

International consensus on sleep problems in pediatric palliative care: paving the way

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International consensus on sleep problems in pediatric palliative care: Paving the way

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ABSTRACT

Objective: Sleep problems constitute a common and heterogeneous complaint in pediatric palliative care (PPC), where they often contribute to disease morbidity and cause additional distress to children and adolescents and their families already facing the burden of life-threatening and life-limiting conditions. Despite the significant impact of sleep problems, clinical evidence is lacking. The application of general pediatric sleep recommendations appears insufficient to address the unique challenges of the PPC dimension in terms of disease variability, duration, comorbidities, complexity of needs, and particular features of sleep problems related to hospice care. Therefore, we initiated an international project aimed at establishing a multidisciplinary consensus.

Methods: A two-round Delphi approach was adopted to develop recommendations in the areas of Definition, Assessment/Monitoring, and Treatment. After selecting a panel of 72 worldwide experts, consensus (defined as $\geq 75\%$ agreement) was reached through an online survey.

Results: At the end of the two voting sessions, we obtained 53 consensus recommendations based on expert opinion on sleep problems in PPC.

Conclusions: This study addresses the need to personalize sleep medicine's approach to the palliative care setting and its peculiarities. It provides the first international consensus on sleep problems in PPC and highlight the urgent need for global guidance to improve sleep-related distress in this vulnerable population and their caregivers. Our findings represent a crucial milestone that will hopefully enable the development of guidelines in the near future.

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1. Introduction

Sleep problems have been identified as a common and significant contributor to symptom burden in children with life-limiting and life-threatening conditions, including those under pediatric palliative care (PPC). The number of children eligible for PPC is estimated at more than 20 million worldwide and is rapidly increasing [1]. The spectrum of conditions involved is broad and diverse, both malignant and non-malignant; chromosomal, metabolic, neurological, and neurodegenerative disorders represent the most prevalent [2]. The duration and complexity of patient care in the PPC setting [3] reflect this heterogeneity and the need to address the wide variety of concerns within each individual situation.

Besides the numerous medical and psychosocial challenges, these children and their families frequently face the additional burden of poor

sleep and the related consequences of mood and behavioral dysregulation, functional impairments, and potential exacerbation of symptoms, such as fatigue and pain [4,5]. However, unlike other aspects of PPC, sleep has received little attention; therefore, sleep problems remain inadequately addressed in this population, profoundly affecting the quality of life (QoL) of the entire family [6,7].

The term “sleep problems” encompasses a wide range of sleep-related concerns that can adversely impact sleep quality, timing, and/or duration. Their prevalence in children and adolescents with PPC needs ranges from 50% to 80%, according to the few available reports [6,8]. Although primary sleep disorders such as sleep disordered breathing may be present, sleep problems more commonly develop in this context as a consequence or complication of the underlying condition [9] and generally result from a combination of intrinsic and extrinsic factors [10], including pain, mental distress, adverse effects of

