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Middle turbinate resection is unlikely to cause empty nose syndrome in first year postoperatively

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ABSTRACT

Purpose: Empty nose syndrome (ENS) is characterized by nasal dryness, crusting, and paradoxical nasal obstruction most commonly after inferior turbinate resection. ENS has also been reported to occur after middle turbinate resection (MTR), and concern for causing ENS is a possible reason surgeons preserve the MT during endoscopic sinus surgery (ESS). The objective was to determine whether MTR during ESS led to ENS.

Materials and methods: This was a prospective case series of 95 consecutive patients that underwent bilateral subtotal MTR during ESS with either Draf IIB or Draf III frontal sinusotomies, for chronic rhinosinusitis with or without nasal polyps, and frontal sinus inverted papillomas. Demographic data and postoperative Empty Nose Syndrome 6-item Questionnaire (ENS6Q) scores were obtained. Nasal crusting was also documented on last postoperative nasal endoscopy.

Results: Pathologies included chronic rhinosinusitis with nasal polyps (69), without nasal polyps (12), and inverted papillomas (14). Fifty-six patients underwent subtotal MTRs during ESS with Draf IIB, and 39 with Draf III. Mean follow-up was 19.4 months (range 12–49). Mean postoperative ENS6Q score was 2.1. Only 2.1% had ENS6Q scores ≥ 11 , and 6.3% had nasal crusting at last follow-up. None of the patients with ENS6Q scores ≥ 11 had nasal crusting at last follow-up. There were no significant differences in outcomes between ages, genders, surgery types, or pathologies.

Conclusions: Patients who underwent bilateral subtotal MTR during ESS were unlikely to develop ENS by at least 1 year postoperatively, based on patients rarely experiencing ENS6Q scores ≥ 11 or persistent nasal crusting.

1. Introduction

Empty nose syndrome (ENS) was first described by Kern and Stenkvist in patients experiencing nasal dryness, crusting, and paradoxical nasal obstruction after partial or total inferior turbinate resection (ITR), despite having widely patent nasal cavities [1,2]. While ENS has also been reported after middle turbinate resection (MTR) [3,4], significantly less attention has been placed on ENS from MTR compared to ITR.

Diagnosing ENS is based largely on patient symptoms, as well as the cotton test in patients who have undergone turbinate surgery [4]. Velasquez et al. also validated the Empty Nose Syndrome 6-item Questionnaire (ENS6Q) to facilitate diagnosing ENS postoperatively. They

showed that patients with ENS6Q scores ≥ 10.5 had an increased likelihood of ENS, with high sensitivity and specificity of 86.7% and 96.6%, respectively [5]. Unfortunately, one cannot predict whether certain patients are predisposed to developing ENS after different degrees of ITR or MTR, due in part to an incomplete understanding of the condition.

ENS has been theorized to be a disorder of abnormal airflow and neurosensory function after nasal surgery [4,6–8]. With regard to abnormal neurosensory function, one theory relates to the function of transient receptor potential melastatin 8 (TRPM8) channels, concentrated in various locations throughout the nasal cavity. TRPM8 is the target receptor for menthol and is part of the nasal trigeminal thermal receptor pathway for perceiving patency amidst cool air [9–11]. A

Abbreviations: CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; ENS, empty nose syndrome; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; ESS, endoscopic sinus surgery; ITR, inferior turbinate resection; MTR, middle turbinate resection; TRPM8, transient receptor potential melastatin 8.

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decrease in nasal cooling receptor density and stimulation causes a sensation of decreased nasal patency and has been proposed as a possible mechanism of ENS after ITR [2–4,12,13]. Patients with ENS after IT reduction or resection have also been shown to exhibit lower (worse) menthol lateralization detection thresholds than normal patients, again suggesting aberrant neurosensory function [6–8]. Additionally, abnormal neural regeneration may cause trigeminal pathway dysfunction, which could explain how ENS can develop in a delayed fashion postoperatively [2–4]. Airflow alteration after turbinate surgery may also contribute to ENS [6–8], with nasal airway resistance decreasing, and nasal airflow increasing with less airflow turbulence [14]. This could lead to less nasal airflow warming and humidification, and the nasal dryness and crusting reportedly associated with ENS.

