Title: PeRiopEratiVE smokiNg CessaTion (PREVENT)- a pilot randomized controlled trial protocol

Ofori Sandra N, MBBS, MSc,[1,2] Flavia Borges, MD, PhD,[1,2,3] Marcucci Maura, MSc, MD,[1,2,3] Conen David, MD, PhD,[2,3] Clara Chow, MBBS, PhD[4,5] Andrew Pipe, MD,[6] Ameen Patel, MD,[Error! Bookmark not defined.] Vikas Tandon, MD,[Error! Bookmark not defined.] Emmanuelle Duceppe, MD, PhD,[7] Emilie P. Belley-Cote, MD, PhD,[Error! Bookmark not defined.,Error! Bookmark not defined.] Michael Jacka, MD, MSc,[8] Joel Parlow,[9] Michael McGillion, RN, PhD; [Error! Bookmark not defined.,Error! Bookmark not defined.] Devereaux PJ, MD, PhD,[1,2,3] on behalf of the PREVENT trial investigators.

Background: Globally, 300 million major surgeries are undertaken annually; 20%-25% of the patients are smokers. Cytisine and text messaging are effective smoking cessation interventions in nonsurgical settings. It is unknown if they are effective in the surgical population. We aim to determine the feasibility of a large randomized controlled trial (RCT) evaluating cytisine versus placebo and text messaging versus standard care for smoking cessation among patients undergoing surgery.

Methods: We designed a multicentre, parallel group, 2x2 factorial RCT to involve 100 patients across 7 Canadian and 1 Australian site. We will include adults aged ≥18 years who smoke ≥10 cigarettes/day during the previous year and have no period of smoking abstinence longer than 3 months, are undergoing surgery within 28 days, have a mobile phone with texting capability, and give informed consent.

Participants will be randomly assigned (1:1) to receive 8 weeks of cytisine or placebo, and in the factorial arm, 8 weeks of semi-personalized text messages (4/week) on random days of the week or standard care. All participants will be followed for 6 months.

The primary outcome is feasibility defined by the ability to recruit 2 patients/center/month and the achievement of 6-month complete follow up on >95% of participants. Secondary outcomes will include i) smoking outcomes- exhaled breath carbon monoxide-verified continuous abstinence at 6 months, self-reported 7-day point prevalence of abstinence at 30 days, 56 days and 6 months, time to first lapse and time to relapse; and ii) clinical outcomes- vascular complications (composite of all-cause mortality and non-fatal myocardial infarction, stroke, cardiac arrest, proximal venous thromboembolism); pulmonary complications (composite of pneumonia and respiratory insufficiency requiring ventilatory support); and wound and infectious complications, length of hospital stay and acute hospital care (composite of emergency room visits and hospital readmissions) since discharge.

The feasibility outcomes will be analyzed using descriptive statistics and 95% confidence intervals (CIs). We will use a variety of exploratory methods to obtain a range of estimates of the relative risks and 95% CIs for the secondary outcomes to inform the design of the full trial.

Conclusion: The PREVENT pilot trial will confirm the feasibility of a large RCT evaluating a smoking cessation strategy utilizing cytisine and text messaging in the perioperative setting. Smoking after surgery remains common and negatively impacts short-and long-term health. PREVENT will evaluate 2 interventions with substantial potential to improve these outcomes.

[1] Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada
[2] Population Health Research Institute, Hamilton, ON, Canada
[3] Department of Medicine, McMaster University, Hamilton, ON, Canada
[4] Westmead Applied Research Centre, University of Sydney, Sydney, Australia
[5] Westmead Hospital, Sydney, Australia
[6] University of Ottawa Heart Institute (Reed, Birnie, Pipe), Ottawa, Ontario
[7] Department of medicine, Faculty of medicine, Université de Montréal
[8] Department of Critical Care Medicine, University of Alberta
[9] Departments of Biomedical and Molecular Sciences, Queen's University Faculty of Health Sciences, Kingston, Ontario, Canada