



# The Role of Eye Color in the Emergence of Tinnitus in Silence

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## Abstract

**Introduction** Previous research suggests that African Americans are less likely than Caucasians to perceive tinnitus in sustained silence.

**Objective** To evaluate the association between non-cutaneous melanin as indicated by eye color and the emergence of temporary tinnitus during a brief period of silence.

**Methods** A cross-section of adults grouped according to their eye color were exposed to silence. A total of 62 adults, aged 18 to 35 years (10 males, 52 females) were required to sit in silence for 10 minutes, after which they filled out a questionnaire to report their eye color and any perception of sounds in the ears or head.

**Results** In total, 63% of the participants perceived tinnitus while sitting in silence, and, of these 95% perceived the tinnitus sounds within 5 minutes of sitting in silence. Though African Americans were less likely to perceive tinnitus in silence, this difference was not significant ( $p = 0.6$ ). After a period of silence, 69% of the subjects with light-colored eyes and 58% of the dark-eyed subjects perceived tinnitus. This difference was not statistically significant ( $\chi^2(1) = 0.77$ ;  $p = 0.38$ ).

**Conclusion** When exposed to reduced auditory stimulation, 3 out of 5 normal-hearing people are likely to experience tinnitus. However, there was no relationship between eye color and the perception of tinnitus in silence. Although melanin has been shown to play a role in the protection of the ear against noise trauma and the effects of age-related hearing loss, its role in the emergence of tinnitus needs further investigation.

## Keywords

- ▶ tinnitus
- ▶ eye color
- ▶ melanin

## Introduction

Tinnitus is the perception of sound in the absence of an auditory stimulus.<sup>1,2</sup> It is often reported as the perception of sound in the ears or the head, and this can be unilateral or bilateral.<sup>3</sup> Tinnitus can be perceived as noise or tones such as ringing, buzzing, humming, whistling, hissing, roaring, cricket-like or like water falling from a height.<sup>4–6</sup> These can be persistent or intermittent. It is estimated that 50 million Americans experience tinnitus;

however, it is persistent in 16 million of these.<sup>7,8</sup> About 7.2% of tinnitus sufferers refer to their tinnitus as a big problem, and an estimated 2% find it debilitating and detrimental to their quality of life.<sup>1,9</sup> Tinnitus has been associated with anxiety, depression, insomnia, and difficulty concentrating.<sup>4,10,11</sup>

Tinnitus is suspected to be the result of compensatory changes in the auditory pathway when exposed to perturbations and reduced auditory input.<sup>12–15</sup> However, there is still a lot that we don't know about the factors that influence

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the emergence of tinnitus, such as why it is present in some people with normal hearing, or why it is not universally present in everyone when they are exposed to reduced auditory input.<sup>1,16</sup> The pathophysiology of tinnitus generation is still unclear, and the treatment of chronic tinnitus remains a challenge.

Silence tends to increase tinnitus perception and awareness in people with tinnitus. To avoid this, people with tinnitus are advised to avoid silence. However, it appears that a majority of adults with no prior history of tinnitus or ear pathology report the perception of temporary tinnitus when exposed to sustained silence.<sup>17-19</sup> There are several possible explanations for this phenomenon. First, the removal of environmental sounds may result in the perception of sounds that were previously masked by an enriched acoustic environment. Another explanation is that following a period of reduced auditory stimulation, the auditory system temporarily undergoes functional changes that manifest as tinnitus.<sup>12</sup> If the latter is the case, studying the perception of tinnitus in silence could improve our understanding of why it is present in some people and absent in others with similar thresholds. The differences that exist between those that perceive tinnitus in silence and those that don't are likely to improve our understanding of the epidemiology of tinnitus and the modifying factors in tinnitus emergence. This is especially relevant for tinnitus resulting from reduced auditory input, often seen in hearing loss from cochlea, middle ear and outer ear pathologies.

