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RESEARCH ARTICLE

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Natural spring water gargle samples as an alternative to nasopharyngeal swabs for SARS-CoV-2 detection using a laboratory-developed test

Sarah Gobeille Paré[1] | Julie Bestman-Smith[1,2] | Judith Fafard[3,4] | Florence Doualla-Bell[3] | Marième Jacob-Wagner[2] | Christian Lavallée[4,5,6] | Hugues Charest[3,4] | Stéphanie Beauchemin[5] | François Coutlée[4,5] | Jeannot Dumaresq[1,7] | Lambert Busque[5] | Manon St-Hilaire[5] | Guylaine Lépine[5] | Valérie Boucher[8] | Marc Desforges[4,9] | Isabelle Goupil-Sormany[10] | Annie-Claude Labbé[4,5,6] | G-SPIT study group

[1]Département de microbiologie-infectiologie et d'immunologie, Faculté de Médecine, Université Laval, Québec, Québec, Canada

[2]Département de microbiologie et d'infectiologie du Centre hospitalier universitaire (CHU) de Québec, Québec, Québec, Canada

[3]Laboratoire de santé publique du Québec, Institut national de santé publique du Québec, Sainte-Anne-de-Bellevue, Québec, Québec, Canada

[4]Département de microbiologie, infectiologie et Immunologie, Université de Montréal, Montréal, Québec, Canada

[5]Département des laboratoires de biologie médicale, Grappe Optilab-CHUM, Centre hospitalier de l'Université de Montréal, Montréal, Québec, Canada

[6]Service de maladies infectieuses, CIUSSS de l'Est-de-l'Île-de-Montréal, Montréal, Québec, Canada

[7]Département de microbiologie et d'Infectiologie, CISSS de Chaudière-Appalaches, Lévis, Québec, Canada

[8]Centre de recherche du CHU de Québec-Université Laval, Québec, Canada

[9]Département clinique de médecine de laboratoire, CHU Ste-Justine, Montréal, Québec, Canada

[10]Direction de la vigie sanitaire, Ministère de la Santé et des Services sociaux du Québec, Québec, Québec, Canada

Correspondence
Annie-Claude Labbé, Service de maladies infectieuses, Hôpital Maisonneuve-Rosemont, 5415 Assomption, Montréal, QC H2J 3Y4, Canada.
Email: ac.labbe@umontreal.ca

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Abstract

The objective of this study was to validate the use of spring water gargle (SWG) as an alternative to oral and nasopharyngeal swab (ONPS) for SARS-CoV-2 detection with a laboratory-developed test. Healthcare workers and adults from the general population, presenting to one of two COVID-19 screening clinics in Montréal and Québec City, were prospectively recruited to provide a gargle sample in addition to the standard ONPS. The paired specimens were analyzed using thermal lysis followed by a laboratory-developed nucleic acid amplification test (LD-NAAT) to detect SARS-CoV-2, and comparative performance analysis was performed. An individual was considered infected if a positive result was obtained on either sample. A total of 1297 adult participants were recruited. Invalid results ($n = 18$) were excluded from the analysis. SARS-CoV-2 was detected in 144/1279 (11.3%) participants: 126 from both samples, 15 only from ONPS, and 3 only from SWG. Overall, the sensitivity was 97.9% (95% CI: 93.7–99.3) for ONPS and 89.6% (95% CI: 83.4–93.6; $p = 0.005$) for SWG. The mean ONPS *cycle threshold* (C_t) value was significantly lower for the concordant paired samples as compared to discordant ones (22.9 vs. 32.1;

$p < 0.001$). In conclusion, using an LD-NAAT with thermal lysis, SWG is a less sensitive sampling method than the ONPS. However, the higher acceptability of SWG might enable a higher rate of detection from a population-based perspective. Nonetheless, in patients with a high clinical suspicion of COVID-19, a repeated analysis with ONPS should be considered. The sensitivity of SWG using NAAT preceded by chemical extraction should be evaluated.

