


# Congenital Cytomegalovirus and Hearing Loss: A Pilot Cross-Sectional Survey of Otolologists' and Pediatric Otolaryngologists' Knowledge

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## Abstract

**Objective.** To evaluate pediatric otolaryngologists, neurotologists, and otologists on awareness and knowledge of congenital cytomegalovirus (cCMV).

**Study Design.** Pilot cross-sectional online survey.

**Setting.** Otolaryngology practices.

**Subjects and Methods.** An electronic multiple-choice questionnaire was sent email listserv to physician members of the American Society of Pediatric Otolaryngology and American Otological Society. The survey assessed demographics, physician awareness, and practice patterns. Data were collected and analyzed.

**Results.** Seventy (14.5%) pediatric otolaryngologists and otologists responded. All responded that they are familiar with cCMV. Most were familiar with symptoms associated with cCMV with the exception of petechia/purpura. Less than 50% knew the incidence/natural history of cCMV-induced hearing loss. Only 63% knew that saliva or urine polymerase chain reaction/culture should be performed prior to 3 weeks of age. Less than half knew the indications for dry blood spot testing, and many incorrectly recommended serologic saliva or urine testing in a child >3 weeks old. Most respondents do not offer any diagnostic testing for cCMV or referral for antiviral therapy for those who may benefit from this treatment. Most either did not know the cCMV screening policy or did not have one at their institution.

**Conclusion.** Despite a relatively low overall response rate, this study suggests several knowledge gaps and underutilization of cCMV testing by physicians who frequently encounter pediatric hearing loss. The findings from this pilot study demonstrate the need for further educational directives focused on cCMV to improve knowledge and incorporation of cCMV best practices.

## Keywords

pediatric hearing loss, etiology for hearing loss, infectious disease, management of pediatric hearing loss, audiology

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Congenital cytomegalovirus (cCMV) has enormous public health implications, as it is the leading cause of neurodevelopmental delay and environmental hearing loss.<sup>1,2</sup> Approximately 90% are asymptomatic with no signs or symptoms and 10% are symptomatic. cCMV is considered symptomatic if a child has 1 or more signs of cytomegalovirus (CMV), including thrombocytopenia, microcephaly, intrauterine growth restriction, hepato/splenomegaly, petechia/purpura, hepatitis, central nervous system (CNS) involvement (microcephaly, intracranial calcifications), chorioretinitis, and sensorineural hearing loss. In children with symptomatic cCMV, hearing loss has been reported in up to 75%; those with asymptomatic cCMV will have a 10% to 15% chance of developing hearing loss.<sup>3</sup> Approximately 15% to 35% of patients with bilateral moderate to profound loss are due to cCMV.<sup>2,4</sup> Frequently, cCMV goes undiagnosed as children

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often do not show visible signs of disease. Currently, there are no standard guidelines for screening or treatment in children with asymptomatic cCMV. Utah, Connecticut, and Iowa have adopted hearing-targeted cCMV screening, where children who fail the newborn hearing screen are evaluated for cCMV within the first 3 weeks of life. Given the high likelihood of hearing loss progression in children with cCMV and hearing loss, a screening program allows children to be identified earlier and closely followed.

Despite the burden of neonatal cCMV infections, the knowledge of its symptoms and transmission was poor among medical providers in multiple studies. In a survey distributed by Muldoon and colleagues,<sup>5</sup> 35.8% of physical and occupational therapists either had low familiarity or never heard of cCMV. Both Cordier et al<sup>6</sup> and Korver et al<sup>7</sup> found that providers in both the Netherlands and France had poor knowledge of cCMV transmission routes and symptoms.

In light of the poor awareness that has been reported in the literature, we wanted to evaluate the knowledge among otolaryngologists, who frequently evaluate pediatric hearing loss. With the impact of early detection of hearing loss and implication of early treatment with children with cCMV, it is important that the physicians who are likely to evaluate these patients have adequate knowledge of this disease process and its management. In this article, we report the results of a cCMV awareness survey conducted among pediatric otolaryngologists and otologists. While this is a descriptive study, we anticipated that our cohort who regularly evaluate pediatric hearing loss (HL) would have a high degree of awareness and knowledge of cCMV.