One possible modifying factor in the perception of tinnitus resulting from reduced auditory stimulation could be melanin. The emergence of tinnitus during sustained silence appears to be less likely in African Americans than in Caucasians.<sup>19</sup> It has also been reported that non-Hispanic whites are more likely to have frequent tinnitus than other racial groups.<sup>8</sup> Temporal bone studies have shown that African Americans have higher levels of cochlear melanin than Caucasians, and research has shown that people with darker iris pigmentation have higher levels of melanin in the cochlea.<sup>20-24</sup> Therefore, higher levels of melanin may offer some protection against the emergence of tinnitus. Melanin is present in the eyes and inner ears, as well as in the skin, in varying proportions that determine the skin color and eye color.<sup>25,26</sup> Melanin is also present in the brain in the form of neuromelanin.<sup>26,27</sup> The same genes that determine eye color are involved in the regulation of melanin, and the level of melanin in the ear can be estimated from eye color.<sup>23,24</sup> The melanin-containing cells synthesized in the intermediate layer of the stria vascularis are thought to actively protect against marginal cell injury and loss.<sup>28</sup> Melanin and its precursors are also thought to play a role in the protection of the inner ear from oxidative stress.<sup>29,30</sup> Furthermore, melanin is an important reservoir for ion pumps, and plays a role in the maintenance of signal transduction; this is true for inner-ear melanin and neuromelanin, which, although not widely researched on, has been postulated to play a role in normal action potentials in neurons.<sup>26,31,32</sup> Susceptibility to noise-induced hearing loss and age-related hearing loss appears to be higher in those with lower levels of melanin or lighter eye colors; furthermore, research has shown that

melanin plays a role in ototoxicity, and that certain drugs reduce the perception of tinnitus by binding to melanin within the cochlea.<sup>14,15,28,30,33,34</sup> Collectively, this suggests that people with higher levels of extracutaneous melanin are less susceptible to the effects of auditory perturbations or injury, and, therefore, less likely to perceive tinnitus. Since we cannot always explain why some people have tinnitus, the study of the role of extracutaneous melanin in tinnitus perception could help improve the current knowledge of the possible risk factors for tinnitus emergence and enrich the existing knowledge of the epidemiology of tinnitus. Additionally, understanding the role of melanin in tinnitus generation will be useful in estimating the individual efficacy of any future tinnitus therapy that targets melanin's ability to bind to chemicals.

The purpose of the present study was to follow up previous research which showed that African Americans were less likely to perceive tinnitus in silence, and to further explore the role of melanin in the emergence of tinnitus after a brief period of sustained silence. This is a role that has previously been explored with respect to noise-induced hearing loss and age-related hearing loss. In the present study, the sounds perceived in silence are referred to as tinnitus, and eye color was used to estimate the level of inner-ear melanin; it is hypothesized that those with lighter eye colors will be more likely to perceive tinnitus in silence than those with darker eye colors. The present study hopes to throw more light on the influence of melanin on tinnitus emergence following reduced auditory stimulation.

## Methods

The participants were 62 adults, 10 males and 52 females, aged 18 to 35 years, who had given their consent to participate in the study. Participants were only included in the study if they had no history of chronic tinnitus, head trauma, neurological disease, ear surgery, or recent ear infections. We studied adults with normal hearing thresholds instead of tinnitus patients in an effort to simulate the effect of sensory deprivation on an intact auditory pathway. This reduces the heterogeneity that often affects studies with tinnitus subjects who frequently have varying sites of auditory pathology.<sup>35</sup> The present was a descriptive cross-sectional study, and approval for it was obtained from the Institutional review board under IRB Number is 18-0066. Fliers and emails were used in the recruitment of participants and convenience sampling was employed. The study was conducted over a two-year period. The sample size was calculated using the effect size and power from similar studies.<sup>17,36</sup> The participants were initially told that the study was about their experience in silence; their attention was not drawn to their auditory system, and tinnitus was not mentioned.

The participants were asked to self-identify their eye color, and 10 (16%) reported that their eyes were either blue or gray, 16 (26%) had green or hazel eyes, and 36 (58%) had brown eyes. All participants had pure-tone hearing thresholds of 25 dBHL or less at octave frequencies between 250 Hz and 8,000 Hz, with type-A tympanograms and

