# ORIGINAL ARTICLE



# Antibiotic prescriptions for child sinusitis varied between specialties after Finnish guidelines were updated in 2018

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## **Abstract**

Aim: We evaluated antibiotic prescriptions issued for Finnish children with acute sinusitis by a nationwide private outpatient clinic network from 2014–2020. Data were compared before and after updated guidelines in 2018.

**Methods:** The study comprised data on 45 296 children aged 2–17 years with acute sinusitis, namely diagnoses, ages, dates, the doctor's specialty and any antibiotics. We measured compliance with the updated 2018 Finnish guidelines, which recommended amoxicillin or amoxicillin-clavulanic acid for children under 12 years old, with doxycycline as an alternative for 12 years plus.

Results: There were 6621–7585 visits per year for acute sinusitis in 2014–2019 and 2954 in 2020. Antibiotics were prescribed for 37.9%–41.6% of patients during the study years. Amoxicillin, including penicillin, accounted for 35.9% of prescriptions, followed by amoxicillin-clavulanic acid (26.9%). Macrolides accounted for 20.6% and, encouragingly, decreased by 38% from 2014–2019. Doxycycline accounted for 5.3%. Paediatricians, general practitioners (GPs) and ear, nose and throat specialists followed the guidelines in 75.1%, 73.8% and 66.7% of cases, respectively. GPs prescribed antibiotics more often than other physicians.

**Conclusion:** Antibiotics were prescribed for about 40% of acute sinusitis visits by Finnish children from 2014–2019. Specialities differed with regard to prescribing rates and whether they followed the guidelines.

# KEYWORDS

acute sinusitis, antibiotics, macrolides, national guidelines, pandemic

# 1 | INTRODUCTION

Viral rhinosinusitis is common during upper respiratory tract infections in children,<sup>1-3</sup> and approximately 7%–8% of cases may lead to acute bacterial infections in the paranasal sinuses.<sup>1-4</sup> Bacterial sinusitis is diagnosed when the infection takes an abnormal clinical

course. Radiological or magnetic resonance imaging and ultrasound scans are not routinely recommended and neither are microbiological or other laboratory tests. <sup>3,5,6</sup> The criteria for bacterial sinusitis in children include persistent presumptive symptoms for more than 10 days, without any considerable improvement. Alternatively, they may include a purulent nasal discharge at onset and fever that lasts

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ENT, ear, nose and throat; GP, general practitioner; RCT, randomised controlled trial.

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for more than 3 days or a biphasic course and/or progressive worsening of symptoms after a transient primary recovery. <sup>1,3,4</sup> These definitions are based more on clinical experience than clinical research.

The major pathogens that are involved in acute bacterial sinusitis are non-capsulated *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Branhamella catarrhalis*. <sup>1,3,5</sup> In Sweden, the incidence of sinusitis in children more than halved from 2003 to 2012 following the implementation of the pneumococcal conjugate vaccinations. <sup>7</sup> Antibiotic treatment may be warranted in children with suspected sinusitis if nasopharyngeal symptoms continue for more than 10 days. <sup>8</sup>

The Finnish Current Care Guidelines, which were updated in 2018, state that the drug of choice for acute bacterial sinusitis in children should be amoxicillin or amoxicillin-clavulanic acid. They recommend a standard oral amoxicillin dose of 40–50 mg/kg/day.<sup>5</sup> Doxycycline is a recommended alternative for adolescents who are at least 12 years of age.<sup>5</sup> In the older guidelines, which were published in 1999, 2006 and 2013, the first-line recommendations were penicillin or amoxicillin without clavulanic acid.<sup>1</sup> Macrolides are effective against *B. catarrhalis*, but they are not recommended as they do not provide sufficient cover for pneumococcal strains.<sup>9</sup> Local mucous membrane constrictors can be used for a short time, in addition to antibiotics, and analgesics, but there has been a lack of research-based evidence on their effectiveness.<sup>5</sup>

The aim of this study was to evaluate antibiotic prescriptions for children treated at home for acute sinusitis between 2014–2020. We also measured prescribing rates in 2019–2020 to see if physicians adhered to the recommendations in the updated Finnish Current Care Guidelines, which were published in 2018. The largest private healthcare company in Finland provided us with access to their national data. This enabled us to estimate the variations in prescriptions by age, study year, hospital region and the specialty of the physician. We paid particular attention to prescriptions for amoxicillin, amoxicillin-clavulanic acid and macrolides.

