PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Evidence-informed and consensus-based statements about SAFEty of Physical Agent Modalities Practice in physiotherapy and rehabilitation medicine (SAFE PAMP): a national Delphi of healthcare scientific societies
AUTHORS	Gianola, Silvia; Bargeri, Silvia; Pellicciari, Leonardo; Gambazza, Simone; Rossettini, Giacomo; Fulvio, Anna; Genovese, Vincenzo; Benedini, Matteo; Proverbio, Emanuele; Cecchetto, Simone; Castellini, Greta; Turolla, Andrea; SAFE PAMP Collaborators, SAFE PAMP Collaborators

VERSION 1 – REVIEW

REVIEWER	Liechti, Fabian Inselspital University Hospital Bern, Department of General Internal Medicine
REVIEW RETURNED	13-Jun-2023

GENERAL COMMENTS	The authors used a Delphi technique to list indications of Physical Agent Modalities. It may be justified to use this technique in this context; however, the aims of the study are not clear and the authors do not sufficiently explain how they generated their “evidence”. Major 1. The aim of the current study is not clear. Does it aim at indications of PAMs or their safety? Also, these terms are not defined throughout the manuscript. 2. The authors need to explain why the present investigation is needed and what it would add to the cited Canadian guideline or other relevant literature. This should also include an elaboration on why to use a Delphi technique. 3. The target group of the recommendations should be mentioned (Which professional groups? Which field? International relevance?) as well as the setting (rehabilitation, acute setting, outpatient?). 4. The findings of the current study should be discussed and compared to previous findings such as the cited Canadian guideline. By reading the current manuscript the reader easily gets the impression that all indications evaluated are safe without any restrictions (which is contradictory to the Canadian guideline and common sense). It is not at all clear what is meant by “evidence” in Appendix 2 and the authors did no formaly assess the level of evidence. 5. The limitations of this study need to be clearly mentioned, i.e., limitations of the Delphi technique. Minor 1) The abstract does name 9 techniques, not indications.

	2) Lines 79 and 80. What do the authors mean by patient-centered healthcare pathways in this context? 3) The abbreviation SAFE PAMP is not needed in this kind of study and can be omitted. 4) It is not clear why the EQUATOR initiative's article on guideline development is cited. 5) Line 108. It is stated "three phases", followed by enumerating four phases. Please clarify. 6) Line 138 ff. Please clearly indicate how the experts were selected. It is not clear on what the sentence "The panel of expert members […]" refers to. Is this already the result of the composition? How did you choose patients and lay members? Were the "voluntary organizations" part of the 28 societies? 7) Table 1 should include number of participants, not only percentages. 8) Line 191 and Fig 2. I'm not sure the word "round" is appropriate here. It should be clear throughout the manuscript what's a "round", including the figure. For example it is stated that there were two "Delphi rounds" but in the figure there are three rounds. 9) Figure 2 should be revised completely. Omit listing the societies in Fig. 2. If "Round 3" were the last one, i.e., the consensus meeting, the number of participants should be 9 and not 17. Also, define "Dropout". "No responses" contradicts with "Not interested" (otherwise you wouldn't know). 10) Line 236. Did some experts represent more than one society or what refers "each" to? 11) The discussion should be shortened but discuss the relevant findings. Please refrain from simplistic statements such as "The absence of evidence is not evidence of absence" unless needed in the context. 12) Line 293 ff. This paragraph is not clear and should be revised. The authors should also distinguish between effectiveness and efficacy. 13) Line 347 ff. The first two paragraphs are not on limitations. Please restructure and omit unnecessary parts (e.g., URL). 14) Line 352. "[…] solid scientific background and external validity […]" should be omitted as a scoping review does not justify this statement. 15) "Evidence-based" should only be used with great caution in this study as it seems that mostly there is no good evidence available, hence, the justification to use a Delphi technique. 16) Revision for English language by a native speaker is necessary.

REVIEWER	Christian, Geroin University of Verona
REVIEW RETURNED	19-Aug-2023

GENERAL COMMENTS	This is a nice study about a shared consensus on safety about Physical Agent Modalities (PAMs) in physiotherapy. Authors aimed to develop evidence-informed and consensus-based indications about safety of PAMs. A RAND-modified Delphi rounds' survey was used to reach a consensus. Authors established a steering committee of the Italian Association of Physiotherapy (Associazione Italiana di Fisioterapia - AIFI) to identify areas and questions for developing indications about the safety of most common used PAMs in physiotherapy and rehabilitation. They invited 28 National Scientific and Technical Societies (STS) as a multidisciplinary and multi-professional panel of experts to evaluate the proposed indications and formulate additional inputs.

