



# Risk factors associated with the development and persistence of pain in adolescents: an international Delphi study

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#### **Abstract**

**Introduction:** Despite significant advancements in research on paediatric pain, a consensus on the primary risk factors (RFs) for the development and persistence of pain in this population has not yet been reached.

**Objectives:** This study aims to establish a consensus among experts on the most significant RFs for the onset and persistence of pain in adolescents.

**Methods:** A modified international e-Delphi study with 4 rounds was conducted. An international and multidisciplinary panel of experts in paediatric pain and/or pain RFs was recruited. The experts were provided with 2 lists of potential RFs (1 for the onset, 1 for the persistence of pain) and were asked to rate the importance of each RF on a 5-point Likert scale. In each round, experts were asked to reconsider their answers in light of other experts' evaluations and comments.

**Results:** A total of 43 experts participated in the study (33 completed all rounds). Forty-six RFs (out of 74) reached consensus for pain onset, and 4 were considered very important. Regarding the persistence of pain, consensus was reached on 56 out of 88 RFs. Eleven of these were found to be very important.

**Conclusion:** This study generated consensus among experts on the importance of several RFs for the development and persistence of pain in adolescents. This consensus will be valuable in informing the design of future longitudinal studies, as well as treatment and preventive programs.

Keywords: Paediatric pain, Risk factors, Consensus

#### 1. Introduction

Musculoskeletal pain is present in adolescents at rates that vary between 4% and 40%. <sup>10</sup> The prevalence rate of chronic multisite pain in adolescents has been estimated at 20.6%. <sup>6</sup> Data indicate that 44% of adolescents report experiencing chronic weekly pain in the last 6 months. <sup>6</sup> In 5% of cases, this pain limits life or work activities of children and is referred to as high impact chronic pain. <sup>13</sup>

Chronic pain (CP) has a negative impact on the development and emotional, psychological, and social functioning of these children. It may be associated with anxiety and depression, sleep difficulties, and poor school performance. <sup>19</sup>

Understanding risk factors (RFs) (ie, any attribute, characteristic, or exposure that increases the likelihood of developing a condition) and the underlying mechanisms that contribute to the transition to CP is highly relevant 16 as this may lead to the

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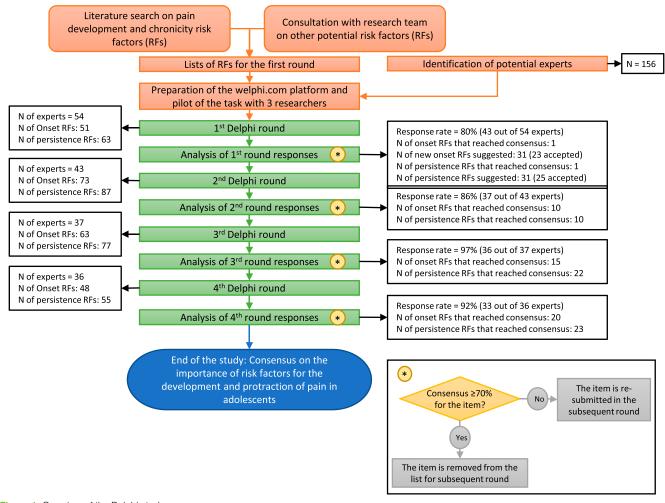


Figure 1. Overview of the Delphi study process.

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development and implementation of preventive interventions<sup>5</sup>; this is particularly relevant since the presence of CP in childhood has been shown to be associated with the persistence of pain,<sup>2</sup> social, and socioeconomic disparities in adulthood.<sup>14</sup>

Recent studies have demonstrated how individual RFs may be associated with the onset and persistence of pain in adolescents. On the other hand, many factors remain unexplored and existing studies have investigated the multifactorial nature of pain from different perspectives. This results in a multitude of heterogeneous and often low-quality studies that are difficult to synthesise. Moreover, these studies frequently fail to investigate associations longitudinally, underscoring the need for further research in the field. <sup>7</sup>

In 2007, Miró et al. <sup>12</sup> published a Delphi study that reached consensus on RFs for CP and disability in children. The authors emphasised the importance of the socio-psychological factors of both adolescents and their parents in the development of CP and related disability. More than 15 years have passed since the consensus. During this time, many new studies have been published, so we cannot exclude the possibility that the information the experts relied on to reach the first consensus is outdated.