# 2 | METHODS

This descriptive, retrospective study was conducted using the electronic health records provided by Terveystalo, the largest private healthcare company in Finland. The company runs more than 300 clinics, which cover all the 20 hospital districts in the country and receives 250000 paediatric visits per year.

The study population comprised children aged 2–17 years who visited Terveystalo outpatient clinics from 1 January 2014 to 31 December 2020 and received a diagnosis of acute sinusitis (Table S1). The number of sinusitis cases was 57159 (50.6% boys) during the seven-year surveillance period (Figure S1). We excluded 4023 cases with lower respiratory tract infections, 6560 with acute otitis media and 1009 with other concomitant bacterial infections. In addition, we excluded 271 cases under 2 years of age, since paranasal sinus infections rarely occur in such small children because the maxillary and frontal sinuses have not yet been formed in that age. They then gradually increase in volume until they reach a significant level in

# **Key notes**

- This study examined data on 45296 children aged 2-17 years with acute sinusitis, with regard to antibiotic prescribing and compliance with the updated 2018 Finnish guidelines.
- Antibiotics were prescribed for about 40% of patients during the study years, and the results included an encouraging 38% decrease in macrolides.
- Paediatricians, general practitioners and ear, nose and throat specialists differed with regard to prescribing rates and whether they followed the guidelines.

teenagers. This meant that 45 296 cases (52.6% boys) with acute sinusitis at 2–17 years of age were included in the present study.

## 2.1 | Data collection

Terveystalo uses the Dynamic Health tool (Tietoevry) to handle its electronic health record data, as previously described. <sup>10</sup> The data collected from the registers comprised information about visits, coded diagnoses and prescribed antibiotics. These were recorded online by practitioners during the child's visit. The antibiotics that were prescribed were identified by the Anatomical Therapeutic Chemical Classification (Table S2).

The patient's date of birth was used to calculate their actual age at the time of any visits in 2014–2020. The data were based on annual cases, rather than individual patients, as some children may have been seen more than once. Children with sinusitis were divided into two age groups: 2.0–11.9 years and 12–17.9 years. The physicians were mainly classified as paediatricians, general practitioners (GPs) and ear, nose and throat (ENT) specialists. Only 2.9% of the cases were treated by other physicians. The years 2019–2020 were chosen to represent the period after the publication of the updated national guidelines in 2018.

# 2.2 | Statistics

SPSS Statistics for Windows, version 26 (IBM Corp), was used for the data management. Basic univariate analyses were conducted using the chi-square test. The 95% confidence intervals (95% CI) for the proportions were calculated using the Wald method and Stata 16.1 software (StataCorp LLC). The age and sex of the child, the specialty of the physician and the year of the visit were included as covariates in the multivariate logistic regression analysis, and the results were expressed as adjusted odds ratios (aOR) and 95% CIs. The results were mostly presented as percentages, to take account of the reduction in respiratory infections as a result of the lockdown measures during the COVID-19 pandemic in 2020. 11,12

### 2.3 | Ethics

This study was part of a quality assessment and development project. All the data were coded and the patients were not contacted. The patient data were actively managed and conformed to the European Union's General Data Protection Regulation and Finland's data security legislation. According to Finnish law, approval by an ethics committee and informed consent were not required. The study was carried out with the promise of the Chief Medical Officer of Terveystalo.

### 3 | RESULTS

The numbers of visits for acute sinusitis between 2014 and 2019 were stable, ranging from 6621–7585 per year, but they decreased to 2954 in 2020, which was 57.1% lower than the previous year (Table 1). The number of sinusitis cases, as a percentage of all respiratory tract infection visits, was highest in 2014 (20.1%) and then gradually decreased to 13.0% in 2020 (Table 1). The patient's ages ranged from 2.0–11.9 years in 40.9% of cases and from 12.0–17.9 years in 59.1% of cases. Antibiotics were prescribed to 37.9–41.6% of patients with sinusitis during the study years, without any constant trend by time (Table 1). The percentage of doctors who prescribed

TABLE 1 Number of children with sinusitis, with and without antibiotic prescriptions

antibiotics for the cases they saw was: GPs (45.3%), ENT specialists (37.1%), paediatricians (32.9%) and others (42.6%) (Table 1).

