 

ORIGINAL ARTICLE

CONTENTS

# Peculiarities of neurovegetative regulation in children and adolescents with sarcopenia according to heart rate variability indicators

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## ABSTRACT

**Aim:** To find what extent the state of neurovegetative regulation in children and adolescents with sarcopenia differs from their peers without signs of sarcopenia.

**Materials and Methods:** The sarcopenic index and hand grip strength, which were simultaneously in the range below the 25th percentile of the reference values of these indicators for the corresponding age and gender, were considered the criteria for sarcopenia. A bioelectrical impedance analyzer, "TANITA MC-780 MA" (Japan), was used to obtain the SI indicator. The functional state of autonomic regulation was assessed using the HRV-scanner hardware and software complex (Biosign, Germany).

**Results:** After processing the examination results according to our algorithm, it became clear that there were no children with signs of autonomic dysfunction in the GWS and BWS subgroups. At the same time, in the GS and BS subgroups, the percentage of children with autonomic dysfunction was 69% (30 out of 42 people) and 74% (28 out of 38 people), respectively.

**Conclusions:** Registration of a standard 5-minute rhythmocardiogram against the background of spontaneous breathing should be supplemented with a 1-minute breathing test in the diaphragmatic breathing mode with an imposed rhythm of 6 breathing movements per minute, which allows for assessing the presence or absence of parasympathetic dysfunction.

**KEY WORDS:** autonomic dysfunction, autonomic nervous system, muscle mass, deep breathing

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## INTRODUCTION

The absolute values of heart rate variability (HRV) parameters and their combinations often do not make it possible to make a reasonable conclusion about the features of the functional state of the patient's autonomic system. In this regard, the methodological approach to HRV analysis proposed by R.D.Beise and M. Hofer, who founded the private research company Biosign in 2000 [1], known for developing HRV-scanner hardware and software complexes, deserves attention. The essence of these scientists' innovative approach to the HRV analysis is that they reduced the significant number of heart rate variability parameters to three groups of indicators that characterize the ANS's tone, dynamics, and flexibility [2].

The tone of the ANS is estimated based on the average values of the R-R interval during the studied period or the heart rate (HR), which are inversely related to each other. The dynamics of ANS are judged by indicators SD1 and SD2, which are obtained by analyzing the Poincaré plot. They are measured in ms and describe the dispersion of heartbeats in a Poincaré diagram. SD1 expresses the width of the point cloud and is more sensitive to rapid high-frequency changes in heart rate, while SD2 describes the length of the point cloud and quantifies long-term HR. At the same time, SD1 is associated with rapid changes in heart rhythm, which mainly depends on parasympathetic activity. SD2 reflects long-term heart rate changes dependent on sympathetic and parasympathetic activity. The SD2/SD1 ratio indicates the balance between short-term and long-term heart rate variability. If this ratio is high (SD2 is significantly greater than SD1), this may indicate increased sympathetic nervous system activity. The flexibility of ANS regulation is judged by the range of heart rate fluctuations (HR). Parameters such as the standard deviation of the duration of R-R intervals, known as SDNN, the coefficient of variation, or the total power of the heart rate spectrum are suitable for this purpose.

For a comprehensive assessment of HRV based on the tone, dynamics, and flexibility of ANS regulation, the HRV-scanner software converts the results of HRV calculations into rank values from 0 to 100% based on the reference values of the parameters obtained during the examination of healthy people of the appropriate age. For example, a 10% flexibility score means that only 10 out of 100 healthy individuals have less flexibility than the subject, and the vast majority of 90% achieve a better value for this parameter. Diagrams 1 and 2 are a graphic illustration of this method of assessing the functional state of the ANS.

However, applying the described technique may lead to incorrect conclusions if the patient's breathing rate changes. The reason for this is the well-known phenomenon of sinus respiratory arrhythmia [3]. In particular, the high frequency of the examinee's breathing (above 12 respiratory movements in 1 minute) minimizes physiological respiratory sinus arrhythmia. It leads to the formation of a low HRV, which is mistakenly considered a manifestation of autonomic dysfunction. Such a situation in children is often associated with chronic psychoemotional stress [4]. Therefore, the authors of the methodology suggest that you must complement the standard 5-minute ECG recording with uncontrolled breathing with the following 1-minute deep breathing test with a frequency of 6 breathing movements per minute. Comparing the results of standard and deep breathing tests allows you to find the reason for the reduced HRV.