## Methods

The Emory University Institutional Review Board granted approval for this study. The American Society of Pediatric Otolaryngology (ASPO) and the American Otological Society (AOS) were contacted for approval and access to their email listserv. ASPO is the largest pediatric otolaryngology society and AOS is the largest otology society in the United States. After access was granted, a multiple-choice survey was sent electronically to members of their respective societies, which includes pediatric otolaryngologists and otologists/neurotologists (**Figure 1**).

The email contained a brief description of our study and the hyperlink for the survey using Survey Monkey (Survey Monkey, San Mateo, California). Prior to proceeding, all respondents signed a consent form. The following demographic variables were addressed: sex, age, years of experience, practice environment, and percentage of patients evaluated for hearing loss in their practice. The questionnaire assessed knowledge of signs and symptoms of cCMV, transmission, prevalence and effect on hearing loss, and diagnosis. The last portion queried the current management of cCMV at the individual's institution. The responses were collected between May and September 2017.

The results were compiled on the online form and then transferred to a spreadsheet using Microsoft Excel (Microsoft Corp, Redmond, Washington). Frequency responses to all

questionnaire items were determined, and overall scores were calculated per questionnaire item. This overall score was based on the sum of the correctly stated true answers, assigning 1 point per correct answer. The maximum achievable score varied between 4 and 11 points, depending on the category of the questionnaire item. Prior to performing statistical analysis, some of the groups were combined to increase the total number within a given subgroup. Since our data were nonparametric, we used the Wilcoxon rank-sum test to compare differences in the median between groups, with statistical significance determined as  $P < .05$ . The median was calculated using the median function in R. This function provides the value at which 50% of observations are above and below that value. Given our skewed data, the median is a better measure of central tendency than the mean.

## Results

### Demographics

A total of 484 members opened the email link (215 ASPO and 269 AOS), of whom 92 clicked on the link (19 AOS, 73 ASPO). We had a 14.5% response rate, with 70 respondents who completed a majority of the questions. All participants were physicians practicing in pediatric otolaryngology, otology, or neurotology. All respondents stated they were familiar with cCMV. Unfortunately, only 23 responded to what their particular specialty was, with 10 (43%) being pediatric otolaryngologists, 12 (52%) neurotologists, and 1 (4%) otologist. Fifty-four (77%) respondents were in an academic practice. The average age of participants was 48 years (range, 33-76 years), with 68% being male. Years of experience in practice varied with the majority either at the beginning of their career (0-5 years, 31%) or late in their career (>20 years, 27%). Interestingly, 83% of participants stated only 1% to 25% of their practice incorporated management of pediatric HL (**Table 1**).

### Symptoms and Transmission of cCMV

A majority recognized some symptoms associated with cCMV, especially hearing loss (100%), and 67% to 94% recognized the other symptoms. Nonetheless, only 25 (36%) identified all the symptoms, and 52 (74%) knew >50% of the symptoms associated with cCMV. Of all the symptoms, most were not aware that petechia/purpura could be associated with cCMV. Furthermore, less than half of respondents knew that cCMV was the most common environmental cause of hearing loss, its incidence, and disease progression.

Respondents did not perform as well when asked about methods of transmission; almost one-third of respondents were not aware of the methods. A transmission route for CMV was correctly identified 46% to 61% of the time. However, 19 (27%) correctly identified all transmission routes, with 29 (56%) recognizing >50% of the transmission routes for cCMV (**Table 2**).

### Diagnosis of cCMV

Sixty-three percent of respondents correctly identified urine and saliva testing with urine confirmation prior to 3 weeks

1. Age \_\_\_\_\_
2. Gender \_\_\_\_\_
3. Type of practitioner: MD/DO
4. Subspecialty
  - a. Pediatrics
  - b. Otology
  - c. Neurotology
5. Years in practice
  - a. 0-5
  - b. 6-10
  - c. 11-15
  - d. 16-20
  - e. >20
6. Practice environment
  - a. Private Practice
  - b. Academic center
  - c. Other \_\_\_\_\_
7. What % of your practice includes management of pediatric sensorineural hearing loss (SNHL)?
  - a. None
  - b. 1- 25
  - c. 26-50
  - d. 51-75
  - e. >75
8. Are you familiar with congenital cytomegalovirus (cCMV)?
  - a. Yes
  - b. No
9. What symptoms are associated with cCMV infection? (pick all that apply)
  - a. **Hearing loss**
  - b. **Intellectual disability**
  - c. **Vision loss**
  - d. **Microcephaly**
  - e. **Motor disabilities**
  - f. **Seizures**
  - g. **Death**
  - h. **Hepatomegaly**
  - i. **Splenomegaly**
  - j. **Intrauterine growth restriction**
  - k. **Petechia and purpura**
  - l. I do not know

