Barriers and enablers to deprescribing benzodiazepines in older adults: elaborating an instrument and validating its content

Facilitadores e dificultadores do processo de desprescrição de benzodiazepínicos em idosos: elaboração de um instrumento e validação de seu conteúdo

Luciana Soares Rodrigues, Marlon Silva Tinoco, Luanna Gabriella Resende da Silva, Clareci Silva Cardoso, Luana Carolaine Campos de Sousa, Ana Maria Rosa Freato Gonçalves, André Oliveira Baldoni

OBJECTIVE: To elaborate and validate an instrument on barriers and enablers to deprescribing benzodiazepines in the patient’s perspective. METHODS: This study was conducted in 3 stages: (1) a methodological stage, (2) a semi-structured pilot interview with 25 older adults undergoing clonazepam deprescribing, and (3) content validation with the Delphi technique. Content validation was performed by 50 specialists with degrees and/or experience with primary health care and/or health care of older adults, such as physicians, pharmacists, and nurses. For evaluating the obtained results, we analyzed the concordance of evaluations with the coefficient of content validity (CCV). We considered values equal to or higher than 0.8 as acceptable levels of concordance. RESULTS: The instrument was considered validated in the first round of evaluation, where all items obtained a CCV of more than 0.8 in the specialists’ assessment. Nevertheless, they proposed improvements that were incorporated to the final version of the questionnaire. CONCLUSION: The instrument represents an important tool to be used by health care professionals for optimizing benzodiazepine deprescribing, with suitable levels of clarity and validity. KEYWORDS: deprescribing; benzodiazepine receptors; eldercare; validation study; questionnaire.

RESUMO

OBJETIVO: Elaborar e validar um instrumento sobre facilitadores e dificultadores do processo de desprescrição de benzodiazepínicos na perspectiva do paciente. METODOLOGIA: Estudo desenvolvido em três etapas, quais sejam: (1) metodológica, (2) entrevista piloto semiestruturada com 25 idosos em desprescrição de clonazepam e (3) validação de conteúdo por meio da técnica de Delphi. A validação deu-se por 50 especialistas com formação e/ou experiência na área da Atenção Primária à Saúde e/ou Saúde do Idoso, entre eles médicos, farmacêuticos e enfermeiros. Como medidas para avaliar os resultados obtidos, foi analisada a concordância da avaliação por meio do coeficiente de validade de conteúdo (CCV). Considerou-se como nível aceitável de concordância o valor maior ou igual a 0,8. RESULTADOS: O instrumento foi considerado validado na primeira roda de avaliação, em que todos os itens avaliados obtiveram CCV superior a 0,8 na avaliação dos especialistas. Entretanto, estes propuseram sugestões de melhorias que foram incorporadas na versão final do questionário. CONCLUSÃO: O instrumento apresenta-se como uma importante ferramenta a ser utilizada pelos profissionais de saúde para a otimização do processo de desprescrição de benzodiazepínicos, possuindo índice de clareza e de validade adequados. PALAVRAS-CHAVE: desprescrições; receptores benzodiazepínicos; assistência a idosos; estudo de validação; questionário.

*Universidade Federal de São João del-Rei — Centro-Oeste Dona Lindu Campus — Divinópolis (MG), Brazil.
*Universidade de São Paulo, Ribeirão Preto Medical School – Ribeirão Preto (SP), Brazil.

Correspondence data
André Oliveira Baldoni – Universidade Federal de São João del-Rei – Rua Sebastião Gonçalves Coelho, 400 – Chanadour – CEP: 35501-296 – Divinópolis (MG), Brazil. E-mail: andreabaldoni@ufsj.edu.br
Received on: 05/17/2021. Accepted on: 10/10/2021.

