices (follow-up currently 76% in DTC.Net). We do not envision excessive difficulties in recruiting and retaining these Internet-ready dental practices.

1. Initial Interest Survey - For HI-QUIT, we will send an initial interest letter that will identify the study as access to a provider information portal for smoking cessation and a free referral resource for patients. Dental providers will be informed that evaluation includes monitoring their use of the website, patient's use of website, and agreement for staff to distribute exit card surveys to patients as they leave their visit. The letter will be accompanied by a form for practices to express interest and initial eligibility.

2. Initial Practice Consent - Interested practices will be sent a more-detailed package with materials explaining the study, and an initial consent. Because the clinical microsystem is the ultimate target of HI-QUIT, consent for this project is complex. The intervention is designed to be integrated into the workflow of practice, and we hope dentists and hygienists will participate along with their patients. We will ask the provider who completed the interest card to discuss the study with all providers in the practice to reach consensus. An initial consent is signed by the interest card provider.

3) Provider Agreement to be Contacted – After the initial consent is signed, the initial consent provider will be asked to assign a contact person (staff member) at the practice. The staff member will be asked to use the data collection form to collect names and emails of all providers (hygienists, dental assistants, dentists) who agree to be contacted with information about the website. We will not limit the number of providers who are eligible to participate, but expect that not all providers in all practices will be actively involved.

4) Run-in Data Collection - Once the initial consent and agreement to be contacted forms are returned, interested practices are asked to complete a run-in phase where baseline patient and practice data are collected and returned. Our recruitment coordinators will call the contact person at the practice who is responsible for data collection to answer any questions.

5) Individual Provider Consent - After the run-in phase is completed, providers will begin to access the website, and begin to refer patients to the intervention. We will broadcast emails to all those who agree to be contacted. Each of these marketing emails will include instructions for opting out. Before accessing the content, providers will read a consent and will have to actively agree by completing check-boxes to 1) allow us to track their activity on the website, 2) allow us to continue to email them with updates, 3) refer patients to the patient intervention. Randomization is described below. Patient recruitment is in Section D6.

Randomization - We will use an online randomization algorithm developed by Dr. Allison.[62] Once providers review the recruitment and consent information online, those that agree to participate will proceed to update their contact information and then click on a link [I AGREE TO PARTICIPATE]. Once they click on this link, a program on the server will randomize their practice to the control or intervention arms in blocks of six to assure roughly equal numbers. Thus, the first provider who logs on will determine the randomization status for all providers and staff within the entire practice. This ensures that the level of randomization is the clinical microsystem (dental practice).

Anticipating attrition – Although data are not complete for follow-up in DTC.Net, we currently have data from 143 of 190 randomized practices (76%) and anticipate a final participation rate at follow-up of 80%. Using these numbers, we plan to recruit 100 practices to the "interested" pool, to obtain 80 practices to be randomized. For power calculations, we have estimated that a range from 30 to 40 practices per arm will complete follow-up data collection. If the practices withdraw from the study prematurely, we will retain their data as for an "intention to treat" analysis. We will compare practices that withdraw with those that do not.

6. Recruitment Phase 2: Patient Recruitment for Outcomes Assessment - Patients will be recruited to participate in the study in two ways, as determined by our analysis plan. First, patients will be recruited to assess providers using brief exit card surveys completed as they are discharged from their clinic appointment. Second, patients will be enrolled as they login to the patient website.

Patient Recruitment Part 1: (Exit Card Surveys) - For *Hypothesis 1* (Processes of Care – including the proportion of patients who are referred to self-management resources will be greater in HI-QUIT practices compared with control practices) we need a measure of provider performance. Provider reports of smoking counseling over-estimate and chart abstraction under-estimates performance.[110-113] Patient reports of provider behavior have also been used.[111-117] The Health Plan Employer Data and Information Set (HEDIS) performance measurement has adopted patient-report of provider tobacco cessation advice using phone

interviews.[118] However, these delayed reports of provider performance may suffer from recall bias due to time elapsed from the patient visit to the time of follow-up assessment. Immediate exit interviews for smoking cessation have been found to correlate with audiotapes.[113]

In DTC.Net, we have developed and evaluated patient-reported provider performance measures that are completed and collected and the time of the visit on "Exit Cards." These patient Exit Cards – brief surveys completed by patients at the end of their appointment – were developed using principles of ecological momentary assessment (EMA). EMA is a method used in health behavior and more recently in health services research to overcome limitations of traditional self-report assessments.[96, 98, 119]

Practices will be provided a set of 100 patient exit cards at each assessment interval. As a baseline, practices will be provided 50 cards in the run-in phase. At each practice, exit cards will be distributed by office staff to consecutive patients (19 and over). Eligible patients will be adults who have completed their visit. In a pilot study for DTC.Net, patients were asked to record the time required to complete the pilot survey. The average time to complete was two minutes and ranged from one to three. The exit cards are administered while the patient is awaiting follow-up instructions and completing payment. A brief statement is included explaining the study, indicating that participation is voluntary, and that their responses will not influence the care that they receive. Importantly, participation is anonymous and no patient identifiers will be included on the Exit Cards. This recruitment is solely to assess provider performance and no patient follow-up is needed.

Each patient is provided a pen to help complete the survey and as a gift. Patients place completed exit cards in an accompanying envelope and then deposit in a sealed collection box. If a patient is not interested in completing the exit card, they write "declined" and return the card to the box. When all exit cards are distributed, the practice returns the collection box to our coordinating center. For each set of 100 exit cards, we estimate 20 to 25 tobacco users will be identified.