**Table 1** Subject demographics

		Frequency	Percentage
Race	Non-Hispanic White	32	51.6
	African Americans	21	33.9
	Hispanic	4	6.5
	Middle-Eastern	2	3.2
	Native American	1	1.6
	Other	2	3.2
	Total	62	100.0
Eye Color	Light eye color	26 (5 males, 21 females)	41.9
	Dark eye color	36 (5 males, 31 females)	58.1
	Total	62	100.0
Gender	Male	10	16.1
	Female	52	83.9
	Total	62	100.0

normal findings on otoscopy. Those who met the inclusion criteria were asked to sit quietly inside a sound-proof booth for a period of ten minutes. We made use of ten minutes of sustained silence because previous research had shown that most participants report an early emergence of tinnitus within the first five minutes, when left in silence.<sup>19</sup>

The noise levels within the sound-proof booth were within American National Standards Institute’s recommendations. Subsequently, the participants completed a short Qualtrics Survey to answer questions about the emergence of tinnitus perception and give a description of the type of sound heard, where it was perceived (ears and/or head), and when it was perceived. The participants that perceived tinnitus while in silence also provided information about the number of sounds heard and the pitch of the tinnitus. Tinnitus perception was defined as sounds heard in the ears and/or the head while sitting in silence.

The participants were divided into two groups according to eye color. The light-eyed group consisted of those with blue, gray, green and hazel eyes, while the dark-eyed group consisted of participants with brown and black eyes. The International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Statistics (IBM Corp., Armonk, NY, US), version 25, was used in the data analysis. The Chi-squared ( $\chi^2$ ) test or its non-parametric equivalent was used in testing for any association between eye color and race, and tinnitus perception *t*-tests were used to examine if the onset of tinnitus perception differed by eye color.

**Results**

**Demographics**

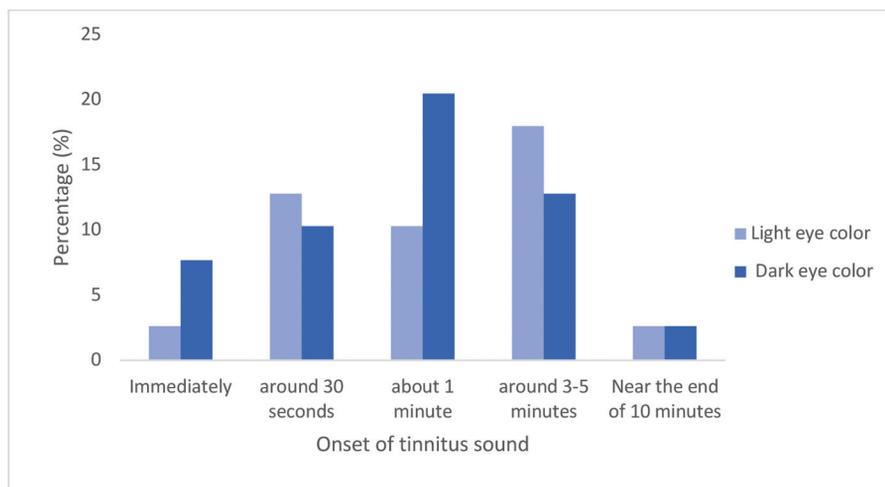
► **Table 1** shows the distribution of the participants by race, eye color and gender. The mean age of the participants was  $22.92 \pm 3.5$  years.

**Perception of Tinnitus during a Brief Period of Silence**

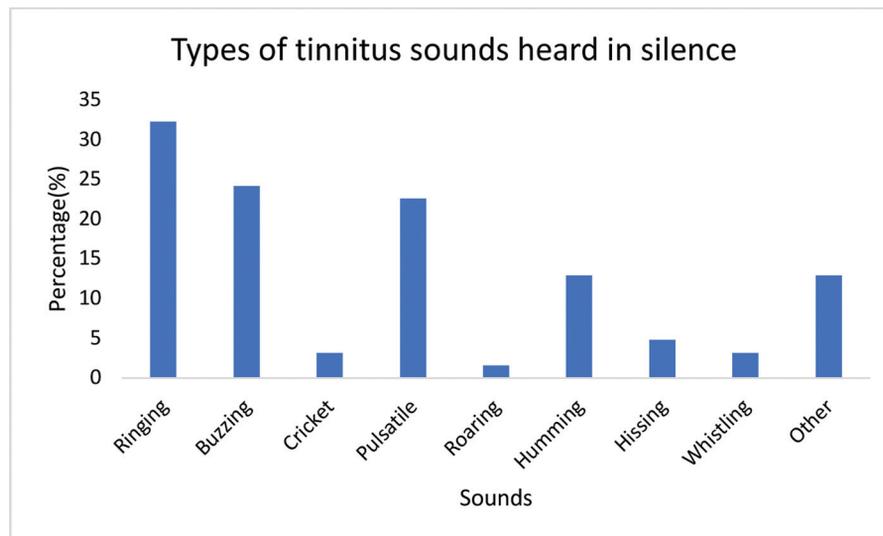
In total, 63% of the participants perceived tinnitus while sitting in silence, and, of these, 95% perceived the tinnitus sounds within 5 minutes of sitting in silence (► **Fig. 1**). A total of 54% of the subjects who perceived tinnitus did so in both ears, and 21% perceived the tinnitus sound in the head; 45% of those who perceived tinnitus described their tinnitus as having 1 sound, while 32% heard 3 or more sounds.