While the aforementioned theories are intriguing, the overwhelming majority of patients undergoing IT or MT surgery do not develop ENS [15,16]. While it is terribly unfortunate that a small proportion of patients develop ENS after turbinate surgery and suffer psychologically [17,18], most clinical studies have focused on ENS after IT surgery, rather than MTR [1,2,4,6,7]. Some patients have sinonasal inflammatory or neoplastic conditions that benefit from MTR during endoscopic sinonasal surgery, and multiple studies have demonstrated low rates of complications like intraoperative cerebrospinal fluid leaks, postoperative epistaxis, frontal sinusitis or mucocele, and ENS [15,19–24]. However, no prospective studies have assessed the likelihood of developing symptoms of ENS after MTR.

With low levels of evidence, uncertainty of whether MTR causes ENS could lead some surgeons to preserve the MT, even if MTR could improve patient outcomes. It would be helpful to determine whether patients undergoing MTR are at risk for developing ENS. The purpose of this prospective series was to determine whether bilateral MTR led to symptoms and endoscopic findings that could be consistent with ENS over at least the first year postoperatively.

2. Materials and methods

This was a prospective case series of 95 consecutive patients from July 2016 to January 2019. The study was approved by Henry Ford Health System's Institutional Review Board. Patients' pathologies included chronic rhinosinusitis with or without nasal polyps (CRSwNP and CRSsNP), and frontal sinus inverted papillomas. Patients with septal perforations were excluded. None of the patients had ENS preoperatively based on them having had no prior IT or MT surgery [1,2]. All CRS patients met symptomatic and objective criteria for CRS [25], and failed at least one 2-week course of oral antibiotics and steroids, as well as 1 month of topical intranasal corticosteroid sprays. All patients with CRSwNP and CRSsNP had partial to complete opacification of all sinuses on sinus computed tomography imaging. All patients underwent bilateral subtotal MTRs during endoscopic sinus surgery (ESS) or endoscopic sinus tumor resection, with either Draf IIB or Draf III frontal sinusotomies (Figs. 1 and 2) [26]. No IT surgery was performed in any patient.

Bilateral subtotal MTRs were performed for a variety of reasons. In CRS cases, MTR was performed to decrease the risk of postoperative MT lateralization and frontal outflow stenosis and to improve topical saline and drug delivery. For frontal sinus inverted papillomas, MTRs were performed during Draf III frontal sinusotomies to achieve complete tumor resections and optimize postoperative tumor surveillance (Fig. 2).

All MTRs were performed by one author (JRC). The first step involved using endoscopic scissors to make the initial cut through the superior portion of the vertical portion of the MT near the axilla of the MT. Cuts were then angled inferiorly away from the cribriform plate, until the vertical portion was released from its common lamella shared with the superior turbinate. The horizontal portion of the MT was then transected from its posterior attachment to the palatine bone, leaving approximately a 5-mm stump. The stump was cauterized with suction monopolar cautery. The MTR was then completed during the Draf IIB or

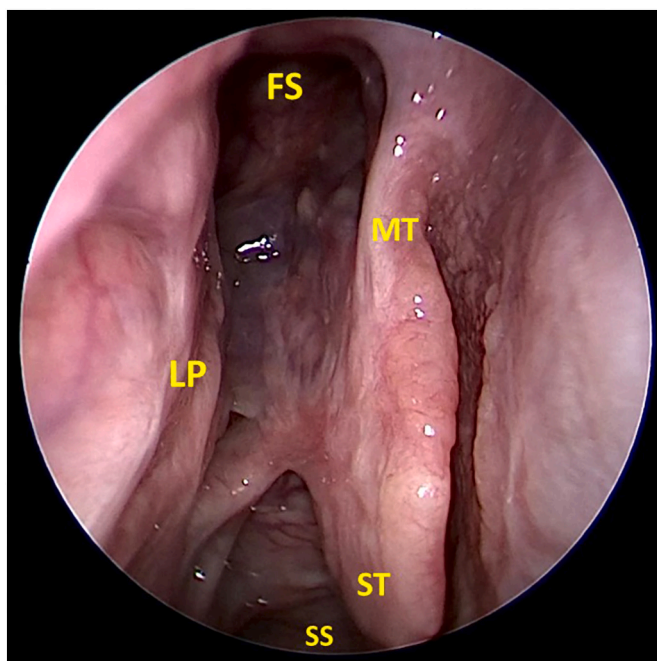


Fig. 1. Postoperative right-sided view after a complete endoscopic sinus surgery with Draf IIB frontal sinusotomy and subtotal middle turbinate resection. FS, frontal sinus; LP, lamina papyracea; MT, middle turbinate; SS, sphenoid sinus; ST, superior turbinate.

