**Notas do Editor:**

1 - Com o objectivo de optimizar a legibilidade do seu artigo e assim incrementar potencialmente as citações do mesmo, recomendamos que os conteúdos redigidos em inglês sejam revistos por um "native speaker", tradutor qualificado ou empresa especializada em serviços de "language polishing"

**Resposta:** De modo a alcançar o solicitado, requisitámos os serviços especializados de um tradutor qualificado e foram realizadas alterações em todo o manuscrito (sublinhadas a amarelo).

2 - O resumo em português necessita de revisão major do ponto de vista linguístico;

**Resposta:** O resumo em português também foi revisto do ponto de vista linguístico.

3 - O resumo e o abstract deverão reflectir fielmente a estrutura do artigo, pelo que é necessário que incluam um parágrafo independente relativo ao capítulo "Discussão";

**Resposta:** Foi incluído o parágrafo independente relativo ao capítulo “Discussão”.

“**Discussion:** The Portuguese version of Current Opioid Misuse Measure was properly translated, adapted and validated; showing good quality in terms of reliability and validity. This isthe first instrument to screen aberrant opioid-related behaviors in Portuguese chronic pain patients. Consequently, will aid and promote the identification of opioid misuse in these patients.

“**Discussão**: A versão portuguesa da Escala de Uso Indevido de Opióides foi, adequadamente, traduzida, adaptada e validada; demonstrando boa qualidade relativamente à confiabilidade e validade. Este é o primeiro instrumento para rastrear comportamentos aberrantes, relativos ao uso de opióides em portugueses com dor crónica. Consequentemente, ajudará e promoverá a identificação do uso indevido de opióides nestes doentes.”

4 - O resumo e o abstract não deverão incluir abreviaturas;

**Resposta:** O resumo e o abstract foram retificados, de modo a não incluir abreviaturas.

5 - No idioma português, as unidades devem ser separadas das casas decimais por vírgulas e não por pontos - estes serão exclusivamente usados nos conteúdos redigidos em inglês;

**Resposta:** Concordámos e fizemos as devidas correções nos conteúdos em português.

6 - Na listagem final de referências, as revistas consultadas deverão ser identificadas na sua forma abreviada (ex: Acta Med Port e não Acta Médica Portuguesa);

**Resposta:** As referências foram retificadas de modo a constar a forma abreviada.

7 - A refª 20 está incompleta. Nomeadamente, não se encontra indicado o local nem a casa publicadora.

**Resposta:** Concordámos e completámos a referência. Entretanto passou a ser a referência 29:

29. Gorsuch RL. Factor Analysis Hillsdale, NJ: Lawrence Erlbaum Associates; 1983.

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**Revisor A:**

Este manuscrito deverá ser publicado na AMP pelo facto de trazer à clínica uma ferramenta fundamental para a compreensão dos comportamentos dos pacientes que tomam o tipo de medicação considerada. A nível nacional poderá ser uma ferramenta com um impacto crucial para a compreensão do panorama geral dos comportamentos dos pacientes com dor crónica, nomeadamente em estudos epidemiológicos.

**Resposta:** Agradecemos o comentário.

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**Revisor B:**

Sem sugestões.

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**Revisor C:**

O manuscrito é relevante para a prática clínica. Permite validar para a
língua portuguesa a utilização de um instrumento útil para o rastreio do
uso indevido de analgésicos opióides.

**Resposta:** Agradecemos o comentário.

Estrutura do Manuscrito

- Título, Resumo e Objectivos bem estruturados.

**Resposta:** Agradecemos o comentário.

- A introdução deveria ser mais focada nos analgésicos opióides nomeadamente nos seus efeitos adversos de modo a salientar a importância da utilização desta ferramenta clínica.

**Resposta:** Agradecemos o comentário e reformulámos a introdução, de modo a salientar a importância desta ferramenta. Deste modo, destacou-se:

- Importância e relevância do uso de opióides na dor crónica

- Efeitos adversos e consequências deletérias da dependência física e do seu uso indevido

- Estimativas da prevalência do uso indevido

- A importância da identificação dos doentes com maior risco de uso abusivo.

