Malnutrition Prevalence in Adult and Older Adults Patients with Leukemia in Pretreatment Phase

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Prevalência de Desnutrição em Pacientes Adultos e Idosos em Fase de Pré-Tratamento de Leucemia Prevalencia de Desnutrición en Pacientes Adultos y Ancianos en la Fase Pretratamiento de la Leucemia

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ABSTRACT

Introduction: The nutritional status in the pretreatment phase may be related to unfavorable clinical outcomes in cancer patients. **Objective:** To assess the nutritional status of adult and older adults patients with leukemia in the pretreatment cancer phase. **Method**: Cross-sectional, retrospective study, involving patients with leukemia in the pretreatment cancer phase. The inclusion criteria were: ≥20 years of age, both genders and enrollment at the National Cancer Institute José Alencar Gomes da Silva (INCA). The exclusion criteria were not having confirmed diagnosis of leukemia, registration of the Patient-Generated Subjective Global Assessment and not having submitted to previous cancer treatment. Chi-square and Student's t tests were used. **Results**: 69 patients were evaluated with leukemia in the pretreatment cancer phase, mostly men (52.2%) under 60 years of age (52.2%). The prevalence of malnutrition was 65.2%, being more expressive in the older adults (78.8%, p=0.023). The prevalence of nutritional risk had the same frequency (65.2%), however it was higher in patients with comorbidities (80.8%, p=0.017) and smoking history (90.9%, p=0.056). **Conclusion**: Most patients with leukemia started their cancer treatment with impaired nutritional status, which was exacerbated for those with chronic leukemia, older adults, with comorbidities and history of smoking.

Key words: Leukemia; Nutritional Status; Malnutrition; Prevalence; Drug Therapy.

RESUMO

Introdução: O estado nutricional em fase pré-tratamento pode estar relacionado a desfechos clínicos desfavoráveis em pacientes com câncer. **Objetivo:** Avaliar o estado nutricional de pacientes adultos e idosos com leucemia em fase de pré-tratamento oncológico. **Método:** Trata-se de um estudo transversal, retrospectivo, envolvendo pacientes com leucemia em fase pré-tratamento oncológico. Os critérios de inclusão foram ≥20 anos de idade; ambos os sexos; e matrícula no Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Os critérios de exclusão foram não ter diagnóstico confirmado de leucemia; registro de avaliação do estado nutricional por meio da avaliação subjetiva global produzida pelo paciente; e não ter recebido tratamento oncológico prévio. Os testes qui-quadrado e *t* de Student foram utilizados. **Resultados:** Foram avaliados 69 pacientes com leucemia em fase pré-tratamento oncológico, sendo em sua maioria homens (52,2%) com menos de 60 anos de idade (52,2%). A prevalência de desnutrição foi de 65,2%, sendo mais expressiva nos idosos (78,8%, p=0,023). A prevalência de risco nutricional apresentou a mesma frequência (65,2%), no entanto, foi maior em pacientes com comorbidades (80,8%, p=0,017) e história de tabagismo (90,9%, p=0,056). **Conclusão:** A maior parte dos pacientes com leucemia iniciou seu tratamento oncológico com o estado nutricional debilitado, o que se exacerbou entre aqueles com leucemia crônica, idosos, com comorbidades e história de tabagismo.

Palavras-chave: Leucemia; Estado Nutricional; Desnutrição; Prevalência; Tratamento Farmacológico.