How to cite this article: Rodrigues LS, Tinoco MS, Silva LGR, Cardoso CS, Sousa LCC, Gonçalves AMRF, Baldoni AO. Barriers and enablers to deprescribing benzodiazepines in older adults: elaborating an instrument and validating its content. Geriatr Gerontol Aging. 2021;15:e0210059. https://doi.org/10.53886/gga.e0210059
https://doi.org/10.53886/gga.e0210059

This article is published in Open Access under the Creative Commons Attribution license, which allows use, distribution, and reproduction in any medium, without restrictions, as long as the original work is correctly cited.
INTRODUCTION

Benzodiazepines (BZD) are among the main medications consumed by older adults, being normally used for treating insomnia and other sleep disorders such as restless leg syndrome, in addition to depression, anxiety, and alcohol abstinence. However, the literature recommends careful use of these drugs, classifying them as potentially inappropriate medications for older adults (PIM) due to the potential risk of adverse events and limited benefits of its chronic use.

The therapeutic effects of these medications are short-term, and long-term use may cause physical and psychological dependence in addition to undesirable effects such as falls, fractures, sedation, car accidents, and cognitive impairment. In this sense, it is important to consider the risks and benefits of continuing using this drug class and propose strategies to rationalize their use, such as deprescribing protocols.

Deprescribing is one of the alternatives for avoiding indiscriminate use of medications and is performed by gradually reducing the dose, resulting in partial or complete medication withdrawal. The process should happen in a planned, systematized, and supervised manner, seeking to improve safety in the use of medications and the patient’s quality of life.

Deprescribing success rates may be achieved when patients are properly guided, with a clear plan, and informed as benefits and possible symptoms of withdrawal. The use of verbal and written information on the benefits and difficulties in deprescribing should be associated to the use of a protocol that helps medical professionals in gradually withdrawing BZD.

Among factors that facilitate deprescribing, we highlight the restoration of sleep control and elimination of the exposure to adverse effects of the drug. Many patients may achieve success with BZD deprescribing, obtaining benefits such as improvements in memory, more natural sleep, and increased self-confidence by achieving medication withdrawal or tapering. On the other hand, there are barriers in the health system and those inherent to patients and professionals, such as doubts regarding the real need for deprescribing and withdrawal symptoms such as anxiety, irritability, and insomnia.

In view of this evidence, this study is justified by the unavailability, in Brazil, of validated instruments that consider enablers and barriers to BZD deprescribing in the patient’s perspective. This way, the elaboration and validation of an instrument may contribute to the work of health professionals in the defying moment of deprescribing BZDs. Therefore, the objective was to develop and validate an instrument that highlights the facilitating and hindering aspects of the BZD deprescription process in the elderly, from the patient’s perspective.

METHODS

This study was conducted in 3 stages:

1. Elaboration of the instrument, represented by a literature review for identifying enablers and barriers to deprescribing BZDs;
2. A semi-structured pilot interview performed with older adults undergoing clonazepam deprescribing; and
3. Validation of the instrument’s content through an analysis by specialists.

Health professionals with degrees and/or experience in primary health care (PHC) and/or health care of older adults were invited to the content validation process.

Elaboration of the instrument

We performed a narrative review of the scientific literature, with a synthesis of studies of the area involving this construct. We did not use specific descriptors or publication periods for selecting studies, and sources were not predetermined. In order to elaborate the data collection instrument, we included studies published in English that approached enablers and barriers to deprescribing. Most of the selected studies were indexed in the PubMed, ScienceDirect, and Scientific Electronic Library Online (SciELO) databases. We considered these search criteria to satisfactorily meet the objectives of this work. Moreover, the synthesis of the evaluated studies was enough for demonstrating problems and positive aspects of tapering medications. The first version of the questionnaire also counted on the expertise of 8 clinical pharmacy professionals for reading the retrieved studies and selecting the items to be contemplated by the instrument.

After reviewing the literature, the concepts of interest for constituting the construct — enablers and barriers to deprescribing BZDs — were selected, dividing the instrument in 3 parts. The first part contemplated questions on the barriers to deprescribing BZDs, considering information on:

1. Insecurity in deprescribing;
2. Difficulty in splitting pills;
3. Difficulty sleeping after guidance on sleep hygiene;
4. and 5. Lack of support by family and/or health professionals; and
6. Withdrawal symptoms when tapering/withdrawing the medication.