Amoxicillin, including penicillin, was the most frequently prescribed antibiotic and it was prescribed for 14.4% of all visits and accounted for 35.9% of prescriptions for antibiotics. This was followed by amoxicillin-clavulanic acid (10.8%, 26.9%), azithromycin (6.3%, 15.8%), cephalosporins (3.0%, 7.6%), doxycycline (2.1%, 5.3%), clarithromycin (1.7%, 4.3%) and sulfadiazine-trimethoprim (1.4%, 3.4%), respectively (Table S3).

As shown in Figure 1, amoxicillin prescription rates varied between 14.1%-15.5% during 2014-2018 and decreased to 12.6% in 2020, while amoxicillin-clavulanic acid prescriptions increased from 10.2% to 12.3%. Our combined analysis of amoxicillin and amoxicillin-clavulanic acid revealed that the prescription rates did not change significantly over time. Macrolide prescriptions decreased from 9.6% to 6.0%, which was a relative reduction of 38% (Figure 1).

When we only included patients who were treated with antibiotics, this showed that amoxicillin, including penicillin, was the most frequently prescribed drug in both age groups. It was prescribed for 36.5% of cases aged 2–11.9 years and 35.5% of cases aged 12–17.9 years. This was followed by amoxicillin-clavulanic acid (29.2%, 25.2%), macrolides (21.8%, 19.8%) cephalosporins (7.2%, 7.9%) and sulfadiazine-trimethoprim (4.6%, 2.6%), respectively. Doxycycline

	Children with acute sinusitis	Children who were treated with antibiotics	Proportion of children treated with antibiotics
	n	n	%
Total	45 296	18117	40.0
Age group			
2–11.9 years	18544	7596	41.0
12-17.9 years	26752	10 521	39.3
Gender			
Male	22684	9061	50.0
Year of visit			
2014	6853/34124(20.1) <sup>a</sup>	2792	40.7
2015	6621/36694(18.0) <sup>a</sup>	2753	41.6
2016	7585/49313(15.4) <sup>a</sup>	3115	41.1
2017	7251/51137(14.2) <sup>a</sup>	2870	39.6
2018	7149/52743(13.6) <sup>a</sup>	2846	39.8
2019	6883/49713(13.8) <sup>a</sup>	2610	37.9
2020	2954/22639(13.0) <sup>a</sup>	1131	38.3
Speciality			
Paediatrician	11662	3837	32.9
General practitioner	21097	9553	45.3
Ear, nose and throat specialist	11207	4161	37.1
Other	1330	566	42.6

<sup>&</sup>lt;sup>a</sup>Proportion (%) of sinusitis cases of all acute upper and lower respiratory tract infection visits in the relevant year.