The exit card will contain brief questions used to assess whether the patient was a tobacco user and whether the provider **Refer**red the patient. We will also assess age, gender, other components of the 5A's, and stage of change: a part of the Transtheoretical Model of behavior change.[120, 121]

We will provide a small reimbursement for data collection (visa debit cards) to the office staff as remuneration for their assistance in distributing exit cards (see budget justification). As discussed in our preliminary data above, from 19,000 exit cards distributed for DTC.Net the response rate has been over 85%.

We had considered collecting exit cards on only smokers, but 1) prior experience with these cards indicates that any instructions other than simply consecutive patients dramatically reduces practices' ability to complete the data collection and 2) in addition to assessing Refer, we also want to assess rates of Ask (screening for smoking by staff) and Advise (staff advising tobacco users to quit). For the assessment of Ask, we need both smokers and non-smokers.

Patient Recruitment Part 2: Website - We will recruit through the website in two layers. First, as they enter the website, patients will be informed that we will monitor use of the website and that reports of total number of uses will be returned to their providers. All patients will be asked to identify their provider (using a unique ID) so that we can provide feedback reports to providers and have data for hypothesis 2. Second, patients will be asked to agree to a six-month follow-up telephone survey similar to the patient exit cards (hypothesis 3). Those who agree will be asked to provide contact information including a phone number and name, again through a SSL online form. Because we want to have as many patients participate in Decide2Quit as possible, we will not require agreement to follow-up as a prerequisite to using the site.

Table 8: Flow of 1,000 patients through the Intervention – REFER to GO to QUIT

	Intervention			**Control**		
Start with 1,000 patient visits	**Total N**	**N**	**%**	**Total N**	**n**	**%**
Total Smokers	1000	200	20%	1000	200	20%
% of Smokers **Refer**red	200	48	24%	200	24	12%
% of Smokers **Referred** who **GO**	48	19	40%	24	4.8	20%
% of Smokers that **GO** who **QUIT**	19	3	15%	5	0.5	10%

Because not all smokers will be interested or ready to be referred, we have estimated the number of smokers per practice that will participate in the website over time. We estimated 1,000 visits by unique patients per year to the dental practice. Based on tobacco use prevalence in DTC.Net, approximately 20% of the patients will be smokers.[7, 122] To be conservative, we assume that we will have only two providers per practice actively participating in the intervention. Using these numbers, we have estimated the number that will

participate per practice yearly (Table 8). In many practices, there will likely be more than one hygienist referring. Thus, the actual number referred may be proportionately higher in each arm.

D7. Data Sources

To test our hypotheses, we need data from multiple sources (Table 9). (Please refer to the power calculations for a description of over sampling to account for dropout and non-response). Data will be maintained and analyzed (using SAS, SAS Institute, Cary, NC) by Dr. Zhu under the supervision of Dr. Joshua Richman, our statistician.

Table 9: Key Data Elements, Their Data Sources, and Hypotheses for quantitative analyses

	Interest Survey	Practice Surveys	Provider Website	Patient Exit cards	Patient Website	Patient Follow-ups
Practice Structure (# MDs)	**B**					
Type of Practice	**B**					
Internet Access	**B**					
Level of Interest	**B**					
Patients per Week	**B**	**B,F**				
Provider Demographics	**B**	**B**				
Proportion of Patients who Smoke	**B**			**B,F**		
Outcome Expectation - Counseling			**B,F**			
Patient contact (hours/week)	**B**		**B,F**			
How Busy is Practice?		**B,F**				
Practice Location		**B**				
Perceived Barriers to Counseling			**B**			
Use of HI-QUIT (Providers)			**F**			
Pre-intervention tobacco counseling				**B**		
Post-intervention Refer				**H1**		
Use of website (Patients)					**H2**	
Type of Tobacco Use				**B**	**B**	**F**
Patient demographics					**B**	**F**
Level of Addiction					**B**	**F**
Medical Comorbidities					**B**	**F**
Past Quit History					**B**	**F**
Readiness to Quit				**H3**		**H3**
Quit Attempts						**H3**
Tobacco Prolonged Cessation*						**H3**

B= baseline covariate, F = Follow-up; H1= Outcome for Hypothesis 1; H2= Outcome for Hypothesis 2; H3= Outcome for Hypothesis 3; *validated by cotinine

1) **Interest Survey and Practice Baseline Survey** – Important covariates including practice organizational structure, workload, reimbursement, and patient population will be available. Because time limitations are a frequently-reported barrier, self-report of practice workload may be an important predictor of the intervention success.

2) **Hygienist Internet Portal (Refer2Quit)** – We will collect two datasets from the provider Internet site – the Basic Profile Questionnaire – Providers (BPQ-Pr) and Participation Tracking. Covariates including provider demographics, smoking counseling attitudes, and self-reported counseling of individual providers will be collected using the BPQ-Pr when providers first access HI-QUIT.

We will also track website activity to assess intensity of participation. We will define four components of participation including frequency of participation (number of logons), total participation (number of pages viewed, cumulative session time), breadth of participation (use of various components – cases, toolbox, provider reports, etc.), and consistency of participation (participation in all months) (see Table 3). We will use these data in analysis to assess mediation of level of participation on outcomes.