## AIM

In this context, we formulated the task of finding out to what extent the state of neurovegetative regulation in children and adolescents with sarcopenia differs from their peers without signs of sarcopenia.

## MATERIALS AND METHODS

The study included 80 healthy children aged 10 to 14 years who underwent rehabilitation at the Transcarpathian Regional Children's Sanatorium «Malyatko» and had signs of sarcopenia. The control group consisted of 40 children of the same age without signs of sarcopenia.

The sarcopenic index (SI, kg/m2) and hand grip strength (GS, kg) of the Handexer Grip Strength Tester digital hand dynamometer (USA), which were simultaneously in the range below the 25th percentile of the reference values of these indicators for the corresponding age and gender, were considered the criteria for sarcopenia. [5,6]. A bioelectrical impedance analyzer, "TANITA MC-780 MA" (Japan), was used to obtain the SI indicator. Height (L, m) was measured using a GIMA height meter (Italy).

The functional state of autonomic regulation was assessed using the HRV-scanner hardware and software complex (Biosign, Germany). This complex allows you to register and analyze the patient's ECG in the 1st standard lead during different time intervals and functional tests and obtain a number of heart rate variability parameters that characterize the activity of different parts of the ANS. A feature of this device that distinguishes it from other similar HRV analyzers is the possibility of simultaneous quantitative assessment of breathing frequency (HR, min-1) and the effect of breathing on heart rate (HR, %) (Fig.1, Fig. 2)

In our study, all examined children underwent a standard 5-minute ECG recording in the mode of uncontrolled spontaneous breathing followed by a 1-minute deep breathing test, during which the ECG was recorded in the mode of controlled deep diaphragmatic breathing with a frequency of 6 respiratory movements per minute. Both tests were performed in the sitting position of the examinee after 10 minutes of adaptation to the conditions of the examination and informing him about the specifics of the diagnostic procedure.

Tone (T, %), dynamics of various divisions of the ANS (D1, % and D2, %), and its flexibility (F, %) were estimated based on the primary HRV parameters according to a special software algorithm that takes into account the reference curves of these parameters for persons of a given age and sex. In addition, the state of the vegetative balance was judged by the D2/D1 ratio.

The main (with sarcopenia) and control (without sarcopenia) groups were divided into subgroups by sex, which included 38 boys and 42 girls and 22 boys and 18 girls, respectively. Statistical processing of the obtained data was conducted after testing the hypothesis about the normality of the distribution of indicators in subgroups using the Student's test for independent samples. The difference between subgroups was considered probable at the significance level of $p<0.05$.

## RESULTS

A comparison of indicators of neurovegetative regulation between subgroups of children with sarcopenia and without signs of sarcopenia, obtained according to the results of a standard 5-minute registration, showed the same type of differences in both girls and boys (Table 1). Thus, in the subgroup of girls with sarcopenia (GS), statistically significantly lower values of tone (T), dynamics of the parasympathetic link of the ANS (D1), and flexibility of autonomic regulation were obtained (F). At the same time, pronounced sympathicotonia was observed in the GS subgroup according to the D2/D1 ratio. Similar differences occurred between the subgroups of boys with sarcopenia (BS) and without signs of sarcopenia (BWS).

**Table 1.** Indicators of neurovegetative regulation obtained as a result of standard 5 min registration (M±SD)

| Indicators (M±SD) | Girls (n=60) | | Boys (n=60) | |
|---|---|---|---|---|
| | With sarcopenia GS (n=42) | Without sarcopenia GWS (n=18) | With sarcopenia BS (n=38) | Without sarcopenia BWS (22) |
| T,% | 65,3±10,4** | 89,9±15,3 | 65,3±10,4** | 82,4±12,3 |
| D1,% | 68,3±14,8** | 92,4±10,7 | 61,8±14,3** | 90,1±14,5 |
| D2,% | 76,3±12,5* | 86,4±14,8 | 76,3±12,5* | 79,3±14,9 |
| D2/D1, од. | 5,91±1,24*** | 2,91±0,82 | 6,04±1,83** | 3,11±0,93 |
| F, % | 66,7±16,8** | 93,5±13,1 | 67,3±14,9* | 89,2±12,4 |
| RR, $min^{-1}$ | 17,3±4,8* | 11,7±3,4 | 18,1±6,2* | 13,2±3,6 |
| BI, % | 12,4±6,8*** | 61,5±7,6 | 17,3±8,7*** | 58,7±13,0 |
| SI, $kg/м^2$ | 4,3±9,8* | 5,9±0,6 | 4,4±0,7* | 6,2±0,8 |
| GS, kg | 17,2±2,8* | 21,7±3,6 | 18,5±3,7** | 24,5±3,9 |