KEYWORDS
COVID-19, diagnosis, gargle, PCR, SARS-CoV-2

1 | INTRODUCTION

The SARS-CoV-2 epidemic that reached the province of Québec at the end of February 2020 mobilized the healthcare network in an unprecedented way. The Laboratoire de santé publique du Québec (LSPQ) rapid development of an in-house nucleic acid amplification test (NAAT) based on Corman and colleagues,[1] followed by the deployment of a dozen of commercial platforms allowed Québec's laboratory network to offer over 39 000 daily tests during the study period.[2]

The exponential increase of COVID-19 cases during the second and third epidemic waves has put a strain on the healthcare system. To meet the increased testing demands, a number of strategies had to be implemented to maintain mass-scale testing. These strategies had to consider the acceptability and cost of the sampling methods, and especially the performance of self-collected samples compared to collection methods by professionals.

The oral and nasopharyngeal swab (ONPS), the most recommended sample collection method for the detection of SARS-CoV-2, remains invasive and requires trained professionals.[3] Less invasive and self-collected specimens, such as saliva or gargle, have been proposed for COVID-19 diagnostic purposes. Systematic reviews on the sensitivity of SARS-CoV-2 testing using saliva revealed a good sensitivity as well as important drawbacks limiting its use, such as specimen viscosity and the inability of some individuals to produce sufficient quantity for testing.[4–6] There have been less publications using gargle as an alternative specimen for SARS-CoV-2 diagnostic.[7–12] Gargles has some advantages over saliva for people who cannot produce or spit out saliva and for the processing of viscous saliva samples that require dilution before processing. However, the limited number of gargle samples studied, and the exclusive use of a saline solution for gargling, a compound incompatible with at least one commercial assay performed in our jurisdiction,[13] required further investigations before large-scale use.

2 | OBJECTIVE

To compare the sensitivity of the SARS-CoV-2 LSPQ-developed NAAT, preceded by thermal lysis, using spring water gargle (SWG) and ONPS.

3 | MATERIALS AND METHODS

3.1 | Study population

The present study was part of the G-SPIT multicenter project comparing the performance of SWG for SARS-CoV-2 detection on various NAAT platforms, in a population at high risk to be infected with SARS-CoV-2. In this substudy, adults presenting at two COVID-19 walk-in clinics in Québec city (healthcare workers; HCW) and Montréal (HCW and general population) for routine testing were eligible to participate if they had a recent contact or symptoms compatible with COVID-19.

3.2 | Sample collection

First, an ONPS was collected by a trained HCW by swabbing the posterior oropharynx and inserting the same flexible swab through one nostril, and rotating for 5–10 s before removing.[14,15] The swab was transported in 3 ml of molecular water (RNase/DNase free). Participants were asked not to eat, drink, or smoke for 15 min before collecting the SWG. They were handed a flexible cup with 5 ml of natural spring water (ESKA®) and were told to rinse their mouth and their throat for a total of 20 s (5 s in the mouth, 5 s in the throat, 5 s in the mouth, 5 s in the throat) and then to spit as much as possible in the initial cup. The content of the cup was emptied into a 15 ml conical tube and sent with the ONPS to the designated laboratory for processing and testing: in Québec City, at the CHU de Québec-Université Laval (CHUQ); in Montréal, at the Hôpital Maisonneuve-Rosemont (HMR). The samples were stored at 4°C and tested within 24–48 h according to the regular laboratory workflow.

3.3 | SARS-CoV-2-detection by NAAT

SARS-CoV-2 testing was performed using an in-house laboratory-developed (LD)-NAAT test targeting the structural protein envelope *E* gene.[1,16] Although the same SARS-CoV-2 primers and probes were used (TaqPath 1-Step Multiplex NO ROX; ThermoFisher Scientific cat no. A28523), the protocols in both laboratories differed in some

aspects. At the CHUQ, 25 µl of the sample were first diluted with 25 µl of RNase-free water containing proteinase K (PK) (Qiagen cat n°19133; 200 µg/ml final concentration) and heated at 56°C for 10 min; at HMR, 50 µl of undiluted sample was used directly. Thermal lysis was performed on a thermal cycler: 90°C for 2 min (CHUQ) or 1 min (HMR), after which microwell plates were placed on a cooling bloc for at least 2 min. Five microliters were then added to 15 µl of SARS-CoV-2 master mixture including human internal controls primers and probes: RNase P at the CHUQ (Forward: AGATTTGGACCTGCGAGCG, Reverse: GAGCGGCTGTCTCCACAAGT, and probe 5ATTO647TTCTGACCTGAAGGCTCTGCGCG 3IAbRQSp) or beta-actin at HMR (Forward: GCGAGAAGATGACCCAGATC, Reverse: CCAGTGGTACGGCCAGAGG, and probe 5′- HEX-CC AGC CAT G/ZEN/T ACG TTG CTA TCC AGG C- IABkFQ-3′).[16]