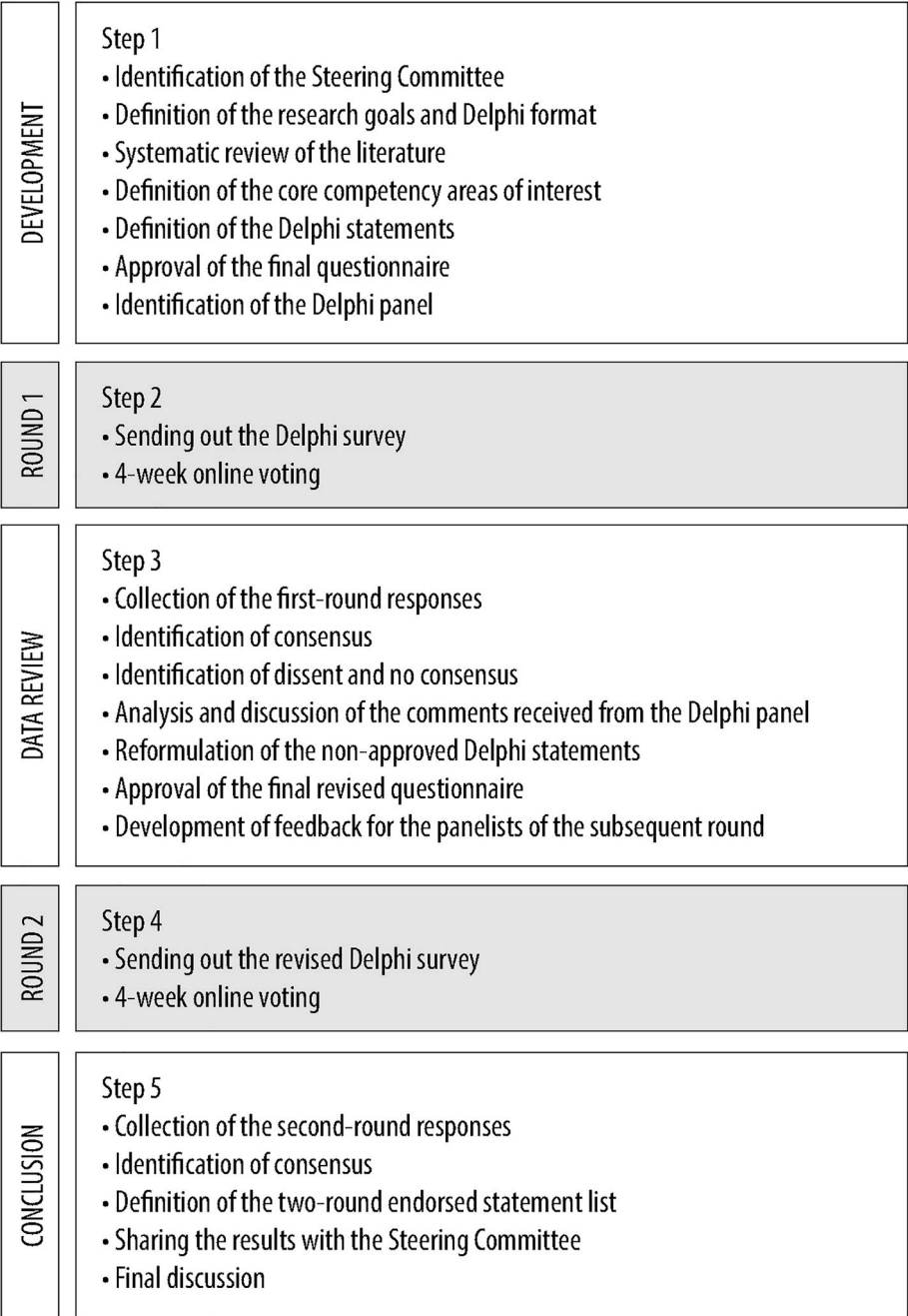


Fig. 1. Project work-flow.

medications, and environmental stressors. The nature of sleep complaints is varied. Difficulty falling and staying asleep, early morning awakenings, poor quality and non-restorative sleep, and excessive daytime sleepiness have been reported, both at home and in hospital settings [11,12]. Frequently, multiple sleep problems are present, either co-occurring or in succession [13].

Few palliative care providers pursue sleep symptoms despite their potential repercussions. These concerns may be perceived as inevitable and untreatable [14] and, in a broader context, viewed as relatively low on the priority list of these patients' problems. In addition, no guidelines or good practices are currently available to approach problematic sleep in PPC.

A more precise profile of the extent, characteristics, impact, and tractability of sleep problems in PPC is urgently needed to address this critical gap.

Our paper presents the results of a Delphi consensus process through which an international group of experts (*Pediatric Sleep and Palliative Care Group*) provided recommendations for defining and managing sleep problems in children and adolescents needing palliative care.

2. Methods

2.1. Study design and participants

This study was part of a more extensive research program investigating the most troublesome PPC symptoms that lack extensive literature [7]. Its primary purpose was to develop an interactive discussion platform to generate consensus among international experts in pediatric sleep and/or PPC through a viable quantitative procedure.

The consensus activity was based on the Delphi method. The project workflow is reported in Fig. 1.

2.1.1. Delphi method

The Delphi method is a widely used consensus method that iteratively and anonymously evaluates the level of agreement (consensus quantification) on a particular topic or issue for which empirical evidence is lacking or limited. It employs rounds of questionnaires in which a committee of identified experts (Steering Committee, SC) contributes independently with suggestions and recommendations (statements) [15]. A panel of experts is then invited to rank their level of agreement with the produced statements and refine them. Additional rounds are completed to eventually reach a consensus among the entire participant group, and each survey iteration is informed by data from the previous round [15].

