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Original articles

# Correlation between auditory thresholds and the response amplitude of otoacoustic emissions in post-COVID-19 adults

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## ABSTRACT

**Purpose:** to verify the auditory acuity and correlate auditory thresholds of pure tone audiometry (PTA) with transient-evoked otoacoustic emissions (TEOAE) and distortion-product otoacoustic emissions (DPOAE) in post-COVID-19 adults.

**Methods:** an analytical cross-sectional study, conducted between October 2021 and October 2022, with 63 post-COVID-19 adults (age range 20-53 years old). The following were performed: PTA, TEOAE, and DPOAE. The results were presented descriptively, and Spearman's correlation test was used.

**Results:** no hearing loss was identified. Most frequency bands were present in both emissions tests. There was a negative and significant correlation between the PTA and TEOAE thresholds in the frequency bands of 500–1500 Hz and 1500–2500 Hz on the left and between the PTA and DPOAE thresholds in the frequency bands of 1000, 2000, and 4000 Hz on the right and 1000, 2000, 3000, 4000, 6000, and 8000 Hz on the left.

**Conclusion:** post-COVID-19 adults presented auditory thresholds within normal limits, with a response to TEOAE and DPOAE. There was a negative correlation between TEOAE and DPOAE and the PTA air threshold, indicating that higher PTA thresholds are associated with lower emission response amplitude.

**Keywords:** Coronavirus Infections; Hearing; Hearing Loss; Adult

A study conducted at the Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil.

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## INTRODUCTION

Coronavirus infection (SARS-CoV-2) was identified in the Wuhan province, China, in late 2019. In March 2020, the World Health Organization declared COVID-19 a pandemic on all continents[1].

It is an infectious disease which is transmitted through the inhalation of droplets of saliva or respiratory secretions, which remain suspended in the air after the infected person coughs or sneezes and/or physical contact with contaminated objects and surfaces[2,3]. Infected individuals may not present apparent manifestations of the disease (asymptomatic), or they may develop mild clinical conditions, similar to flu symptoms, or severe ones, such as Pneumonia and Severe Acute Respiratory Syndrome (SARS). Depending on the clinical condition of the infected person, at risk of death, more invasive interventions are necessary[4,5].

It is known that viral infections, such as Cytomegalovirus, Rubella, and Measles, can cause sensorineural hearing loss[6,7], whose consequences differ according to the type of virus and include direct damage to the structures of the inner ear, such as cell death, to indirect damage, such as inflammation or vascular impairment, depending on the treatment for each virus. Therefore, SARS-CoV-2 infection, as a cause of hearing loss, remains under study[8].

Growing evidence suggests that hearing loss may be part of the clinical spectrum of COVID-19 and may, in some cases, signal the onset of the disease[8]. The literature points to cases in which sudden hearing loss was found to be the only symptom presented by patients[9,10]. Relationships with conductive hearing loss have also been verified[11,12]. Some authors suggest that otitis media should be considered a manifestation or symptom of COVID-19[12]. Knowledge of this presentation became important during the pandemic to prevent infection spread through isolation and to define strategies to begin treating hearing loss[9].

Regarding auditory acuity and performance in the transient-evoked otoacoustic emissions (TEOAE) testing in individuals affected by COVID-19, asymptomatically, the first report in the literature showed a significant increase in PTA air thresholds at frequencies of 4,000, 6,000, and 8,000 Hz, with a lower mean response amplitude in TEOAE, when compared to the control group, suggesting impairment in the functioning of the cochlear hair cells[13]. Thus, studies indicate that this disease has neurotropic properties, with manifestations in the sensory epithelium, such as in the labyrinth, which reinforces the importance of detailed assessment of cochlear function in patients with SARS-CoV-2 infection[8].

Given that evoked otoacoustic emissions (EOEs) testing detects changes even before the emergence of symptoms related to auditory acuity, its application proves to be crucial in the early detection of possible damage to cochlear function[8,13]. Therefore, it is essential to perform these EOE tests, both through transient and distortion-product otoacoustic emissions (DPOAE), in individuals who have had COVID-19, regardless of whether they were asymptomatic or not.

