

FSFW HEALTH, SCIENCE, AND TECHNOLOGY WAVE 2 REQUESTS FOR PROPOSALS

TOPIC 3: IMPROVING THE EFFECTIVENESS OF CESSATION AND HARM REDUCTION INTERVENTIONS: SMOKER CHARACTERIZATION AND TAILORING OF QUITTING/SWITCHING APPROACHES

SMOKER CHARACTERIZATION AND TAILORING OF QUITTING/SWITCHING APPROACHES: INTRODUCTION

The challenge of smoker characterization

Smokers are a heterogeneous population, in terms of both their risk of harm from smoking and level of difficulty they face in trying to quit. Most say that they want to quit. Many try, often multiple times, but very few succeed.¹ A broad range of products and services are available to help smokers quit, but none have shown high effectiveness across the entire population of smokers.²

There are a number of dimensions to this heterogeneity:

Smoking history and behaviors clearly affect the risk of disease, and also appear to impact motivation to quit and likelihood of successful cessation. For example, cessation success has repeatedly been shown to be (negatively) correlated with behaviors that suggest nicotine dependence, such as the number of cigarettes smoked per day and the time to first cigarette after waking.³ Smoking behaviors are also gendered.⁴

Biological factors both drive risk and influence cessation. Research is identifying a growing number of these. For example, low activity of the DNA repair enzyme 8-oxoguanine DNA N-glycosylase (OGG) has been associated with a higher risk of lung cancer, suggesting that smokers with reduced OGG activity might be particularly at risk.⁵ And on influencing cessation, genetically slow metabolizers of nicotine (modulated via CYP2A6 activity) appear to be less dependent than fast metabolizers.⁶ Recent genome-wide association studies also suggest that a broader range of nicotine receptor subtypes than initially thought may play a role in nicotine dependence.⁷ Sex differences are also relevant,⁸ as are differences

¹ WHO: <http://www.who.int/news-room/fact-sheets/detail/tobacco>

² EY-Parthenon report on smoking cessation: https://www.smokefreeworld.org/sites/default/files/ey-p_smoking_cessation_landscape_analysis_key_findings.pdf

³ Hyland A, Li Q, Bauer JE, et al. Predictors of cessation in a cohort of current and former smokers followed over 13 years. *Nicotine & Tobacco Research* 2006 6: S363-S369

⁴ Bottorff J et al. Gender, smoking, and tobacco reduction and cessation: a scoping review. *International Journal for Equity in Health* 2014; 13:114

⁵ Paz-Elizur T, Krupsky M, Blumenstein S, et al. DNA repair activity for oxidative damage and risk of lung cancer. *J Natl Cancer Inst* 2003 Sep 3; 95(17): 1312-1319

⁶ Benowitz NL. Pharmacology of nicotine: addiction, smoking-induced disease, and therapeutics. *Annu Rev Pharmacol Toxicol* 2009; 49:57-71

⁷ Harmey D, Griffin PR, Kenny PJ. Development of novel pharmacotherapeutics for tobacco dependence: progress and future directions. *Nicotine Tob Research* 2012 Nov; 14(11): 1300-1318

⁸ FDA presentation 'Opioid and Nicotine Use, Dependence, and Recovery: Influences of Sex and Gender'. Scientific Conference Sept 27-28 2018'. <https://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/UCM620084.pdf>

between women who use oral contraceptives and those who do not.⁹

Psychological factors may also be relevant, beyond the well-known associations of smoking with schizophrenia, depression and anxiety. Applications of the Five Factor Model (FFM) of personality have consistently shown that smokers score higher than non-smokers on the neuroticism dimension, and that smokers with higher levels of neuroticism are more likely to experience problems when trying to quit. These smokers might therefore benefit from cessation approaches that explicitly address this component of their personality.¹⁰

Socioeconomic and demographic factors, including education, employment, income, and access to healthcare, are important for driving both quit attempts and success rates. In one study, for example, smokers with fewer smoking friends, and smokers whose friends gave up smoking, were more likely to try to quit and to succeed in doing so.¹¹

Given this heterogeneity, there is unlikely to be a ‘one size fits all’ approach for helping smokers to quit. However, current guidelines and approaches for smoking cessation do not fully take this heterogeneity into account. At best, some factors are evaluated and considered, such as level of nicotine dependence (via, for example, the Fagerström Test for Nicotine Dependence), or nicotine dependence and some elements of smoking history (National Comprehensive Cancer Network smoking cessation guidelines for cancer patients).

The challenge of tailoring approaches to quitting or switching

Historically, the randomized clinical trial (RCT) has been the main tool used to test and evaluate clinical interventions (e.g., pharmacological, surgical or behavioral therapies). These prospective studies are designed to control for sources of error and bias through randomization, blinding and subject inclusion/exclusion criteria. In the area of smoking cessation, RCTs have been used to determine that nicotine replacement therapy (NRT) and prescription medication (e.g., varenicline, bupropion) can modestly improve success in quitting smoking, although the effect appears to be stronger in men than in women.¹²

The same rigorous methods that make RCTs the gold standard for assessing clinical interventions also challenge their applicability to more diverse “real world” populations and treatment settings. The US FDA recently has acknowledged the value of real-world evidence in informing regulatory decisions, improving process efficiency, enhancing safety, and lowering the cost of product development.

Assessing the potential role of ANDS (whether as quitting tools or for switching) faces the additional complication that unlike the pharmaceutical products and medical devices commonly used in RCTs, ANDS are widely available consumer products in most countries. This removes the possibility of blinding, introduces the potential for consumer bias or product preference, makes it difficult to control the type and amount of product used, and introduces the risk of product characteristics changing (and of products becoming unavailable) over the course of a study.