In this project, the level of agreement was assessed using a Likert scale (1–5; 1 = total disagreement; 5 = total agreement), and consensus was established when $\geq 75\%$ of voters expressed a vote equal to 4 or 5 [16]. A two-round Delphi voting was conducted online using the SurveyMonkey software. Two professional methodologists and one study facilitator supervised the whole Delphi process.

2.1.2. Identification of the Steering Committee

Participants were recruited based on significant contribution and expertise in the field of pediatric sleep and/or PPC, following these criteria: role/function, related fields of expertise, years of experience, and advanced educational degrees.

The SC consisted of five pediatric sleep experts and five PPC specialists from eight countries worldwide, across different disciplines - including clinicians, a psychologist, and a nurse - and backgrounds. The Committee was charged with reviewing the most relevant literature on the topic, defining the core competency areas, producing a list of statements for the online survey, and nominating the members of the Delphi panel.

2.1.3. Establishing the Delphi Panel of experts

The SC nominated 117 candidates with at least five years of clinical

experience and active scientific publication in pediatric sleep and/or PPC, again targeting different geographic areas, disciplines, and backgrounds. Each potential participant was sent an email invitation introducing the project.

2.2. Development and validation of the Delphi questionnaires

PubMed, Google Scholar, Cochrane Library, Web of Science, and Scopus databases were systematically reviewed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The SC defined three core competency areas of utmost relevance to achieving consensus on sleep problems in PPC: 1) Definition, 2) Assessment/Monitoring, and 3) Treatment. Two members of the SC were identified as referees for each area of expertise. The first questionnaire was created based on the literature review and feedback from the remaining members, who were asked to provide statements relying mainly on their clinical experience. Overall, 105 statements were collected; the two referees identified the most significant ones, which were then reviewed and collegially agreed upon for inclusion in the final questionnaire.

The second questionnaire was revised according to the Panel's responses and comments.

2.2.1. Instructions for Delphi Panel of experts

A secure online link to participate anonymously was emailed to the participants. The survey included a personal information sheet and a list of statements to vote on and provide feedback comments. Instructions on voting were shared through a written procedure guide, with directions to skip the statements beyond a panelist's area of expertise.

2.3. Data collection and analysis

The first Delphi survey was sent out for the Panel vote in August 2023; 4 weeks were allowed for completion, with two reminders sent as needed. Afterward, the SC discussed the outcomes and provided alternative formulations for the statements that had yet to reach a consensus, considering the comments received from the panelists.

The same experts participating in the first round were invited to the second round. The second Delphi survey, including the reformulated statements, was carried out in December 2023 using the same previous methodology.

Consensus was achieved only for the statements voted by more than half of the Panel. Statements not reaching an agreement were classified as "no consensus."

All data were analyzed with descriptive statistics.

3. Results

The final Delphi Panel comprised 72 experts from 18 countries worldwide with different expertise (Fig. 2). 65 experts (90.2%) participated in the second Delphi round.

Respondents' rates varied for each statement. By the end of the two voting sessions, a consensus was reached for 53 of 61 (87%) statements: 14 in definition, 16 in assessment/monitoring, and 23 in treatment. The statements endorsed are presented in the consensus statements section below. Tables 1–3 show the detailed results of each round; Table 4 summarizes the quantitative data.

3.1. First round

Consensus was reached for 35 of 52 statements (67%); in detail, for 11 of 16 (69%) in Definition, 10 of 15 (67%) in Assessment/Monitoring, and 14 of 21 (67%) in Treatment.