	The level of agreement was measured with a 9-points Likert scale. Consensus in the Delphi rounds was assessed using the rating proportion with a threshold of 75%. Authors identified 61% out of 28 STS participated involving their most representative expert member. Experts composing the panel were mainly clinicians (88%) reporting multiple expertise in musculoskeletal (47%), pelvic floor (24%), neurological (18%) and lymphatic (6%) disorders with a median experience of 30 years (IQR=17-36). Two Delphi rounds were necessary to reach a consensus. The final approved criteria list comprised nine indications about the safety of PAMs in adults (electrical stimulation neuromodulation, extracorporeal shock wave therapy, laser therapy, electromagnetic therapy, diathermy, hot thermal agents, cryotherapy and therapeutic ultrasound) with a general note about populations subgroups. Authors summarized evidence-based indications regarding the safe application of PAMs in physiotherapy and rehabilitation and suggested that future studies are needed to extend this consensus on pediatric, adolescent, and frails patients. It's a well-written manuscripts and I don't have any comment.

REVIEWER	Matteo, Cioeta IRCCS San Raffaele Roma
REVIEW RETURNED	21-Aug-2023

GENERAL COMMENTS	Dear authors, from my point of view the manuscript is of great interest to the scientific community and appropriate for this journal. It is also clearly written and has no deficit. However I have two clarifications to ask for: 1. At line 77 you stated "they are prescribed and applied by healthcare professionals in various medical specialties (e.g., neurology, orthopedics, geriatrics, pediatrics, oncology, urogynecology) to carry on patient-centered healthcare pathways". What are the evidences for this statemant? In which way physical agent modalities can enhance a patient-centered care? Are there any guidelines that suggest that? 2. At line 222 you declared "17 out t of 28 (61%) invited STS responded to the questionnaire. The Delphi process flow chart with the STS participants list is reported in Figure 2". Figure 2 describes the process correctly, but it would be interesting to list all the 28 scientific societies involved initially; inidicare which companies did not respond and who was not interested. It would also be interesting to understand why the two companies mentioned in the flow chart did not care. In my view this is important for complete data transparency.

VERSION 1 – AUTHOR RESPONSE

bmjopen-2023-075348 - "Evidence-informed and consensus-based indications about SAFEty of Physical Agent Modalities Practice in physiotherapy and rehabilitation medicine (SAFE PAMP): a national Delphi of healthcare scientific societies"

We thank the editor for the interest in our manuscript bmjopen-2023-075348. All changes were made in track changes. Additionally, we have uploaded a clean version of the manuscript to enhance its readability (with references to specific lines and pages within the clean version).

We revised the whole manuscript according to the Reviewer's comments. In particular:

- We deepen the rationale for using the Delphi technique;
- We better specified the target of indications;
- We added a paragraph in the discussion, “comparison with previous literature”, to better make our study compared to previous consensus studies (e.g., Canadian guideline);
- We revised the strength and limitation sections (both abstract and discussion);
- We maintained the SAFE PAMP acronym in the title according to the published literature, even if reviewer 1 suggested omitting it. However, we leave the editor with the final decision about this.

Best regards
Silvia Bargeri, on behalf of all authors

Editor's Comments to Author:

- Please revise the ‘Strengths and limitations of this study’ section of your manuscript (after the abstract). This section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. The novelty, aims, results or expected impact of the study **should not** be summarised here.

Author response
We thank the editor and we ameded the section ‘Strengths and limitations of this study’ accordingly.

Formatting Amendments (where applicable):

- No Corresponding author email address:

Please provide a Corresponding author email address to your main document. Email address should be placed within the title page.
Author response
Added
Reviewer: 1
Dr. Fabian Liechti, Inselspital University Hospital Bern Comments to the Author:
The authors used a Delphi technique to list indications of Physical Agent Modalities. It may be justified to use this technique in this context; however, the study's aims are unclear and the authors do not sufficiently explain how they generated their “evidence”.
Author response
We thank the Reviewer for the precious comments and the careful review that helped to improve our manuscript. We have now revised the aim of the study. We started with a scoping review (Bargeri 2023) that mapped the evidence about adverse events from 117 systematic reviews on PAMs reporting no important harms. However, since in literature it is known that adverse events are under-reported in the primary studies, to be more conservative and bridge the existing gaps between the available literature and clinical practice, we aimed to consider the involvement of experience from a panel of experts. These were the ground bases for an evidence-informed and expert consensus-based on the safety of PAMs using the Delphi technique, primarily used by researchers when the available knowledge is incomplete or subject to uncertainty. Introduction, Line 87-92 page 5, Methods-design lines 100-102 page 6.

Major

1. The aim of the current study is not clear. Does it aim at indications of PAMs or their safety? Also, these terms are not defined throughout the manuscript.

Author response

We thank the Reviewer for this comment. We focused on safety, which we named as “indication of safety”. We have now revised the rationale and aim of this Delphi study to address this point better. Introduction, Lines 84-92 page 5. We better defined all these terms throughout the manuscript.

2. The authors need to explain why the present investigation is needed and what it would add to the cited Canadian guideline or other relevant literature. This should also include an elaboration on why to use a Delphi technique.

Author response

We thank the Reviewer for this comment. We tried to explain the investigation's need in the first comment, and we better clarify it in the manuscript (Introduction, Lines 84-92 page 5, Methodsdesign lines 100-102 page 6.)