The aim of the current study is to update the consensus reached by Miró et al. 12 on the importance of RFs for the chronicity of pain in adolescents, as well as to reach consensus on the most important RFs related to the development of pain in adolescents. This consensus, achieved with leading experts in

the field of paediatric pain, will inform the design of future longitudinal studies aimed at identifying RFs for the development and persistence of pain in adolescents. This study's findings will inform the development of preventive interventions aimed at reducing pain onset and the transition from acute to CP in this population.

#### 2. Methods

#### 2.1. Design

The study was designed and conducted following the recommendations on Conducting and Reporting Delphi Studies (CREDES guidelines). It took place between January and April 2023 and followed an international modified e-Delphi methodology. An online platform (wephi.com) facilitated the study, ensuring the experts' completed the survey anonymously throughout the process; even the steering committee was not able to trace the answers and comments back to the individual experts. All correspondence was in English.

#### 2.2. Participants

A convenience sample of experts was identified between October 2022 and January 2023. The experts had to meet the following eligibility criteria: (1) willing to participate AND (2)  $\geq$ 1 criterion: (A) first or last author of  $\geq$ 1 peer-reviewed publication on pain in

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Table 1

Demographics and qualifications of the panel of experts.

No. of participants	Invited (n = 156)	Completed round 1 (n = 43)	Completed round 2 (n = 37)	Completed round 3 (n = 36)	Completed round 4 (n = 33)
Sex, n (%) Female Male Prefer not to say	102 (65.4) 54 (34.6)	29 (67.4) 13 (30.2) 1 (2.3)	26 (70.3) 10 (27.0) 1 (2.7)	25 (69.4) 10 (27.8) 1 (2.8)	23 (69.7) 9 (27.3) 1 (3.0)
Age (y), mean (SD)	N/A	47 (11)	47 (12)	48 (12)	48 (12)
Profession, n (%) Chiropractor Epidemiologist Medical doctor Nurse Occupational therapist Physiotherapist Psychologist Researcher (not specified)	4 (2.6) 4 (2.6) 35 (22.4) 8 (5.1) 3 (1.9) 39 (25.0) 46 (29.5) 17 (10.9)	1 (2.3) 3 (7.0) 7 (16.3) 5 (11.6) 1 (2.3) 15 (34.9) 10 (23.3) 1 (2.3)	1 (2.7) 2 (5.4) 5 (13.5) 3 (8.1) 1 (2.7) 15 (40.5) 9 (24.3) 1 (2.7)	1 (2.8) 2 (5.6) 5 (13.9) 3 (8.3) 1 (2.8) 15 (41.7) 8 (2.2) 1 (2.8)	0 (0.0) 2 (6.1) 4 (12.1) 3 (9.1) 1 (3.0) 15 (45.5) 7 (21.2) 1 (3.0)
Affiliation, n (%) Australia Belgium Canada Germany Iceland Italy Latvia Netherland Norway Portugal South Africa Spain Sweden Switzerland United Kingdom United States of America Not specified/other	19 (12.2) 3 (1.9) 22 (14.1) 7 (4.5) 1 (0.6) 3 (1.9) 1 (0.6) 6 (3.8) 7 (4.5) 4 (2.6) 2 (1.3) 5 (3.2) 9 (5.8) 6 (3.8) 13 (8.3) 29 (18.6) 19 (12.2)	5 (11.6) 1 (2.3) 5 (11.6) 1 (2.3) 1 (2.3) 3 (7.0) 1 (2.3) 1 (2.3) 2 (4.7) 2 (4.7) 1 (2.3) 2 (4.7) 3 (7.0) 2 (4.7) 4 (9.3) 8 (18.6) 1 (2.3)	5 (13.5) 1 (2.7) 5 (13.5) 0 (0.0) 1 (2.7) 1 (2.7) 1 (2.7) 1 (2.7) 1 (2.7) 2 (5.4) 1 (2.7) 2 (5.4) 2 (5.4) 2 (5.4) 2 (5.4) 4 (10.8) 7 (18.9) 1 (2.7)	5 (13.9) 1 (2.8) 4 (11.1) 0 (0.0) 1 (2.8) 1 (2.8) 1 (2.8) 1 (2.8) 1 (2.8) 2 (5.6) 1 (2.8) 2 (5.6) 2 (5.6) 2 (5.6) 2 (5.6) 4 (11.1) 7 (19.4) 1 (2.8)	4 (12.1) 0 (0.0) 4 (12.1) 0 (0.0) 1 (3.0) 1 (3.0) 1 (3.0) 1 (3.0) 2 (6.1) 1(3.0) 2 (6.1) 2 (6.1) 2 (6.1) 4 (12.1) 6 (18.2) 1 (3.0)
Highest academic degree, n (%) PhD MSc		40 (93.0) 3 (7.0)	34 (91.9) 3 (8.1)	33 (91.7) 3 (8.3)	31 (93.9) 2 (6.1)
Experience (y), mean (SD) In the field of pain Of which with adolescents	_	19 (10) 12 (10)	19 (10) 13 (10)	19 (10) 13 (10)	20 (10) 13 (10)
Professional activity, n (%) Mainly clinical Mainly research 50% clinical, 50% research		7 (16.3) 12 (27.9) 14 (32.6)	5 (13.5) 12 (32.4) 12 (32.4)	5 (13.9) 12 (33.3) 11 (30.6)	4 (12.1) 11 (33.3) 10 (30.3)
Only clinical Only research	_	0 (0.0) 10 (23.3)	0 (0.0) 8 (21.6)	0 (0.0) 8 (22.2)	0 (0.0) 8 (24.2)