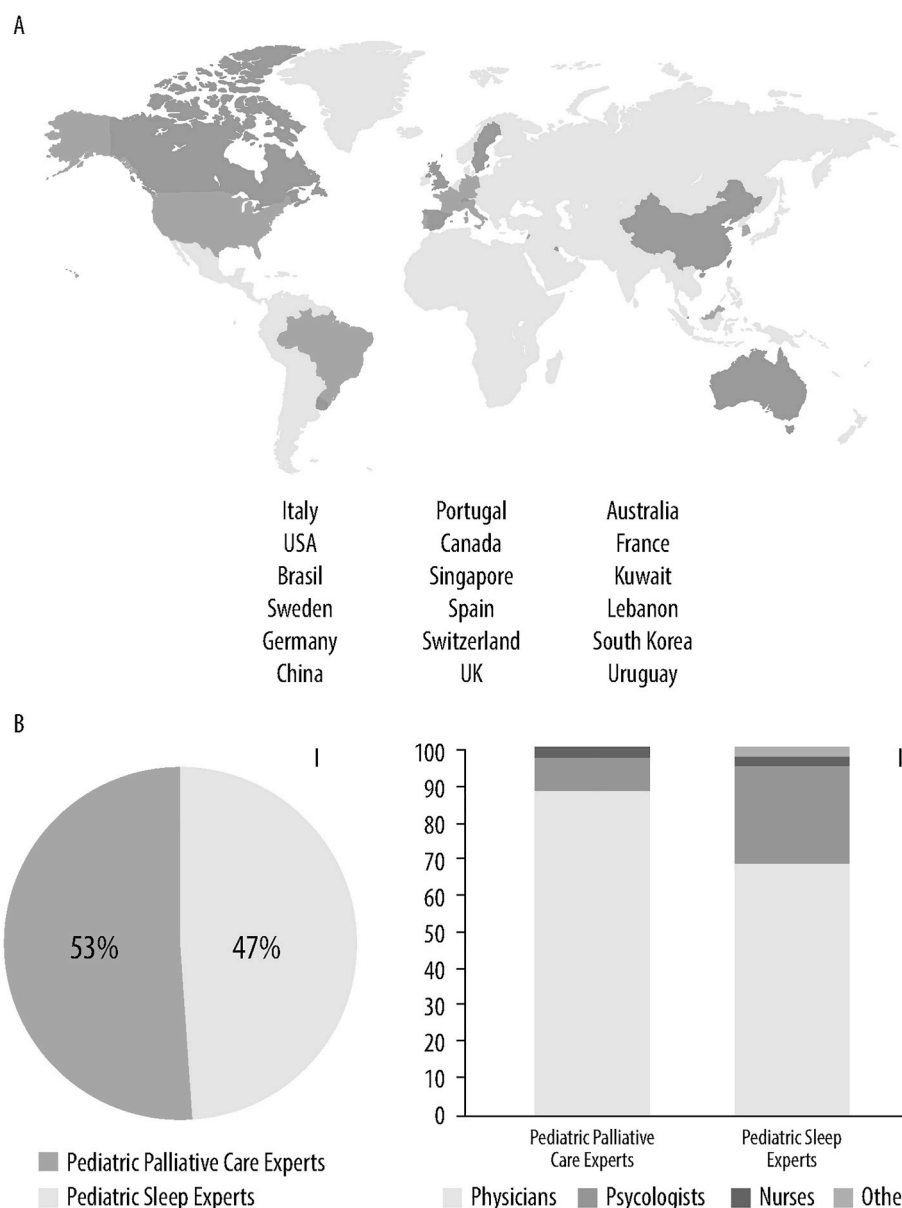


Fig. 2. Composition of the Delphi Panel according to A. geographic location (in order of prevalence) and B. expertise (I) and discipline (II).

3.2. Second round

According to the Panel's suggestions, nine statements not approved in the first round were reformulated, seven were split into two new statements, and one was split into three new statements to improve clarity and correctness.

26 statements (seven in Definition, nine in Assessment/Monitoring, and 10 in Treatment) were voted in the second round. The consensus was reached for 19 of them (73%): three of seven (43%) in Definition, six of nine (67%) in Assessment/Monitoring, and 10 of 11 (91%) in Treatment.

3.3. Consensus statements

3.3.1. Definition of sleep problems in PPC

- Strong consensus was reached on the recognition that the **etiology** of sleep problems in the PPC setting is **multifactorial** (statement 1; 99% of agreement) and, similarly, on possibly having **different**

sleep disorders in the same patient (statement 2; 90% of agreement).

- **Pain** was strongly identified as an essential factor to consider in difficulty falling or staying asleep (statement 4R.2; 95% of agreement), while a causative role of primary underlying conditions and concomitant medications in sleep problems was not (statements 3R; no consensus). Neither was hypersomnia correlated with drug-drug interactions nor with the use of sedative medications for pain relief (statements 5R.1 and 5R.2; no consensus). At the same time, anxiety and fear failed to gain consensus as the most relevant psychological factors for insomnia (statement 4R.1; no consensus).
- Conversely, **medical and nursing procedures** were acknowledged as a frequent reason for nocturnal awakenings, along with **musculoskeletal alterations** and **postural demands**, contributing to sleep problems (statements 9, 10 and 16; 77%, 86% and 88% of agreement, respectively).
- Sleep disruptions were also correlated with **opioid-induced respiratory alterations** (statements 14R; 78% of agreement). Likewise,

Table 1
Results of the Delphi survey on sleep problems in PPC - Definition.