- As recomendações sobre a identificação deste grupo de doentes

Página 4, linha 10:

“Opioid analgesics are therapeutic options for those experiencing both cancer-related or noncancer-related chronic pain9. There are enormous variations in opioid use across the globe, and even within regions, similar variations are observed8. In Portugal, the prevalence of its use by patients with chronic pain is estimated to be 4.37%10. Opioids should only be introduced when strictly necessary and with due regard to an ongoing risk benefit analysis8. They should be used as part of a multifaceted strategy that includes all necessary adjuvant analgesics, non-drug interventions, psychological support and rehabilitation8. Opioid use in chronic pain treatment is complex, as patients may derive both benefit and harm. Common side effects of opioid administration include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression11. With all opioids, respiratory depression and death are the most feared complications11.

Physical dependence and addiction are clinical concerns that may prevent proper prescribing and in turn inadequate pain management11. Although long-term opioid therapy can be an effective chronic pain management treatment, a recent meta-analysis identifies rates of misuse between 21% and 29% of patients with chronic pain in opioid treatment12. Identification of individuals currently misusing opioids is important given the substantial recent increases in prescription rates and consequent increases in morbidity and mortality12. Activity limitations in daily life, co-morbidities, such as depression and anxiety, and lack of social relationships can contribute to misuse of opioid therapy 9. Clinical guidelines emphasize the need for regular assessment and management of risk associated with misuse as an integral part of safe opioid prescribing practices 13. Strategies such as pill counts, urine toxicology screeners, and prescription drug monitoring programs may provide potentially useful information about risk, however, each of these strategies has important limitations14. Self-report instruments may be one viable strategy for capturing aberrant opioid-related behaviors14. Aberrant opioid-related behaviors are a wide range of behaviors that fall outside those expected in opioid treatment15. They range from borrowing or stealing opioid medication from others, to patient-initiated dose escalation or concurrent use of an illicit substance16.

Current practice guidelines recommend using the Current Opioid Misuse Measure (COMM) to assess patients who are prescribed opioid therapy 13. The COMM, developed by Butler et al.17, is a validated self-reported instrument to screen aberrant opioid-related behaviors in chronic pain patients. This instrument has been translated to other languages18, but so far there is no Portuguese version. “

- Métodos: Deve ser explicado como fizeram o cálculo da amostra de 98 doentes.

**Resposta:** Não existem regras absolutas para a determinação do tamanho da amostra em estudos de validação de questionários. No nosso estudo, seguimos as recomendações sobre a validação de questionários na área da dor 1, e foi aplicada uma razão de participante/item de 5/1. Deste modo, dado que esta escala contém 17 itens, a amostra deveria incluir 85 participantes (5 x 17 = 85). Estimando que houvesse 15% de questionários incompletos ou mal preenchidos definimos que deveríamos aplicar o questionário em 100 participantes. Sendo assim, aplicámos o questionário a 100 participantes. No entanto, 2 participantes não completaram o questionário, o que resultou num total de 98 questionários contabilizados. Se considerarem pertinente, podemos acrescentar esta informação nos métodos.

 “***Sample size***

*Guidelines for the respondent-to-item ratio ranged from 5:1[50] (i.e., fifty respondents for a 10-item questionnaire), 10:1,[30] to 15:1 … Given the variation in the types of questionnaire being used, there are no absolute rules for the sample size needed to validate a questionnaire.[53] As larger samples are always better than smaller samples, it is recommended that investigators utilize as large a sample size as possible. The respondent-to item ratios can be utilized to further strengthen the rationale for the large sample size when necessary.*”

1. *Tsang S, Royse CF, Terkawi AS. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. Saudi J Anaesth. 2017 May;11(Suppl 1):S80-S89. doi: 10.4103/sja.SJA\_203\_17. PMID: 28616007; PMCID: PMC5463570.*

- Porque é que para a fase teste-reteste usaram apenas 17 doentes?