Figure 1. (continued)

10. Which of the following statement(s) regarding cCMV is/are true (pick all that apply)
- Up to 15% of children with asymptomatic cCMV can develop hearing loss**
  - Up to 30 % of children with asymptomatic cCMV can develop hearing loss
  - Up to 75% children with symptomatic cCMV will develop hearing loss**
  - Up to 95% of children with symptomatic cCMV will develop hearing loss
  - cCMV is the most common environmental cause of hearing loss**
  - I do not know
11. Of children with cCMV with hearing loss, what percent will have progressive hearing loss
- 5%
  - 20%
  - 35%
  - 50%**
  - I do not know
12. What test(s) can be performed to diagnose cCMV status (pick all that apply)
- Dried blood spot CMV PCR at any age**
  - Serologic CMV IgG testing at any age
  - Urine PCR/culture at any age
  - Saliva CMV Culture at any age
  - Dried blood spot (DBS) prior to 3 weeks of age**
  - Serologic IgM testing at any age
  - Urine PCR/culture prior to 3 weeks of age**
  - Saliva CMV Culture with confirmation with Urine PCR/Culture prior to 3 weeks of age**
  - I do not know
13. Which of the following are routes of transmission for CMV (pick all that apply)
- Kissing**
  - Changing diapers**
  - Breast milk**
  - Blood transfusion**
  - Sexual Intercourse**
  - Sharing food with children**
  - Sneeze**
  - I do not know
14. Which test(s) can definitively establish a diagnosis for cCMV in children >3 weeks of age (pick all that apply)
- Dried blood spot testing**
  - Serology for IgM and IgG for CMV
  - Imaging studies including CT and MRI
  - Urine PCR/culture for CMV
  - Saliva culture for CMV
  - I do not know

Figure I. (continued)

15. A child with hearing loss undergoes dried blood spot CMV PCR testing. The results are negative for CMV. How do you counsel this patient?
- Etiology of your hearing loss is not attributed to CMV
  - This test must be repeated
  - CMV cannot be ruled out as an etiology for hearing loss**
  - I do not know
16. Do you incorporate **any type** of cCMV testing for children with SNHL?
- Always
  - Sometimes
  - Rarely
  - Never
17. Do you offer DBS CMV PCR testing for your patients?
- Yes
  - No
18. Does your institution or hospital offer hearing targeted early cCMV screening?
- Yes
  - No
  - I do not know
19. Does your institution or hospital offer universal cCMV screening?
- Yes
  - No
  - I do not know
20. Do you offer antiviral therapy or refer to infectious disease specialist for antiviral therapy for cCMV infected children?
- Yes, only if they are symptomatic
  - Yes, for symptomatic children and asymptomatic children that fail the hearing screen
  - No
  - I do not know

**Figure 1.** Congenital cytomegalovirus awareness survey. Correct answers are in bold.

of age will definitively diagnose cCMV. However, the responses were less clear with definitive diagnosis using the dried blood spot. Only 33% knew that this assay could be used at any age. There was also a poor understanding on what diagnostic methods could be used to definitively diagnose cCMV when the child is >3 weeks old. Only 36% responded correctly with dried blood spot as the only method. Other incorrect answers of using serology, imaging, urine, or saliva testing were selected by 11% to 39% of the respondents. Most participants (64%) did acknowledge that a negative dried blood spot test could not rule out cCMV as the etiology of hearing loss (**Table 3**).

### Practice Patterns

Fifty-eight percent of respondents rarely or never incorporate CMV testing for children with idiopathic sensorineural hearing loss. Seventy-six percent do not offer a dried blood spot CMV PCR test. Seventy-four percent either did not have or did not know if early hearing targeted or universal

cCMV screening was offered at their institution. Most physicians did not know when to refer a cCMV-infected child for antiviral therapy (**Table 4**).