Thermal cycling, performed on a Roche LightCycler 480 II instrument (Roche) at the CHUQ and on a QuantStudio™ 6 Real-Time PCR System (Thermo Fisher) at HMR, included a reverse transcription step 53°C/10 min, a denaturation step 95°C/2 min, 45 amplification cycles 95°C/15 s–60°C/30 s and a cooling step 40°C/30 s. Gene amplifications were analyzed by ATTO647 (IC) and FAM (E gene) fluorophores.

SARS-CoV-2 was considered positive when cycle threshold (C_t) values were ≤37 and negative beyond 37 or without amplification of the target. A result was deemed invalid in the absence of amplification of the internal control.

At the CHUQ, sample pairs were also tested by the same LD-NAAT after chemical extraction using MagNA Pure with the FLOW Solution (Roche Molecular Diagnostics). At HMR, a subset of sample pairs was tested by one of two commercial molecular assays: the Simplexa™ COVID-19 Direct (DiaSorin Molecular LLC), which is CE-approved on saliva samples for SARS-Cov-2 detection,[17] and the cobas® SARS-CoV-2 test (Roche Molecular Diagnostics).[15]

3.4 | Questionnaire

Participants were asked to answer few questions: age, contact with COVID-19, presence, and duration of COVID-19 symptoms.

3.5 | Statistical analysis

In the absence of a gold standard for SARS-CoV-2 NAAT, data were first analyzed using a contingency table to assess the positive percent agreement (PPA), negative percent agreement (NPA), overall percent agreement (OPA), and κ statistics,[18] with 95% confidence intervals (CIs) calculated. The clinical sensitivity of the assay on ONPS and SWG samples was calculated using the exact Clopper–Pearson test based on infection status: a participant was considered infected if a positive result was obtained from either the ONPS or the SWG. This reference standard was chosen because no current gold standard exists and false-negative nasopharyngeal swab (NPS) NAAT results have been reported.[19–21] Differences in clinical sensitivity were calculated using the McNemar test. Differences in C_t values (delta C_t [$\Delta C_t = C_{tSWG} - C_{tONPS}$]) were assessed using the Wilcoxon sign rank test. Statistical analyses were done using Stata® 16 (StataCorp LLC). Figures were produced using Prism 9 (GraphPad Software).

3.6 | Ethics

The study received ethical approval from the review boards of each participating institution. Verbal informed consent was obtained from each participant.

4 | RESULTS

4.1 | LD-NAAT results and agreement between sample types

Between November 19 and December 14, 1297 participants provided paired samples. As shown in Table 1, invalid results were obtained for 18 samples, leaving 1279 valid pairs for analysis. Of the 144 positive paired samples, a concordant result (positive on both ONPS and SWG) was obtained in 126 pairs, while a positive result only on ONPS was obtained in 15 pairs, and only on SWG in three pairs. The PPA was 89.4% (95% CI: 83.1–93.9) and the overall agreement was excellent, as reflected by a κ value of 0.93 (95% CI: 0.89–0.96).

TABLE 1 Detection of SARS-CoV-2 RNA in ONPS and SWG, using an LD-NAAT (n = 1297)

Results				Agreement (95%CI)			
	ONPS						
SWG	+	−	INV	PPA	NPA	OPA	κ
+	126	3	0	89.4	99.7	98.6	0.93
−	15	1135	12	(83.1–93.9)	(99.2–100)	(97.8–99.2)	(0.89–0.96)
INV	0	6	0				

Note: PPA (positive percent agreement): proportion of positive ONPS results paired with positive SWG results; NPA (negative percent agreement): proportion of negative ONPS results paired with negative SWG results; OPA (overall percent agreement): proportion of concordant results (positive ONPS and positive SWG, or negative ONPS and negative SWG) among all results

Abbreviations: CI, confidence interval; INV, Invalid; LD-NAAT: laboratory-developed nucleic acid amplification test; ONPS, oronasopharyngeal swab; SWG, spring water gargle.