3) **Patient exit cards** (**Hypothesis 1**) – We will use patient exit cards to assess providers' performance, focusing on **Refer**. Fiore et al. have used patient exit interviews to assess implementation of tobacco cessation counseling and treatment in previous clinical trials.[114] Provider self-reports often overestimate actual activities, and the National Committee for Quality Assurance's Health Plan Employer Data and Information Set (HEDIS) has recently incorporated a patient survey-based measure of tobacco counseling.[118] As discussed above, patients will complete exit cards as they leave their appointment.

4) **Patient Website and information prescriptions (Hypothesis 2)** – We will use the patient website to track number of patients who participate per practice for Hypothesis 2. The number who are referred will be collected by the website in the intervention group, but we must use the information prescriptions in the control (see Section D8, Main Evaluation Measures). In addition, as each patient accesses the intervention or control websites, we will collect a Basic Profile Questionnaire – Smokers (BPQ-SM). The BPQ-SM will be used to

target content of the website to individual patients and as covariates in our analysis of cessation rates of those who participate in the website (H2). Using tracking data, we will also create variables related to participation similar to those of providers described above.

5) **Patient follow-up assessment** (**Hypothesis 3**) – Tobacco cessation behaviors will be assessed by follow-up telephone interviews at six months from website enrollment. We will have three measures of tobacco cessation behavior: 1) Tobacco cessation, 2) Quit Attempts, and 3) Stage of Change (Transtheoretical Model).[120] As recommended in the new standard criteria for evaluation smoking cessation trials, smoking cessation will be validated at six months using cotinine.[123] We have had experience in previous studies in validating cessation by using mailed salivary cotinine measures. Currently, we are using Salimetric's mailed salivary cotinine test.

D8. Main Evaluation Measures

As depicted in Figure 4, HI-QUIT is designed to have a sequence of effects on the process of care within each clinical microsystem. Thus, we have designed our main evaluation to assess several key areas of influence that we have abbreviated as **Refer -> GO -> QUIT**. For our hypotheses, we have three primary dependent variables. Each of the outcomes is collected at the patient level and is used to create a proportion. The first link in the chain of evaluation is of course to assess the performance of the provider. We will use the exit cards to assess the proportion of smokers who are referred. This is assessed at discrete time points (Patients recruited in 3 cohorts at intervention Time 0 (I_0) (pre-intervention), I_0 + 6 months, I_0 + 12 months,). This analysis is solely to assess provider performance and data are collected from patients anonymously.

The proportion of smokers who are referred who GO to the website (H2), and the subsequent proportion who QUIT (H3) are assessed continuously throughout the study. For H2, the numerator is the number who GO, as tracked by HI-QUIT and the control website. The denominator is the number referred. Because of the nature of the Internet versus paper referral system, by definition, the continuous assessment of the number of patients who are referred is different by study arm. Our interest in H2 is the proportion of patients referred who logon, or 'GO', to the website (% who go = number who visit/number referred). In the intervention group, the webserver collects the number of patients entered into the system per practice (i.e.: denominator, the number referred). In the control group, patients are not entered into an electronic system, but are referred using an "information prescription." In both groups, the intervention and control websites collect the number of patients who visit the site. Thus, assessment of the numerator is the same, but assessment of the denominator is systematically different by arm. We have developed protocol for more accurately measuring the denominator and the number referred in the control group by using the information prescription pads with a leave-behind notation of when the patient was referred. We will collect the empty prescription pads from the control practices to assess the number of patients referred for the denominator.

Table 10: Dependent (outcome) variables (**Refer -> GO -> QUIT**)

Label	Question	Source	Collected	Numerator	Denominator
Refer (H1)	During your provider's visit TODAY did anyone: Refer you to Decide2Quit* - a website with information about tobacco?	Patient Exit Card	Discrete Intervals (baseline, 6 and 12 Months)	Number **Refer**red	Number of Smokers
GO (H2)	Proportion of patients from the practice who log onto website	Website tracking and information prescriptions	Continuous	Number who **GO**	Number **Refer**red‡
QUIT (H3)	Do you currently smoke cigarettes (smoked even 1 puff in the last 7 days)?	6 month survey†	Continuous	Number who **QUIT**	Number **Refer**red‡

* control website for Controls; † validated using mailed cotinine saliva kit.
‡ Assessed by web tracking in intervention, in control by leave-behind receipts from information prescriptions

For H3, the dependent variable is point prevalent cessation (QUIT). Smoking cessation trialists have recommended assessment of smoking cessation in randomized trials using both measures of 1) point

prevalence cessation, and 2) continuous or sustained abstinence.[106, 123] Continuous abstinence is preferred when participants have a defined quit date and face-to-face meetings with staff. The HI-QUIT trial is defined as a **cessation-induction study** – a test of treatment to prompt cessation among all smokers, including those who are not currently trying to quit.[106] Provider advice to quit smoking and telephone quitlines are classic examples of cessation induction trials. Like most cessation-induction studies, patients in our study will come into contact with the intervention at irregular intervals after their initial office visit and we will encourage repeated exposures (website visits) in the intervention. As Hughes and colleagues for the Society for Research in Nicotine and Tobacco workgroup on measurement note, point prevalence cessation is often the best measure for cessation-induction trials.[106] We will also collect a measure of prolonged cessation.