Statements	n	Response (%) ^a					Consensus score, % (n)	Final result
		1	2	3	4	5		
Q1 Sleep problems in children in palliative care have a multifactorial etiology.	71	0	0	1	11	88	99 (70)	Yes
Q2 Different sleep disorders often coexist in the same patient.	71	0	1	8	25	65	90 (64)	Yes
Q3 Sleep disorders in children with non-cancer conditions most commonly involve chronic insomnia, circadian rhythm sleep-wake disorder, and sleep-related movement disorder.	69	1	7	23	49	18	67 (47)	No
Q3R ▶ Sleep problems are commonly a symptom of another primary disorder or pharmacological side effects in this population.	63	2	8	27	35	28	63 (40)	No
Q4 Insomnia related to anxiety and fear is a prevalent cause of sleep-wake difficulties in oncologic patients needing PPC.	70	0	4	21	37	36	73 (52)	No
Q4R.1 ▶ Anxiety and fear are the psychological factors most associated with insomnia.	63	2	10	24	38	27	65 (41)	No
Q4R.2 ▶ Pain is an important cause to consider when addressing difficulty falling asleep or maintaining sleep.	62	0	2	3	19	76	95 (59)	Yes, 2 nd round
Q5 Hypersomnia is frequently correlated with pain and the use of sedative medication.	70	0	11	28	46	13	59 (42)	No
Q5R.1 ▶ Hypersomnia frequently correlates with the use of sedating medications to relieve pain.	62	0	5	23	63	10	73 (45)	No
Q5R.2 ▶ Hypersomnia frequently arises from drug interaction in complex treatment regimens.	61	0	2	25	59	15	74 (45)	No
Q6 A bi-directional relationship exists between poor quality sleep and pain, fatigue, and poor quality of life.	71	0	0	3	18	79	97 (69)	Yes
Q7 A bi-directional relationship exists between sleep problems and more intense feelings of depression and hopelessness .	70	0	4	9	34	53	87 (61)	Yes
Q8 Sleep deprivation is associated with higher rates of anxiety in children with PC needs and their caregivers.	68	0	0	7	43	48	91 (63)	Yes
Q9 Night awakenings in PPC are often related to medical and nursing procedures (such as change of position, aspiration, administration of drugs, and feeding).	71	0	4	18	38	39	77 (55)	Yes
Q10 Musculoskeletal alterations contribute to sleep problems.	68	0	1	10	44	42	86 (60)	Yes
Q11 Sleep disorders correlate with increased disease burden of children in PPC, as reported by patients/caregivers.	71	0	1	8	41	49	90 (64)	Yes
Q12 Parents of children receiving home-based care fear their child will pass away during their parents' sleep.	68	0	4	25	34	36	70 (48)	No
Q12R ▶ Caregivers of children receiving home-based terminal care may fear their child will pass away when they are asleep and tend to develop an inadequate wake-sleep routine.	63	0	6	11	40	43	83 (52)	Yes, 2 nd round
Q13 Most parents of children needing PPC suffer from poor sleep.	68	0	0	9	33	56	89 (62)	Yes
Q14 Opioid-induced respiratory alterations correlate with sleep disruptions, possibly exacerbating excessive daytime sleepiness.	65	2	15	30	27	25	52 (34)	No
Q14R ▶ Opioid-induced respiratory alterations during sleep may determine sleep disruptions, possibly exacerbating excessive daytime sleepiness.	59	0	10	12	47	31	78 (46)	Yes, 2 nd round
Q15 The use of corticosteroids is associated with circadian rhythm disruption.	66	0	3	16	39	40	79 (53)	Yes
Q16 Postural needs influence sleep quality.	67	0	0	10	43	45	88 (60)	Yes

^aPercentage results have been rounded up. Endorsed statements are reported in blue.
Q=question; n=number of voters.

- corticosteroids were involved in circadian rhythm disruptions (statement 15; 79% of agreement).
- Furthermore, the panelists largely agreed on the **bi-directional relationship** between poor-quality sleep and pain, fatigue, poor QoL, and more intense feelings of depression and hopelessness (statements 6 and 7; 97% and 87% of agreement, respectively), as well as the association between deprived sleep and higher rates of anxiety in both patients and their caregivers (statements 8; 91% of agreement), and between sleep disorders and a higher disease burden (statement 11; 90% of agreement).
 - Interestingly, it was agreed that most **parents/caregivers** of children needing PPC also experience poor sleep (statement 13; 89% of agreement). Among the reasons endorsed was the fear that their child will pass away while they are asleep (statement 12R; 82% of agreement).