4.2 | Characteristics of study participants and prevalence of SARS-CoV-2 infection

Mean age was 36.5 (range: 18–78), 80.1% had symptoms compatible with COVID-19 and 29.9% reported contact with a known case of COVID-19 (Table 2). Among the 1197 individuals for whom the information was available for both symptoms and contact history, 179 (15.0%) reported both. The median duration between symptom onset and sampling was 2 days (interquartile range: 1–3 days; $n = 864$). Symptomatic participants recruited in Québec City sought COVID-19 screening earlier than those in Montréal (mean of 1.9 vs. 3.2 days; $p < 0.001$).

A total of 144 (11.3%) participants were considered infected. Prevalence was six times higher among participants recruited in Montréal (112/468; 23.9%) than in those recruited in Québec city (32/811; 4.0%). Individuals reporting symptoms were eight times more likely to get a positive result (13.6% vs. 1.6%).

4.3 | LD-NAAT clinical sensitivity, overall and by participants' characteristics, according to sample types

As detailed in Table 3, the global clinical sensitivity of the LD-NAAT from SWG (89.6% [95% CI: 83.4–93.6]) was significantly lower compared to the ONPS (97.9% [95% CI: 93.7–99.3]; $p = 0.005$). Differences in sensitivity varied widely across the different subgroups (city, age, history of contact or symptoms compatible with COVID-19). When symptomatic participants were further subdivided according to the duration of symptoms, ONPS and SWG sensitivity was similar among participants ($n = 566$; prevalence 12.9%) whose symptoms started less than 3 days before testing (95.9% [95% CI: 87.8–98.7] versus 93.2% [95% CI: 84.4–97.2]; $p = 0.48$), while the difference reached 35.7% (100% [95% CI: 76.8–100]) versus (64.3% [95% CI: 35.0-85.7]; $p = 0.02$) among those whose symptoms started at least seven days before testing ($n = 51$; prevalence 27.5%).

TABLE 2 Characteristics of the study population ($N = 1279$) and prevalence of SARS-CoV-2 infection*

	Québec city	Montréal	Total
Age (years) ($n = 1279$)			
18–29	15/299 (5.0)	23/122 (18.9)	38/421 (9.0)
30–49	13/427 (3.0)	56/235 (23.8)	69/662 (10.4)
≥50	4/85 (4.7)	33/111 (29.7)	37/196 (18.9)
Contact ($n = 1222$)			
Yes	15/251 (6.0)	41/114 (36.0)	56/365 (15.3)
No	14/514 (2.7)	66/343 (19.2)	80/857 (9.3)
Symptoms ($n = 1241$)			
Yes	29/558 (5.2)	106/436 (24.3)	135/994 (13.6)
No	3/226 (1.3)	1/21 (4.8)	4/247 (1.6)
Duration of symptoms (days) ($n = 864$)			
0-2.9	25/347 (7.2)	48/219 (21.9)	73/566 (12.9)
3.0-6.9	3/70 (4.3)	45/177 (25.4)	48/247 (19.4)
≥7.0	1/11 (9.1)	13/40 (32.5)	14/51 (27.5)
Total	32/811 (4.0)	112/468 (23.9)	144/1279 (11.3)

*Data are expressed as no. (%) of participants.

4.4 | Agreement between the thermal lysis LD-NAAT and comparative assays

Agreement with the three comparator assays was excellent, as expressed with κ values varying from 0.93 to 0.96 (Table 4). The LD-NAAT detected more positive SWG samples after chemical extraction than when thermal lysis was used (PPA 87.9%; 95% CI: 71.0–95.6). All 18 SWG samples that were positive with the Simplexa™ COVID-19 Direct assay were also positive with the thermal lysis LD-NAAT. When compared with the cobas® SARS-CoV-2 test, the PPA for SWG samples was 90.7% (95% CI: 82.3–95.3). Mean comparator C_t values was significantly higher on discordant SWG samples (thermal lysis LD-NAAT negative/comparator positive) than on concordantly positive SWG samples: 32.5 versus 27.6 ($p = 0.04$) for the LD-NAAT preceded by chemical extraction, and 34.8 versus 27.9 ($p < 0.001$) for the cobas® SARS-CoV-2 test.