Furthermore, considering that hearing loss may not always occur immediately after disease contagion and that damage may occur subclinically[8], studies are necessary to develop clinical guidance and multidisciplinary approaches based on evidence[14]. The global dimension and the proportion of patients who had COVID-19 made it essential to know about the behavior of the virus in the auditory pathway and its possible hearing damage. Thus, this study aimed to verify auditory acuity and the correlation between PTA auditory thresholds and TEOAE and DPOAE response amplitude in post-COVID-19 adults.

## METHODS

This is a cross-sectional, analytical study conducted in a clinic. Data collection took place between October 2021 and October 2022, and it was initiated upon approval by the Human Research Ethics Committee (CEPSH) of the Universidade Federal de Santa Catarina, Brazil, under opinion number 5.019.582 and CAAE number 515455210.0.0000.0121.

The collection period and lack of funding justify the non-probabilistic convenience sample. The sample consisted of adult individuals of both sexes who had symptomatic COVID-19, with diagnosis confirmed by the RT-PCR test (reverse transcriptase reaction followed by polymerase chain reaction), without other comorbidities. All participants signed the Informed Consent Form (ICF).

Adults of both sexes with a positive PCR test for COVID-19 who did not require hospital admission, had no otological complaints prior to the infection, and had no noise exposure habits were included.

Exclusion criteria were malformation of the outer, middle, or inner ear, tumors involving the auditory system, previous otological surgery, acoustic trauma, and head trauma (found at anamnesis), obstructive earwax found on the date of the evaluation, conductive changes observed in the PTA and the measurement of

acoustic immittance, and failure to perform all audiological procedures.

The information obtained from the sample was extracted through anamnesis, and all tests were conducted in an acoustically treated booth.

## Assessment procedures

- **Anamnesis:** data on general health history, including concomitant diseases, use of medications, previous otorhinolaryngological diseases, and possible audiological complaints. Before the audiological procedures, the outer ear canal was inspected using the Heine Mini 3000 otoscope to rule out earwax obstructions.
- **Pure Tone Audiometry (PTA):** evaluation of the type, degree, and audiometric configuration. Made in a soundproof booth, with *Otometrics* audiometer, *MADSEN Astera2* model, and *SENNHEISER HDA 200* headphones. Air tone thresholds were investigated at frequencies of 250, 500, 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz and, for individuals with air thresholds greater than or equal to 20 dBHL, bone conduction tone thresholds were researched at the respective frequency, between 500 and 4,000 Hz, with the B-71 bone vibrator positioned on the mastoid. The method used was descending. The threshold was defined at the lowest intensity at 50% stimulus identification. The criterion for classifying normality was that adopted by Silman and Silverman (1997)[15]; therefore, thresholds ≤ 25 dBHL, at any frequency assessed, were considered within normal standards.
- **Transient evoked otoacoustic emissions (TEOAE):** assessment of the functioning of the outer hair cells of the cochlea. It helped in the early diagnosis of cochlear auditory changes, as they can show changes in patients with normal PTA. Searched on *Eclipse EP25* equipment, *Interacoustics*, with click stimulus with a frequency spectrum of 500–1,500 Hz, 1,500–2,500 Hz, 2,500–3,500 Hz, 3,500–4,500 Hz, and 4,500–5,500 Hz at 80 dBSPL intensity, presentation rate at 21.1/s, and total 2,000 stimuli, 12 ms window and maximum noise level 48.47 dBSPL. For present responses, the following were accepted: signal/noise ratio > 3 dB, general reproducibility ≥ 75% and minimum stability of 70%[16].
- **Distortion-Product Otoacoustic Emissions (DPOAE)**: they were triggered by two different pure tones and informed the functioning of the outer cochlear hair cells with frequency specificity. *Eclipse EP 25 Interacoustics equipment,* at frequencies 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz, with F1/F2 ratio of 1.22, with L1 intensity of 65 dB SPL and L2 of 55 dB SPL. For present responses, it was considered: signal-to-noise ratio ≥ 6 dB, stability greater than 80%, number of rejected stimuli < 20% of total presentations[17].

## Statistical analysis

The figures presented descriptive data on PTA air auditory thresholds and TEOAE and DPOAE response amplitude.

The Spearman's correlation test was applied to verify the relationship between TEOAE and DPOAE response amplitudes between PTA air auditory thresholds. The significance level adopted was 5% ($p < 0.05$), and the analyses were conducted using the Jamovi software version 2.3.21.