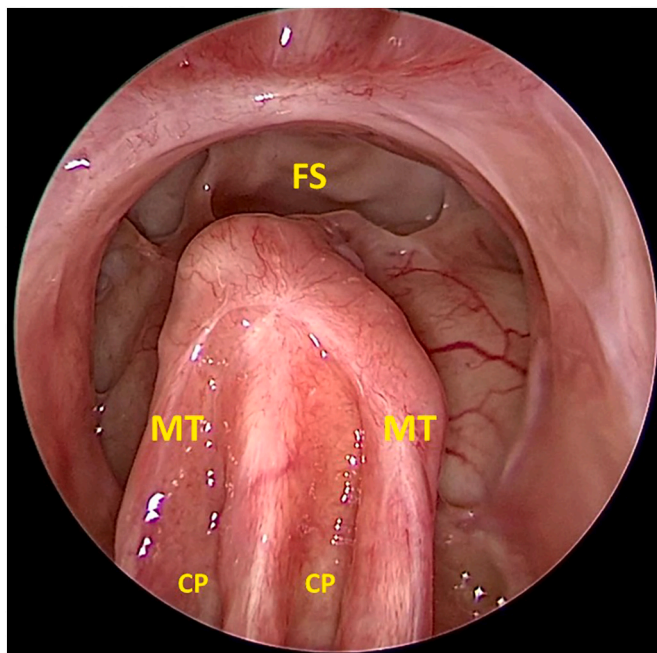


Fig. 2. Postoperative view of a Draf III frontal sinusotomy and bilateral subtotal middle turbinate resections. FS, frontal sinus; MT, middle turbinate; CP, cribriform plate.

III frontal sinusotomy, by removing the majority of the vertical portion of the MT superiorly to its insertion onto the frontal sinus floor. Note that at least 0.5–1 cm remnants of both the middle and superior turbinates were maintained along their insertions to the cribriform plates to maintain intraoperative landmarks and prevent cerebrospinal fluid leaks (Fig. 1).

Demographic data, postoperative Empty Nose Syndrome 6-item

Questionnaire (ENS6Q) scores, and nasal crusting at the last postoperative nasal endoscopy were collected prospectively. The percentage of patients with ENS6Q scores ≥ 11 was calculated, as these scores could be consistent with ENS [5]. Nasal crusting was defined as any removable crusting on any of the sinonasal mucosal surfaces. If patients had ENS6Q scores ≥ 11 , individual scores to the six questions in the questionnaire were reported. The aforementioned postoperative outcome measures were also compared between different genders, pathologies, Draf IIB versus Draf III frontal sinusotomies, and primary versus revision surgery.

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). Continuous variables were compared between 2-level groups using independent 2-group *t*-tests. Categorical variables were compared between groups using chi-square tests or Fisher's exact tests. Statistical significance was set at $p < 0.05$. A power analysis was also conducted to determine an appropriate sample size. Assuming an incidence of ENS of 1%, in order to detect a small effect size of 0.25, a two-group independent *t*-test would require 12,813 patients (127 with ENS and 12,686 without ENS) to achieve 80% power. As this sample size was deemed infeasible, the study was conducted with a sample size commensurate with previous studies.