N/A, not available.

adolescents within the past 5 years OR (B) first or last author of  $\geq$ 1 peer-reviewed publication on RFs for the development/persistence of pain within the past 3 years.

Given the broad scope of the subject matter, no restrictions were imposed on the professional background of the experts. As there is no consensus on an adequate sample of experts, a minimum number of 30 experts was set, aligning with a previous similar study in the field. 12

PubMed electronic library was searched for individuals meeting the inclusion criteria. The experts were, therefore, sought globally. Potential panellists were then contacted by email, informing them of the study and asking them about their willingness to participate. Moreover, a snowballing strategy was adopted by the recruiting author (A. Folli), requesting experts who agreed to participate to suggest additional potential eligible participants. A. Folli verified on PubMed that the suggested experts met the inclusion criteria and then invited them.

#### 2.3. List of potential predictors

The lists of predictors for the first round were formulated by the steering committee of the Delphi study. The committee was composed of the authors. Two separate RFs lists were drawn up: 1 for the development of pain and 1 for the persistence of pain (chronicity).

Initially, a search was conducted on PubMed for factors associated with the development and persistence of pain in adolescents and adults. Several factors were extracted from the studies for the first version of the lists. After preliminary lists had been compiled, the committee met to discuss and adapt them to make them as comprehensive as possible (eg, the committee added factors that had not emerged from the literature but which they considered potentially relevant). The 2 final lists that were submitted to the experts in the first round are presented in Appendix 1 (available at http://links.lww.com/PR9/A292) and consisted of 51 factors for pain onset, and 63 for pain persistence.

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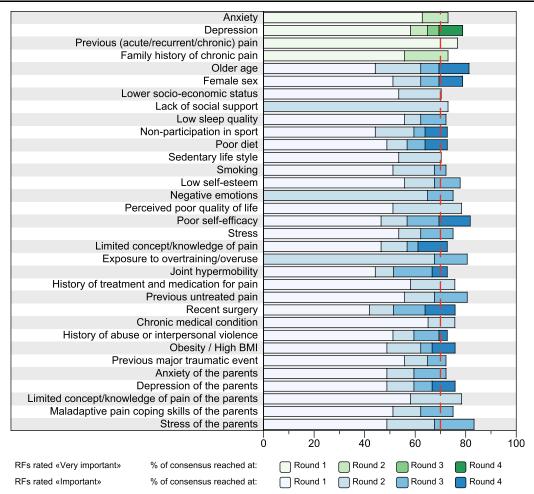


Figure 2. Incremental agreement for RFs rated "very important" or "important" for pain onset. For each RF, the evolution of the expert panel consensus is shown. Each colour refers to a specific round. RFs that reached consensus with the rating "very important" are shown in green, while those rated "important" are displayed in blue. BMI, body mass index; RF, risk factor.

## 2.4. Delphi procedure

Once they agreed to participate in the study by email, experts were invited to participate in the first round. Before participating in round 1, all participants had to consent to data processing and participation in the study, directly via the online platform, and answer a series of questions regarding their sex, age, citizenship/country of their first affiliation, professional background, highest academic qualification (and year), years of experience in the field of pain (clinical and/or research experience), years of experience in the adolescent pain field, professional activity in the field of pain (clinical/research), number of publications in the field of pain in adolescents, and number of publications in the field of pain RFs. For each round, the experts received several invitation and reminder emails (between 4 and 5 emails).