Cohen's parameters were considered when interpreting correlation values: values between 0.10 and 0.29 indicated no or weak correlation, values between 0.30 and 0.49 indicated a moderate correlation and values between 0.50 and 1 were interpreted as signs of a strong correlation[18].

## RESULTS

Sixty-three adults met the inclusion criteria (20 males and 43 females), aged between 20 and 53 years, with a mean age of 32.7 (± 7.53 years).

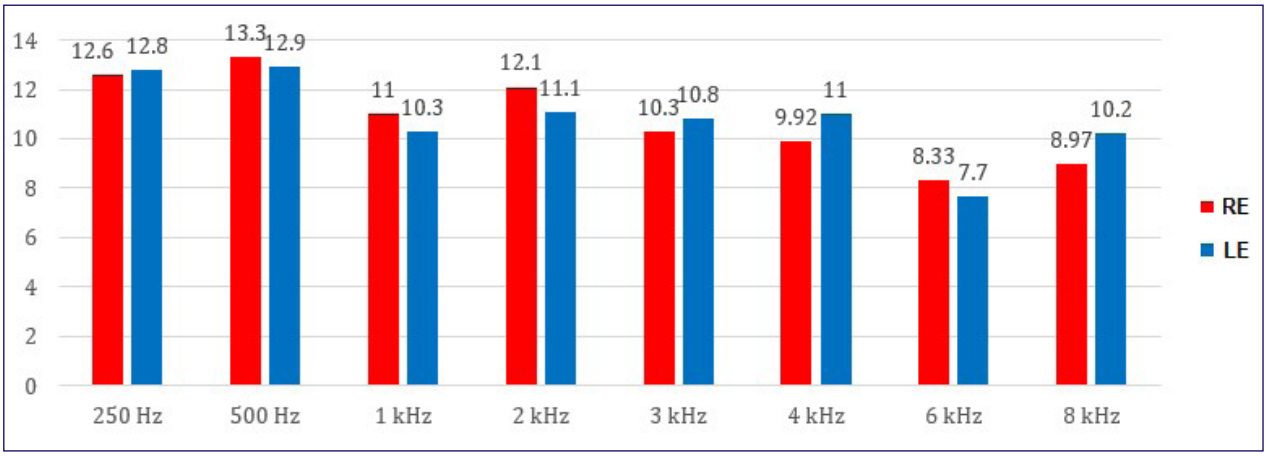
On the date of collection, more than half of the individuals had already been vaccinated (57.14%); there were reports of the use of "preventative" medications, such as ivermectin, or to mitigate the symptoms above, such as paracetamol and dipyrone by 33.33%. Auditory symptoms such as tinnitus, ear fullness, vertigo, and otalgia were reported by individuals (Table 1).

**Table 1.** Relative frequency of auditory symptoms reported by the COVID-19 group (63 participants)

| Variables | Yes (%) |
|---|---|
| Tinnitus | 25.39 |
| Ear Fullness | 20.63 |
| Vertigo | 14.28 |
| Otalgia | 4.76 |

Legenda: (%) – Porcentagem.