4.5 | Analytical comparisons of LD-NAAT between ONPS and SWG

As illustrated in Figure 1, mean C_t value for positive samples was lower for ONPS (23.9; standard deviation [SD] ± 5.5) than for SWG samples (29.7; SD ± 3.9; $p < 0.001$). The ΔC_t between the two sample types varied considerably (−7.5 to 15.3), with a mean ΔC_t among concordant positive samples of 6.7 (SD ± 4.6). Mean ONPS C_t value was significantly lower for concordant paired samples (paired SWG also positive) as compared to discordant ones (paired SWG negative): 22.9 vs. 32.1; $p < 0.001$. The distribution of ONPS and SWG C_t values is depicted in Figure 2, showing a bimodal curve for ONPS but not for SWG.

5 | DISCUSSION

This study demonstrates that SWG is a less sensitive sampling method than ONPS to diagnose SARS-CoV-2 when used with thermal lysis and LD-NAAT in a COVID-19 high-risk population. When symptomatic participants were stratified according to the duration of their symptoms, the difference in sensitivity between the SWG and

TABLE 3 Clinical sensitivity of the LD-NAAT according to participant characteristics and sample types

	Results			Sensitivity* (95% CI)		
		ONPS				
	SWG	+	−	ONPS	SWG	Difference (95% CI) *p* value**
Total	+	126	3	97.9% (93.7–99.3)	89.6% (83.4–93.6)	8.3% (2.0–14.6)
	−	15	1135			*p* = 0.005
City						
Montréal	+	99	1	99.1% (93.8–99.9)	89.3% (82.0–93.9)	9.8% (2.9–16.8)
	−	12	356			*p* = 0.002
Québec	+	27	2	93.8% (77.2–98.5)	90.6% (73.7–97.1)	3.1% (−13.7 to 19.9)
	−	3	779			*p* = 0.65
Age (years)						
18–29	+	30	2	94.7% (80.5–98.7)	84.2% (68.4–92.9)	10.5% (−6.3 to 27.4)
	−	6	383			*p* = 0.16
30–49	+	63	1	98.6% (90.1–99.8)	92.8% (83.5–97.0)	5.8% (−2.5 to 14.1)
	−	5	593			*p* = 0.10
≥50	+	33	0	100% (97.7–100)	89.2% (73.8–96.0)	10.8% (−1.9 to 23.5)
	−	4	159			*p* = 0.05
Contact						
Yes	+	47	1	98.2% (87.9–99.8)	85.7% (73.6–92.8)	12.5% (0.7–24.3)
	−	8	309			*p* = 0.02
No	+	71	2	97.5% (90.4–99.4)	91.3% (82.6–95.8)	6.3% (-2.2 to 14.7)
	−	7	777			*p* = 0.10
Symptoms						
Yes	+	119	3	97.8% (93.3–99.3)	90.4% (84.1–94.4)	7.4% (1.0–13.8)
	−	13	859			*p* = 0.01
No	+	2	0	100% (40.0–100)	50.0% (4.0–96.0)	50.0% (-24.0 to 124)
	−	2	243			*p* = 0.16
Duration of symptoms (days)						
0–2.9	+	65	3	95.9% (87.8–98.7)	93.2% (84.4–97.2)	2.7% (−6.2 to 11.7)
	−	5	493			*p* = 0.48
3.0–6.9	+	45	0	100% (92.6–100)	93.8% (81.9–98.0)	6.3% (-2.7–15.2)
	−		199			*p* = 0.08
≥7.0	+	9	0	100% (76.8–100)	64.3% (35.0–85.7)	35.7% (3.5–68.0)
	−	5	37			*p* = 0.03

Abbreviations: CI, confidence interval; LD-NAAT: laboratory-developed nucleic acid amplification test; ONPS, oronasopharyngeal swab; SWG, spring water gargle.

*A participant is considered infected by SARS-CoV-2 when at least one of the two paired samples (ONPS or SWG) is positive. This infection status is used to estimate sensitivity, assuming 100% specificity for both samples.