* - p<0,05; ** - p<0,01; *** - p<0,001.

**Table 2.** Indicators of neurovegetative regulation obtained as a result of the deep breathing test (M±SD)

| Indicators (M±SD) | Girls (n=60) | | Boys (n=60) | |
|---|---|---|---|---|
| | With sarcopenia GS (n=42) | Without sarcopenia GWS (n=18) | With sarcopenia BS (n=38) | Without sarcopenia BWS (22) |
| T,% | 75,3±12,2** | 92,2±14,7 | 75,3±12,5** | 85,7±13,7 |
| D1,% | 79,6±15,8 | 90,4±13,7 | 81,8±13,6 | 89,2±13,2 |
| D2,% | 60,2±11,9* | 76,6±10,8 | 56,3±10,2* | 69,2±12,6 |
| D2/D1, од. | 4,66±1,35*** | 2,35±0,89 | 5,44±1,73** | 2,47±0,94 |
| F, % | 74,8±17,2 | 91,5±15,8 | 77,3±18,4 | 68,9±16,5 |
| RR, $min^{-1}$ | 6,0 | 6,0 | 6,0 | 6,0 |
| BI, % | 22,1±5,8*** | 71,5±7,9 | 27,4±9,9*** | 68,1±12,6 |

* - p<0,05; ** - p<0,01; *** - p<0,001.

Respiratory rate (RR) was likely to be higher in children with sarcopenia compared to children without signs of sarcopenia, both among girls and boys. No significant differences were found between the subgroups regarding the impact of breathing on HRV (BI). However, the reason for this may not be the absence of the influence of breathing but the insufficient accuracy of measuring this indicator with the given number of observations, as indicated by its relatively large root mean square deviation.

Using rank values of indicators of neurovegetative regulation, expressed as a percentage of the reference values of these parameters, allows for identifying children with signs of autonomic dysfunction in the examined subgroups. Since there are currently no generally accepted criteria for autonomic dysfunction based on the proposed parameters, we accepted as such a criterion the simultaneous finding of at least 3 of the 4 ranking indicators of neurovegetative regulation in the range below the 25th percentile for this age category. After processing the examination results according to this algorithm, it became clear that there were no children with signs of autonomic dysfunction in the GWS and BWS subgroups. At the same time, in the GS and BS subgroups, the percentage of children with autonomic dysfunction was 69% (30 out of 42 people) and 74% (28 out of 38 people), respectively, illustrated in Fig. 3.

Taking into account the fact that children with signs of sarcopenia probably had a higher respiratory rate during standard registration, it can be assumed that low values of tone and dynamics of neurovegetative regulation in them are associated with excessive activation of the sympathetic link of the ANS. This, in turn, probably leads to reciprocal suppression of the parasympathetic link of the ANS and worsens the functional state of neurovegetative regulation. However, in the case of a decrease in the functional tension of the sympathetic link, it is quite possible to return to the optimal state of autonomous regulation. To discover this possibility, we used a deep breathing test, in which the subject makes controlled breathing excursions for 1 minute with a frequency of 6 breathing movements per minute. This breathing mode is a potent stimulator of the parasympathetic link of the ANS and can significantly increase the physiological