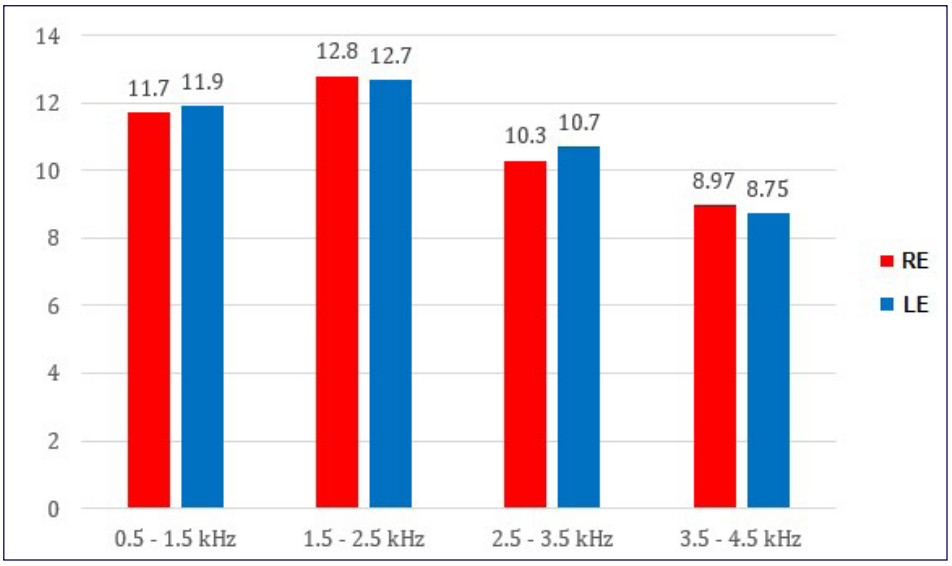
Most of those evaluated in the PTA had thresholds less than or equal to 25 dBHL. An air threshold of 30 dBHL was observed at 2,000 Hz in the right ear and one at 3,000 Hz in the left ear (the thresholds being bone conduction coupled in these situations), one at 30 dBHL at 8,000 Hz in the left ear, and two at 35 dBHL also at 8,000 Hz bilaterally. The mean auditory threshold values for both ears are presented in Figure 1.




Captions: RE = right ear; LE = left ear.

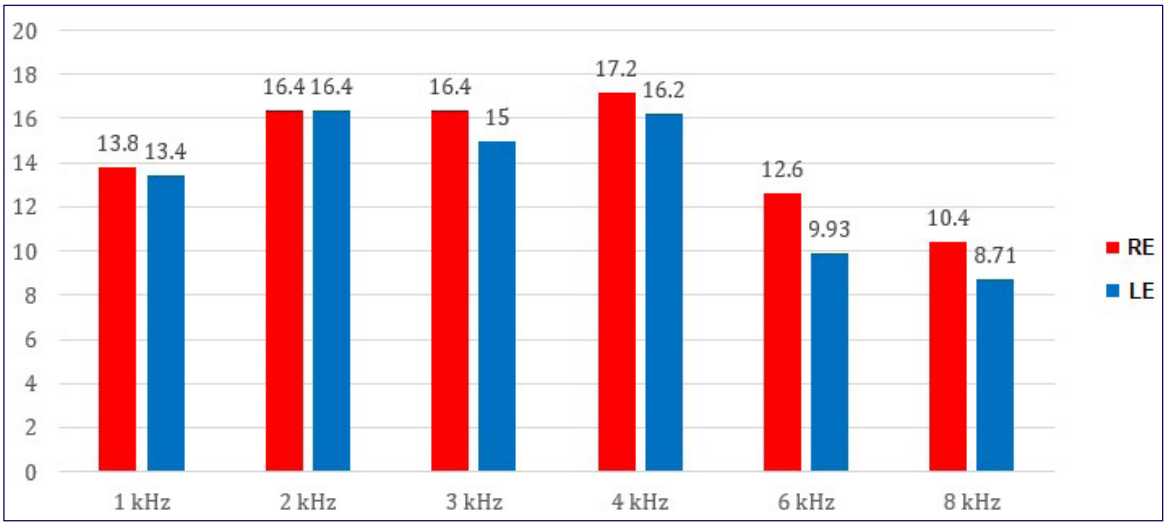
**Figure 1.** Mean values of pure tone audiometry air thresholds in individuals who had COVID-19, in both ears

In both the TEOAE and DPOAE tests, individuals showed a bilateral response in most frequency bands, and the mean values for both ears are presented in Figures 2 and 3, respectively.




Captions: RE = right ear; LE = left ear.

**Figure 2.** Mean values of response amplitude in the transient evoked otoacoustic emissions testing in individuals who had COVID-19, in both ears




Captions: RE = right ear; LE = left ear.

**Figure 3.** Mean values of response amplitude in distortion-product otoacoustic emissions testing in individuals who had COVID-19, in both ears

When verifying the relationship between PTA auditory thresholds and TEOAE response amplitude, a moderate, negative, and significant correlation was observed at 1,000 and 2,000 Hz in the left ear. This indicates that the higher the PTA air threshold, the lower the TEOAE response amplitude at these frequencies (Table 2; *Spearman's* correlation).