About Canadian guidelines or other relevant literature, we better contextualize it in the introduction (Lines 84-86 page 5) and we added a new paragraph in discussion “Comparison with literarature” (Pages 13-14).

In particular:

- Different time covered. Canadian guideline was published in 2010. Considering the advancing technologies, some new PAMs could not be comprised and could be outdated. Then, we proposed indications based on a recent scoping review that covered the last ten years of publications (the scoping review's search strategy started in 2011).
- Different focus. Canadian guideline mainly focused on precautions and contraindications, whereas we aimed at safety indications (regarding absence/low rate of adverse events). We better explain in methods “*phase II, generation of indications*” page 8)

3. The target group of the recommendations should be mentioned (Which professional groups? Which field? International relevance?) as well as the setting (rehabilitation, acute setting, outpatient?).

Author response

We thank the Reviewer for this comment. In the paragraph *Phase II. Generation of indications*, we added the target groups for the indications as well as the fields (conditions/population) and relevance (page 8): *“Indications were developed for different target conditions/population. PAMs were delivered by expert healthcare professionals (who had undergone formal education and training) to ensure patient safety in inpatient and outpatient settings. They were presented within the relevant rehabilitation field, along with a list of patient conditions in which the PAMs were indicated as safe and supported by evidence and clinical expertise. Evidence was recently summarized in a scoping review, which gathered information about the safety of PAMs from 117 systematic reviews in physiotherapy and rehabilitation medicine. Clinical expertise was assured by content experts of AIFI (e.g., musculoskeletal disorders, orthopedic and neurological physiotherapy and pelvic floor rehabilitation)”*

In addition, in results section (Page 12) and Appendix 2. Final criteria list details about the target group, the specific fields (conditions/population) for each indication are also reported.

4. The findings of the current study should be discussed and compared to previous findings such as the cited Canadian guideline. By reading the current manuscript the reader easily gets the impression that all indications evaluated are safe without any restrictions (which is contradictory to the Canadian guideline and common sense). It is not at all clear what is meant by “evidence” in Appendix 2 and the authors did no formaly assess the level of evidence.

Author response

We thank the Reviewer for this comment.

- We added a paragraph in the discussion section “comparison with literature” (page 1314) to contextualize our consensus. In particular, the Canadian guidelines and others published in the early 2000s are outdated. It is claimed that guidelines should be updated within 3 to 5 years or when new information becomes available

(https://www.bmj.com/content/323/7305/155).

- The resulting indications are safe with restriction to the adult population in the reported rehabilitation field. We now deeply explain this in the results and discussion section to better underline this. Page 12, Lines 257-61, page 13 lines 280-82
- We took advantage to better specify in methods “Generation of indications” what we meant by “evidence” and by “expertise” (page 8, lines 166-170). We also amended Appendix 2, adding an introduction and provided as raw data the Survey Monkey questionnaire sent to the panel of experts in all rounds (https://osf.io/w8kgs/)
- In the discussion limitation section, we underlined that the scoping review does not aim to assess the level of evidence but to map safety on population and area of intervention (page 17, lines 371-74).

5. The limitations of this study need to be clearly mentioned, i.e., limitations of the Delphi technique.

Author response

We thank the Reviewer for this comment. We added limitations of the Delphi technique. Pgae 16, Lines 366-70

Minor

1) The abstract does name 9 techniques, not indications.

Author response

Amended

2) Lines 79 and 80. What do the authors mean by patient-centered healthcare pathways in this context?

Author response

We amended the sentence: "However, clinicians and patients must be informed about the safety of the proposed treatments”

3) The abbreviation SAFE PAMP is not needed in this kind of study and can be omitted.

Author response

We thank the Reviewer for this comment. However, we have a priori published the protocol of this Delphi study with the *SAFE PAMP* acronym and sent all rounds and documents to the panel of experts taking into account this acronym. Then we took advatanges from literature adopting this term “PAM”:

- Physical agent modalities: a position paper - PubMed (nih.gov)
- Applied Sciences | Free Full-Text | Role of Physiotherapy and Physical Agent Modalities for Musculoskeletal Disorders: Present and Future (mdpi.com)
- Do physical agent modalities fit under an occupational therapy scope of practice? - Ted Brown, 2015 (sagepub.com)
- Physical Agent Modalities / Minnesota Board of Occupational Therapy Practice (mn.gov)
- Physical Agent Modalities (PAMs) Free Trial - Pass The OT
- Physical-Agent-Modalities.pdf (therapistsforarmenia.org)

For all these reasons we preferred to maintain the term PAM if it is possible. However, we will leave the final decision to the editor.

4) It is not clear why the EQUATOR initiative’s article on guideline development is cited.

Author response

The reporting guideline for the Delphi studies is the CREDES, which is reported on the

EQUATOR website. https://www.equator-network.org/reporting-guidelines/credes/
We removed the sentence about Equator Initiative, adding in substitution the reference of the website. Thank you for the clarification.