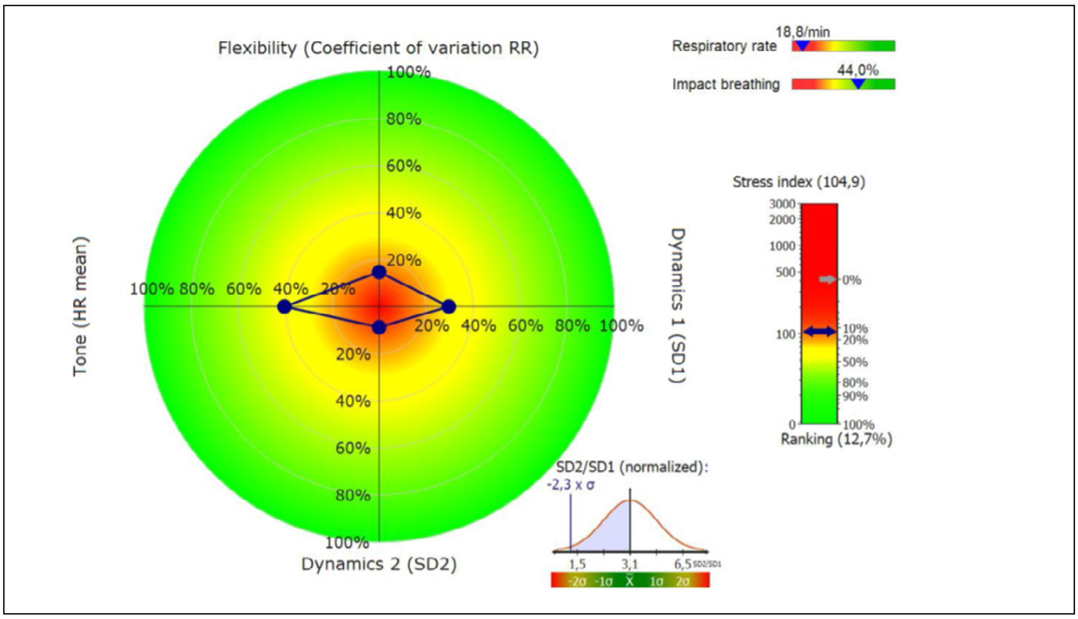


**Fig. 1**. An example of a visual representation of the results of a standard 5-minute registration of HRV of the examined P. (13 years old).

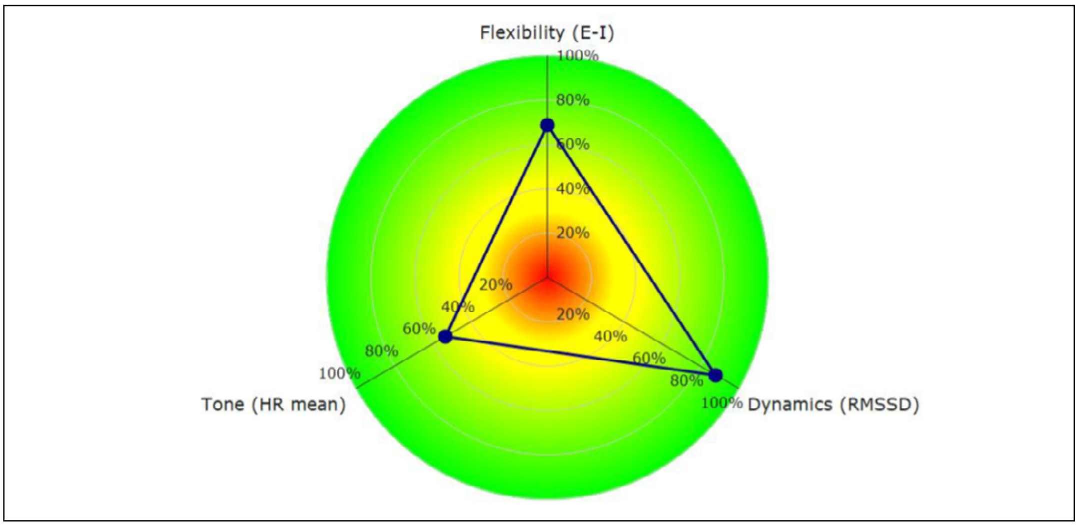


**Fig. 2.** An example of a visual representation of the results of the deep breathing test of the examined P. (13 years old).

sinus respiratory arrhythmia. However, this ability is preserved only in those examined who do not have parasympathetic autonomic dysfunction of organic origin. Thus, the breathing test helps to distinguish functional changes in parasympathetic regulation from pathological changes associated with morphological damage to the structures of the ANS.