### Comparison among the Groups

In **Table 5**, we compared the median scores within each group. Overall, most participants across all groups had their best scores with questions geared toward cCMV symptoms. When looking at the median across all categories, most answered questions regarding the effect on hearing loss and diagnosis of cCMV incorrectly. Within the subset of individuals who saw  $\geq 26\%$  of patients with pediatric HL (12 participants), they performed well in most categories, with the exception of diagnosis (mean score 67). In fact, these individuals outperformed respondents whose practice included  $\leq 25\%$  of pediatric HL with respect to symptoms, diagnosis, and prevalence ( $P < .05$ ). Although the median value for transmission was also higher for this group, it was not statistically significant. We also identified that

**Table 1.** Demographics of the Respondents and Type of Professional Practice.

Characteristic	Number of Respondents	Total Percent
<b>Age, y</b>		
30-45	30	43
46-60	30	43
61-76	8	11
Did not answer	2	3
<b>Sex</b>		
Male	46	66
Female	22	31
Did not answer	2	3
<b>Type of practitioner</b>		
MD	70	100
DO	0	0
<b>Specialty</b>		
Pediatric otolaryngologist	10	14
Neurotologist	12	17
Otologist	1	1
Did not answer	48	69
<b>Years in practice</b>		
0-5	22	31
6-11	7	10
11-15	8	11
16-20	14	20
>20	19	27
<b>Practice environment</b>		
Private	13	19
Academic	55	79
Other	2	3
<b>Percentage of practice includes management of pediatric sensorineural hearing loss</b>		
0%	0	0
1%-25%	58	83
26%-50%	10	14
51%-75%	1	1
>75%	1	1
<b>Are you familiar with congenital cytomegalovirus?</b>		
Yes	70	100
No	0	0

participants in academic medicine or in practice  $\leq 15$  years performed slightly better compared to those in private practice or in practice  $\geq 16$  years, but these differences did not reach statistical significance in any category.

## Discussion

This pilot survey suggests several knowledge gaps and insufficient implementation of cCMV testing by physicians who are expected to be the most competent to treat pediatric HL. Pediatric otolaryngologists or neurotologists, whose practice encompassed  $\geq 26\%$  of pediatric sensorineural hearing loss (SNHL), outscored their counterparts who evaluated or treated fewer pediatric HL patients. Even this group, however, did not demonstrate an impressive understanding of how to diagnose these patients. This may in part be due

to the lack of awareness and the intricacy involved in understanding the virology of cCMV. Furthermore, familiarity of symptoms and transmission may stem from initial training in medical school; however, after this period, there may not be much of an emphasis on cCMV in residency training or as part of continuing medical education, which may account for the results.

All of the physicians who participated in our survey were familiar with cCMV but had little understanding of associated symptoms, natural history, and mode of transmission. Korver et al<sup>7</sup> performed a similar study evaluating physician knowledge in the Netherlands. Most respondents in this study were unaware of transmission through breast milk (34.6%), changing diapers (22.8%), and sexual intercourse (39.8%). Symptoms associated with cCMV were correctly

**Table 2.** Symptoms and Transmissions of cCMV.

Question	Correct Responses	
	Number	Percentage
What symptoms are associated with cCMV infection? (Pick all that apply)		
True		
Hearing loss	70	100
Intellectual disability	65	94
Vision loss	57	81
Microcephaly	54	77
Motor disabilities	52	76
Seizures	51	72.9
Death	42	61
Hepatomegaly	46	67
Splenomegaly	42	60
Intrauterine growth restriction	52	79
Petechia and purpura	32	49
False		
I do not know	4	6
Which of the following are routes of transmission for CMV? (Pick all that apply)		
True		
Kissing	42	61
Changing diapers	32	46
Breast milk	37	53
Blood transfusion	43	61
Sexual intercourse	36	51
Sharing food with children	33	47
False		
I do not know	20	29
Which of the following statement(s) regarding cCMV is/are true? (Pick all that apply)		
True		
Up to 15% of children with asymptomatic cCMV can develop hearing loss	27	39
Up to 75% children with symptomatic cCMV will develop hearing loss	21	30
cCMV is the most common environmental cause of hearing loss	33	47
False		
Up to 30% of children with asymptomatic cCMV can develop hearing loss	24	34
Up to 95% of children with symptomatic cCMV will develop hearing loss	5	7
I do not know	14	20
Of children with cCMV with hearing loss, what percent will have progressive hearing loss?		
True		
50%	31	44
False		
5%	2	3
20%	9	13
35%	10	14
I do not know	17	26