5) Line 108. It is stated “three phases”, followed by enumerating four phases. Please clarify.

Author response
We apologize for this typo, amended as “four phases”.

6) Line 138 ff. Please clearly indicate how the experts were selected. It is not clear on what the sentence “The panel of expert members […]” refers to. Is this already the result of the composition? How did you choose patients and lay members? Were the “voluntary organizations” part of the 28 societies?

Author response
We thank the Reviewer for allowing us to explain this point better. The steering committee invited all the national multidisciplinary and multi-professional STS involved in physiotherapy and rehabilitation care (n=26) and the STS dealing with forensics (n=1). These STS were identified by the published list of the Italian Ministry of Health and are entitled to generate national clinical practice guidelines. In addition, we invited Cittadinanzattiva as the largest Italian organization for patient representatives (35,100 members throughout the national country, https://www.cittadinanzattiva.it/chi-siamo/organizzazione.html, date: 31/12/2020), which promotes citizen activism for the protection of rights, the care of common goods, and support for people in conditions of weakness. For privacy, we uploaded the full list of all STS invited that did not answer as row data at the following link: https://osf.io/w8kgs/.

7) Table 1 should include number of participants, not only percentages.

Author response
Added, thank you. We also splitted the “other category” into lay and forensic members for a clearer interpretation.

8) Line 191 and Fig 2. I’m not sure the word “round” is appropriate here. It should be clear throughout the manuscript what’s a “round”, including the figure. For example it is stated that there were two “Delphi rounds” but in the figure there are three rounds.

Author response
We thank the Reviewer for underline this inappropriatness and understanding this point. We now substituted round 3 with “workshop meeting”, making clear in the manuscript the distinction between these two. We amended Figure 2 accordingly.

9) Figure 2 should be revised completely. Omit listing the societies in Fig. 2. If “Round 3” were the last one, i.e., the consensus meeting, the number of participants should be 9 and not 17. Also, define “Dropout”. “No responses” contradicts with “Not interested” (otherwise you wouldn’t know).

Author response
We apologize for the typo. Nine STS joined the workshop. However, all STS (100%) approved the final criteria list. Reasons for dropouts were now explained in the text. Two STS answered that they were uninterested in involvement, and nine did not. We amended Figure 2 accordingly.

10) Line 236. Did some experts represent more than one society or what refers “each” to?

Author response

Experts represent one society in which they are the main representatives. We better explain it in methods and results. Lines 140-41 page 7, line 226-27 page 11

11) The discussion should be shortened but discuss the relevant findings. Please refrain from simplistic statements such as “The absence of evidence is not evidence of absence” unless needed in the context.

Author response
We shortened the discussion, and we amended simplistic statements.

12) Line 293 ff. This paragraph is not clear and should be revised. The authors should also distinguish between effectiveness and efficacy.

Author response
We thank the Reviewer for this comment. To shorten the discussion, we incorporated this paragraph in implications for clinicians (page 14)

13) Line 347 ff. The first two paragraphs are not on limitations. Please restructure and omit unnecessary parts (e.g., URL).

Author response
We revised the whole paragraph.. We changed it into strengths and limitations (page 16)

14) Line 352. “[…] solid scientific background and external validity […]” should be omitted as a scoping review does not justify this statement.

Author response
We agreed with the Reviewer; we changed it accordingly.

15) “Evidence-based” should only be used with great caution in this study as it seems that mostly there is no good evidence available, hence, the justification to use a Delphi technique. Author response

We now revised the abstract and manuscript conclusion to replace the term 'evidence-based' with 'consensus-based' indications.
We took advantage to better specify in methods “Generation of indications” what we meant by “evidence” and by “expertise” (page 8, lines 411-415). We also amended Appendix 2, adding an introduction and provided as raw data the Survey Monkey questionnaire sent to the panel of experts in all rounds (https://osf.io/w8kgs/)
In the discussion limitation section, we underlined that the scoping review does not aim to assess the level of evidence but to map safety on population and area of intervention (page 17, lines 371-72).

16) Revision for English language by a native speaker is necessary.

Author response
We carefully revised the English language. Done

Reviewer: 2
Dr. Geroin Christian, University of Verona Comments to the Author:
This is a nice study about a shared consensus on safety about Physical Agent Modalities (PAMs) in physiotherapy. Authors aimed to develop evidence-informed and consensus-based indications about safety of PAMs. A RAND-modified Delphi rounds’ survey was used to reach a consensus. Authors established a steering committee of the Italian Association of
Physiotherapy (Associazione Italiana di Fisioterapia - AIFI) to identify areas and questions for developing indications about the safety of most common used PAMs in physiotherapy and