Cotinine biochemical verification: In 2002, the SRNT Subcommittee on Biochemical Verification published recommendations and evidence to aid the decision-making in choosing biochemical verification. This article divided studies into clinic-based trials (usually with less than 500 participants) where misclassification is higher and the need for biochemical verification is high and participation in biochemical verification is also high, versus population-based studies where misclassification is low and biochemical verification is less needed, and is in fact less feasible (with non-response rates up to 70%).[124] In planning the study, we feel that HI-QUIT is closer to a clinic-based trial. The connection to the clinical microsystem makes this study more intense than public health interventions and may change the demand characteristics. To increase participation rates for the mailed salivary cotinine, we will provide an additional incentive of $50 for completing this sample. However, we acknowledge that not all patients may complete cotinine validation by mail. For patients who self-report quitting at six months, but fail to return their cotinine saliva sample, we will use their self-report data, acknowledging that those who do not return their cotinine sample will be more likely to mis-report cessation. We will carefully assess for differential misclassification comparing intervention and control. First, we will compare participation rates for returning the cotinine sample by intervention and control. Next, we will assess self reported cessation among those that do and do not return the cotinine sample (comparing intervention and control). Finally, we will compare the misclassification rates among those that did return the sample (again intervention vs. control). If differences are detected, this would represent a case of non-ignorable missing data. Using these rates, we will conduct sensitivity analyses to assess the impact of differences in participation and misclassification on our main outcome and use pattern mixture approaches to assess how much our main analysis might change.[125]

D9. Analysis Plan: For each practice, HI-QUIT is available for 20 months (see Figure 3, section D1). We plan to assess the impact of the intervention throughout this interval.

Unit of Inference. Our unit of randomization is at the practice level, but, all our outcomes are assessed at the patient level. With data at the patient level, we have the flexibility to set our unit of inference at the practice level, or at the patient level (with the second two using modeling techniques to account for clustering). We have carefully considered the unit of inference for each hypothesis. A recent article by Donner[126] discusses the unit of inference and notes that it is often most appropriately set at the unit where the effect is most important to the investigators. As discussed, the HI-QUIT intervention is designed to target all aspects of the clinical microsystem (patients, providers, and processes within the practice). Both dentists and hygienists will have a role in implementing the system and it is anticipated that the roles of dentists and hygienists in Refer2Quit will vary from microsystem to microsystem – although we anticipate that hygienists will usually be the driving force behind Refer2Quit. Considering the unit of inference is particularly important for Hypothesis 1, assessing rates of referral. There are multiple sources of effects, including the providers and patients. Thus, our analysis should be designed to evaluate these sources. We will use hierarchical modeling to explicitly test the sources of variance in using HI-QUIT.

Hypothesis 1: The proportion of patients Referred to self-management resource websites will be larger in HI-QUIT practices (24% of smokers) compared to control practices (12% of smokers).

Data Definitions for Hypothesis 1 (H1): The main dependent variable is the dichotomous outcome of "Refer", indicating whether a patient is referred, as ascertained by the patient exit cards at discreet intervals (6 and 12 months). As secondary dependent variables, we will also test differences in the other provider performance measures assessed by the exit card (screening for tobacco use, provider advice to quit). The primary independent variable is assignment to intervention or control. Considering the unit of inference is particularly important for Hypothesis 1 (assessing rates of referral). There are multiple sources of effects, including the

providers and patients. Thus, our analysis should be designed to evaluate these sources. To this end we will use multilevel modeling to explicitly evaluate the sources of variability in HI-QUIT usage.

Analyses for H1: We will assess differences between intervention and control in three ways.

As our **primary analysis**, we will use patient-level data and multilevel modeling to account for practice-level effects and adjusting for the complex effects of patient and provider variables in multivariable analyses. We have chosen this as the primary analysis for two reasons: 1) because this analysis represents a detailed understanding of the effects of the clinical microsystem intervention, and 2) because we have empirically-driven intraclass correlation coefficients to guide our power calculations.

Thus, to test the overall effect of HI-QUIT, we will use data from all post-intervention evaluation time points together. The hypothesis will be tested by using logistic regression, using patient-level data and incorporating practice-membership as a design factor. An important consideration in handling correlated data resulting from group-randomization is properly accounting for the correlations in the analysis. For example, positive correlations will result in the underestimation of standard errors of the between-practice effects and overestimation of the standard errors of the within-subject effects.[127] Generalized Estimating Equations (GEE),[128] specifically designed for correlated outcomes that can be modeled with a generalized linear model (GLM) including logistic regression, will be used. PROC GENMOD can easily accommodate GEE methods adjusting for clustering.[127] For multivariable analyses logistic regression will be used again, with accounting for clustering. These models will allow adjustment for patient and practice variables described in Section D7. We will also test the hypothesis using data from each individual time point.

Hypothesis 2: The proportion of patients referred who GO to the patient self-management website will be larger in HI-QUIT practices (40%) compared to control practices (20%).

Data Definitions for H2: The primary dichotomous outcome will be whether or not each referred patient goes to the website. The number who visit will be recorded by the website itself which links each visitor to their provider at login. The number referred is continuously registered directly for intervention practices and can be obtained by referral receipts for control practices (see description of information prescriptions and main outcomes above). The analysis will again be done at the patient level with adjustment for clustering within practices.