**McNemar test.

TABLE 4 Agreement between the thermal lysis LD-NAAT and other assays, by sample type

		Thermal lysis LD-NAAT		Agreement (95% CI)			
				PPA	NPA	OPA	κ
LD-NAAT preceded by chemical extraction (n = 809)							
		ONPS +	ONPS −				
ONPS	+	30	5	85.7% (69.2–94.1)	100% (99.5–100)	99.4% (98.6–99.8)	0.93 (0.85–0.99)
	−	0	774				
		SWG +	SWG −				
SWG	+	29	4	87.9% (71.0–95.6)	100% (99.5–100)	99.5% (98.7–99.9)	0.93 (0.86–1.00)
	−	0	776				
Simplexa™ COVID-19 Direct (n = 75)							
		ONPS +	ONPS −				
ONPS	+	20	1	95.2% (70.2–99.4)	98.1% (87.5–99.7)	97.3% (90.7–99.7)	0.93 (0.73–0.99)
	−	1	53				
		SWG +	SWG −				
SWG	+	18	0	100% (93.7–100)	98.2% (88.1–99.8)	98.7% (92.8–100)	0.96 (0.76–0.96)
	−	1	56				
cobas® SARS-CoV-2 test (n = 358)							
		ONPS +	ONPS −				
ONPS	+	87	3	96.7% (90.0–98.9)	99.3% (97.0–99.8)	98.6% (96.8–100)	0.96 (0.90–0.99)
	−	2	266				
		SWG +	SWG −				
SWG	+	78	8	90.7% (82.3–95.3)	100% (98.7–100)	97.8% (95.6–99.0)	0.94 (0.88–0.94)
	−	0	272				

Note: PPA (positive percent agreement): proportion of positive thermal lysis LD-NAAT samples, among positive comparative assay samples; NPA (negative percent agreement): proportion of negative thermal lysis LD-NAAT samples, among negative comparative assay samples; OPA (overall percent agreement): proportion of concordant results (positive thermal lysis LD-NAAT and positive comparative assay, or negative thermal lysis LD-NAAT and negative comparative assay) among all results

Abbreviations: CI: confidence interval; LD-NAAT: laboratory-developed nucleic acid amplification test; ONPS, oronasopharyngeal swab; SWG, spring water gargle.

ONPS sampling methods was statistically significant only for the group of subjects sampled at least 7 days after symptom onset. This is consistent with other studies on alternative sampling methods showing that the assay can fail to detect RNA when viral shedding diminishes.[19,22–24] This needs to be considered when investigating an outbreak with backward tracing, as ONPS might be a better alternative in these circumstances. However, the loss of sensitivity of SWG after the first week of symptom onset might be mitigated by the fact that this population is likely to be less contagious at the time of sampling.[25–27]

The larger difference in sensitivity observed in Montréal (9.8%) than in Québec city (3.1%) is intriguing. It could be due, at least in part, to differences in positivity rate and characteristics of the study population. For example, the symptomatic HCW recruited in Québec city had symptoms for a shorter period of time before sampling compared to symptomatic participants in Montréal (Table 2). Another possibility would be the use of proteinase K (PK) in the CHUQ protocol. Indeed, some studies suggested that pretreatment of samples with PK increased the sensitivity of direct rRT-PCR for SARS-CoV-2 detection,[28,29] particularly in low positive samples with high C_t values.[13] It has been suggested that PK could degrade or inactivate RNAses, allowing to purify a better quality of RNA.[30] Another study showed that sputum specimens pretreated with PK for homogenization before nucleic acid extraction for RT-PCR had a higher

detection rate than those pretreated with saline only. The authors suggested this could be because PK is able to digest mucous protein, resulting in an increased concentration of extracted RNA.[31] Although SWG specimens are less mucous than sputum, they may have benefited from PK pretreatment.