RESUMEN

Introducción: El estado nutricional en la fase de pretratamiento puede estar relacionado con resultados clínicos desfavorables en pacientes con cáncer. **Objetivo:** Evaluar el estado nutricional de pacientes adultos y ancianos con leucemia en fase de pretratamiento de cáncer. **Método**: Este es un estudio transversal, retrospectivo, que involucra a pacientes con leucemia en la fase de pretratamiento de cáncer. Los criterios de inclusión fueron ≥20 años de edad; ambos os sexos; e inscripción en el Instituto Nacional del Cáncer José Alencar Gomes da Silva (INCA). Los criterios de exclusión fueron no tener un diagnóstico confirmado de leucemia; registro de la evaluación del estado nutricional a través de la Valoración Subjetiva Global-Generada por el Paciente; y no haber recibido tratamiento previo contra el cáncer. Se utilizaron las pruebas de Chi-cuadrado y *t* de Student. **Resultados**: Se evaluaron 69 pacientes con leucemia en la fase de pretratamiento de cáncer, en su mayoría hombres (52,2%) menores de 60 años (52,2%). La prevalencia de desnutrición fue del 65,2%, siendo más expresiva en los ancianos (78,8%, p=0,023). La prevalencia del riesgo nutricional tuvo la misma frecuencia (65,2%), sin embargo, fue mayor en pacientes con comorbilidades (80,8%, p=0,017) y antecedentes de tabaquismo (90,9%, p=0,056). **Conclusión**: La mayoría de los pacientes con leucemia comenzaron su tratamiento con un estado nutricional deteriorado, que se exacerbó entre aquellos con leucemia crónica, ancianos, con comorbilidades y antecedentes de tabaquismo.

Palabras clave: Leucemia; Estado Nutricional; Desnutrición; Prevalencia; Quimioterapia.

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INTRODUCTION

The incidence and mortality by cancer are increasing in the world. Estimates of the Global Cancer Observatory show in 2018 an incidence of leukemia of 249 thousand cases for men, ranking tenth among the most incident tumors in the world. For women, 187 thousand cases are estimated, being in the twelfth position[1,2]. In Brazil, for each year of the triennium 2020-2022, 5,920 new cases of leukemia are estimated for men and 4,890 for women[3].

The World Health Organization (WHO) classifies leukemias in myeloid and lymphoid based in the type of white cells affected. Thus, there are four main leukemias: acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML) and chronic lymphocytic leukemia (CLL)[4,5]. Among these, the most prevalent in adults are AML, CML and CLL[6].

Scarce are the studies that portray the nutritional status in adult and older adult patients with leukemia, most of the studies are with children[7-9]. In addition, it is believed that malnutrition is an underrecognized problem in hospitals[10]. The European Society of Clinical Nutrition and Metabolism (ESPEN) and the American Society of Parenteral and Enteral Nutrition (ASPEN) recommend early screening of the nutritional status of all the inpatients[11,12].

Of the several tools of assessment of nutritional status, the Patient-Generated Subjective Global Assessment (PG-SGA) was developed and validated for nutritional assessment of oncologic patients and ESPEN and ASPEN[11-13] recommend its use. In addition, recent studies are demonstrating the relation between debilitated nutritional status assessed by PG-SGA and clinical outcomes as the extension of the hospitalization and lower survival in patients with hematologic cancer[7,14].

Considering the relevance of the assessment of the nutritional status and the scarcity of this data in patients with leukemia in adults and older adults, the objective of this manuscript was to assess the nutritional status in the groups of patients in oncologic pre-treatment phase.

METHOD

Retrospective, cross-sectional study with sample by convenience conducted through analysis of patients charts with leukemia enrolled at the Hematologic Clinic of the National Cancer Institute José Alencar Gomes da Silva (INCA), between January 2009 and December 2013. The Institutional Review Board of the institution approved the study, number CAAE 14452919,0,0000,5274.

According to the eligibility criteria, the patients selected should be: ≥20 years old, confirmed diagnosis of leukemia, enrollment at INCA in the period of interest, register of the nutritional status evaluation through PG-SGA and not submitted to previous oncologic treatment.

The inclusion criteria were ≥20 years old, both genders, enrollment at INCA in the period of interest. The exclusion criteria were not having confirmed diagnosis of leukemia, no register of nutritional status evaluation through PG-SGA and not submitted to previous oncologic treatment.

Trained investigators extracted data of interest in the pre-treatment period and registration in the specific form as: gender (male *vs.* female), age (<60 *vs*. ≥60 years), skin color (Caucasian *vs.* Non-Caucasian), education (until complete high school *vs*. university), employment bond (yes *vs.* no), personal income (<1 *vs.* ≥1 minimum wage), presence of comorbidities – arterial hypertension and diabetes *mellitus* – (yes *vs.* no), smoking history (is smoking and/or quit smoking: yes *vs.* no), alcoholism history (is drinking and/or already used alcohol: yes *vs*. no) and PG-SGA (classification: A *vs*. B+C; global score: <9 *vs*. ≥9 points). Later, all the data of the review of the physical and electronic charts were typed in electronic spreadsheet in specialized software.