3. Results

Table 1 demonstrates demographic and outcome measures data for the whole study population. Of the 95 patients, mean age was 56 years, and 59% were male. Mean overall follow-up was 19.4 months (range 12–49). Frequencies of different pathologies were as follows: CRSwNP (72.6%), CRSsNP (12.6%), and inverted papillomas (14.7%). Regarding frontal sinusotomies performed with subtotal MTRs, 56 patients underwent Draf IIB (59.0%), while 41 underwent Draf III (41.0%). Sixty-eight patients underwent primary surgery (67.4%), and 32 had revision surgery (32.6%). No intraoperative cerebrospinal fluid leaks

Table 1
Demographic and clinical data for the 95 patients who underwent bilateral subtotal MTRs.

	Means \pm SD or frequencies (n)
Age (years)	56.0 \pm 14.3
Gender	
Male	58.9% (56)
Female	41.1% (39)
Type of frontal sinusotomy	
Draf IIB	58.9% (56)
Draf III	41.1% (39)
Primary versus revision surgery	
Primary	67.4% (64)
Revision	32.6% (31)
Pathologies	
CRSwNP	72.6% (69)
CRSsNP	12.6% (12)
Inverted papilloma	14.7% (14)
ENS6Q (postoperative)	2.1 \pm 2.7
Proportions of patients with ENS6Q <11 or ≥ 11 (postoperative)	
ENS6Q <11	97.9% (93)
ENS6Q ≥ 11	2.1% (2)
Nasal crusting (postoperative)	
Absent	93.7% (89)
Present	6.3% (6)
Follow-up (months)	
Mean \pm SD	19.4 \pm 9.5
Range	12–49
12–23	72.6% (69)
24–35	17.9% (17)
36–47	8.4% (8)
48+	1.1% (1)

MTR, middle turbinate resection; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; SD, standard deviation.

occurred.

Mean postoperative ENS6Q score at last follow-up was 2.1 ± 2.7 , and 2.1% of patients had ENS6Q scores ≥ 11 . At last follow-up, 93.7% of patients had no crusting on nasal endoscopy. Neither of the 2 patients with ENS6Q ≥ 11 had nasal crusting at their last follow-up endoscopy. Table 2 demonstrates pathologies, frontal surgery types, follow-up durations, and scores to each of the 6 questions in the ENS6Q for the 2 patients with ENS6Q scores ≥ 11 .

Table 3 shows comparisons of the outcome measures between patients who underwent Draf IIB versus Draf III frontal sinusotomies, and primary versus revision surgeries. There were no significant differences between Draf IIB versus Draf III with regard to mean postoperative ENS6Q, proportions of patients with ENS6Q ≥ 11 , or nasal crusting at last follow-ups. Note that no Draf IIB patients, and 5.1% of Draf III patients had ENS6Q scores ≥ 11 ($p = 0.166$). With regard to primary versus revision surgeries, the mean ENS6Q of 1.7 ± 2.3 for primary surgery was lower than 2.9 ± 3.4 for revision surgery ($p = 0.043$). There were no significant differences in nasal crusting at last follow-ups between primary and revision surgeries (7.8% versus 3.2%, $p = 0.660$).

Table 4 demonstrates comparisons of outcome measures between genders and the different pathologies. When comparing between genders, there were no significant differences between males and females with regard to ENS6Q scores, or proportions of patients with ENS6Q ≥ 11 . Females did have more nasal crusting at last follow-up ($p = 0.041$). When comparing between different pathologies, there were no significant differences with regard to ENS6Q, proportion of patients with ENS6Q ≥ 11 , or nasal crusting. The proportions of patients with ENS6Q scores ≥ 11 in CRSwNP, CRSsNP, and sinus inverted papillomas, were 2.9%, 0%, and 0%, respectively ($p = 1.000$).

4. Discussion

ENS was first described in patients experiencing nasal crusting, dryness, and paradoxical nasal obstruction after partial or total ITR, despite having patent nasal cavities [1,2]. A 2006 case report described a patient who developed ENS after left subtotal MTR during ESS, without IT surgery [3]. That patient underwent a left septal submucoperichondrial acellular dermal implant to mimic the lost MT tissue volume, and his symptoms improved [3]. Since that case report, little evidence has supported MTR causing ENS, and no prospective studies have assessed the occurrence of ENS after MTR. Tan et al. published a retrospective cohort study comparing 93 patients with partial MTR to 84 patients with MT preservation during ESS. Based on telephone surveys, they showed that 10% of all patients had postoperative ENS6Q scores ≥ 11 , with no differences between MTR and MT preservation groups. They concluded that partial MTR did not cause ENS in patients undergoing ESS for CRS [15].