Analysis for H2: A significant challenge for this hypothesis is how to count the number of patients referred (the denominator) from control practices. For intervention practices, patients will be directly referred into the HI-QUIT system by the providers using Refer2Quit. Thus, for these HI-QUIT intervention practices, we can construct a proportion (number who GO/those who are Referred) using webserver data. However, we have chosen a control to represent a current innovation in referrals, the "information prescription." Thus, patients will not be logged into the system and we cannot use the system to create a proportion. To calculate the denominator for the control practices, we will use the leave-behind receipts from the control "information prescription" pads to tally the number of referrals from each practice. This will allow us to calculate an exact proportion.

The main patient-level analysis will again use logistic regression to model the probability that a referred smoker goes to the website where the independent variable is the group assignment of their referring practice. Because each website links patients back to their practice, we will again use GEE methods to account for clustering within practices. The main hypothesis will be tested by whether the coefficient for treatment assignment is significant in the model corrected for clustering.

Secondary analysis: Our primary approach does have the potential for errors resulting from lost, damaged, or mis-used "information prescription" pads in the control. This would result in a differential misclassification in the control as compared to the intervention group. As much of this error would underestimate the control denominator, it would still provide a conservative estimate. However, it is true that the inherent difference in the intervention and control creates a difference in the assessment of the denominator. Thus, as a secondary analysis and as safeguard against these error sources, we will repeat the analysis using the number of patients who GO as the outcome, with careful adjustment for *patient volume, proportion of smokers, and rates of referral as assessed by the exit cards at discrete time points.* This will allow us to check for consistency of results. The secondary analysis for the number who GO will use linear regression to model the number of patients per practice who go to the website by treatment assignment adjusted as above, where the test of H2 will be the significance of the coefficient for treatment assignment.

Hypothesis 3: The proportion of smokers who are referred who QUIT at six months will be larger among intervention compared with control because of the additional connectivity of HI-QUIT.

Data Definitions for H3: The main dependent variable for H3 is the dichotomous outcome of patient tobacco cessation (quit). The primary independent variable is assignment to intervention or control group. We have designed a patient-level analysis around point prevalence cessation based on the following question: "Do you currently smoke cigarettes (smoked even 1 puff in the last 7 days)?"

We will approach this analysis in two ways. In both approaches, the numerator will be the number of patients who report cessation at six-month follow-up calls. In our primary analysis, we will use an intent-to-treat analysis in that we will include all practices (regardless of whether they actually use the intervention) and will include all smokers who are referred (the same denominator used in H1) regardless of whether they GO to the website. This represents a conservative assessment since we assume that many patients will not GO, and for the purposes of analyses, we will assume that these patients will not have quit. The most conservative analysis would be to use the total number of smokers seen in the practices as the denominator. However, we will not know this number exactly. Our exit cards give an estimate but we do not have a continuous measure of total smokers.

As a secondary analysis, we will assign the denominator as the number of patients who GO to the website. For this secondary analysis, consistent with current guidelines for smoking cessation trials, we will assume that patients who are lost to follow-up, including those who GO and do not agree to follow-up, are smokers.[123]

We have assumed a control cessation rate of 17% among those with completed cases (follow-up complete) in the control group based on a range of completed case and intent-to-treat evaluations of prior internet smoking cessation interventions[31-39] (Table 11). For the purposes of power calculations, we estimate a 9% difference in cessation among those with completed cases in the intervention group. Those who do not agree to follow-up will be considered smokers. The intent-to-treat cessation rates are calculated as the sum of the completed case rate (the proportion who quit among those who complete follow-up), and the rate among those that do not agree to follow-up (assigned as 0% cessation). We conservatively have anticipated that 60% of website participants will agree to follow-up. Thus, we anticipate an intent-to-treat cessation rate among those who go to the website of 15% in the intervention group (See Table 11). Based on this rate we have also calculated the more conservative assessment needed for our primary analysis, assuming that all those patients referred who do not GO are not abstinent.

Table 11: Six-month cessation anticipated among completed cases, those who go to the website, and those referred from 80 practices.

	Six-month cessation among Completed Cases*†		Cessation among those who GO		Cessation among those who are referred‡ (Primary Analysis)	
	n/N	Proportion	n/N	Proportion	n/N	Proportion
Intervention	120/456	26%	120/760	16%	120/1920	6%
Control	20/120	17%	20/200	10%	20/960	2%

* Completed Cases are those with completed six-month telephone surveys
† Assumes 60% follow-up among those who GO (see Table 8 for number who go per practice) and assigns not abstinent to those without follow-up
‡ Assumes those who are referred and do not go are **not abstinent**, based on estimates of those referred from Table 8 multiplied by the number of practices

The prevalence of tobacco cessation will be assessed at six months. Secondary dependent variables for H3 include reports of prolonged cessation, the number of quit attempts, and change in readiness to quit. Models will be constructed treating the number of quit attempts both as a continuous variable and as a Poisson variable. We will conduct additional analyses for quit attempts and change in stage.

Analyses for H3: We will first test the hypothesis for the main outcome (quit rate) and will conduct H3 at the patient level. Because we are comparing rates in all instances between intervention and control practices, we will use a two-group chi-square test of equal proportions to test the statistical difference between the quit rates. Due to the different referral mechanisms and the implications of referral for the providers, we expect that there may be differences in the characteristics of referred smokers between study groups. For instance, it is entirely possible that only those smokers who express a high readiness to change will be referred in the

control practices, while smokers in the intervention practices will be referred less selectively. To address this we will use a GLM with a logit link to model tobacco cessation by treatment assignment adjusted for readiness to change as entered into the website by the patient. Clustering by practice will be accounted for by employing generalized estimating equations as in our other analyses. We will do several multivariable analyses with separate models for overall quit rate, quit attempts, and change in stage. Patient and practice level variables will be used for adjustment in a similar manner to that described for H1. As an additional covariate, initial stage of change will be used to adjust models where the dependent variable is quitting or attempts.