#### 2.4.1. Round 1

During the first round, the experts were presented with the lists of RFs defined by the steering committee. Experts had to assign each RF a level of importance on a 5-point Likert scale: "not important," "low importance," "neutral," "important," "very important." They were first presented with the list of RFs relating to the development of pain and then the list of RFs relating to the persistence of pain (development of CP). Experts also had the option to leave comments justifying their assessment for each item if they deemed it necessary. After evaluating each item, they had the opportunity to suggest further items to be added to the list.

#### 2.4.2. Subsequent rounds (2, 3, and 4)

In round 2, the lists of RFs were expanded following the experts' suggestions, after discussion within the study steering group. The experts received feedback on all suggestions made during round 1 and comments from the steering committee on why these were included or not included in the lists for the next round (Appendix 2, available at http://links.lww.com/PR9/A292). In all subsequent rounds, experts were given the results of the previous round. including the items that had reached consensus (with also the percentage of responses distributed on the Likert scale). The feedback also included any explanations requested by the experts in the comments of the previous round. In responding to the questionnaire, the experts were provided with their own answer from the previous round, the distribution of the group's answers from the previous round (in percentages), and the anonymous comments left by all experts, relating to each RF. Figure A and Figure B in Appendix 3 (available at http://links.lww. com/PR9/A292) show a reproduction of the Welphi platform, which shows how the content of previous rounds was presented to the experts.

#### 2.5. Statistical analysis

After each survey round, the responses were analysed and reorganised for resubmission to the experts in the next round. It was defined a priori that the study would be terminated after 4

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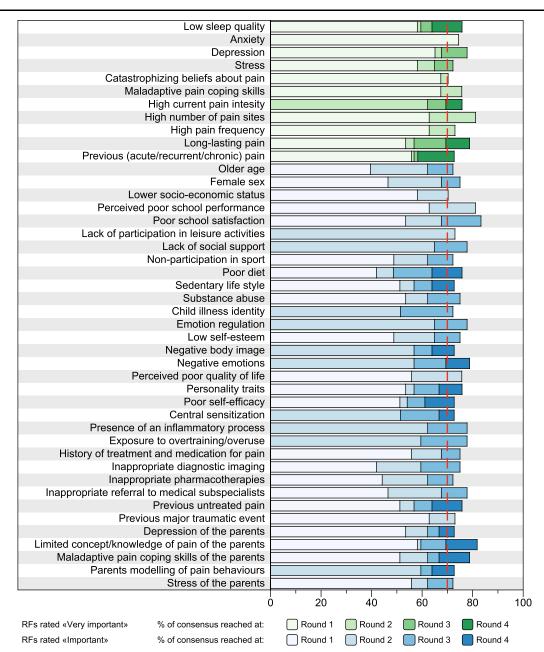


Figure 3. Incremental agreement for RFs rated "very important" or "important" for pain persistence. For each RF, the evolution of the expert panel consensus is shown. Each colour refers to a specific round. RFs that reached consensus with the rating "very important" are shown in green, while those rated "important" are displayed in blue. RF, risk factor.

rounds and that each item would reach consensus when  $\geq$ 70% of the experts provided the same rating. Furthermore, any item that reached the minimum level of consensus was to be excluded from the list for the next round.

#### 3. Results

The process of this international modified Delphi study is summarised in Figure 1.

### 3.1. Participating panel

A total of 122 experts on pain in adolescents (who fulfilled inclusion criterion A) and 34 experts on pain RFs (who fulfilled inclusion criterion B) were invited to participate. Of these, 54

decided to participate, 16 refused to participate (5 because they did not consider themselves sufficiently experienced in the field, 11 due to lack of time), and 52 did not respond. Of the 54 experts who selected to participate in the study, 43 completed the first round (response rate = 80%), 37 completed the second round (response rate = 86%), 36 completed the third round (response rate = 97%), and 33 completed the last round (response rate = 92%). The overall study response rate was 61%. The demographics and qualifications of the participants who completed the different rounds are summarised in **Table 1**.

#### 3.2. Consensus on risk factors for the development of pain

Regarding the onset of pain, 46 RFs out of 74 achieved the minimum predefined consensus rate of 70%. Of these, 4 RFs were

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rated "very important" in the development of pain: "previous (acute/recurrent/chronic) pain" (reaching a consensus of 77% in the first round), "anxiety" and "family history of CP" (both achieving 73% consensus in the second round), and "depression" (78.8% in the fourth round). Also, 29 RFs that reached consensus were rated "important" and 13 "neutral." **Figure 2** shows the evolution of agreement for the items that were rated "important" or "very important" for pain development from at least 70% of the panel. Table A in Appendix 4 (available at http://links.lww.com/PR9/A293) shows the evolution of the consensus of all RFs related to the onset of pain, in all rounds conducted in this Delphi study.