The second part of the instrument contemplated enablers of deprescribing, with questions regarding:

1. The patient’s comprehension of the importance of deprescribing;
2. The importance of in-person meetings and/or supervised remote support by health professionals;
3. Improvements in general health status; and
4. The importance of support by the health professional.

Answers were presented in a Likert scale format and numbered 1–3 as follows: 1 = “yes, it happened to me;” 2 = “it happened a few times but was not important;” and 3 = “no, this did not happen.”

Finally, in the third part, we included further information, with 2 questions. One of them asked the patient to describe the barriers or enablers that might not have been mentioned by the multiple-choice questions and the other was about the possible recommendation of the deprescribing process to friends and family members. This last question had the following answer categories: “Yes, definitely;” “I would have to think about it;” or “No.” It is important to note that, after all questions, there were dedicated spaces for observations.

Semi-structured pilot interview

After a literature review, we applied a questionnaire to older adults undergoing clonazepam deprescribing for assessing their perception of this process and conducting it during the semi-structured pilot interview.

The questionnaire was applied by 4 trained researchers to 25 older adults undergoing clonazepam deprescribing who came from 2 inland cities in Minas Gerais and were cared for at 5 PHC units.

All researchers received the field manual and were instructed to read every question in a suitable voice tone, repeating if necessary, but without using other terms for explaining them. Moreover, they were trained on cordiality, the use of an identification tag, and scheduling of a time and place (health unit or the patient’s home) that were appropriate to the patient’s preference.

We performed 5 biweekly meetings (totaling 2 and a half months) and, at every meeting, the clonazepam dose was reduced by 25% according to the protocol elaborated and validated by Baldoni et al.,7 aiming to cater for the reality of older adults assisted mainly by the Unified Health System (SUS). After applying the questionnaire, we made changes to the instrument for incorporating all suggestions from the interview in order to facilitate comprehension by older adults.

Content validation

Content validation was performed by specialists including medical, pharmaceutical, and nursing professionals via the Delphi technique. The participation of a group of specialists is one of the main characteristics of this technique.14 When elaborating instruments in Delphi studies, researchers may use structured, open-ended, or scaled-response questions. In this study, the answers followed a Likert scale where 0 represented “Inadequate/does not satisfy” and 10 represented “Adequate/satisfies.” Moreover, after each question there was a dedicated field for comments and suggestions.14

Data collection was performed electronically via Google Forms, and specialists received e-mail invitations requesting their collaboration in content validation, describing the objective and target population (BZD deprescribing in older adults at primary care), and offering instructions for accessing the instrument. The evaluation round took place during 14 consecutive days.

All data collected by the forms were subjected to verification of concordance through the coefficient of content validity (CCV). Items with final CCV (CCVf) equal to or higher than 0.8 were considered valid.15

This study was approved by the Municipal Health Departments of the participating municipalities and by the Committee for Ethics in Research on Human Beings (CEPES) of Universidade Federal de São João del-Rei, Centro-Oeste Dona Lindu campus (UFSJ/CCO), protocol No. 3 490 485 and Certificate of Presentation for Ethical Appreciation (CAAE) No. 89367218100005545. The whole project was conducted according to Resolution 466/2012,16 and older adults who agreed to participate in the study signed a free and informed consent form.

RESULTS

Based on the narrative literature review17–21 on questionnaires that approach enablers and barriers to medication deprescribing, we obtained an instrument with 12 questions, of which 11 had 3 answer options and 1 was an open-ended question (Chart 1).