**Resposta:** De igual modo, não existem regras absolutas sobre o número de doentes que participam na fase teste-reteste. Após revisão da literatura sobre estudos de validação de questionários na área da dor 1,2,3, a fase teste-reteste é aplicada em cerca de 5 a 20% do total dos participantes. Sendo assim, optámos por aplicá-la em 17 doentes, que corresponde a 20% dos 98 participantes.

*1. Santos JG, Brito JO, de Andrade DC, et al. Translation to Portuguese and validation of the Douleur Neuropathique 4 questionnaire. The journal of pain : official journal of the American Pain Society. 2010;11(5):484-490.*

*2. Sa AC, Sousa G, Santos A, Santos C, Abelha FJ. Quality of Recovery after Anesthesia: Validation of the Portuguese Version of the 'Quality of Recovery 15' Questionnaire. Acta medica portuguesa. 2015;28(5):567-574.*

*3. Zhao Y, Li Y, Zhang X, Lou F. Translation and validation of the Chinese version of the Current Opioid Misuse Measure (COMM) for patients with chronic pain in Mainland China. Health and quality of life outcomes. 2015;13:147.*

- Resultados: a apresentação e análise dos dados é rigorosa? São claros e convincentes? Os quadros e tabelas são legíveis, elaborados de forma correcta?

**Resposta:** Na nossa opinião, a apresentação e análise dos dados e tabelas é rigorosa e correta.

- Discussão: Existem alguns aspectos na discussão que devem ser reformulados:

1- “There are no Portuguese validated tools regarding follow-up of
chronic pain patients treated with opioids.“ Além de não ser correcto, é importante explicitar que o COMM é somente um instrumento de rastreio de comportamentos de abuso em relação aos opioides.

**Resposta:** Os autores pretendiam enfatizar que não existia nenhum instrumento validado para a língua portuguesa sobre o uso indevido de opióides. Concordámos que este instrumento apenas permite o rastreio do uso indevido de opióides.

De modo a clarificar esta ideia, foram introduzidas alterações no parágrafo salientado (página 9, linha 7):

“Self-report instruments may be one viable strategy for screening aberrant opioid-related behaviors14. Until now, there were no Portuguese versions of these instruments; therefore, the Portuguese version of COMM is the first instrument that will allow this screening in Portuguese chronic pain patients. “

2- Em Portugal o uso de medicamentos “emprestados” é algo muito
enraizado entre a população. Como tal, a explicação dada para as
diferenças encontradas deve ser reformulada.

**Resposta:** Concordámos que a explicação dada para as diferenças encontradas fosse reformulada. Desse modo, acrescentámos informação nesse parágrafo (ver em baixo). No entanto, apesar de poder existir a perceção de que “em Portugal o uso de medicamentos emprestados é algo muito enraizado entre a população”, não existem estudos sobre este assunto no nosso país.

Página 9, linha 15:

“…These questions allude to the concept of taking/borrowing medication from someone else. In a recent systematic review, which comprised 19 studies from 9 countries (8 conducted in the United States, 4 in Australia, 2 in New Zealand, and 1 each in Canada, Nigeria, Malaysia, Qatar, and Ireland), the prevalence estimates for borrowing someone’s prescription medication varied between 5% to 51.9% 27. There are no estimates regarding this concept in Portugal and this should be addressed in future studies. Differences in cultures, health care systems, economics, education, and medication use behaviors could explain differences among countries. Misuse can take many shapes and be characterized by a whole range of behaviors. Once the concepts of taking/borrowing medication try to measure one dimension of misuse, one can postulate that, if it exists, the act of borrow and take medication belonging from someone does not appear to be frequent or relevant in our setting. However, concealment of information due to fear of reprisals cannot be ruled out.…..”

**Revisor D:**

RELEVANCE: In my opinion this manuscript is very important for the  clinical practice, clearly addresses a topic of extreme importance in health,  given that chronic pain is a common pathology in Portugal. Involves clinical, scientific and social factors in healthcare.

**Authors’ answer:** We thank the comment.

ORIGINALITY: In addition to being a up-to-date topic with great  potential
for analysis, the adaptation and validation of a questionnaire widely validated to a Portuguese case is undoubtedly an added value for the  área under study, and can be considered an originality.