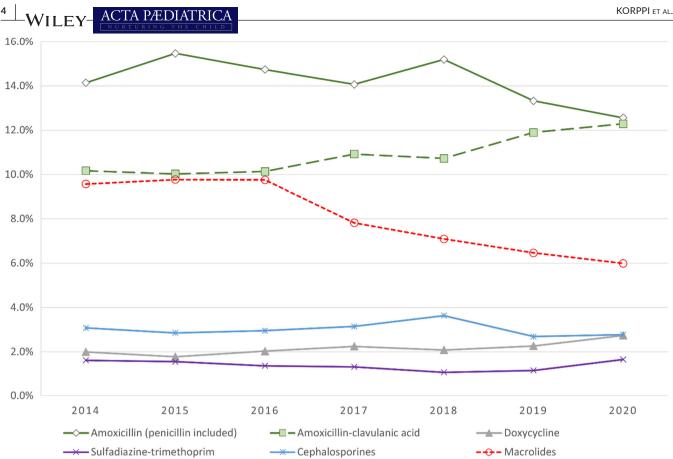


FIGURE 1 Annual antibiotic prescription rates for children with sinusitis

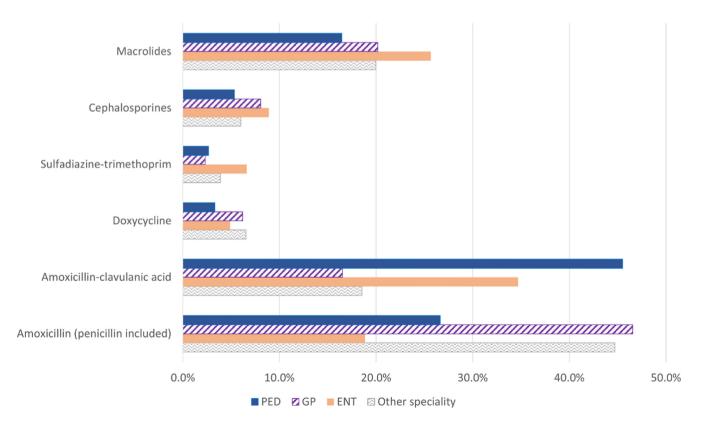


FIGURE 2 Prescribed antibiotics by specialty of the physician

was prescribed to 8.7% of children who were at least 12 years of age (Figure S2).

When looked at how many doctors chose amoxicillin and amoxicillin-clavulanic acid when they prescribed antibiotics, the respective figures for the two treatment regimens were: paediatricians (26.6%, 45.5%), GPs (46.5%, 16.5%) and ENT specialists (18.8%, 34.7%) (Figure 2). This means that 62.8% of patients who received antibiotics were treated with amoxicillin or amoxicillin-clavulanic acid: 72.1% for paediatricians, 63.0% for GPs and 53.5% for ENT specialists. The total percentage treated with macrolides was 20.6%: 16.4% for paediatricians, 20.2% for GPs and 25.6% for ENT specialists (Figure 2).

# 3.1 | Following the guidelines

Physicians were considered to follow the 2018 guidelines if they prescribed amoxicillin or amoxicillin-clavulanic acid for children of all ages, with the additional option of doxycycline for children who were at least 12 years old. The first-line recommendations in the previous 2013 guidelines were penicillin or amoxicillin without clavulanic acid. The results varied substantially between the clinics in different hospital districts across the country (Figure S3).

We assessed this data separately for paediatricians, GPs and ENT specialists for 2014–2017 and 2019–2020. This covered the periods before and after the updated guidelines released in 2018. The respective figures for these two periods were: paediatricians (73.8%, 75.1%), GPs for paediatricians, (67.4%, 73.8%) and ENT specialists (53.2%, 66.7%) (Table 2). The age distributions of the children varied significantly according to the specialty of the physician they visited (Figure S4).

We also carried out multivariate analyses. The age and sex of the child and the specialty of the physician were incorporated into the logistic regression analysis, along with whether they followed the guidance (Table 3). Before the 2018 guidelines were issued, the aOR for age was 1.04. When paediatricians were the reference group, the aOR was 0.65 for GPs and 0.36 for ENT specialists. After the 2018 guidelines were issued, the figures were 1.03 for age, 0.86 for GPs and 0.63 for ENT specialists. The results suggest that before the 2018 guidelines were issued, the adjusted risk of receiving prescriptions for antibiotics that were not recommended was 54% higher when visiting GPs rather than paediatricians. The figure for ENT specialists was much higher compared to paediatricians, at 175%.

TABLE 2 Whether the guidelines were followed before and after the 2018 updated Finnish guidelines for the treatment of sinusitis in children were issued.

Physicians' specialty	Before guidelines <sup>a</sup> 2014-2017% (n)	After guidelines 2019- 2020% (n)	p Value
Paediatricians	73.8 (1842/2496)	75.1 (605/806)	0.478
General practitioner	67.4 (4270/6338)	73.8 (1279/1733)	<0.0001
Ear, nose, and throat specialists	53.2 (1252/2355)	66.7 (702/1052)	<0.0001
Others	68.0 (232/341)	74.7 (112/150)	<0.0001

<sup>&</sup>lt;sup>a</sup>The 2013 guidelines were in place during this period.

After the updated guidelines were issued, the adjusted risks were 16% higher for GPs than paediatricians and 59% higher for ENT specialists (Table 3).