Qualitative Process Analysis – How Practice Characteristics Impact Use of the Referral System:
Case-Comparison study - Our main analyses above are to test overall differences, Intervention versus Control. However, based on our prior experience, adoption of the intervention will vary. Some hygienists and practices will have high rates of referral and, despite our efforts, some practices may use Refer2Quit very little. Consistent with the framework for evaluation of complex interventions,[105] we plan a second qualitative analysis to answer questions including: What organization and process factors are related to adoption, or not adoption, of the intervention? To accomplish this task, we plan to conduct semi-structured interviews with a random sample of providers.

The design is a case-comparison study, a subset of the multimethod assessment process (MAP).[129-132]
Sample: We will use a selective sampling strategy.[133] Selective sampling is defined as sampling subjects according to a preconceived, but reasonable initial set of criteria to obtain a broad array of informants. As the goal of our qualitative research is to obtain a range of opinions related to workflow processes, barriers, facilitators and other themes related to adoption, we will target specific practices and providers. Our first layer of selective sampling is to identify 1) high and 2) low-adopting practices. We also would like to obtain larger and smaller practice sizes. Thus, we will interview hygienists and dentists from an initial random sample of 8 high and 8 low-adopting practices among the 40 intervention practices (also split by large and small practice size).

Many qualitative research studies use a combination of selective sampling and theoretical sampling.[133] We will conduct iterative analyses and may find that we do not reach theme saturation in some strata of our selective sampling after 16 practices.[134] We have budgeted resources for up to 20 practices to provide for the needs of theoretic sampling and theme saturation.

Interviews - We will develop a Semi-Structured interview guide. The interview guide will be reviewed by our team and two participating practices that are not top adopters. The interview guides will be developed to encourage participants to “tell the story” of how patients receive care. DPBRN Coordinating Center staff will recruit and conduct the semi-structured interviews. Our goal will be three telephone interviews per practice. A verbal consent will be obtained and the interview will be recorded.

Analysis - Interviews will be transcribed and anonymized. Because one of primary goals is to describe the processes of care, we will use a combination of thematic summary and narrative summary.[135] Narrative summary is best used when qualitative data follow a logical order (such as patient care) and frequently used in triangulation with quantitative data.[136] The transcribed interviews will be reviewed by two independent reviewers (Gilbert, Houston) to develop preliminary themes. To develop themes, we will use an open-coding approach to be maximally inclusive. Each open-ended question in the interview guide will be assessed separately, and then the reviewer will generate larger summary themes for the overall interview. The themes will then be reviewed with the larger investigator group in the steering committee meeting to resolve disagreements. From the themes, we will create summary tables of key points. We will complete this method twice while collecting interviews. In this way, we will assess for theme saturation and further revise our data collection methods for the second wave of interviews to focus on details of interest.

D10. Power Calculations - All power calculations were made using nQuery Advisor v.6.01, and the primary analysis are carried out at the patient-level with sample sizes adjusted for the clustering of patients within practices. To do this, we used practice-level Intraclass correlations derived from DTC.Net. For all power calculations, we have built in two **conservative assumptions** that impact our power calculations.

1) We have estimated the power based on one year of access, but the intervention will actually have availability for 20-months, thus number of smokers referred will be somewhat higher.
2) We assume that only two providers per practice will be actively involved in referring patients. Thus, for some practices more providers may participate and the number of patients referred (say if four hygienists and dental assistants refer) may be considerably greater.

Hypothesis 1: This analysis will test whether HI-QUIT practices refer patients at a higher rate than control practices. The literature supports estimating the mean baseline referral rate of 12% for control practices.[1] Power was estimated using a two-sided chi-square test for a difference in proportions with a Type 1 error rate of 0.05. To take a conservative approach, power was calculated assuming an average of 66 smokers per practice responding to the exit cards. Due to clustering within practices and clustering within providers, these will not all be independent observations. The standard practice is to adjust the sample size by an inflation factor D = [1 + (m-1) r] where r is the intra-class (practice-level) correlation (ICC) and m is the number of subjects per group (practice). Pilot data from DTC.Net revealed a relatively large ICC of 0.15 for rates of advice to quit smoking within dental practices. Assuming equal ICCs of 0.15 for Refer and a cluster size of 66 smokers per practice gives D= 10.75, or an effective sample size per practice of approximately 6 patients. With these numbers only 29 practices per arm are required to achieve 80% power to detect a significant difference in referral rates of 0.12.