Most of the 25 patients who participated in the semi-structured pilot interview were female, with a mean age of 64 years (61 to 91), and average schooling of 4 years of schooling. According to the participants’ perception, many factors contributed as enablers and/or barriers to deprescribing. Considering barriers, 44% (n = 11) reported feeling insecure to reduce the medication dose due to fear of not being able to sleep without their usual dose. Regarding signs and symptoms of withdrawal, 20% (n=5) thought about giving up at some point, but only one participant returned to the initial dose. The most reported signs and symptoms that made the patient rethink whether he or she would continue with clonazepam tapering were hallucinations, mentioned by 8% (n = 2), insomnia, also cited by 8% (n = 2), and dizziness and weakness at the same time, which were reported by 1 patient (4%).
As for the enabling aspects, 96% (n = 24) considered it was important to know that they counted on the support of health professionals during the process, which helped them proceed with tapering. It is important to note that, when asked if they would recommend deprescribing to those close to them, 88% (n = 22) answered “Yes,” 8% (n = 2) answered “I would have to think about it,” and only 4% said they would not recommend it. All participants of the study mentioned the support of friends and family regarding deprescribing. None of the patients reported any other barrier or enabler during clonazepam tapering, regarding the last question in the questionnaire (Table 1).

Aiming at a better comprehension by older adults, some modifications were made to the instrument: the term “clonazepam” was substituted by “benzodiazepines;” 2 similar questions at the beginning of the questionnaire were merged together; a question on the lack of support by the health team as a barrier to deprescribing was added; the sequence, format, and wording of some questions

Table 1. Enablers and barriers mentioned by patients after clonazepam deprescribing in 2 inland cities in Minas Gerais (n = 25).

<table>
<thead>
<tr>
<th>Barriers</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insecurity in reducing the dose</td>
<td>11</td>
<td>44</td>
</tr>
<tr>
<td>Difficulty in executing the technique (pill spilling)</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Difficulty sleeping</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Signs and symptoms of withdrawal (hallucinations, insomnia, dizziness, weakness)</td>
<td>5</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enablers</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support of health professionals</td>
<td>24</td>
<td>96</td>
</tr>
<tr>
<td>Knowledge on the risk of using benzodiazepines* for long periods</td>
<td>24</td>
<td>96</td>
</tr>
<tr>
<td>In-person meetings with health professionals</td>
<td>23</td>
<td>92</td>
</tr>
<tr>
<td>Improvements in general health status, wellbeing, and disposition</td>
<td>15</td>
<td>60</td>
</tr>
</tbody>
</table>

*In this case, clonazepam.

Chart 1. First version of the “Enablers and barriers to deprescribing benzodiazepines, in the patients’ perspective” questionnaire applied to older adults undergoing clonazepam deprescribing.
were changed for a better comprehension by older adults (Table 2); and then the questionnaire underwent validation by specialists.

For validating the content of this instrument, we sent 95 invitations to specialists in the medicine, pharmacy, and nursing areas, with degrees and/or experience in PHC. We obtained 50 answers at the first evaluation stage. Among the specialists/judges who participated in validation, 80% (n = 40) were female, of which 52% (n = 26) were nursing professionals, 40% (n = 20) were pharmacy professionals, and 8% (n = 4) were physicians.

The total CCV (CCVt) was 93.0%, and 100% of the items obtained a CCVf of over 0.8 in the first round of

### Table 3. Final coefficient of content validity of specialists’ evaluations of the instrument content.

<table>
<thead>
<tr>
<th>Items referring to the instrument</th>
<th>CCVf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitability of instructions to the interviewer</td>
<td>0.93</td>
</tr>
<tr>
<td>Suitability of instructions to the interviewee</td>
<td>0.92</td>
</tr>
<tr>
<td>Language clarity for older adults</td>
<td>0.90</td>
</tr>
<tr>
<td>Clarity of affirmatives for applying the questionnaire</td>
<td>0.95</td>
</tr>
<tr>
<td>Identification of enablers of deprescribing</td>
<td>0.93</td>
</tr>
<tr>
<td>Identification of barriers to deprescribing</td>
<td>0.92</td>
</tr>
<tr>
<td>Suitability of the logical sequence of the content</td>
<td>0.96</td>
</tr>
<tr>
<td>Applicability of the instrument to outpatients</td>
<td>0.93</td>
</tr>
</tbody>
</table>

CCVf: final coefficient of content validity.
Support instrument for deprescribing

evaluations (Table 3). Even though all items had a CCVf
higher than 0.8 in the first round, some questions were
reformulated according to suggestions for improving
instrument comprehension and quality. Among these
changes, in the “barriers” section, we included questions
on the access to other pharmaceutical forms that would
facilitate dose adjustments, in addition to difficulties in
understanding each dose reduction. In the “enablers” sec-
tion, we included pharmacological and non-pharmaco-
logical measures such as sleep hygiene and the need to
purchase the medication.