Zhao and colleagues have published multiple studies using computational fluid dynamics (CFD) modeling to study ENS pathophysiology after turbinate surgery, though mostly for IT surgery. Li et al. studied 27 ENS patients who underwent at least IT reductions, and 2 patients underwent total MTRs. ENS patients exhibited airflow trajectories concentrated toward the middle meatus, as opposed to normal patients with airflow distributed more evenly along the entire nasal cavity. However, the sample size was too small to assess airflow dynamics after isolated MTR [7]. Maza et al. compared airflow patterns after MTR during endoscopic skull base surgery between 2 patients with ENS, and 2 patients without ENS. They also demonstrated ENS patients having airflow trajectories directed at the middle meatus rather than along the inferior turbinates [8], similar to Li et al. [7]. Based on these CFD studies, turbinate surgery may cause ENS in patients with middle meatal airflow trajectories. However, since the majority of patients undergoing IT and MT surgery do not develop ENS [4,16,27,28], more clinical research is necessary to understand ENS pathophysiology.

The current study demonstrated that bilateral subtotal MTRs were unlikely to cause ENS by at least the first year postoperatively, based on

Table 2

Patient factors and scores for individual questions on the ENS6Q for the patients with ENS6Q scores ≥ 11 .

Patients	Patient factors in those with ENS6Q ≥ 11		ENS6Q Items					
	Pathology and frontal surgery type	Follow-up duration (months)	Dryness	Sense of diminished airflow	Suffocation	Nose feels too open	Nasal crusting	Nasal burning
1	CRSwNP, Draf III	46	1	4	1	1	2	2
2	CRSwNP, Draf III	27	3	4	2	0	5	1

CRSwNP, chronic rhinosinusitis with nasal polyps; ENS6Q, Empty Nose Syndrome 6-item Questionnaire.

Table 3

Comparisons of the outcome measures between patients who underwent Draf IIB versus Draf III frontal sinusotomies, and primary versus revision surgery.

	ESS + Draf IIB	ESS + Draf III	p-Value	Primary ESS	Revision ESS	p-Value
Postoperative ENS6Q (mean \pm SD)	1.8 \pm 2.3	2.5 \pm 3.2	0.185	1.7 \pm 2.3	2.9 \pm 3.4	0.043
ENS6Q <11 or ≥ 11						
ENS6Q <11	100% (56)	94.9% (37)	0.166	98.4% (63)	96.8% (30)	0.548
ENS6Q ≥ 11	0% (0)	5.1% (2)		1.5% (1)	3.2% (1)	
Nasal crusting						
Absent	92.9% (52)	94.9% (37)	1.000	92.2% (59)	96.8% (30)	0.660
Present	7.1% (4)	5.1% (2)		7.8% (5)	3.2% (1)	

ENS6Q, Empty Nose Syndrome 6-item Questionnaire; ESS, endoscopic sinus surgery; SD, standard deviation.

Significant p-values are bolded.

low mean postoperative ENS6Q scores, very low rates of patients with ENS6Q scores ≥ 11 , and low nasal crusting rates. This was true regardless of gender, inflammatory versus neoplastic pathologies, Draf IIB versus III frontal sinusotomies, and primary versus revision surgery.

There are some important points to consider in the 2 patients who may have developed ENS based on having ENS6Q scores ≥ 11 . Both patients had CRSwNP, underwent Draf IIIs during their ESSs, and had relatively long follow-up periods (46 and 27 months). Larger future studies will be important to determine whether Draf III increases the chance of ENS after MTR, and whether such follow-up durations are necessary to detect ENS. There are also some points that bring into question whether these patients truly had ENS. Since both patients had CRSwNP, they could have had sinonasal symptoms that directly affected their ENS6Q scores. For example, both patients scored 4/5 on “sense of diminished airflow,” which could have been more representative of their underlying disease, rather than from ENS. They also both scored low on feelings of suffocation, nose feeling too open, and nasal burning. Measuring ENS6Q changes after medical therapy could have been helpful in determining whether patients’ higher ENS6Q scores were due

to their underlying CRSwNP rather than ENS, and this could be considered in future studies.