H1: Number of subjects needed per group for 80% power with a two-sided χ^2 test of equal proportions and α=0.05, adjusting for clustering in practices

	1	2	3	4
Control proportion, π_1	0.12	0.12	0.12	0.12
HI-QUIT proportion, π_2	0.24	0.22	0.20	0.19
Unadjusted n needed per group	176	240	354	447
Adjusted n needed per group*	1,892	2,580	2,805	4805
Number of practices needed per group	29	39	58	73

* Design factor (D = [1 + (m-1) r]) inflates n to account for clustering

Hypothesis 2: This analysis will test the proportion of patients referred who GO to the website, comparing HI-QUIT practices and control practices. As discussed above, a conservative base rate for control practices is for 12% of smokers to be referred and for approximately 20% of those to GO to the website[1]. We expect these proportions to increase for the intervention group to 24% and 40%, respectively. We then need to examine statistical power to detect a 20% difference (40%-20%) in the proportion of referred patients who GO between the two groups, which corresponds to an odds ratio of 2.8. Based on approximately 200 smokers per practice per year and the referral rates above, we expect averages of 24 and 48 smokers to be referred from each control and intervention practice, respectively (Table 8).

Because of the group randomization, our effective sample size must again be reduced by a design factor for each group. Because “GO” to the website is more patient-directed, we have assumed a lower ICC of 0.05 for this analysis. Conservatively assuming an ICC of 0.05, we calculated design factors of 2.2 and 3.6 for the control and intervention groups, respectively. Incorporating the design factors gives an effective sample size per practice of 12 for the control group and 14 for the intervention group. Using a two-sided chi-square test with Type 1 error rate of 0.05, only 10 practices per arm are required to achieve 80% power. If we assume a smaller effect where only 30% of referred smoker in the intervention group GO, 30 intervention practices and 30 control practices are sufficient to achieve 80% power.

Hypothesis 3: This analysis of patient cessation outcomes is again conducted at the patient level. As detailed in the analysis plan we will approach this hypothesis in two ways and power calculations will be presented for each. For both approaches, this hypothesis will be tested as a two-sided chi-square test for equality of proportions and the number who quit will be assessed at follow-up among those who visited the website.

As the primary analysis, and most conservative approach, we will test whether those patients referred through HI-QUIT are more likely to quit than control patients who received information prescription referrals. As in H1), we expect 48 referrals from each intervention practice and 24 from each control practice. Based on ICCs from DTC.Net, we will use an ICC of 0.017 to account for clustering within practices. We further again assume that 20% of referred control patients will GO as will 40% of referred intervention patients. We will

assume that the cessation rate was 0% among those referred who did not GO. Assuming an intent-to-treat cessation rate of 10% among control patients who GO and 15% for the intervention group (See Table 11), we arrive at overall cessation rates of 2% for the control group and 6% for the intervention group. Only 8 practices per group are required to achieve 80% power to test this hypothesis with a Type 1 error rate of 0.05. If power is reduced by assuming that only 30% of referred intervention group smokers GO, 36 practices per group are required for 80% power.

In summary, evidence suggests that there is ample power to detect clinically significant differences for the three main hypotheses with conservative assumptions.

E. HUMAN SUBJECTS

This study is pending expedited approval from the Institutional Review Board. In the development phase of our study, we will conduct individual "Think Aloud' usability interviews with local hygienists and patients. These formative data will inform the development of the interactive web-based approach. Written consent will be obtained from each participant. Participants in these formative studies will not be included in the RCT.

The main study will involve recruitment of community-based dental practices in the Dental PBRN to a randomized trial of an Internet-delivered intervention. As discussed above, providers will be contacted by mail with an interest survey, and those interested will be sent additional materials, as discussed above. Providers who agree to participate will agree to: 1) review the contents of a website (intervention or control); 2) allow us to send the follow-up emails with reminders for updates; 3) encourage other hygienists from their practice to participate in the intervention; 4) agree to allow us to recruit patients as they exit their visit to participate in the evaluation using exit card surveys; and 5) allow us to contact a sample of patients participating in websites.

We will recruit patients from the practices to complete exit cards in the waiting rooms after their visit. Exit cards (brief postcard-sized surveys) will be presented to consecutive patients as they leave the office. The exit cards will come with an envelope explaining the study, explaining that participation is voluntary, and that responses will be. Exit cards will be completed anonymously. Participants will seal the exit card in the envelope and place it in the return box before they leave the practice.

For patients referred by hygienists using refer to quit, patient consent is layered and matched to the risk and burden to the patient. Patient consent is not obtained at chairside after they agree to be enrolled. At this level of participation, only patient email is collected. Intervention patients will receive emails after being referred to the intervention website by providers. To minimize risk, the emails will only contain a reminder to go to the website, but will not identify the purpose of the website. No personal health information will be in the emails. Because risk is low and it is not feasible to obtain informed consent without changing the processes of care themselves, we will not obtain informed consent at this level (similar to prior Fax-to-Quit studies).

If patients choose to log onto the web-based system, they will be asked to complete an online consent process where they agree to specific line items (agree to allow us to track their use of the site, agree to follow-up) by online check boxes verified with a username and password they create. If they agree, they will provide telephone numbers for follow-up. If they do not wish to participate in follow-up, they can use the online system without providing additional identifying information. Because participation is again optional, and because requiring written consent would likely greatly decrease use of the online system, we will not obtain written informed consent at this phase. Once the patient is called for follow-up, we will complete a verbal consent procedure for participating in the interview. If the patient reports smoking cessation, we will obtain written informed consent when the specimen is collected. Thus, signature documentation is only obtained for the subset of patients for whom biologic specimens are obtained. This layered procedure has been used in prior studies including DTC.Net and the NCI-funded Smoking Coach study referenced in the application.