In addition to these changes, we changed some terms
such as “deprescribing” (to “withdrawal”), “sleep hygiene”
(which received an explanation), “obstacles” (to “difficul-
ties”), “medications” (to “drugs”), and titles (“you” was sub-
stituted by “Mr./Mrs.”) for better comprehension of the
instrument by patients. We also altered the order of the
questions for improving cohesion and logical sequence at
the interview (Chart 2).

**DISCUSSION**

The systematized process of elaborating the instrument
allowed us to obtain a structured, robust questionnaire applied
to the reality of Brazilian older adults, especially those at the
SUS. The use of this instrument allows us to identify the

---

**Chart 2. Final version of the questionnaire titled “Enablers and barriers to deprescribing benzodiazepines, in the patients’ perspective”**

<table>
<thead>
<tr>
<th>Barriers</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Was it difficult to obtain other pharmaceutical forms for better adjusting the dose?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Was it difficult to understand how I could take the drug after each dose reduction?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. I was afraid of not being able to sleep if I stopped taking/reduced the drug dose [say the name of the benzodiazepine].</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. It was difficult to split pills at home (reduce the dose) [or to correctly count drops].</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Even though I was following guidance on sleep hygiene, which is for sleeping better, I could not sleep well at night knowing that I had reduced the dose of my drug [say the name of the benzodiazepine].</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. During withdrawal of the drug [say the name of the benzodiazepine], it was complicated not having the support of my family, friends, or neighbors.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. During withdrawal of the drug [say the name of the benzodiazepine], it was complicated not having the support of the health care team.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. During dose reduction until complete withdrawal of the drug, I felt something that bothered me. Obs. (if yes, describe the possible signs or symptoms): ______________________________________</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enablers</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Guidance on sleep hygiene, which is for sleeping better, was something that helped me during the reduction of the drug dose [say the name of the benzodiazepine].</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. The fact that I did not have to buy the [say the name of the benzodiazepine] helped me during reduction/withdrawal of the drug.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. I understood very well the importance of not using [say the name of the benzodiazepine], and this increased my willpower to stop taking it or reducing the dose, thus overcoming difficulties.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. During the reduction of the drug dose [say the name of the benzodiazepine], I was able to observe improvements in my general health status, wellbeing, and disposition, which very much motivated me to continue with drug withdrawal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. In-person meetings and the support, even if remote, of the health professional comforted me and helped me during reduction/withdrawal of the drug [say the name of the benzodiazepine].</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. It was important for me to know that I could count on the support of health professionals during the process, and this helped me continue.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Would you recommend the same drug withdrawal treatment [say the name of the benzodiazepine] to your friends or family members? [ ] Yes, definitely [ ] I would have to think about it [ ] No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Besides these questions, would you like to cite some other factor(s) that enabled or constituted a barrier to withdrawing the drug? [ ] Yes [ ] No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>if yes, which one(s)?” ______________________________________________</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1: No, this did not happen; 2: It happened a few times but was not important; 3: Yes, it happened to me.
potential enablers and barriers to deprescribing BZD in the patient’s perspective — the focus of the intervention — with content validation by health professionals caring for older patients at the PHC frontline.