Overall, 28 (74%) of those who perceived tinnitus while sitting in silence described it as having a pitch, and more than half of these had high-pitched tinnitus (54%). Only 3 (11%) thought that their tinnitus was low-pitched.

► **Fig. 1** shows the reported onset of tinnitus perception for each eye-color group. A greater proportion of dark-eyed participants perceived tinnitus after one minute of exposure to silence. However, there was no statistically significant difference in the onset of tinnitus perception when both groups were compared ( $t_{37} = 0.72$ ;  $p = 0.48$ ). Both groups were more likely to report that they heard 2 or more sounds while in silence ( $t_{36} = -0.23$ ;  $p = 0.82$ ).



**Fig. 1** The onset of tinnitus perception in silence by eye color.



**Fig. 2** Types of tinnitus sounds heard.

► **Fig. 2** shows the types of sounds heard and the proportion of participants.

#### Race Distribution of Tinnitus Perception during a Brief Period of Silence

In total, 23 (72%) of non-Hispanic whites perceived tinnitus in silence, while 11 (52%) of African Americans perceived tinnitus in silence. A Fisher exact test did not show a significant association between tinnitus perception and race (Fisher = 3.99;  $p = 0.6$ ).

The relative risk of perceiving tinnitus was 1.4 times higher in Caucasians than African Americans. The odds of perceiving tinnitus in silence was two times higher in Caucasians than in African Americans.

#### Eye Color and Tinnitus Perception in Silence

Overall, 18 (69%) of the light-eyed subjects and 21 (58%) of the dark-eyed subjects perceived tinnitus after a period of

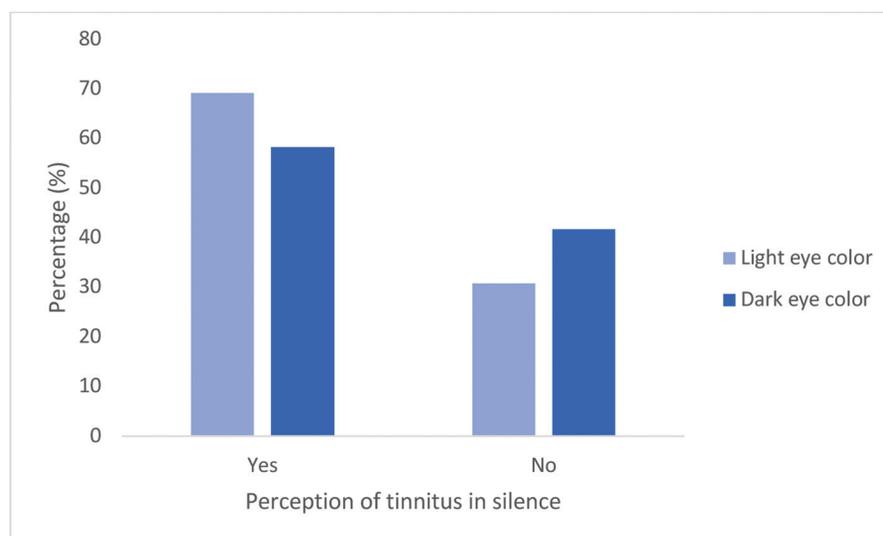
silence (► **Fig. 3**). This difference was not statistically significant ( $\chi^2(1) = 0.77$ ;  $p = 0.38$ )

The relative risk of perceiving temporary tinnitus in silence was 1.2 times higher in those in the light-eye-color group than in those in the dark-eye-color group. The light-eyed subjects were 2.25 times more likely to perceive tinnitus in silence than not, while the dark-eyed subjects were 1.4 times likely to perceive tinnitus in silence than not. Therefore, the odds of perceiving tinnitus when exposed to silence was 1.6 times higher in the light-eyed group when compared with the dark-eyed group.