A Data Safety and Monitoring Board (DSMB) will be established that includes three individuals, at least two of whom are not associated with UAB. The DSMB will provide reports to the NIDCR and the UAB IRB. The DSMB will meet before the study begins to review the protocol, assess safety, and approve plans for data integrity. For this type of study, evaluating a new type of health care delivery using all approved interventions, there will most likely not be any type of interim data analysis to assess probability of statistically significant group differences. The main purpose of the DSMB will be to monitor success of recruitment, assess data integrity, and monitor for adverse events. Risks to study participants relate mostly to misinterpretation of what

is research and what is usual care and loss of confidentiality. The DSMB will carefully evaluate how the study is described and that study subjects are informed not to report urgent symptoms through email communications. The DSMB will be convened every six months

Risks and Benefits.

Our study involves two sets of participants: Providers and their patients.

The risks to dental staff in this study are minimal, especially in relation to the importance of the knowledge that may be expected to follow from this study. Certainly there will be a burden of time required to learn about and implement tobacco control using HI-QUIT. The major risk is the accidental disclosure of provider-specific information; however, every precaution will be taken to prevent this and the study team has an excellent track record of protection of confidential data. In no way will individual patient- or provider-level data be released to the public or cited in a publication. We have substantial experience with implementing these methods successfully. As part of the intervention and evaluation activities, we will feed back data; however, participating providers will only receive their own coded performance data, and only aggregate peer performance data will be disseminated.

A major risk of the study to patients is the accidental disclosure of patient-identified information; however, every precaution will be taken to prevent this and the study team has an excellent track record of protection of confidential data. Dr. Richman and Ms. Causey in the Data Information and Statistics Core will organize data security and archiving. The group has over 20 years of combined experience in entering and securing confidential information collected from studies with human subjects. All personnel involved in the study have completed training in human subjects research and HIPAA. We will allow patients to complete the patient exit cards anonymously. We will provide an envelope with each exit card so that patients can seal the envelopes and then place them in the sealed return box at the practice. Printed on the envelope will be information about the study informing them that participation involves completing a series of questions on the enclosed postcard and that participation is voluntary. The telephone number of the HI-QUIT project office and the UAB IRB will be provided on each exit card to call with questions. We will assure patients that providers have agreed not to review the cards, and that individual patient reports will not be disclosed to the provider. Thus, participation or non-participation will not impact their care. The sealed postcard will be returned within the return box.

Both providers and patients will be participating in the intervention and control websites. For both websites, we will develop an online consent form with a series of check-boxes that require participants to actively agree to specific line items in the consent. In previous studies, we have found that these check-boxes are necessary in online consents to have participants actually read the information. All participants will be provided the telephone number of our HI-QUIT project office to call if they have questions related to the consent.

For Phone Interviews (Follow-up assessment of website participants to assess smoking cessation (H3): Research assistants will obtain verbal consent to participate in the brief telephone survey. For quality assurance of data collection, a ten percent sample of telephone surveys will be audiotaped. The selected patients will also be asked if they are willing to be audiotaped. If the patient declines to be taped, they will be allowed to participate in the interview without the audiotape.

Patients who have quit at six months will be asked if they agree for us to mail them a saliva test kit for a salivary cotinine sample. If they consent, a collection tube from Salimetrics and instructions for use will be sent. The patient will mail the collection tube directly to the lab in a postage-paid envelope.

Risks to patients also include the burden of completing the exit interviews and follow-up surveys. We will provide a small compensation to offset the effort of participating in the follow-up telephone interviews and cotinine validation. Patients may certainly benefit from the training their providers have received in the form of more appropriate counseling.

Gender and Minority Inclusions

The population sampled for exit surveys will be inclusive of the general dental care population (patients age 19 and over) without restriction to gender, race/ethnicity, or socioeconomic status. Based on data from our previous Internet-delivered trials, 18% of the patients are ethnic minorities, and 7% use public assistance to help pay for their dental care. Seven percent of the providers in our prior Mi-Plus study (See Table 2) are ethnic minorities. We are well aware of race/gender disparities in quality of care, which may also result in differential application of tobacco control guidelines.

Children

For our study we will only include those age 19 or older. Adolescents have unique factors related to use of tobacco and their stage of personal development such as issues of noncomformity, parental supervision, sales to minors, use of other recreational drugs and the influence of peers. The HI-QUIT intervention we are developing will not adequately address these issues initially. We know that adolescents are patients at some community-based dental practices, and may potentially benefit from the training that the providers receive. However, because of the scope of information already planned for HI-QUIT, we will not be able to adequately cover specific information for adolescents. Thus, we will not recruit them as part of our evaluation of the microsystem intervention. Providers will be allowed to use the patient handouts for those under 19 who smoke in their practice, but we will not recruit them as subjects because the focus of our training is not tobacco cessation counseling for minors.

TABLE 12 : Projected Characteristics of Enrolled Patients*

	HI-QUIT	Control
	%	%
Gender		
Male	50	50
Female	50	50
Age		
Less than 30	20	20
30 to 45	43	43
46 to 60	35	35
Over 60	2	2
19-45 years old	38	38
Ethnicity		
White	82	82
African-American, Hispanic, Asian	10	10

* Adult Patients (over 18), data based on Free2Quit study

F. VERTEBRATE ANIMALS: Does not apply.

G. Select Agent Research: Does not apply.

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I. Multiple PI Leadership Plan: Does not apply.

J. Consortium/Contractual Arrangements: none

K. Resource Sharing: Does not apply.