Previously trained institution nutritionists applied the PG-SGA. The tool is formed by two parts. The first involves the assessment of four different domains: i. Changes of body weight (score ≤5 points); ii. Food intake (score ≤4 points); iii. Presence of symptoms of nutritional impact (score ≤24 points); and iv. Functioning (score ≤3 points). Based in this part of the tool, a global score is generated with the sum of the points of each one of the four domains and can range from 0 to 36 points (as higher the score, higher is the nutritional risk). Patients with global score >9 points were considered in nutritional risk[13]. The second encompasses the history of the patient with data as diagnosis, age, metabolic demand, use of corticosteroids and physical exam, including loss of subcutaneous fat, loss of muscle mass and edema or ascites. In the end of the evaluation of the complete tool, each patient was classified as well nourished (A), moderately malnourished (B) or severely malnourished (C).

The analysis of the data was performed in the software STATA ® (Stata Data Analysis and Statistical Software; Stata Corp., College Station, Texas, USA), version 13.0. The descriptive statistics were expressed as percent (%) absolute or relative and mean and standard deviation (SD) as needed. The test Kolmogorov-Smirnov was utilized to evaluate the distribution of the numerical variables. To evaluate the differences among the groups according to the type of leukemia (chronic and acute) and the nutritional status, the chi-square test for proportions for categorical variables and test t of Student to evaluate the difference

between means of the PG-SGA global score and for each type of leukemia were utilized. The results were considered statistically significant when p<0.05, with confidence intervals of 95%.

RESULTS

Of the 313 individuals enrolled in INCA Hematology Clinic between January 2009 and December 2013, after verification of the electronic chart, 267 individuals remained. Of these, 210 physical charts were analyzed and were included in the final sample of 69 patients, the main reason for exclusion was missing information of the PG-SGA (45.0%) nutritional status (Figure 1).

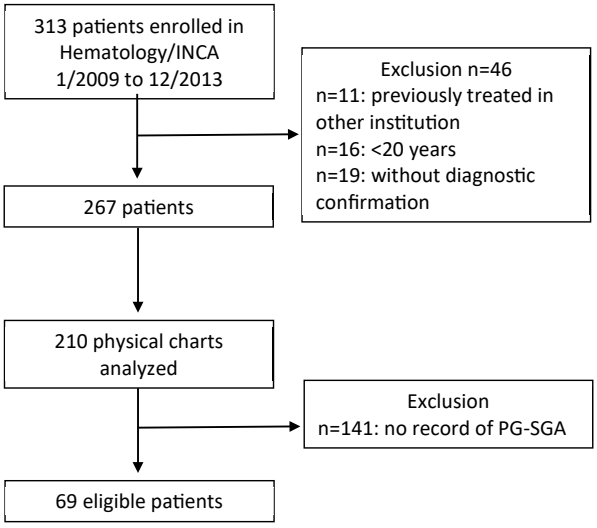

Figure 1. Flowchart of patients selection

Captions: INCA=National Cancer Institute José Alencar Gomes da Silva. n=Number of observation. PG-SGA=Patient-Generated Subjective Global Assessment.

Most of the patients with leukemia in oncologic pre-treatment were males (52.2%), under 60 years old with prevalence of malnutrition and nutritional risk of near 65.2% (Table 1).

The sample was divided in two groups: those who were diagnosed with chronic leukemia (n=33) and those who were diagnosed with acute leukemia (n=36). In the group with chronic leukemia, it occurred high prevalence for older adults (p=0.012) in nutritional risk(p=0.023) (Table 1).

According to Figure 2, which demonstrates the global score of PG-SGA according to the type of leukemia, patients with chronic leukemia have more nutritional risk with higher score than those with acute leukemia [13 (SD: 7) vs. 9 (SD: 5) points, p=0.034).