Table 2 presents the data obtained from the deep breathing test in all four subgroups. In contrast to the standard 5-minute recording in the spontaneous breathing mode, the studied subgroups did not statistically significantly differ in many parameters of neurovegetative regulation. In particular, no difference was found between the D1 and F indicators between the subgroups of GS and GWS and BS and BWS. Probable differences were preserved in these subgroups according to T and D2/D1 indicators. The analysis of the presence of children with signs of autonomic dysfunction in the subgroups of GS and BS according to the results of the breathing test showed that their number significantly decreased compared to the standard 5-minute registration (Fig. 4) and amounted to 52 % (22 out of 42 people) and 39%, respectively (15 out of 38 people).

## DISCUSSION

Sarcopenia is a pathological condition of the musculoskeletal system, which is characterized by a loss of muscle mass and strength and is traditionally associated with adults and older people. However, in recent years, the opinion that it can also develop in children, especially against the background of other diseases or pathological conditions, is increasingly common in the literature [7]. Sarcopenia can have a significant negative impact on a child's physical,

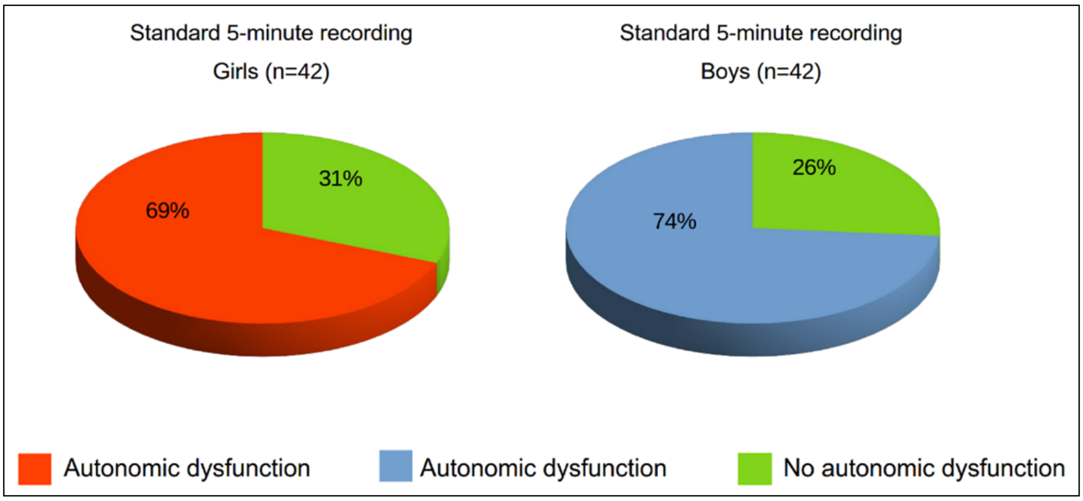


**Fig. 3.** The ratio of children with autonomic dysfunction and without signs of autonomic dysfunction according to the results of a standard 5-minute recording.

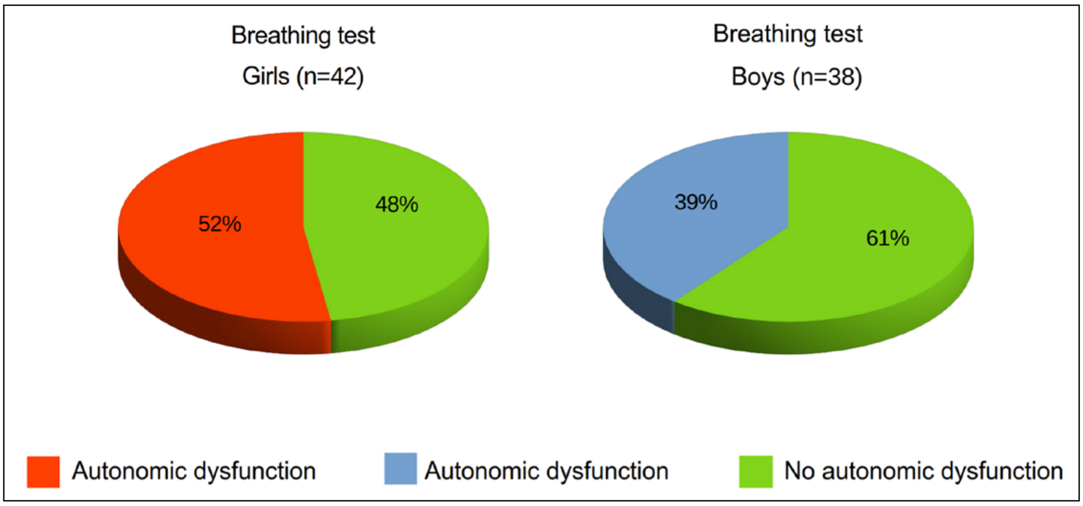


**Fig. 4.** The ratio of children with autonomic dysfunction and without signs of autonomic according to the results of the breathing test.