## Discussion

#### Perception of Tinnitus in Silence

The proportion of participants with normal hearing thresholds who perceived tinnitus in the present study was similar to the 64% reported by Tucker et al.,<sup>19</sup> 2005, but much lower



**Fig. 3** Eye color and perception of tinnitus.

than the proportion reported in the study by Heller and Bergman,<sup>18</sup> 1953 (94%). This may be because the participants in the present study were younger and were confirmed to have normal hearing thresholds to exclude any confounding factors that may be introduced by hearing impairment. In the study by Heller and Bergman,<sup>18</sup> 1953, the participants were older, ranging from 18 to 60 years in age, and were not objectively confirmed to have normal hearing thresholds. The proportion of participants who perceived tinnitus in the present study is also lower than the proportion reported by Del Bo et al.,<sup>17</sup> 2008, in whose study an initial 83% of the participants reported the perception of tinnitus sounds in silence, with an increase to 92% when a non-functioning loudspeaker was present in the sound proof booth. This may be attributed to the difference in the instructions given to the participants. Whereas Del Bo et al.,<sup>17</sup> 2008 instructed the participants to listen for a sound, in the present study, no attention was drawn to the auditory system, and the participants were instructed to sit quietly and report any experience after the period of silence. Therefore, the higher proportion of tinnitus perception reported in the study by Del Bo et al.,<sup>17</sup> 2008, may be attributed to the use of auditory attention in their study. Tinnitus perception in silence appears to be enhanced by auditory attention.<sup>36</sup>

#### Eye Color, Race and Perception of Tinnitus in Silence

In the present study, tinnitus perception did not show a significant variation regarding the different races or eye colors. Our findings of no racial differences in the perception of tinnitus in silence are contrary to those reported by Tucker et al.,<sup>19</sup> 2005. This difference is unlikely to be attributed to our sample size being smaller than the one in that study. In the study by Tucker et al.,<sup>19</sup> 2005, they had 120 participants with an effect size that was double what we observed in the present study. They reported that 78% of the Caucasians and 38% of the African American participants perceived tinnitus in silence. The relative risk of tinnitus perception in their study was 2.1 times higher in Caucasians than in African Americans, while it was 1.4 times higher in the present study. The odds of perceiving tinnitus in silence was 6 times higher in Caucasians than African Americans in the study by Tucker et al.,<sup>19</sup> 2005. However, in the present study, the odds of perceiving tinnitus were just two times higher in Caucasians than in African Americans. The observed differences between the findings of the present study and those of Tucker et al.,<sup>19</sup> 2005, may imply that any role race might play in tinnitus perception varies widely within the population, and requires further investigation.

To the best of our knowledge, very few researchers have studied the racial differences in the incidence and prevalence of tinnitus. Shargorodsky et al.,<sup>8</sup> 2010, reported that non-Hispanic Caucasians were more likely to experience persistent tinnitus, while Cooper,<sup>37</sup> 1994, reported that a greater proportion of African Americans had bothersome tinnitus; however, in the study by Cooper,<sup>37</sup> 1994, the researcher did not ask about non-bothersome tinnitus. Reports from studies on racial differences in hearing impairment imply that the odds of having hearing loss is lower in African Americans

than in Caucasians, and in dark-skinned Hispanics in than light-skinned Hispanics.<sup>38–40</sup> Some researchers have also reported that age-related hearing loss is more common in Caucasians than in African Americans.<sup>39,41</sup> Although these studies imply that melanin may play a protective role against hearing loss and age-related changes in the auditory pathway, they did not look at the differences in terms of tinnitus perception. It is possible that the protective effects of melanin are activated in pathological changes, such as hearing loss, but not physiological responses to silence, as examined in the present study. This may explain why studies have shown that the protective effect of melanin in noise-induced hearing loss is only observed at damaging levels of loud noise.<sup>34,42</sup> In future studies, the level of cutaneous melanin in the participants could be determined using spectrophotometry technology. Additionally, a future investigation could examine the relationship between variations of pigmentation-related genes and tinnitus perception.