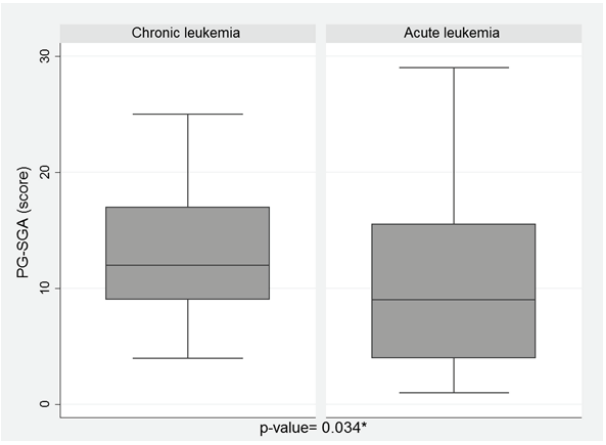

Figure 2. Global score of the patient-generated subjective global assessment according to the type of leukemia (N= 69)

Captions: PG-SGA=Patient-Generated Subjective Global Assessment. Mean global score of PG-SGA in patients with chronic leukemia =13 (standard-deviation: 7) points; acute= 9 (standard deviation: 5) points. *p-value, test t of Student.

The prevalence of malnutrition in the total sample was higher in older adults (78.8%, p-value=0.023). The prevalence of nutritional risk was bigger in patients with comorbidities (80.8%, p-value=0.017) and smoking history (90.9%, p-value=0.056) (Table 2).

DISCUSSION

The present study showed that the greatest part of the patients with leukemia already initiated their oncologic treatment in debilitated nutritional status, defined by the presence of malnutrition and/or nutritional risk in elevated proportions. The prevalence of these disorders was more expressive among those with chronic leukemia, older adults, with comorbidities and smoking history.

As nutritional status is one of the potentially modifiable factors and related to unfavorable clinical outcomes, its monitoring should be early, continuous and individualized through the entire course of the disease. It is critical in the oncologic pre-treatment for the early diagnosis of nutritional disorders, serving as base for the planning of a nutritional therapy specialized and individualized[13].

The PG-SGA stands out as the proper method for this purpose as it is a simple, little invasive and low-cost clinical tool through which adverse factors that influence the nutritional status can be evaluated[15]. In addition, despite the subjective assessment of malnutrition provided by the tool (A, B or C), its global score allows the objective interpretation and more accurate monitoring of the individual variations of the nutritional status, identifying patients who need urgent nutritional intervention and helping to prevent or reduce the symptoms during all the lines of oncologic treatment that may be established[16].

Table 1. Prevalence of selected variables according to the type of leukemia (N= 69)

Variable		Leukemia		p-value*
	Total n (%)	**Chronic** (n=33) n (%)	**Acute** (n=36) n (%)	
Age (years)				
<60	36 (52.2%)	12 (33.3%)	24 (66.7%)	
≥60	33 (47.8%)	21 (63.6%)	12 (36.4%)	**0.012**
Gender				
Male	36 (52.2%)	17 (47.2%)	19 (52.8%)	
Female	33 (47.8%)	16 (48.5%)	17 (51.5%)	0.916
Skin color white**				
Yes	38 (55.9%)	20 (52.6%)	18 (47.4%)	
No	30 (44.1%)	13 (43.3%)	17 (56.7%)	0.446
Education				
≤ high school	58 (84.0%)	28 (48.3%)	30 (51.7%)	
≥ university	11 (16.0%)	5 (45.5%)	6 (54.5%)	0.864
Employment bond**				
Yes	26 (41.9%)	10 (38.5%)	16 (61.5%)	
No	36 (58.1%)	20 (55.6%)	16 (44.4%)	0.184
Personal income**				
<1 minimum wage	19 (33.9%)	12 (63.2%)	7 (36.8%)	
≥1 minimum wage	37 (66.1%)	21 (56.8%)	16 (43.2%)	0.645
Comorbidities**				
Yes	26 (41.3%)	13 (50.0%)	13 (50.0%)	
No	37 (58.7%)	20 (54.0%)	17 (46.0%)	0.751
Smoking**				
Yes	11 (17.7%)	6 (54.5%)	5 (45.5%)	
No	51 (82.3%)	24 (47.1%)	27 (52.9%)	0.652
Alcoholism**				
Yes	19 (31.1%)	9 (47.4%)	10 (52.6%)	
No	42 (68.9%)	21 (50.0%)	21 (50.0%)	0.849
PG-SGA (classification)				
A: no malnutrition	24 (34.8%)	9 (37.5%)	15 (62.5%)	
B+C: malnutrition	45 (65.2%)	24 (53.3%)	21 (46.7%)	0.210
PG-SGA (global score)				
<9: no nutritional risk	24 (34.8%)	7 (29.2%)	17 (70.8%)	
≥9: nutritional risk	45 (65.2%)	26 (57.8%)	19 (42.2%)	**0.023**

Captions: PG-SGA=Patient-Generated Subjective Global Assessment. *p-value: Chi-square test for proportions. **Variables with missing data, therefore, with relative frequency.