We performed ad hoc supplementary analyses for the post-guideline years 2019–2020, which included hospital districts as covariates in the multivariate model. The post-guideline aOR (95% CI) was 1.04 (1.02–1.06) for age. It was 0.82 (0.65–1.03) for GPs and 0.591 (0.47–0.74) for ENT specialists, when paediatricians were the reference group. This shows that GPs lost their statistical significance, but the direction of the results did not change (Table 3).

We performed ad hoc sensitivity analyses, by focusing on the 2019 data and excluding the 2020 data to eliminate the effects of the COVID-19 pandemic. The aOR (95% CI) was 1.02 (1.00–1.05) for age. When paediatricians were the reference group, the aORs (95% CIs) were 0.83 (0.65–1.06) for visits to GPs and 0.60 (0.47–0.78) for visits to ENT specialists. Age and visits to GPs lost their statistical significance, but the direction of the results did not change.

The revisit rate within 30 days after the initial visit was 2.9%. During the revisits, macrolides were prescribed as frequently (37.5%) as amoxicillin with or without clavulanic acid together (37.5%).

### 4 | DISCUSSION

This was a real-life, register-based study based on antibiotic prescriptions issued in 2014–2020 for more 45 000 cases aged 2–17 years with acute sinusitis. There were three key findings. First, antibiotics were prescribed for approximately 40% of the children with sinusitis during the seven-year study period, without any consistent trends by time. Second, there were substantial differences in prescription rates among physician's specialties and geographical areas when we looked at who followed the guidance and where they were based. Third, antibiotic prescriptions changed significantly after the 2018 national guidelines, which were previously updated in 2013.

Although many studies have reported antibiotic prescription rates for respiratory tract infections over time, and following new guidelines, <sup>13-15</sup> there are scarce data for children with sinusitis. In one French emergency department, antibiotic prescriptions for childhood sinusitis decreased from 66.7% in 2005 to 59.1% in 2009 after national guidelines for respiratory tract infections were released in November 2005. <sup>16</sup> However, there were only 141 patients with sinusitis out of 53055 children with respiratory tract infections. <sup>16</sup> In another French study of more than 220000 paediatric

TABLE 3 Whether guidelines were followed for antibiotic prescriptions for sinusitis in children before and after the 2018 updated Finnish guidelines for the treatment of sinusitis in children were issued.

Before updated guidelines (years 2014-2017)				
Factor	aOR (95% CI)	p Value		
Age	1.04 (1.03-1.05)	< 0.001		
Sex (boy)	1.027 (0.95-1.11)	0.509		
Paediatrician	1.0 (reference)	-		
General practitioner	0.65 (0.58-0.72)	< 0.001		
ENT specialist	0.36 (0.32-0,41)	< 0.001		
Others	0.66 (0.51-0.84)	0.001		
After updated guidelines (years 2019-2020)				
Factor	aOR (95% CI)	p Value		
Age	1.03 (1.01-1.05)	0.007		
Sex (boy)	1.07 (0.92-1.23)	0.373		
Paediatrician	1.0 (reference)	-		
General practitioner	0.86 (0.70-1.05)	0.139		
ENT specialist	0.63 (0.53-0.78)	< 0.001		
Others	0.88 (0.58-1.32)	0.534		

*Note*: Multivariate logistic regression. Only 2.9% were treated by other doctors; Age was included as a continuous variable.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ENT, ear. nose and throat.

visits for respiratory tract infections, antibiotics were prescribed for 68.9% of 751 children with sinusitis.<sup>17</sup> Thus, the 40% prescription rate in the present study was lower than in previous studies, but there are still a lack of comparable data.

Differences were observed between physicians with different specialties when we only analysed patients who were treated with antibiotics. The treatment of choice was amoxicillin-clavulanic acid for paediatricians (45.5%), amoxicillin GPs (46.5%) and macrolides for ENT specialists (25.6%). A national study of French GPs and paediatricians, which covered 2015–2017, found that the respective figures were higher for amoxicillin (52.5%, 65.5%) and lower for amoxicillin-clavulanic acid (11.5%, 13.5%). Previous studies have shown some differences in antibiotic prescriptions between specialists, for acute otitis media 18-21 and upper and lower respiratory tract infections. 17.22

There were no substantial changes by time in our study when amoxicillin and amoxicillin-clavulanic acid prescriptions were jointly analysed. Macrolide prescriptions decreased by 38% during the seven-year study period. This was a desirable outcome, because macrolides do not show appropriate effectiveness against the bacteria involved in sinusitis. Doxycycline, which is effective against most bacterial pathogens in sinusitis, was only prescribed for 8.7% of cases aged 12 years and over. There were no other notable associations between age and selected antibiotics.