# 3.3. Consensus on risk factors for the persistence (chronicity) of pain

Regarding the persistence of pain, 56 RFs out of 88 achieved the minimum predefined consensus threshold of 70%. Of these, 11 were rated as very important. These "very important" RFs include psychosocial factors such as "anxiety," "depression," and "stress" (percentage agreement of 74.4% at round 1, 77.8% at round 3 and 72.2% in round 3, respectively). Other 2 factors considered "very important" are related to attitudes and beliefs about pain: "catastrophising beliefs about pain" and "maladaptive pain coping skills" (70.3% and 75.7%, respectively, both in round 2). Also several RFs pertaining to the clinical presentation of pain in adolescents were considered "very important": "high number of pain sites" (81.1% in round 2), "high pain frequency" (73% in round 2), "high current pain intensity" (75.8% in round 4), "long-lasting pain" (78.8% in round 4), and "previous (acute/recurrent/chronic) pain" (72.7% in round 4). Also "low sleep quality" was rated "very important" (75.8% in round 4). Moreover, 33 RFs that reached consensus were rated "important" and 12 "neutral." Figure 3 shows the evolution of agreement for the items that were rated "important" or "very important" for pain persistence from at least 70% of the panel. Table B in Appendix 4 (available at http://links.lww.com/PR9/A293) shows the evolution of the consensus of all RFs related to the persistence of pain, in all rounds conducted in this Delphi study.

#### 4. Discussion

This study sought to reach new consensus among experts on paediatric pain on the importance of RFs for the development and persistence of pain in adolescents. The results highlight the experts' recognition of the multifactorial nature of pain in adolescents. Four RFs were deemed "very important" in the context of pain development, and 11 in the context of pain persistence over time. This discussion focuses on some of the RFs that achieved an "important" or "very important" rating.

Nevertheless, several RFs were considered "neutral" by the panel of experts; a rating that is not straightforward to interpret. This result might suggest that the expert panel did not consider these RFs as significant for the onset or persistence of pain. Alternatively, it could indicate that the experts did not feel confident expressing a clear opinion on the importance of these potential RFs.

#### 4.1. Comparison to previous literature

Of the several factors that were rated "very important," "previous (acute/recurrent/chronic) pain" was the first to reach consensus in the first round regarding pain onset. One of the experts also commented "I suspect this would be the most important factor." To the best of our knowledge, there are no studies that have investigated the association of the presence of pain in the past

with the occurrence of a new episode of pain or CP in the general population in this age group.

In the present study, the panel agreed that the presence of depression, anxiety, and stress is very important for both the development and persistence of pain. The frequent association between anxiety, depression, and pain is well studied in the literature. Some models suggest that these are associated factors, <sup>17,18</sup> and some studies provide evidence in favour of a causal association, classifying the presence of negative emotional symptoms as a RF for the development of pain. <sup>7</sup> The expert panel opinion within this study supports this relationship. Despite the clear association between the presence of negative emotional symptoms and the development of musculoskeletal pain highlighted in the review by Huguet et al. <sup>7</sup> and based on moderate quality studies, it appears that the association between this RF and the persistence of pain cannot be confirmed due to confounding factors and the low quality of the evidence. <sup>7</sup>

The panel also recognized a family history of pain as an important RF for the onset of pain in adolescents, a stance that is well-substantiated by existing literature. Although this Delphi panel failed to reach a consensus on the relevance of this aspect for the persistence of pain, from the first round and throughout the study, more than 90% of the experts rated a family history of CP as "important" or "very important." The presence of previously untreated pain also constitutes a point of convergence between the consensus reached by the 2 studies, being considered by both expert groups as important for chronicity.

Maladaptive pain coping skills (eg, fear avoidance) and catastrophizing beliefs about pain were also identified by the expert panel in the current study as relevant factors with respect to pain persistence (chronicity). While numerous studies in the literature support an association between the presence of catastrophising or maladaptive pain coping skills and CP, <sup>11,20</sup> the causality of this association, as with other factors, remains a hypothesis based on cross-sectional studies and models not confirmed by robust longitudinal studies.<sup>1</sup>

The present study also highlights the importance of factors related to pain characteristics as a high number of pain sites (widespread pain), long lasting pain, high current pain intensity and pain frequency, as well as the presence of a past pain experience. Even if characteristics of pain presentation were considered important also in the consensus study by Miró et al., 12 to the best of our knowledge, there are no studies in the literature confirming the association between the presence of these characteristics as predisposing or RFs for the persistence of pain in adolescents.