Therefore, the knowledge of nutritional status of the patient with cancer is an essential part of the clinical treatment. The prevalence of malnutrition in patients with cancer varies nearly from 20% to more than 70% in world studies, with differences related to age, type and cancer stage. It is estimated that death rates of patients with cancer are 10% to 20% attributed to malnutrition and not to the disease's malignancy[17,18]. In addition, malnutrition is associated to unfavorable outcomes as loss of muscle mass, immune compromise with increase of infections, psychosocial stress, poor quality of life, toxicity of the treatment and more time of hospitalization with cost increase[11].

Studies demonstrated that the prevalence of malnutrition specifically in hematologic patients at

Table 2. Selected variables according to the nutritional status (N=69)

Variables	Malnutrition*		p-value***	Nutritional Risk**		p-value***
	No	Yes		No	Yes	
Age (years)						
<60	17 (47.2%)	19 (52.8%)	**0.023**	16 (44.4%)	20 (55.6%)	0.078
≥60	7 (21.2%)	26 (78.8%)		8 (24.2%)	25 (75.8%)	
Gender						
Male	16 (44.4%)	20 (55.6%)	0.078	16 (44.4%)	20 (55.6%)	0.078
Female	8 (24.2%)	25 (75.8%)		8 (24.2%)	25 (75.8%)	
Skin color white**						
Yes	13 (43.3%)	17 (56.7%)	0.218	11 (29.0%)	27 (71.0%)	0.339
No	11 (28.9%)	27 (71.1%)		12 (40.0%)	18 (60.0%)	
Education						
≤ high school	20 (34.5%)	38 (65.5%)	0.904	19 (32.8%)	39 (67.2%)	0.418
≥ university	4 (36.4%)	7 (63.6%)		5 (45.5%)	6 (54.5%)	
Employment bond**						
Yes	12 (46.2%)	14 (53.8%)	0.210	12 (46.2%)	14 (53.8%)	0.210
No	11 (30.6%)	25 (69.4%)		11 (30.6%)	25 (69.4%)	
Personal income**						
<1 minimum wage	8 (42.1%)	11 (57.9%)	0.474	6 (31.6%)	13 (68.4%)	0.644
≥1 minimum wage	12 (32.4%)	25 (67.6%)		14 (37.8%)	23 (62.2%)	
Comorbidities**						
Yes	6 (23.1%)	20 (76.9%)	0.063	5 (19.2%)	21 (80.8%)	**0.017**
No	17 (45.9%)	20 (54.1%)		18 (48.6%)	19 (51.4%)	
Smoking**						
Yes	4 (36.4%)	7 (63.6%)	0.946	1 (9.1%)	10 (90.9%)	**0.056**
No	18 (35.3%)	33 (64.7%)		20 (39.2%)	31 (60.8%)	
Alcoholism**						
Yes	8 (42.1%)	11 (57.9%)	0.396	6 (31.6%)	13 (68.4%)	0.753
No	13 (30.9%)	29 (69.1%)		15 (35.7%)	27 (64.3%)	

Captions: *Diagnosis of malnutrition defined through patient-generated subjective global assessment. **Nutritional risk defined through patient-generated subjective global assessment. ***p-value: Chi-square test for proportions.

hospital admission utilizing the PG-SGA varied from 17.5% to 47.7%[14,19,20]. This range of values can be justified by the different types of hematologic cancers included in these samples. In studies that assessed only patients with acute leukemia, lower prevalence and less variations were observed, from 15% to 27.9%[7,21].