**Table 2.** Correlation between the response amplitudes of transient-evoked otoacoustic emissions and pure tone audiometry air thresholds, in the COVID-19 group

| Comparisons | Spearman's rs | p-value |
|---|---|---|
| 1000 Hz PTA and 500–1500 Hz TEOAE RE | -0.117 | 0.362 |
| 2000 Hz PTA and 1500–2500 Hz TEOAE RE | -0.193 | 0.130 |
| 3000 Hz PTA and 2500–3500 Hz TEOAE RE | 0.037 | 0.775 |
| 4000 Hz PTA and 3500–4500 Hz TEOAE RE | 0.396 | 0.396 |
| 1000 Hz PTA and 500–1500 Hz TEOAE LE | -0.372 | 0.003* |
| 2000 Hz PTA and 1500–2500 Hz TEOAE LE | -0.382 | 0.002* |
| 3000 Hz PTA and 2500–3500 Hz TEOAE LE | -0.058 | 0.649 |
| 4000 Hz PTA and 3500–4500 Hz TEOAE LE | -0.229 | 0.071 |

Captions: PTA = Pure tone audiometry; TEOAE= Transient-evoked otoacoustic emissions; RE = right ear; LE = left ear; Hz = Hertz; * = statistically significant

Likewise, the relationship between PTA auditory thresholds and DPOAE response amplitude was significant at 1,000, 2,000, and 4,000 Hz for the right ear and at 1,000, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz for the left ear. All correlations were negative, showing that the higher the PTA air threshold, the lower the DPOAE response amplitudes at these frequencies. The strength of the correlation was weak in the right ear and moderate to strong in the left ear at most frequencies (Table 3; *Spearman's correlation*).

**Table 3.** Correlation between the response amplitudes of distortion-product otoacoustic emissions and pure tone audiometry air thresholds in the COVID-19 group

| Comparisons | Spearman's rs | p-value |
|---|---|---|
| 1000 Hz PTA and 1000 Hz DPOAE RE | -0.288 | 0.022* |
| 2000 Hz PTA and 2000 Hz DPOAE RE | -0.280 | 0.028* |
| 3000 Hz PTA and 3000 Hz DPOAE RE | -0.227 | 0.074 |
| 4000 Hz PTA and 4000 Hz DPOAE RE | -0.280 | 0.026* |
| 6000 Hz PTA and 6000 Hz DPOAE RE | -0.181 | 0.156 |
| 8000 Hz PTA and 8000 Hz DPOAE RE | 0.057 | 0.656 |
| 1000 Hz PTA and 1000 Hz DPOAE LE | -0.333 | 0.008* |
| 2000 Hz PTA and 2000 Hz DPOAE LE | -0.530 | < .001* |
| 3000 Hz PTA and 3000 Hz DPOAE LE | -0.488 | < .001* |
| 4000 Hz PTA and 4000 Hz DPOAE LE | -0.324 | 0.010* |
| 6000 Hz PTA and 6000 Hz DPOAE LE | -0.344 | 0.006* |
| 8000 Hz PTA and 8000 Hz DPOAE LE | -0.260 | 0.040* |

Captions: PTA = Pure tone audiometry; DPOAE= Distortion-product otoacoustic emissions; RE = right ear; LE = left ear; Hz=Hertz; * = statistically significant

## DISCUSSION

Following the COVID-19 pandemic, there has been a growing interest in understanding the persistent clinical manifestations that affect infected individuals. Reports of auditory and vestibular symptoms are described in the literature, in addition to hearing loss and its association with tinnitus and vertigo[19-21]. The participants in this study did not present complaints of hearing loss. However, they described that during the course of the disease, they had tinnitus (25.39%) and vertigo (14.28%), which may be associated with damage to the inner ear, without manifesting auditory acuity, and also ear fullness (20.63%), and otalgia (4.76%), which may have occurred due to nasopharynx inflammation during the disease period.

Thus, the auditory acuity of adult individuals after SARS-CoV-2 infection was verified and it was observed that most participants had tonal thresholds ≤ 25 dBHL. It may suggest that, in quantitative terms, the hearing of these individuals was not affected by the disease.