There are multiple reasons MTR could be less likely to cause ENS compared to ITR. First, histopathologically, the MT has fewer sinusoidal capacitance vessels and contributes less to regulation of nasal airway resistance than the IT [29]. Therefore, MTR should cause less of a decrease in nasal airway resistance compared to ITR and a lower chance of paradoxical nasal obstruction. In a CFD study by Dayal et al., 20 CFD airflow simulations were created after virtual total ITR and MTR (10 CFD simulations for each turbinate surgery type). They showed that after total MTR, while nasal heating and humidification decreased, the decrease was not as significant as with total ITR. Importantly, total MTR did not result in a significant change in surface area stimulated by mucosal cooling, whereas total ITR did [14]. This suggested that nasal airflow conditioning should remain functional after total MTR, as long as the ITs are intact.

While debate will continue with regard to MTR causing ENS, physicians should be aware that there has been a preponderance of clinical benefit with MTR [15,19,21,30–41], with low intraoperative and postoperative risks [15,19,24,32,35,42].

Limitations with this study also deserve mention. First, there was no comparison made to MT preservation surgery, and preoperative ENS6Q scores were not included. While these factors would have strengthened the study’s findings that MTR was unlikely to cause ENS, this prospective series provided valuable preliminary data for future studies. Second, while the 95 patient sample size was comparable to the number of partial MTRs reported by Tan et al. [15], the study was still underpowered. While the incidence of ENS after turbinate surgery is unknown, it is presumably $\leq 1\%$, and therefore obtaining an adequate sample size to achieve statistical power will be challenging, if not impossible. The follow-up duration was also potentially too short to detect ENS, since previous reports have reported it occurring years after surgery [2]. However, the literature is unclear on this point, and future studies would be helpful to determine how likely ENS is to develop after the first year postoperatively. Another point of criticism could be that cotton tests were not performed in the 2 patients with ENS6Q scores ≥ 11 . However, the cotton test has not been validated for detecting ENS after MTR, and its utility in this scenario requires further study. Lastly, it would have been beneficial to analyze psychological comorbidities in patients preoperatively and postoperatively, as multiple studies have demonstrated significant psychological disturbances in ENS patients [17,18].

Table 4

Comparisons of the outcome measures between male versus female genders, and the different pathologies.

	Male	Female	p-Value	CRSwNP	CRSSNP	Sinus IP	p-Value
Postoperative ENS6Q (mean \pm SD)	2.3 \pm 3.1	1.8 \pm 2.2	0.414	2.2 \pm 2.9	2.7 \pm 2.9	0.9 \pm 1.3	0.194
ENS6Q <11 or ≥ 11							
ENS6Q <11	96.4% (54)	100% (39)	0.511	97.1% (67)	100% (12)	100% (14)	1.000
ENS6Q ≥ 11	3.6% (2)	0% (0)		2.9% (2)	0% (0)	0% (0)	
Nasal crusting							
Absent	98.2% (55)	87.2% (34)	0.041	92.8% (64)	91.7% (11)	100% (14)	0.652
Present	1.8% (1)	12.8% (5)		7.3% (5)	8.3% (1)	0% (0)	

CRSSNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; ENS6Q, Empty Nose Syndrome 6-item Questionnaire; IP, inverted papilloma; SD, standard deviation.

Significant p-values are bolded.

5. Conclusion

Patients who underwent bilateral subtotal MTR during ESS were unlikely to develop ENS by at least 1 year postoperatively, based on patients rarely experiencing ENS6Q scores ≥ 11 or persistent nasal crusting.

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CRedit authorship contribution statement

Richard H. Law: Conceptualization, Methodology, Data curation, Writing-original draft preparation, Editing.
Abdelwahab M. Ahmed: Data Curation, Writing-original draft preparation, Editing.
Meredith Van Harn: Conceptualization, Methodology, Data curation, Formal analysis, Writing-reviewing and editing.
John R. Craig: Conceptualization, Methodology, Supervision, Writing-reviewing and editing.

Declaration of competing interest

None.

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