This study portrayed higher prevalence rates of malnutrition and nutritional risk (65.2%) than those reported previously. Despite the clinical heterogeneity of chronic leukemias, the sample is formed solely by inpatients, symptomatic and needing immediate beginning of the oncologic treatment, which, probably justifies the strong expressivity of the deficit or nutritional risk verified. It is reaffirmed, therefore, the early necessity of nutritional support in individuals with cancer[11].

In addition, among the patients with chronic leukemia, it is noticed a higher proportion of older adults (p=0.012) in nutritional risk (p=0.023), with more elevated means of global score of PG-SGA (p=0.034). These leukemias are almost exclusive of individuals older than 40 years, with emphasis for CLL with mean age older than 70 years at the diagnosis. Most of the patients is diagnosed at an early and asymptomatic stage, initiating therapy years later, which increases the mean age of the first oncologic treatment[6].

Because of population ageing and increase of life expectancy of older adults, the number of older patients

with chronic leukemia increases in parallel. Studies show that older adults with malignant tumors are more propense to malnutrition, reduction of functionality, reduction of cognitive capacities and increase of inflammation, leading to loss of lean body mass, more energetic expenditure and increase of thermogenesis[22-25].

In addition, many chronic diseases associated to older adult reduce the intake and absorption of food, which affects the nutritional status negatively[26]. Santo et al.[27], in a Brazilian study report that 65.6% of older adults with cancer have difficulties in feeding themselves and the most mentioned symptoms were dry mouth, intestinal constipation, loss of appetite and early satiety[27]. Another study revealed still that more than half of the older adults with hematologic tumors have nutritional status deficit[28].

It is concluded in these findings that the prevalence of moderate (B) and severe (C) malnutrition was bigger in older adults (78.8%, p-value=0.023). Corroborating these results, a study developed in Brazil by Pinho et al.[29], with 4,783 patients with different types of cancer showed that there is high risk of older adults to present malnutrition (OR: 1.83; CI: 1.59-2.11), also evaluated by PG-SGA[29]. A study with 68 patients with acute leukemia showed that adults older than 60 years old are associated to severe malnutrition[21].

Nutritional risk was more prevalent in patients with comorbidities (80.8%, p-value=0.017) and with smoking history (90.9%, p-value=0.056). It is known that patients with pre-existing comorbidities to cancer or smoking history have specific metabolic and physiologic conditions where nutritional risk is more frequent[30,31].

Malnutrition led to several unfavorable outcomes[25,32], considering still that the patient evaluated herein is in pre-treatment and will be submitted to several oncologic therapeutic, that potentially exacerbate the nutritional deficits with consequential increase of risks of unfavorable outcomes[11]. Therefore, it is important the role of the nutritionist in the early nutritional assistance with other health professionals to promote the improvement of the nutritional status of these patients even before the beginning of the oncologic treatment.

The results of the present study can help to devise hypothesis for new studies about the importance of the nutritional status in patients with leukemia. Methodological limitations need to be addressed. PG-SGA-based nutritional diagnosis may have some level of compromise because of possible memory bias as some patients can have difficulty in responding about the domain of weight loss in the last six months accurately and specify the food intake during the last month. The sample involved a relatively small number of patients of only one institution and with different types of leukemia. Therefore, the development of more studies with bigger, more homogeneous samples and multicentric is paramount. Because of the small sample, more robust statistical analyzes were not performed. However, as the data about nutritional status in patients with hematologic cancer are scarce, the strength of the work is to explore a field less studied and important, utilizing an internationally recognized tool with translation and cultural adjustment.

CONCLUSION

With these findings, the conclusion is that most of the patients diagnosed with leukemia initiated its oncologic treatment already with nutritional compromise (malnutrition and/or nutritional risk) and for those with chronic leukemia, comorbidities and smoking history (is smoking and/or quit smoking), this compromise was exacerbated.

Additionally, based in the PG-SGA scores, most of the patients needed nutritional intervention, being highlighted the importance of the early nutritional diagnosis and action of the multi-disciplinary team, including the nutritionist in order to offer proper treatment emphasizing nutritional therapy.

CONTRIBUTIONS

Thiago Huaytalla Silva and Livia Costa de Oliveira contributed substantially for the conception and design of the study, gathering, analysis and interpretation of the data, wording and critical review. All the authors approved the final version to be published.

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DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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