The first Finnish guidelines on sinusitis treatment were published in 1999 and updated in 2006 and 2013. These versions

recommended amoxicillin or penicillin as a first-line therapy. In the 2018 update, penicillin was no longer recommended and amoxicillin-clavulanic acid, together with amoxicillin, became the first-line antibiotic treatment of choice.<sup>5</sup> The number of paediatricians who followed the 2013 and 2018 guidelines was particularly high, at around three-quarters of those studied.

Children visiting GPs or ENT specialists were less likely to receive antibiotics in line with the guidelines at both timepoints than those visiting paediatricians. However, after the 2018 guidelines were issued, compliance rose by 9.5% in GPs and 25.3% in ENT specialists. Lastly, during the post-guideline years of 2019–2020, 70.9% of children up to 11 years of age received amoxicillin or amoxicillinclavulanic acid and 72.8% of children aged 12 years or more received amoxicillin, amoxicillin-clavulanic acid, or doxycycline, in line with the updated 2018 guidelines. To our knowledge, there have not been any previously published studies on how many doctors complied with the guidelines for antibiotic prescriptions for children with acute sinusitis.

The usefulness of prescribing antibiotics for children with suspected bacterial sinusitis remains unclear. A systematic review that was published in 2013 found that only four randomised controlled trials (RCTs) had been carried out on children with acute sinusitis over a 25-year period. The accompanying meta-analysis found that the recovery rates were about twice as high in children treated with antibiotics than those who received a placebo. However, the studies were small and heterogeneous. The studies compared amoxicillin in 90 cases, amoxicillin-clavulanic acid in 28 cases, cefuroxime in 35 cases and antibiotics in general in 161 cases. Placebos were given to 28–55 controls. After 2010, we did not find any further RCTs published on antibiotics in children with sinusitis.

The COVID-19 pandemic started in Wuhan, China, at the end of 2019 and the first diagnosed case in Finland was at the end of January 2020 in a tourist from that region. Studies have commonly reported that the circulation of respiratory viruses has been lower during the pandemic, than at the same times in earlier years. This has been explained by social distancing, other restrictions and enhanced hygiene. <sup>11,12</sup> In the present study, the number of visits for sinusitis in 2020 was less than half of the annual visits in 2014–2019. Since our data have mostly been presented as ratios, it is unlikely that changes in the number of visits had any significant effect on the results of antibiotic prescriptions or the number of doctors who followed the guidelines.

### 4.1 | Strengths and limitations

The main strength of the present study was that the data we analysed came from outpatient clinics covering different areas of the country and comprised more than 45 000 sinusitis cases aged 2–17 years. The information was electronically registered by the physician online during the visit and was obtained from the company's centralised and uniformly coded electronic health record system. However, our retrospective study had some limitations. The data came from the private sector and may not fully represent the

entire child population in Finland. There might be some differences between living in urban or rural area or differences concerning the socioeconomic status between those who visited Terveystalo clinics and those who did not. Unfortunately, we were not able to collect that kind of information. The revisit rate in our clinics was <3%, but it was not possible to assess how often revisits took place in public or other companies' clinics. Such low rate is not likely to substantially influence the overall results. We were able to measure how well doctors complied with the guidance when they selected antibiotics, but not reliability of the sinusitis diagnoses and whether the children were under- or over-treated with antibiotics.

# 5 | CONCLUSION

Antibiotics were prescribed for approximately 40% of our cohort of more than 45 000 children aged 2–17 who had been diagnosed with acute sinusitis in 2014–2020. Nearly 75% of paediatricians and GPs complied with the updated 2018 guidance and so did more than 65% of ENT specialists. The results highlight the important role that the national guidelines played in Finland. Less frequent prescribing of macrolides was one desirable outcome. Repeated guideline updates are needed to ensure that physicians provide the best evidence-based treatments for common diseases, such as sinusitis in children.

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# **CONFLICT OF INTEREST**

The authors have no conflicts of interest to declare.

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# SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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