**Authors’ answer:** We thank the comment.

MISCONDUCT: No plagiarism or other fraud was detected.

**Authors’ answer:** We thank the comment.

STRUCTURE OF THE MANUSCRIPT

- The Title is instructive and has the ideal size in order to summarize the manuscript;

- The Abstract reflect the contents of the manuscript, it is well structured and summarizes its content. Describes the methodology, presents the results as well as their discussion;

- The Introduction is brief but nevertheless manages to make a good framing of the theme, with current and pertinent references. Regarding the way in which authors are referenced, being only a  suggestion, the introduction of the author's name and the year of publication is, in  my opinion, an added value for the article, facilitating its reading. The purpose of the study is described as well as its relevance;

- The Methodology used is very well described. As regards the translation and adaptation of the questionnaire into the Portuguese version, all the principles of good practice were followed. In this way, it guaranteed the quality of the questionnaire obtained and consequently ensured that the statistical analysis of the results and the consequente conclusions could be validated. The process of data collection is  perfectly described, a convenience sample was used as a case study requires. The authors give a brief description of the sample, using correctly  descriptive statistical measures for this purpose. Details can be found in the  attached tables. The use a retest in a random sample a finally the use of a panel  of experts in chronic pain provides statistical and medical validity. The description of the statistical methods used is enough, it presents some references. Once again, I preferred the authors' names and the  publication year. The choice of the statistical techniques is adequate to the data under study, allowing to respond to the proposed objectives.

- The Results are presented clearly; make sense in statistical terms and are therefore convincing. The tables are well designed and support all results. Regarding the application of the Factor Analysis would be interesting the reference to some paper that supported the  obtained results.

- The Discussion presents the relevance of the results obtained, always making a parallel between the case of Portugal and the original questionnaire. It is supported by a set of references. It presents the advantages of the study but also its weaknesses, not forgetting the potential the areas in need for future studies.

-The Conclusions are relevant, but the authors could have invested a little more, it is quite succinct. Are based on the results and are consistent with the objectives.
- References: Regarding the adequacy of the references, it seems to me that the minimum requirements are met. In my area of  expertise are referenced several articles, applied to the area under study, which seems quite appropriate. In a general I consider the literature review to be adequate; the citations are correct; I believe that the percentage of recente references are satisfactory and it follows the AMP’s style.

- In Tables the message is clear. All the tables are clearly identified and legible.

- Acknowledgments: No financial support is declared, nor any conflicts of interest are declared.

**Authors’ answer:** We thank the comments.

In the discussion, we have included a reference regarding the support to our comparisons in Factor Analysis (page 10, line 15).

Regarding the conclusions, we have followed your advice and expanded it.

Page 11, line 14:

“This questionnaire is expected to offer clinicians a tool to aid and promote the screening of aberrant opioid-related behaviors, in Portuguese chronic pain patients currently on opioid therapy, beside to assess their treatment compliance.

Consequently, the implementation of this questionnaire may reduce the incidence and morbimortality related with opioid misuse; and should improve chronic pain treatment in Portugal, namely by reducing physician’s concerns related to opioids prescription and by increasing patient’s awareness of the responsibility of being on opioid therapy.”

EXTENSION: In my opinion there is no need to reduce the paper. All tables are clear, and I believe that all are important to support the results discussion.

**Authors’ answer:** We thank the comment.

PRESENTATION: Is the manuscript clearly and logically presented? Yes, in my opinion it is.

**Authors’ answer:** We thank the comment.

RECOMMENDATION REGARDING PUBLICATION: Do you think the manuscript should  be published in AMP? Yes, in my opinion it should be.  It is an innovative
study, supported on statistically validated results with potential to assist physicians in making key decisions. There are obviously some weaknesses that can be addressed in future studies.

**Authors’ answer:** We thank the comment.

PRIORITY REGARDING PUBLICATION: In which ranking regarding priority in publication would you consider the manuscript? Within the first 10% to 20%.

**Authors’ answer:** We thank the comment.