The risk of perceiving temporary tinnitus in silence was 1.2 times higher in light-eyed group than in those with the dark eyes. However, there was no significant difference between the proportion of light- and dark-eyed subjects who perceived tinnitus in silence. This may be a consequence of the grouping method used, in which the participants with intermediate levels of melanin concentration in the iris were grouped along with the blue-eyed subjects who had the least amount of melanin. Da Costa et al.,<sup>34</sup> 2008, and Sallustio et al.,<sup>43</sup> 1998, used the same method in the grouping of their subjects. Both observed that dark-eyed subjects were less likely to develop noise-induced hearing loss than light-eyed subjects, but this difference was only significant in the study by Da Costa et al., 2008.<sup>34</sup> Hannula et al., 2012,<sup>44</sup> observed the opposite, that dark-eyed respondents with a history of noise exposure were more likely to have hearing impairment than light-eyed respondents. However, they did not control for the level of noise or duration of noise exposure. Another explanation could be that the protective effects of melanin may only be evident when the ear has undergone a challenge or injury.<sup>42</sup> Its effect seems to be more evident at higher noise levels; therefore, authors report that pure-tone thresholds do not differ in normal-hearing individuals with different iris pigmentations who have not been exposed to an acoustic challenge that would cause auditory stress.<sup>34,45,46</sup> The same might be true for the role of melanin in the emergence of tinnitus in silence. It is likely that the temporary absence of acoustic stimulation during the period of silence resulted in a compensatory increase in the burst firing rate, burst duration and spikes per burst in the central auditory pathway.<sup>12</sup> This increase in gain is likely to be responsible for the perception of tinnitus by some of the participants, and melanin may not have a role in this pathway.<sup>47–49</sup> However, we did not measure the activity in the central auditory pathway, and are only able to hazard a guess as to the mechanisms behind the perception of tinnitus among the study participants.

One limitation of the present study is the reliance on reports from participants for tinnitus characteristics. Examining individuals with normal hearing thresholds gives us an

idea of the relationship between melanin and tinnitus emergence in apparently normal auditory systems, it also offers a glimpse into the response of the auditory system to reduced auditory stimulation, but it may not be generalizable to all patients with tinnitus.

The results from the present study offer a foundation for further exploration of the role of melanin in the epidemiology of tinnitus. Our results indicate that more research is needed to understand the role of melanin as a risk factor in tinnitus emergence. Research into the risk factors involved in tinnitus perception will help clinicians counsel tinnitus patients and provide explanation for some of the previously unexplained cases of tinnitus perception in individuals with apparently normal auditory systems.

## Conclusion

The present study shows that 3 out of 5 individuals with normal hearing thresholds and without a history of tinnitus are likely to perceive tinnitus when they are in sustained silence. However, this perception did not differ by eye color or race. A greater knowledge of the factors that influence tinnitus emergence and perception will be useful in the counselling of tinnitus patients and in understanding the factors that determine tinnitus perception or absence in silence. The results from the present study imply that although melanin has been shown to play a role in the protection of the ear against noise trauma and the effects of age-related hearing loss, its role in the emergence of tinnitus needs further investigation. To further explore the role of melanin in tinnitus emergence following reduced auditory stimulation, it may be beneficial to look at the response of those with the smallest amount of inner-ear melanin and those with the greatest amount. A comparison of the response of individuals with blue eyes and those with brown eyes may provide a clearer glimpse into the role of melanin in the emergence of tinnitus in silence. Studies on tinnitus in silence have shown that a greater proportion of participants perceived tinnitus when they were instructed to direct their attention to the auditory system.<sup>17,36</sup> Therefore, future studies focused on attention and awareness as possible factors contributing to the emergence of tinnitus in reduced auditory stimulation may help expand our knowledge of the risk factors for tinnitus perception. These can be obtained by comparing late auditory-evoked responses in those that perceive tinnitus and those who do not perceive tinnitus in silence. Counselling is an integral component of tinnitus therapy, and a more comprehensive idea of the risk factors behind tinnitus perception will aid clinicians in providing answers to tinnitus patients.

### Conflict of Interests

The authors have no conflict of interests to declare.

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