rehabilitation. They invited 28 National Scientific and Technical Societies (STS) as a multidisciplinary and multi-professional panel of experts to evaluate the proposed indications and formulate additional inputs. The level of agreement was measured with a 9-points Likert scale. Consensus in the Delphi rounds was assessed using the rating proportion with a threshold of 75%. Authors identified 61% out of 28 STS participated involving their most representative expert member. Experts composing the panel were mainly clinicians (88%) reporting multiple expertise in musculoskeletal (47%), pelvic floor (24%), neurological (18%) and lymphatic (6%) disorders with a median experience of 30 years (IQR=17-36). Two Delphi rounds were necessary to reach a consensus. The final approved criteria list comprised nine indications about the safety of PAMs in adults (electrical stimulation neuromodulation, extracorporeal shock wave therapy, laser therapy, electromagnetic therapy, diathermy, hot thermal agents, cryotherapy and therapeutic ultrasound) with a general note about populations subgroups.
Authors summarized evidence-based indications regarding the safe application of PAMs in physiotherapy and rehabilitation and suggested that future studies are needed to extend this consensus on pediatric, adolescent, and frails patients. It's a well-written manuscripts and I don't have any comment.
Author response
We are very thankful for your interest in our manuscript.

Reviewer: 3
Dr. Cioeta Matteo, IRCCS San Raffaele Roma Comments to the Author:
Dear authors, from my point of view the manuscript is of great interest to the scientific community and appropriate for this journal. It is also clearly written and has no deficit. However I have two clarifications to ask for:

1. At line 77 you stated "they are prescribed and applied by healthcare professionals in various medical specialties (e.g., neurology, orthopedics, geriatrics, pediatrics, oncology, urogynecology) to carry on patient-centered healthcare pathways". What are the evidences for this statemant? In which way physical agent modalities can enhance a patient-centered care? Are there any guidelines that suggest that?
Author response
We thank the Reviewer for this comment. Now, we rephrased the sentence. Page 5, lines 83-4.

2. At line 222 you declared "17 out t of 28 (61%) invited STS responded to the questionnaire. The Delphi process flow chart with the STS participants list is reported in Figure 2". Figure 2 describes the process correctly, but it would be interesting to list all the 28 scientific societies involved initially; inidicare which companies did not respond and who was not interested. It would also be interesting to understand why the two companies mentioned in the flow chart did not care. In my view this is important for complete data transparency.
Author response
We added as row data in the OSF repository all lists of STS contacted.

Reviewer: 1
Competing interests of Reviewer: None.

Reviewer: 2
Competing interests of Reviewer: None

Reviewer: 3
Competing interests of Reviewer: I declare no competing interests.

VERSION 2 – REVIEW

REVIEWER	Liechti, Fabian Inselspital University Hospital Bern, Department of General Internal Medicine
REVIEW RETURNED	03-Nov-2023

GENERAL COMMENTS	General remarks The authors have revised the manuscript throughout and it has indeed improved a lot. The Introduction is much better with clearly identifying the knowledge gap and indicating the aim of the study. The methods section has also improved a lot. Adding the 'Comparison with literature' section in the Discussion is valuable. I also recognize that definitions are used more carefully with being more precise in the wording. The message that a panel of important stakeholders considers the 9 PAMs investigated as safe is helpful for users internationally. However, there are still some limitations the authors should address. Major Abstract: '… to evaluate the proposed indications' is somehow misleading. In fact they assessed only the 9 PAMs with the indications given as additional information. Please revise. The authors comment that they 'aimed at safety indications (regarding absence/low rate of adverse events)'; however, this is not clear from the manuscript. Also, this doesn't preclude discussing and evaluating specific contraindications and precautions, such as mentioned in the Canadian guideline. Many of the concerns raised in 2000 may still be valid. The current manuscript gives the impression that all nine treatment methods can be used without any safety concern in all adult people – which is contradicting the mentioned Canadian guideline. This is a major problem and should be clearly addressed in the discussion section. Line 166: In this paragraph it's not clear how the steering committee worked out the indications. How were the different experts involved? What was done when disagreeing? It seems the authors put a lot of effort in preparing this list of indications and this should be more accessible for the reader. Line 166 and 177: In these paragraphs it should be better explained that for each PAM a list of indications with distinction of evidence and expertise was provided and that the participants indeed used a Likert scale to rate the safety of each of the 9 PAMs with indications from the final list in appendix 1. Otherwise this is only clear when accessing the monkeysurvey questions. I also suggest replacing the word 'voting' with 'rating' to be more precise. The discussion section should still be more concise and should be shortened. I especially recommend better structuring within the paragraphs. For example the Main Findings section is very repetitive on excluding children. Instead it would be interesting to know if other populations should also be excluded, e.g. hemato-