Although the ΔC_t between the ONPS and the SWG was variable among the concordant positive samples, it was mostly in favor of the ONPS. Again, this suggests a lower amount of SARS-CoV-2 RNA in SWG compared to ONPS, which would explain the loss of clinical sensitivity of SWG among samples with a low viral load. Indeed, the vast majority of false-negative SWG were paired with high C_t-value ONPS samples (Figure 2). The analysis of SWG samples using more sensitive NAAT platforms or using several primer pairs might mitigate this loss of clinical sensitivity. Nonetheless, in patients with a high clinical suspicion of COVID-19 and a negative SARS-CoV-2 screening result on SWG, a repeated analysis with ONPS should be considered. In the province of Québec, automated messages included in negative reports suggest repeat testing if symptoms do not resolve by themselves after 48 h. From a population-based perspective, being non-invasive, the higher acceptability of SWG might compensate for the loss of sensitivity and enable a higher rate of detection in symptomatic individuals and contacts of infected persons.

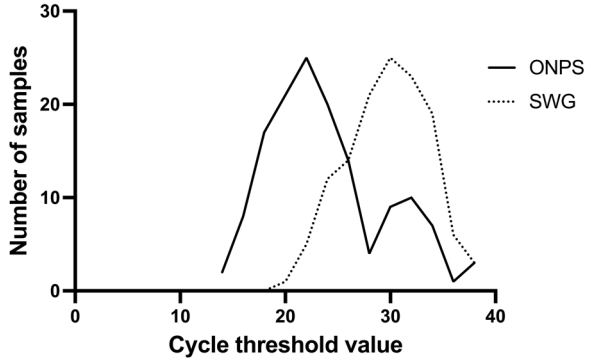

FIGURE 1 Distribution of cycle threshold (C_t) values according to specimen type. ONPS, oronasopharyngeal swab (n = 141); SWG, spring water gargle (n = 129)

The results of this study are important because they differ from others reported in the literature. Goldfarb et al.[7] and Kandel et al.[32] reported that gargling performance was superior or similar to HCW-collected NPS. Differences between studies could account for this discrepancy. First, there was a smaller number of positive paired samples in those previous studies, resulting in a lower power (decreased ability to detect any difference). The gargling procedure included a supplementary mouth and throat cycle, which might have increased the amount of viral RNA collected and thus, the sensitivity of the gargle samples. In addition, the comparator used in those studies was an NPS, which might be slightly less sensitive than the combined ONPS we used. A small study from Michel et al.[33] reported similar results to ours, with a lower sensitivity of water mouthwash compared to ONPS. This study included individuals at high risk of COVID-19. Thus, its results, as ours, may not apply to a low-risk population.

Participants were asked to use 5 ml of spring water to gargle, which is slightly more than the amount of molecular water (3 ml) used to transport the ONPS. This volume was chosen to allow participants to have enough liquid in their mouth to gargle effectively and is