A new element emerging from the consensus reached by the experts in the present study is the quality of sleep of adolescents. Even in the case of sleep deprivation, the causality of the association between poor sleep and pain is subject of speculation and model formulation but has not yet been clearly defined. 3,21

Comparing the results of the 2 consensuses also reveals further differences. One of the aspects considered important in the study by Miró et al. 12 was the child's tendency to somatise. Although this can be considered a correlate of several items in the present study that were considered important (eg, "personality traits"), it was not investigated directly. Furthermore, treatment-related aspects were considered primary by the panel of consensus in 2007. In the current study, it was found that the same characteristics (eg, "history of treatment and medication for pain," "inappropriate diagnostic imaging," "inappropriate pharmacotherapies," "inappropriate referral to medical subspecialists") were important but not considered among the priority factors by the expert panel.

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The consensus reached in this study appears to be in line with the results of a recent systematic review that identified that many of the factors explored in this study are also considered to be important for the prognosis of persistent musculoskeletal pain (eg, multisite pain, pain intensity, high number of pain sites, etc.). <sup>15</sup>

#### 4.2. Methodological considerations

The pool of experts in this study were from multiple disciplines and were active in research as well as in clinical practice. Moreover, the experts on the panel are spread all over the world. These characteristics confer validity to the results of the study. Nevertheless, the study has some limitations that must be considered when interpreting the results. First, it must be considered that the methodology of Delphi studies ensures that a consensus is reached between experts, which does not necessarily equate to factual accuracy. Many of the factors presented in the list have not been studied in the literature. These results are, therefore, to be understood as a mere consensus among the experts who participated and may be valuable for the design of future studies, but they do not constitute a representation of the evidence. In addition, the results may also have been influenced by the professional background of the experts (specific profession and distribution of work between research and clinical practice). Furthermore, the opinion and consensus reached by the Delphi panellists may differ from those identified experts who declined to participate; thus, the results may not fully represent the opinion of all experts in the field.

Another limitation to be considered is related to the lists of potential RFs submitted to the experts; although efforts were made to make them as comprehensive as possible and the experts had the opportunity to add other RFs, it is not possible to claim that the lists are complete, and some potentially relevant RFs may have been omitted. Furthermore, some RFs were generic or did not specify a direction. Moreover, since it was decided a priori to end the Delphi study in round 4, the factors that were suggested by the experts in round 1 had less opportunity to reach consensus.

Another aspect characterising this study is that musculoskeletal pain in adolescents was considered without reference to specific pathologies. A focus on more homogeneous populations might have led to different outcomes among the experts.

#### 4.3. Clinical and research implications

This study aimed to identify consensus on important RFs for the onset and the persistence of pain in adolescents. The expert panel reached consensus on the importance of 46 out of 74 factors with respect to pain onset and 56 out of 88 factors with respect to pain persistence. The results underscore the multifactorial nature of pain development and persistence in adolescents. The results offer clinicians and researchers insights into potential RFs that may play a role in this process. In the clinical field, this knowledge could be applied in the development of preventive programmes by health professionals or educational systems, aimed at addressing modifiable RFs that could lead to the development of pain and/or the transition to persistent pain in adolescents (eg, negative emotions, lifestyle, etc.). These results can also be a valuable foundation for the design of future research. Indeed, it has become apparent that many potential RFs are not adequately studied. Risk factors that have been assessed as "very important" or "important" in this consensus could be a first starting point for studying causal associations through longitudinal studies.

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#### **Disclosures**

The authors have no conflicts of interest to declare.

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An abstract of this study was presented at a local research congress (Giornata della Ricerca e dell'Innovazione in Medicina Umana della Svizzera italiana, Lugano, Switzerland, 2023) and as a poster at the International Federation of Orthopaedic Manipulative Physical Therapists Congress (IFOMPT, Basel, Switzerland, 2024) and at the European Paediatric Physiotherapy Congress (EUPPT, Zurich, Switzerland, 2024).

Data availability statement: The data that support the findings of this study are available from the corresponding author, A. Folli, upon reasonable request.

#### Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PR9/A292 and http://links.lww.com/PR9/A293.

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