	oncological patients with severe immunocompression or coagolupathy. The discussion needs to address risks of the proposed PAMs. If the authors think that the concerns raised in the Canadian guideline they should argue against them. It would also be interesting to know if any experts mentioned specific risks in the free text or in the panel discussion. If so, this should be mentioned in a paragraph of the results section. I have problems with the term 'indication', which suggests that a particular medical treatment is necessary. However, the authors did not evaluate indications but rather asked for a consensus if a treatment methods was safe – which is not the same as having an indication to use it. I therefore think that the use of the term 'indication' should be revised in this context. Minor Title: The authors indicated well why to use the abbreviation "SAFE PAMP" in the title and PAM throughout the manuscript. 'Strengths and limitations of this study' section: I suggest adding the limitation that safety may be underreported To improve readability consider using less abbreviations, e.g. STS. Line 166: '… different target conditions/populations.' Omit population because it suggests a particular group of people (e.g. older people, from different geographic regions, etc.) not necessary related to the condition. Line 182: '… how to vote for indications'. Should it rather read '…the voting for indications'? Line 147, unclear to what ref. 24 refers to Lines 211-214 should it read 'highly appropriate' instead of 'critical' and 'highly inappropriate' instead of 'limited importance' to be in agreement with the Likert scale as in lines 185-6? Line 321: 'e.g. … frail people' should be omitted. References: Please check with the journal's guideline if all items listed as references should indeed be listed there, e.g. ref. 20 and 25 should probably only be referred to in the text. Figure 2. It should be differentiated between non-response and rejection after invitation (such as in the manuscript's text). Also I think this figure would profit from showing the flow process more stringently (e.g. comparable to CONSORT flow charts). The authors added a Supplement 2 which is helpful to make the methods used more comprehensible. I did not see a reference in the manuscript to the link. If the authors decide to keep this data available, I suggest adding this document or the link to it in the manuscript.

REVIEWER	Matteo, Cioeta

	IRCCS San Raffaele Roma
REVIEW RETURNED	20-Dec-2023

GENERAL COMMENTS	This version fully responds to comments made earlier and now the manuscript is ready to be published.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Fabian Liechti, Inselspital University Hospital Bern Comments to the Author:

General remarks

The authors have revised the manuscript throughout and it has indeed improved a lot. The Introduction is much better with clearly identifying the knowledge gap and indicating the aim of the study. The methods section has also improved a lot. Adding the 'Comparison with literature' section in the Discussion is valuable. I also recognize that definitions are used more carefully with being more precise in the wording. The message that a panel of important stakeholders considers the 9 PAMs investigated as safe is helpful for users internationally. However, there are still some limitations the authors should address.

Author response

We are very thankful for your precious comments that improved our manuscript. We now hope to have addressed all remaining concerns.

Major

Abstract: '… to evaluate the proposed indications' is somehow misleading. In fact they assessed only the 9 PAMs with the indications given as additional information. Please revise.

Author response

We thank the reviewer, amended.

The authors comment that they 'aimed at safety indications (regarding absence/low rate of adverse events)'; however, this is not clear from the manuscript. Also, this doesn't preclude discussing and evaluating specific contraindications and precautions, such as mentioned in the Canadian guideline. Many of the concerns raised in 2000 may still be valid. The current manuscript gives the impression that all nine treatment methods can be used without any safety concern in all adult people – which is contradicting the mentioned Canadian guideline. This is a major problem and should be clearly addressed in the discussion section.

Author response

We understand the point well. Thank you. We made it clearer that our aim was at safety indications. Surely, this doesn't preclude discussing and evaluating specific contraindications and precautions, such as those mentioned in the Canadian guideline, but it is still valid guidance.

In the discussion section, we added that *"We did not aim to report specific contraindications as we started collecting evidence from systematic reviews that reported safety outcomes from primary studies, which may not always encompass real-world conditions, such as the presence of comorbidities (e.g., active deep vein thrombosis). In addition, evidence-informed by systematic reviews did not find enough information about risk for a specific* population *(e.g., hematooncological patients with severe immunocompromised or coagulopathy). However, based on the principle of precaution, the panel agreed to add a general note about precaution in specific subgroups of the population in the absence of literature. Generally, all these indications should be adhered to in conjunction with the guidelines and standards established by professional associations, equipment manufacturers' manuals and regulatory bodies.(48)."*

We also added, in the discussion section, the following paragraph:

Overall, the Canadian document(7) represents the most comprehensive guidance on this topic.

However, our Delphi is the most recent consensus on PAMs focusing on statements about safe PAMs application as clinical practice indications (e.g. field) sustained by literature and clinical expertise. This does not mean that the contraindications and precautions mentioned in the Canadian guideline(7) are in contrast to our findings. Simply, we use a complementary perspective. Our Delphi agree to define the common safe applications stratifying by fields/conditions, whereas the Canadian one describes the contraindications and precautions about these common applications in particular situations or under certain circumstances. For instance, both documents recognize cryotherapy and electrical stimulation as commonly safe PAMs in musculoskeletal applications, such as treating ankle sprains and osteoarthritis. However, the Canadian guideline recommends precaution when combining compression with cryotherapy to ensure the preservation

of circulation and nerves. Furthermore, the guideline contraindicated the use of electrical

stimulation in the presence of implanted electronic devices. Although the evidence presented in the Canadian guideline was not systematically collected (Canada and the United States experts in conjunction with multiple sources such as textbooks), it is reasonable to assume that many precautions and contraindications still remain applicable. Nevertheless, it is important to note that guidelines should be updated every three to five years or when new information becomes available.(32, 33)

We also added this consideration in the implications for clinicians (page 15, lines 513-514) as well as in the conclusion of the manuscript.