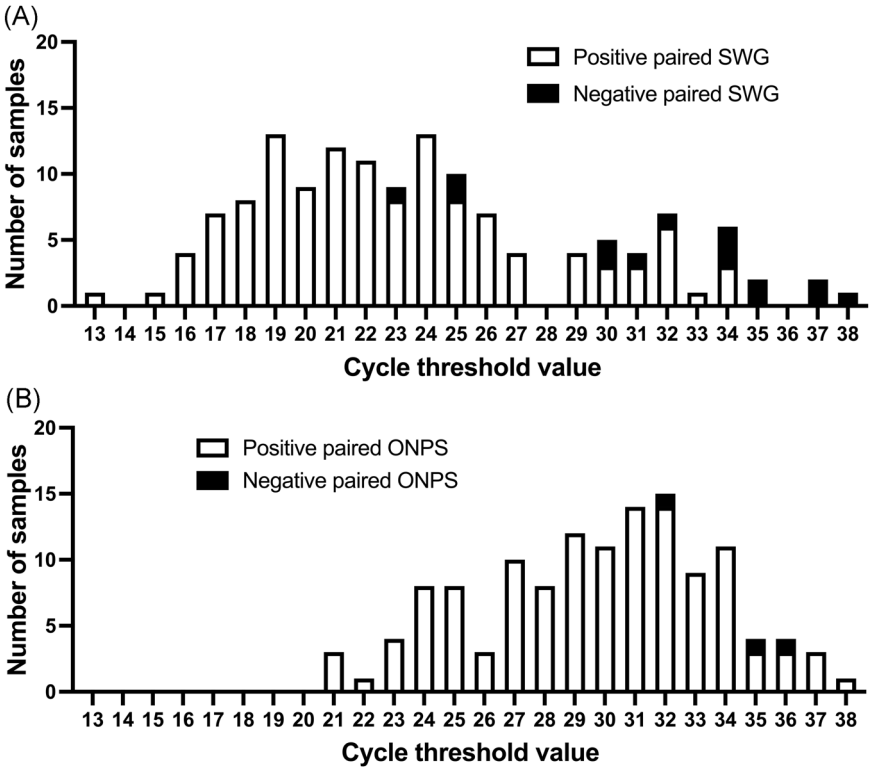

FIGURE 2 Distribution of cycle threshold (C_t) values according to specimen type and SARS-CoV-2 laboratory-developed nucleic acid amplification test (LD-NAAT) results obtained from the paired samples. (A) Distribution of ONPS C_t values according to SARS-CoV-2 LD-NAAT SWG result (n = 141).
(B) Distribution of SWG C_t values according to SARS-CoV-2 LD-NAAT ONPS result (n = 129). ONPS, oronasopharyngeal swab; SWG, spring water gargle

similar to that used by Goldfarb et al.[7] However, it might have diluted the viral RNA collected through the SWG and slightly impacted its sensitivity (~by 1–2 C_t value).

The thermal lysis followed by LD-NAAT being slightly less sensitive to diagnose SARS-CoV-2 than other available assays, false-negative results may occur more frequently, especially when viral load is close to the limit of detection. Indeed, in our study, the thermal lysis LD-NAAT was positive in 88% and 90% of SWG samples that were positive with the LD-NAAT preceded by chemical extraction and cobas® SARS-CoV-2 test, respectively. Interestingly, the LD-NAAT was positive in all SWG samples positive with the Simplexa™ COVID-19 Direct, which is CE-approved on saliva samples for SARS-Cov-2 detection.[17]

Despite the limitations discussed above, the SWG coupled with thermal lysis remains the most affordable method currently available for SARS-CoV-2 detection. Compared to an LD-NAAT preceded by chemical extraction, it offers accelerated turn-around time and is less vulnerable to reagents shortages.

6 | CONCLUSION

This study demonstrates that SWG is a less sensitive sampling method than ONPS when tested with an LD-NAAT preceded by thermal lysis. However, this loss of clinical sensitivity occurs mainly among samples with a lower amount of RNA. Being noninvasive, the higher acceptability of SWG might compensate the loss of sensitivity and enable a higher rate of detection on a population-based perspective. Nonetheless, in patients with a high clinical suspicion of COVID-19, a repeated analysis with ONPS should be considered.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTION

Investigation, *formal analysis*, *data curation*, *data interpretation*, *visualization*, *writing—original draft*: Sarah Gobeille Paré. *Conceptualization*, *methodology*, *writing—review and editing*, *supervision*: Julie Bestman-Smith. *Conceptualization*, *funding acquisition*, *methodology*, *formal analysis*, *data interpretation*, *writing—review and editing*: Judith Fafard. *Project administration*: Florence Doualla-Bell. *Investigation*, *formal analysis*, *writing—review and editing*: Marième Jacob-Wagner, Manon St-Hilaire, and Guylaine Lépine. *Formal analysis*, *statistical analysis*, *writing—review and editing*: Christian Lavallée. Conceptualization, *writing—review and editing*: Hugues Charest and Isabelle Goupil-Sormany. *Investigation*, *methodology*, *project administration*: Stéphanie Beauchemin. *Conceptualization*, *methodology*, *data interpretation*, *statistical analysis*, *writing—review and editing*: François Coutlée. *Conceptualization*, *methodology*, *writing—review and editing*: Jeannot Dumaresq and Marc Desforges. *Project administration*, *formal analysis*, *writing—review and editing*: Lambert Busque. *Project administration*, *software*, *writing – review and editing*: Valérie Boucher. *Conceptualization*, *funding acquisition*, *methodology*, *formal analysis*, *statistical analysis*, *writing—original draft*, *review and editing*, *supervision*: Annie-Claude Labbé.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

ORCID

François Coutlée http://orcid.org/0000-0002-2025-8928
Annie-Claude Labbé http://orcid.org/0000-0001-8936-3307

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