Some authors also found no significant difference in the hearing of patients who had COVID-19, Battha *et al.* (2022)[22] conducted a prospective study in eight institutes, with 331 individuals in the COVID-19 group, and reported that 3.2% of patients had mild conductive hearing loss, but returned to normal in the following three months; also, this finding was not significant. Yıldız (2022)[23]performed audiometry on 240 patients aged 18 to 50 years in the first and third months after the end of the infection, finding minimal impairment, also restored in the third month, with no significant changes observed that would indicate hearing loss associated with COVID-19.

However, even with reports of recovery after a certain period of the infection, individuals who have been infected must investigate their auditory acuity, even without complaints of reduced auditory capacity. Different studies, with symptomatic or asymptomatic cases, have shown that the infection can raise hearing thresholds, especially at frequencies above 2,000 Hz[6,8,13,21-23].

Therefore, it is known that changes in the auditory pathway caused by viral infections may differ according to the type of virus. These infections can cause direct or indirect damage to the structures of the inner ear, and the outcome of this infection in the structures of the auditory system is variable[8].

One characteristic of EOE testing is that it detects a failure in the cochlear mechanism before verifying changes in auditory thresholds. When one-third of the outer hair cells changes, the PTA remains normal but with reduced response amplitude in the EOEs. Therefore, some studies have investigated the presence and response amplitude in this test[13,24,25].

As observed in this study, participants had a response, both in TEOAE and DPOAE, in most frequency bands evaluated. This investigation of the response amplitude in the different frequency bands of both types of EOEs made it possible to verify the power of the cochlear amplifier after SARS-CoV-2 infection in individuals without auditory complaints before the disease.

In fact, it is expected that as tonal thresholds increase, the response amplitude of the EOEs will decrease and even disappear in the event of hearing loss, which characterizes the deterioration of the outer hair cells as a result of the decrease in the ability to hear. This condition is more easily perceived in EOEs than in PTA, in which cochlear responses are less captured[26].

Different studies have sought to analyze this correlation. Thus, Öztürk et al. (2022)[25], when comparing the results of TEOAE and DPOAE in groups of adults without hearing complaints, whether or not they had COVID-19, they observed that the TEOAE amplitudes at 1,500 Hz, 2,000 Hz, and 4,000 Hz and the DPOAE amplitudes at 4,000 Hz were significantly lower in the group that had the disease.

Similarly, Dorobisz et al. (2023)[27] evaluated the amplitudes of TEOAEs in a population of post-COVID-19 adults and found a reduction in the response amplitudes, suggesting that this result is due to a possible complication of COVID-19[27].

Therefore, research justifies that the decrease in blood vessel supply due to the formation of clots in the vessels that irrigate the auditory system or even cell apoptosis impacts the results of EOEs13.25. Furthermore, there is scientific evidence that COVID-19 leads to hypoxia, causing greater damage to the inner ear structures initially detected by EOEs[27].

On the other hand, Yildiz (2022)[23], when evaluating PTA results and TEOAE amplitudes among adult individuals divided into three groups: control group, COVID-19 group without pneumonia, and COVID-19 group with pneumonia, found no significant differences in test results between the participants evaluated. Therefore, there are still controversies in the literature regarding the possible damage to hearing resulting from contamination by the SARS-CoV-2 virus.

Finally, the results found in this study demonstrate that individuals who had COVID-19 and who did not have hearing loss before the infection require a detailed investigation of the auditory function to confirm the damage obtained. Audiological monitoring is recommended to investigate long-term sequelae or until the audiological condition evolves after several exposures to the virus. Cohort studies with larger, probabilistic samples will contribute to better understanding the mechanisms underlying the relationship between COVID-19 and hearing.

## CONCLUSION

Post-COVID-19 adult individuals presented thresholds within normal limits, with a response to TEOAE and DPOAE tests. There was a negative correlation between TEOAE, DPOAE, and the ATL airway threshold, indicating that higher PTA thresholds are associated with lower emission response amplitudes.

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**Authors' contributions:**

CP: Conceptualization; Data curation; Investigation; Methodology; Writing - Original draft.

GER: Formal analysis; Writing - Review and editing.

DPCS: Formal analysis; Methodology; Supervision; Writing - Review and editing.

**Data sharing statement:**

The data will be publicly accessible, indefinitely or permanently. If additional information or specific supplementary data are needed, those interested may contact the study authors directly to request them.