In this context, the Foundation will fund research to develop a useful and validated smoker segmentation tool. It will also fund work to examine pragmatic trial methods for evaluating ANDS and their potential for quitting or switching. We also welcome expressions of interest from organizations interested in leading or participating in such studies.

⁹ Benowitz NL et al. Femal sex and oral contraceptive use accelerate nicotine metabolism. *Clin Pharmacol Ther* 2006 May; 79(5):480-8

¹⁰ Zvolensky MJ, Taha F, Bono A, Goodwin RD. Big five personality factors and cigarette smoking: a 10-year study among US adults. *J Psychiatr Res*. 2015 Apr; 63: 91-96

¹¹ Hitchman SC, Fong GT, Zanna MP, et al. The relation between number of smoking friends, and quit intentions, attempts, and success: findings from the International Tobacco Control (ITC) four country survey. *Psychol Addict Behav*. 2014 Dec; 28(4): 1144-1152

¹² Perkins KA, Scott J. Sex differences in long-term smoking cessation rates due to nicotine patch. *Nicotine Tob Res* 2008 Jul; 10(7):1245-50

REQUEST FOR PROPOSAL 3A: DETERMINANTS OF A SMOKER CHARACTERIZATION TOOL

Issue date:	January 18, 2019
Question window ends:	March 18, 2019
Closing date:	April 18, 2019
Closing time:	5pm US Eastern Standard Time
Contact information:	support@smokefreeworld.org
Submit questions to:	support@smokefreeworld.org
Submit proposals to:	See submission instructions in RFP
Financing instrument:	Scoping grant (3 grants available)
Financing amount:	Up to US\$ 200,000
Financing duration:	Up to 3 months

(Please review the Topic 3 Introduction document as well for further background)

SCOPING RESEARCH QUESTION

What is the current fact base on factors that could be used to characterize smokers?

The heterogeneity of smokers was described in the introduction to this section. Understanding this heterogeneity is important: offering each smoker the most appropriate support requires a good understanding of his/her risks from smoking and which approaches to quitting are most likely to be successful.

The knowledge base on this heterogeneity is currently dispersed. We seek to bring it together into a structured fact base that can serve as a starting point for designing, testing and validating tools for characterizing smokers.

Deliverables

An initial fact base including relevant biological, psychological, socioeconomic and historic factors, including the gender issues in these factors, and the evidence relating each factor to:

1. Risk of harm from smoking
2. Likelihood of successful quitting
3. Most successful approach to quitting.

Design and delivery of 2-3 workshops with gender-balanced groups of international experts to discuss the fact base and develop perspectives on what an evidence-based and pragmatic smoker segmentation tool would look like.

Research proposal to develop and validate a smoker segmentation tool, based on the above fact base and expert input, to guide the choice of cessation intervention.

Expected qualifications

- Demonstrated experience in conducting academic literature reviews, synthesizing and presenting findings, and designing and delivering workshops
- Demonstrated experience designing guidelines and tools for use in clinical practice.

Geographic focus

Global

Estimated budget and duration

Up to \$200k and up to three months

(We will issue up to 3 grants in parallel in order to explore different approaches.)

Submission Instructions

Applications should be submitted through our online portal which can be accessed [here](#). This link will always start a new application form.

You may save a started application at any time by using the 'Save & Finish Later' button at the end of each page. If you do so please use [this link](#) to return to the log-in screen to access the saved form.

A list of application portal FAQs can be found [here](#).

For all access inquiries, please contact us at support@smokefreeworld.org

REQUEST FOR PROPOSAL 3B: DESIGNING CLINICAL TRIALS AND EVALUATION METHODS FOR READILY AVAILABLE CONSUMER PRODUCTS

Issue date: January 18, 2019
Question window ends: March 18, 2019
Closing date: April 18, 2019
Closing time: 5pm US Eastern Standard Time

Contact information: support@smokefreeworld.org

Submit questions to: support@smokefreeworld.org

Submit proposals to: See submission instructions in RFP

Financing instrument: Scoping grant

Financing amount: Up to US\$ 200,000

Financing duration: Up to 3 months

(Please review the Topic 3 Introduction document as well for further background)



SCOPING RESEARCH QUESTION

The challenges of using RCTs to assess ANDS and other products or services that are commercially available were described in the introduction to this section. In order to evaluate the potential role of such tools to help smokers quit or reduce their risk of harm, pragmatic trial methods must be developed urgently. The Foundation is interested in funding work that informs the development of such methods.

Deliverables

An initial fact base on study designs which includes:

1. An overview of existing major studies assessing the potential of ANDS for cessation or harm reduction, and of the study designs being used, and to what extent these studies included or focused on women
2. Examples of successful study designs which have been used to evaluate consumer behavior in the real world (e.g., nutrition, exercise).

2-3 workshops with gender-balanced groups of international experts to review the above fact base and develop recommendations for best practices in pragmatic trials of ANDS, including how trial designs may vary by subpopulation, geographic region and smoker type, and how innovations in technology (e.g., wearables, mobile) might play a role in trial design.

Final report with workshop findings and recommendations.

Expected qualifications

1. Demonstrated expertise in trial design, particularly those involving consumer behavior
2. Familiarity with smoking cessation and harm reduction.

Geographic focus

Global

Estimated budget and duration

200k over 3 months

Submission Instructions

Applications should be submitted through our online portal which can be accessed [here](#). This link will always start a new application form.

You may save a started application at any time by using the 'Save & Finish Later' button at the end of each page. If you do so please use [this link](#) to return to the log-in screen to access the saved form.

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