Abbreviations: cCMV, congenital cytomegalovirus; CMV, cytomegalovirus.

identified by more than 50% of the cohort. Within the subset of physicians, 13 were otolaryngologists; they were correct approximately half of the time with respect to transmission route, natural history, and symptoms.

Only 44% of our surveyed physicians knew that hearing-impaired children with cCMV are likely to develop worse

hearing. With respect to the severity of cCMV, 39% correctly identified the percentage of asymptomatic patients and 30% identified the percentage of symptomatic patients likely to experience progressive hearing loss. Only 47% of respondents knew that cCMV is the most common environmental cause of hearing loss. In addition, 26% “did not

**Table 3.** Diagnosis of cCMV.

Question	Correct Responses	
	Number	Percentage
What test(s) can be performed to diagnose cCMV status? (Pick all that apply)		
True		
Dried blood spot CMV PCR at any age	23	33
Dried blood spot prior to 3 weeks of age	28	41
Urine PCR/culture prior to 3 weeks of age	44	63
Saliva CMV culture with confirmation with urine PCR/culture prior to 3 weeks of age	44	63
False		
Serologic CMV IgG testing at any age	11	16
Urine PCR/culture at any age	10	14
Saliva CMV culture at any age	6	9
Serologic IgM testing at any age	7	10
I do not know	14	20
Which test(s) can definitively establish a diagnosis for cCMV in children >3 weeks of age?		
True		
Dried blood spot testing	25	36
False		
Serology for IgM and IgG for CMV	27	39
Imaging studies including CT and MRI	9	13
Urine PCR/culture for CMV	16	23
Saliva culture for CMV	8	11
I do not know	20	29
A child with hearing loss undergoes dried blood spot CMV PCR testing. The results are negative for CMV. How do you counsel this patient?		
True		
CMV cannot be ruled out as an etiology for hearing loss	45	64
False		
Etiology of your hearing loss is not attributed to CMV	9	13
This test must be repeated	1	1
I do not know	15	21

Abbreviations: cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; CT, computed tomography; IgG, immunoglobulin G; IgM, immunoglobulin M; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

know” the percentage of progressive hearing loss, and 20% did not know the prevalence of hearing loss within the symptomatic or asymptomatic groups.

One of the most concerning findings from our survey is that many physicians did not know how to diagnose cCMV. Forty-seven percent of respondents did not know that either urine only or saliva with urine confirmation PCR/culture within 3 weeks is required to definitively diagnose cCMV. Sixty-seven percent did not know that dried blood spot testing could be used to diagnose cCMV at any time, even after 3 weeks. In fact, 39% incorrectly believed that immunoglobulin G and immunoglobulin M serology or urine PCR/culture (23%) could definitively diagnose cCMV in children older than 3 weeks. In addition, 20% did not know what test could be performed to definitively diagnose cCMV prior to 3 weeks, and 29% did not know what to order after 3 weeks.<sup>8,9</sup> Given this lack of knowledge with diagnostic testing, it is perhaps not surprising that only 11% of

respondents routinely order CMV testing for idiopathic SNHL. An international group of pediatric otolaryngologists published a consensus statement recommending that cCMV testing should be done first for idiopathic pediatric SNHL.<sup>10</sup> Park et al<sup>11</sup> reported that 30% of children who presented with idiopathic SNHL were determined to have cCMV when testing was incorporated into a hearing loss evaluation algorithm. They also found that when CMV testing is performed first, this approach had the lowest cost for all types of hearing loss except in the case of auditory neuropathy spectrum disorder. In that case, imaging had the lowest cost when ordered first.

