Progress/Final Report for Network for Canadian Oral Health Research:
New Frontier Seed Grant Program (2018)

Study Title: A multi-centered stepped wedge cluster randomized controlled trial (RCT) of the de-adoption of oral chlorhexidine prophylaxis and implementation of an oral care bundle for mechanically ventilated critically ill patients (The CHORAL study)

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Study Summary:

Background
Critical illness and invasive mechanical ventilation contribute to painful oral conditions including xerostomia, mucositis as well as the accumulation of oral bacteria linked to the development of infection-related ventilator associated complications (IVACs), including ventilator-associated pneumonia (VAP). These issues led to the introduction of topical oral chlorhexidine mouth rinse to prophylactically control oral bacteria and reduce the risk of IVACs.

Study Rationale
New studies reevaluating oral chlorhexidine prophylaxis identify non-significant reduction of VAP and a statistically significant increase in mortality (OR 1.25, CI 1.05 - 1.50) in non-cardiac surgery patients. Patients report development of oral disease and pain. In response, scientific study of oral chlorhexidine de-adoption and implementation of improved oral care processes are warranted.

Methods
We conducted a multi-centered stepped wedge cluster randomized controlled trial (RCT) of the de-adoption of oral chlorhexidine prophylaxis and implementation of an oral care bundle for ventilated critically ill patients. We identified 6 ICUs and randomized each to one of 6 wedges. Within this design, we provided multifaceted education and support to the participating units as they rolled out a 4 element comprehensive oral care bundle (assessment, tooth brushing, oral moisturization and suctioning). All ICUs received the intervention by the end of the 14-month study period. For control and intervention periods, we used the iCORE registry, a highly reliable and validated ICU clinical registry, to measure our primary outcome of mortality. Secondary outcomes included IVACs and oral health status. We undertook a concurrent mixed-methods process evaluation to understand how the intervention was actively delivered to inform future clinical application.

Results
A total of 3260 patients were enrolled; 1560 patients (mean age, 60.3 years; 604 women [38.7%] during the baseline period (control) and 1699 (mean age, 59.4 years; 644 women [37.9%]) during the intervention phase. We found no difference in overall ICU mortality between groups, with 332 (21.3 %) and 400 (23.5 %) deaths

respectively (adjusted OR, 1.11; 95% CI, 0.81-1.52; P = 0.51).

Infection-related ventilator-associated complications were not significantly changed. Oral health dysfunction scores (using the Beck Oral Assessment Scale) were worse during the control phase indicating better oral health during the intervention 11.3 (3.9) vs. (10.5 (3.2); P < 0.023). There was no difference in mean (SD) procedural pain (CPOT) scores in the control period vs. intervention periods (2.34 vs. 2.29; P = 0.825)

Among 348 randomly observed oral care encounters, we identified a significant reduction in oral chlorhexidine use between control and intervention periods (61.3% vs. 0%; P < 0.0001). Delivery of 4 elements of the oral care bundle increased in the intervention phase: oral assessment, 12.6% vs. 46.3%, P < 0.0001; tooth brushing, 36.7% vs. 72.6%, P < 0.0001; oral moisturization, 49.3% vs. 100%, P < 0.0001; and lip care, 48.1% vs. 81.5%, P < 0.0001. No difference was noted for oral suctioning (94.3% vs. 89.4%; P = 0.1046). The mean duration of oral care per episode was longer in the intervention period compared to control: 4.5 minutes vs 3.7 minutes; P < 0.0005.

Completed qualitative data include 131 clinician interviews about the practice change comprising 62 baseline and 69 post-intervention interviews.

Implications
Our study comprises the largest prospective study of oral care in mechanically ventilated adults to date. The finding of no significant mortality difference between groups differs from that of recent meta-analyses reporting increased mortality in patients exposed to daily chlorhexidine oral care. Outcomes for practice include robust evidence supporting chlorhexidine de-adoption and implementation a comprehensive oral care bundle for improved oral health.

Alignment with NCOHR and CIHR priorities
This study represents a novel collaboration between interprofessional researchers, knowledge users, and patients to improve the oral care offered to critically ill Canadians. Diverse stakeholder involvement in this research aligns with Canada's patient-oriented research strategy by engaging stakeholders in research that is relevant to patients' concerns.

Adherence to study timeline
We experienced delays beyond the 14-month intervention period with respect to validating data at our participating sites for our primary outcome. Some of the delay emerges from the absence of dedicated site registry data collectors who maintain the database and would normally respond to data queries at each site. Our RA and statistician worked tirelessly to resolve this issue.

Knowledge translation (KT)
We have submitted our primary results manuscript to the Journal of the American Medical Association (JAMA). Qualitative process evaluation data will be published in a separate manuscript. Our KT materials include two videos: (1) oral care instruction and (2) patient touchpoints regarding the importance of oral care. These are available to our study partners as durable resources.

Budget
The majority of our budget was spent on study personnel as planned. The remainder was used for transcription services and printing educational material for our study sites.