Line 166: In this paragraph it's not clear how the steering committee worked out the indications. How were the different experts involved? What was done when disagreeing? It seems the authors put a lot of effort in preparing this list of indications and this should be more accessible for the reader.

Author response

We thank the reviewer for giving us the possibility to better explain this step. We have now better addressed this point. *"The steering committee formulated indications based on evidence and clinical*

expertise. Particularly, evidence was summarized from a scoping review(10) and its supplementary materials, which gathered information about the safety of the nine PAMs from 117 systematic reviews in physiotherapy and rehabilitation medicine (e.g. safety of PAMs for low back pain, osteoarthritis, stroke, urinary incomitance). Clinical expertise was assured by content experts of AIFI (e.g., musculoskeletal disorders, orthopaedic and neurological physiotherapy and pelvic floor rehabilitation), adding examples of clinical conditions for which they commonly safely apply PAMs in their specific field. Disagreements between experts were resolved through discussion. Page 8 lines 203-228

Line 166 and 177: In these paragraphs it should be better explained that for each PAM a list of indications with distinction of evidence and expertise was provided and that the participants indeed used a Likert scale to rate the safety of each of the 9 PAMs with indications from the final list in appendix 1. Otherwise this is only clear when accessing the monkeysurvey questions. I also suggest replacing the word 'voting' with 'rating' to be more precise.

Author response

We thank the reviewer.

In the paragraph ***Phase II.*** **Generation of statements** we now modified as follows: "*The steering committee formulated indications for each PAM (with distinction of evidence and expertise), ensuring that all the potentially relevant topics in the field would be included in the initial list of questions for the first Delphi round"*.

In the paragraph ***Phase III. Rating of statements through Delphi Rounds*** we explained the scale used to rate the 9 PAMs. ***"****The panel of experts evaluated the proposed statements and formulated additional comments using a free text box to ensure complete topic coverage. According to the RAND method, the panel of experts used a 9-point Likert scale (i.e., 1-3 = highly inappropriate, 4-6 = undecided, 7-9 = highly appropriate) for rating the level of concordance for each statement"*.

Page 9, lines 271-275

According to the reviewer's suggestion, we replace the word 'voting' with 'rating' to be more precise across all manuscript.

The discussion section should still be more concise and should be shortened. I especially recommend better structuring within the paragraphs. For example the Main Findings section is very repetitive on excluding children. Instead it would be interesting to know if other populations should also be excluded, e.g. hemato-oncological patients with severe immunocompression or coagolupathy.

Author response

We thank the reviewer. We shortened the discussion section to better-structured paragraphs. We now added in the main findings that "*for precautionary purpose (35) (36, 37), developed indications were not generally extended to other subgroups, such as children and adolescents (due to biological tissue in growth phases(38, 39)), and frail people (e.g., immunocompromised patients), since limited and insufficient literature on harm is available."*

In the limitation section, we also reported that: "We did not aim to report specific

contraindications as we started collecting evidence from systematic reviews that reported safety outcomes from primary studies, which may not always encompass real-world conditions, such as the *presence of comorbidities (e.g., active deep vein thrombosis). In addition, evidence-informed by*

systematic reviews did not find enough information about risk for a specific population (e.g., hemato-oncological patients with severe immunocompromised or coagulopathy). However, based on the principle of precaution, the panel agreed to add a general note about precaution in specific subgroups of the population in the absence of literature. Generally, all these indications should be adhered to in conjunction with the guidelines and standards established by professional associations, equipment manufacturers' manuals and regulatory bodies.(48)."

The discussion needs to address risks of the proposed PAMs. If the authors think that the concerns raised in the Canadian guideline they should argue against them.

Author response

We thank the reviewer.

We added in the discussion that "*Although the evidence presented in the Canadian guideline was not systematically collected (Canada and the United States experts in conjunction with multiple sources such as textbooks), it is reasonable to assume that many precautions and contraindications still remain applicable. Nevertheless, it is important to note that guidelines should be updated every three to five years or when new information becomes available"*

Also, in implication for research, we added that*: "Lastly, future studies can better expand our statements to ensure the safest and optimal modality application of the proposed PAMs (e.g., optimal voltage, amperage, frequency, current density, dose), contraindications and precautions, especially for the subgroups mentioned (e.g., children, immunocompromised people)"*

It would also be interesting to know if any experts mentioned specific risks in the free text or in the panel discussion. If so, this should be mentioned in a paragraph of the results section.

Author response

We thank the reviewer for this suggestion. We collected in free-text any inputs. Thus, we have now added a supplementary including all expert's comments.

I have problems with the term 'indication', which suggests that a particular medical treatment is necessary. However, the authors did not evaluate indications but rather asked for a consensus if a treatment methods was safe – which is not the same as having an indication to use it. I therefore think that the use of the term 'indication' should be revised in this context.

Author response

We thank the reviewer; we have adopted "statements" rather than "indications."