Kimberlin et al<sup>8</sup> studied the impact of treating symptomatic CMV-infected infants younger than 1 month of age with the antiviral drug, valganciclovir. They reported that these infants treated for 6 months had better hearing and neurocognitive scores than those treated for 6 weeks. An earlier trial demonstrated better hearing outcomes in treating



**Table 4.** Individual Institutional Practice.

Question	Number	Percentage
Do you incorporate any type of cCMV testing for children with SNHL?		
Always	8	11
Sometimes	22	31
Rarely	20	29
Never	20	29
Do you offer DBS CMV PCR testing for your patients?		
Yes	16	23
No	52	76
Does your institution or hospital offer hearing targeted early cCMV screening?		
Yes	18	26
No	28	40
I don't know	24	34
Does your institution or hospital offer universal cCMV screening?		
Yes	8	11
No	37	53
I don't know	25	36
Do you offer antiviral therapy or refer to infectious disease specialist for antiviral therapy for cCMV-infected children?		
Yes, only if they are symptomatic	15	21
Yes, for symptomatic children and asymptomatic children who fail the hearing screen	28	40
No	12	17
I don't know	15	21

Abbreviations: cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; DBS, dried blood spot; PCR, polymerase chain reaction; SNHL, sensorineural hearing loss.

**Table 5.** Comparison of cCMV Awareness between Groups.<sup>a</sup>

Characteristic	No.	Median Symptom Score, %	Median CMV Effect on Hearing Loss Score, %	Median Diagnosis Score, %	Median Transmission Score, %
% of practice associated with pediatric SNHL					
1%-25%	58	<b>73</b>	<b>25</b>	<b>50</b>	50
≥26%	12	<b>100</b>	<b>75</b>	<b>67</b>	91.5
P value <sup>b</sup>		<b>.006</b>	<b>&lt;.0001</b>	<b>.009</b>	.052
Years of experience					
0-15	37	91	50	67	50
≥16	33	73	50	50	50
P value <sup>b</sup>		.42	.72	.43	.53
Type of practice					
Private	13	55	25	50	33
Academic	55	91	50	50	50
Other	2	10.5	1.5	1.5	6
P value <sup>c</sup>		.058	.36	.19	.10

Abbreviations: cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; SNHL, sensorineural hearing loss.

<sup>a</sup>Significant findings are in bold.

<sup>b</sup>Using the nonparametric equivalent of the unpaired *t* test, the Wilcoxon rank-sum test.

<sup>c</sup>Other was not included in calculation of *P* value.

symptomatic cCMV infants younger than 1 month of age with ganciclovir compared to those untreated infants. These findings have resulted in a national consensus that symptomatic CMV-infected infants younger than 1 month should be treated with antiviral therapy when diagnosed. However,

despite this national consensus,<sup>12</sup> only 21% of the respondents either referred or treated with antiviral therapy infants with symptomatic cCMV. Seventeen percent did not treat or refer to infectious disease, and 21% did not know. The lack of knowledge regarding treatment was also noted in a

survey evaluating cCMV awareness among medical students. In that study, 58% of second- through fourth-year medical students either were not aware or did not know treatment existed.<sup>13</sup>

The main limitation of our study is a low response rate of 14.5% and a total of 70 participants. In addition, we were not able to determine the specific otolaryngology specialty for most respondents as they did not respond to this question. We cannot exclude correct answers due to guessing as opposed to knowledge. Regardless of these limitations, we believe this initial survey demonstrates a clear lack of knowledge on the diagnosis and treatment of a common condition for otolaryngologists.

## Conclusions

Our pilot study highlights the significant knowledge gaps and underutilization of cCMV testing among pediatric otolaryngologists, neurotologists, and otologists. Due to the time sensitivity of definitive diagnosis of cCMV and the high likelihood for otolaryngologists to see this population, we recommend that all otolaryngologists become well versed in diagnosis and management of cCMV. We have proposed the incorporation of additional education directives through our national boards and at the major otolaryngology meetings. Larger studies will be planned over the next 5 to 10 years to reevaluate knowledge and practice patterns after increasing awareness.

## Author Contributions

**Kavita Dedhia**, conception and design of work, analysis of data, drafting and revising manuscript, and final manuscript approval; **Jennifer Tomlinson**, acquisition of data, manuscript revision and final manuscript approval; **Nancy Murray**, analysis of data, manuscript revision and final manuscript approval; **Albert Park**, conception and design of work, revising manuscript and final manuscript approval.

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