The participation of patients who finished the BZD deprescribing process in the elaboration of this instrument was important because it took their perspective into consideration when selecting items; this stage, together with the literature review, is recommended considering the importance of the selected items.22

BZD deprescribing allows the rationalization of the use of this medication, avoiding long-term use in older adults and reducing negative effects to health such as cognitive decline, mental confusion, falls, and hospitalizations. It is nevertheless necessary to understand the enablers and barriers to this process for successfully withdrawing the medication with the least damage to the patient’s health and quality of life.23

At PHC, the Family Health Team (ESF) is the main strategy for patients to access health care, and nursing professionals are a part of the minimal composition for the team to function.23 In this study, more than half of the evaluating judges (52%) were nurses. In health care units, these professionals manage comprehensive patient care, act in the decision-making process seeking interaction between users and the team, and organize the work process.24

In addition to the nursing professionals, instrument validation had the participation of physicians, which are also required in the minimal composition of the ESF, and pharmacy professionals, who act in the Expanded Center for Family Health and Primary Care (NASF-AB) together with the team in planning assistance and providing comprehensive care.25 We thus managed to have a multidisciplinary team of judges for evaluating the instrument through the Delphi technique.25 According to this assessment, the level of language clarity for older adults is easily comprehensible by the target population. In order to extract reliable data from an instrument, in addition to the proposal of choice by the researcher, the participant should comprehend the text used in the construct of interest.26

As for the identification of enablers, one of the items mentioned by specialists was that the patient should comprehend the importance of withdrawing or tapering the medication. Acceptance of this measure by the patients, based on the perspective that their medications may be unnecessary and/or harmful to health, is one of the factors that enable deprescribing. Other factors that may also simplify the process are: the use of deprescribing protocols that guarantee patient follow-up, monitoring collateral effects and guaranteeing their safety; and the reduction in the number of medications taken by the patient, in addition to their associated costs.27

Barriers to tapering or withdrawing medications include the lack of follow-up by health professionals in shorter time intervals, the lack of confidence in the physician responsible for deprescribing, and the fear of being without the drug.27 The lack of knowledge on the reason for deprescribing and resistance to change are also barriers to this process.28

Concomitant strategies, including patient education/guidance and non-pharmacological treatments28 (such as cognitive behavioral therapy2 and guidance on sleep hygiene and healthy life habits),7 are fundamental for minimizing the impact of barriers to deprescribing.

Among suggestions recommended by specialists, we highlight the inclusion of an item on access to other pharmaceutical forms that may help with dose adjustments. One of the barriers to tapering is the fact that the patient is not able to split pills, hence substituting it for the medication in its liquid form would be an option.7 However, the drug is not always available in this pharmaceutical form, which could result in additional costs to the patient even though it is a low-cost medication.7,29

As limitations of this study, we note the use of the instrument in a specific population (users of the SUS) and the absence of an assessment with scores given by older adults to each item of the instrument; however, its application in patients who finished BZD deprescribing revealed its viability. Even before specialists’ suggestions, the patients managed to score the main characteristics observed during deprescribing. To the best of our knowledge, there is no validated Brazilian instrument for identifying enablers and barriers to BZD deprescribing in older adults at the SUS.

**CONCLUSION**

The construction of this instrument comprehended relevant aspects of BZD deprescribing in older adults in the context of Brazilian health care, and content validation with the Delphi technique was pertinent since only one round resulted in all items with CCVf values over 0.8, which was the cut-off point for validation.

Therefore, the instrument represents a relevant strategy for optimizing BZD deprescribing in Brazilian older adults. Studies of its application to older adults should
still be performed for verifying its comprehension, viability, and effectiveness in identifying enablers and barriers to deprescribing.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

AUTHORS' CONTRIBUTIONS

LSR: formal analysis, conceptualization, data curation, writing - original draft, writing - review & editing. MST: formal analysis, conceptualization, data curation, writing - original draft, writing - review & editing. LGRS: formal analysis, conceptualization, data curation, writing - original draft, writing - review & editing. LCCS: formal analysis, conceptualization, data curation, writing - original draft, writing - review & editing. AMRFG: formal analysis, conceptualization, data curation, writing - original draft, writing - review & editing. AOB: formal analysis, conceptualization, data curation, writing - review & editing.

REFERENCES