Minor

Title: The authors indicated well why to use the abbreviation “SAFE PAMP” in the title and PAM throughout the manuscript.

Author response

We thank the reviewer for underlining this. The final letter P stay for “practice”. As reported in the peer response r1, we maintained the same acronym of our published protocol. However, we now took the opportunity to insert the term “practice” in the manuscript as appropriate.

‘Strengths and limitations of this study’ section: I suggest adding the limitation that safety may be underreported

Author response

We strongly agree. Done, thank you.

To improve readability consider using less abbreviations, e.g. STS.

Author response

Done, thank you. We have now removed STS abbreviations.

Line 166: ‘… different target conditions/populations.’ Omit population because it suggests a particular group of people (e.g. older people, from different geographic regions, etc.) not necessary related to the condition.

Author response

Amended as appropriate throughout the manuscript.

Line 182: ‘… how to vote for indications’. Should it rather read ‘…the voting for indications’?

Author response

Amended, thank you.

Line 147, unclear to what ref. 24 refers to

Author response

Reference 24 investigated some characteristics of the Delphi methodology, such as the required sample size and the number of participating experts.

Lines 211-214 should it read ‘highly appropriate’ instead of ‘critical’ and ‘highly inappropriate’ instead of ‘limited importance’ to be in agreement with the Likert scale as in lines 185-6?

Author response

We thank the reviewer, and we have now changed it to “highly appropriate.”

Line 321: ‘e.g. … frail people’ should be omitted.

Author response

Thank you. This section has now been rephrased. We now added examples of frailty, such as immunocompromised patients.

References: Please check with the journal’s guideline if all items listed as references should indeed be listed there, e.g. ref. 20 and 25 should probably only be referred to in the text.

Author response

Thank you, checked

Figure 2. It should be differentiated between non-response and rejection after invitation (such as in the manuscript’s text). Also I think this figure would profit from showing the flow process more stringently (e.g. comparable to CONSORT flow charts).

Author response

We followed the reviewer’s suggestion about the use of standards for reporting. For instance, we used the information reported in the Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES) and adapted the figure accordingly. Thus, we tried to improve figure 2, indicating the invitation, participation and completion to differentiate the phases and relative responses. We took advantage of adding the invitation, participation, and completion rate in the main text.

The authors added a Supplement 2 which is helpful to make the methods used more comprehensible. I did not see a reference in the manuscript to the link. If the authors decide to keep this data available, I suggest adding this document or the link to it in the manuscript.

Author response

Thank you, it is linked here. Page 8, line 213

Reviewer: 3

Dr. Cioeta Matteo, IRCCS San Raffaele Roma Comments to the Author:

This version fully responds to comments made earlier and now the manuscript is ready to be published.

Author response

Thank you for your precious comments

Reviewer: 1

Competing interests of Reviewer: None.

Reviewer: 3

Competing interests of Rev

VERSION 3 – REVIEW

REVIEWER	Liechti, Fabian Inselspital University Hospital Bern, Department of General Internal Medicine
REVIEW RETURNED	16-Feb-2024

GENERAL COMMENTS	Reviewer's coments The authors have revised the manuscript according to my suggestions. Thank you also for adding the valuable comments from the experts in the appendix. Some minor issues should still be addressed. 1. Please rephrase and be aware to spell out abbreviations on first mentioning; e.g. 'strength and limitations', first paragraph. 2. I recommend careful and thorough revision of the text by a native English speaker as many phrasings should be more precise. This would increase readability a lot. 3. Please, take also care of formatting issues throughout the manuscript, e.g. a. 'Delphi rounds, Round 2', b. "In fact, for safety purposesprecautionary purpose. (35-37) developed indicationstatements were not generally extended to other subgroups, such as children and , adolescents […]" After careful revision improving readability I think the manuscript will be ready for publication.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 1
Dr. Fabian Liechti, Inselspital University Hospital Bern
Comments to the Author:
Reviewer's coments
The authors have revised the manuscript according to my suggestions. Thank you also for adding the valuable comments from the experts in the appendix. Some minor issues should still be addressed.
1. Please rephrase and be aware to spell out abbreviations on first mentioning; e.g. 'strength and limitations', first paragraph.
Author response
We thank the reviewer for the precious suggestions. In the first paragraph of strength and limitations the abbreviation PAMs is spelled out in line 95 page 5. We took the opportunity to check all abbreviations.

2. I recommend careful and thorough revision of the text by a native English speaker as many phrasings should be more precise. This would increase readability a lot.
Author response
Thank you. We checked the English of the whole manuscript

3. Please, take also care of formatting issues throughout the manuscript, e.g.
a. ‘Delphi rounds, Round 2’,
Author response
Thank you. Checked

b. “In fact, for safety purposesprecautionary purpose. (35-37) developed indicationstatements were not generally extended to other subgroups, such as children and , adolescents […]”
After careful revision improving readability I think the manuscript will be ready for publication.
Thank you. We checked the English of the whole manuscript

Reviewer: 1
Competing interests of Reviewer: None.