psychological, and social development, as skeletal muscle plays an important role in metabolism and overall health throughout the life cycle. New evidence suggests that prenatal (maternal diet during pregnancy and genetic defects) and postnatal factors (physical activity, hormones, dietary protein, and obesity) influence the acquisition of muscle mass and strength early in life [8]. As a result, low muscle mass and strength contribute to many adverse health outcomes in childhood. In particular, studies have demonstrated an inverse relationship between muscle mass and strength with individual and clustered metabolic risk factors [9]. The literature also consistently reports low muscle mass and strength are associated with decreased bone parameters during growth, increasing the risk of osteoporosis in old age[10]. In addition, increased muscle mass is associated with improved neural development in the early years of life [11].

Despite the growing interest in childhood sarcopenia, this concept still needs to be implemented in terms of identification criteria [12]. Advances in research in this area will allow practitioners to recognize sarcopenia better, not only in pediatric patients with chronic diseases but possibly also in otherwise healthy children. In our opinion, it became possible to identify children with signs of sarcopenia due to the widespread introduction into clinical practice of non-invasive and highly informative bioimpedance analysis of the component composition of the body. This method makes it possible to quantitatively characterize the total content of skeletal muscles in the subject's body and their content in individual regions of the body. It is the appendicular mass of skeletal muscles, related to the square of height, that is considered an informative sarcopenic index. If you combine this indicator with the results of standard hand dynamometry, you can get a fairly accurate criterion of sarcopenia. In our study, the finding of both parameters in the range below the 25th percentile of their reference values for a given age and gender is considered a criterion. Subgroups of girls and boys with sarcopenia, separated in this way, demonstrated significant differences in the functional state of the ANS compared to their peers without signs of sarcopenia. These differences were reduced to a decrease in the tone of neurovegetative regulation, a decrease in the dynamics of the parasympathetic link of the ANS, and the flexibility of autonomic regulation in general. Such features of the ANS in this contingent, in our opinion, significantly reduce the adaptive reserve of the children's body and are a risk factor for the occurrence of metabolic disorders, cardiovascular pathology, and growth retardation.

The results of our study showed that the use of a standard 5-minute ECG recording to calculate HRV leads to overdiagnosis of autonomic dysfunction in children with sarcopenia. The reason for this, in our opinion, is insufficient consideration of the effect of breathing frequencies on HRV indicators. In many of the examinees, a high respiratory rate neutralizes the physiological impacts of sinus respiratory arrhythmia and artificially lowers HRV. At the same time, if you record ECG in the diaphragmatic slow breathing mode with an imposed rhythm of 6 respiratory movements per minute, the activation of the parasympathetic link can significantly increase HRV. This approach to diagnosing autonomic dysfunction in the HRV-scanner hardware and software complex uses a 1-minute deep breathing test. With its help, our study found that standard registration overestimated the number of individuals with autonomic dysfunction among girls and boys by 17% and 35%, respectively.

## CONCLUSIONS

1. In children and adolescents with sarcopenia, there is a high probability of the formation of autonomic dysfunction, which is manifested in a decrease in the tone, dynamics, and flexibility of neurovegetative regulation.
2. For the instrumental diagnosis of autonomic dysfunction, it is advisable to study heart rate variability with the help of modern hardware and software complexes, particularly the HRV scanner (Biosign, Germany).
3. Registration of a standard 5-minute rhythmocardiogram against the background of spontaneous breathing should be supplemented with a 1-minute breathing test in the mode of diaphragmatic breathing with an imposed rhythm of 6 breathing movements per minute, which allows assessing the presence or absence of parasympathetic dysfunction.

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## CONFLICT OF INTEREST

The Authors declare no conflict of interest

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