3.3.2. Assessment and Monitoring of sleep problems in PPC

- There was strong consensus on the necessity of **exploring sleep** to provide an effective PPC program (statement 17; 92% of agreement).
- According to the Panel, the **full spectrum of sleep disorders** should be considered in the assessment phase, given the possibility of a concomitant occurrence (statement 23R.1; 98% of agreement).

- Moreover, the panelists confirmed that sleep assessment and monitoring can best be performed using **standardized sleep questionnaires** and **sleep diaries** completed by parents (statements 18R and 24; 87% and 97% of agreement, respectively).
- It was also established that when sleep disorders are present, it is essential to adequately investigate the patient's **psychological profile** (statement 25; 80% of agreement).
- Evaluating **indirect indicators** (e.g., crying, alteration of physiological indicators, discomfort) and **potential contributors** (such as anxiety, depression, nighttime care, and effects of concomitant medications) to sleep disturbances helps address problematic sleep (statements 19, 22, 23R.2; 80–100% of agreement overall), as does monitoring pain and identifying its causes (statement 21; 93% of agreement).
- Assessing the child's **sleep routine and schedule** was almost unanimously recognized as a mainstay of insomnia (statement 30; 99% of agreement).
- Remarkably, referral to a **sleep study** was strongly identified as limited to treatment goals (statement 26R.1; 94% of agreement). Actigraphy was not consensually considered a feasible and reliable method for assessing and monitoring sleep disturbances and 24-hour sleep duration over multiple days/nights, nor was video-somnography (statements 26R.2, 26R.3, and 27R; no consensus).

Table 2
Results of the Delphi survey on sleep problems in PPC - Assessment/Monitoring.

Statements	n	Response (%)					Consensus score, % (n)	Final result
		1	2	3	4	5		
Q17 Collecting data on sleep constitutes an essential step in defining an effective PPC program.	68	0	1	4	23	69	92 (64)	Yes
Q18 Validated questionnaires should always be used to assess sleep in children and adolescents with life-limiting conditions.	69	0	13	14	37	34	71 (50)	No
Q18R ► Sleep questionnaires may be helpful as additional tools for monitoring sleep problems.	62	0	0	13	35	52	87 (54)	Yes, 2 nd round
Q19 Evaluation of indirect sleep-related parameters (such as crying, alterations of physiological parameters, associated movements, and refusal of the ventilator or oximeter monitoring) helps define the contributors to sleep problems in PPC.	70	0	3	17	44	36	80 (56)	Yes
Q20 It is essential to raise awareness among professionals regarding the importance of evaluating the sleep quality of caregivers of children with complex chronic diseases.	70	0	1	0	7	92	99 (69)	Yes
Q21 Monitoring pain and identifying its causes are essential to address sleep problems in children needing PPC.	70	0	0	7	11	82	93 (65)	Yes
Q22 The role of concomitant drugs must be considered during the evaluation of sleep problems.	70	0	0	1	17	82	99 (69)	Yes
Q23 Sleep apnea and sleep-related movement disorders must be excluded when evaluating sleep problems in PPC.	69	9	11	16	24	39	63 (44)	No
Q23R.1 ► The full spectrum of sleep disorders should be considered when evaluating sleep complaints, as more than one sleep disorder may be present in the same child.	63	0	0	2	25	73	98 (62)	Yes, 2 nd round
Q23R.2 ► Sleep assessment must include evaluation of indirect sleep-related parameters, such as anxiety, depression, discomfort, and interruptions due to nighttime care.	63	0	0	0	19	81	100 (63)	Yes, 2 nd round
Q24 A sleep diary completed by parents can provide important information about the child's sleep-wake pattern in the home setting.	70	0	1	1	39	58	97 (68)	Yes
Q25 It is necessary to investigate the psychological profile to address sleep disorders adequately, consistent with age and cognitive level.	69	1	3	14	39	41	80 (56)	Yes
Q26 In order to diagnose specific sleep disorders in PPC, sleep protocols, actigraphy, and polysomnography are useful tools.	69	1	3	21	30	43	73 (51)	No
Q26R.1 ► Considerations for referring a patient for a sleep study must include the study's goals related to possible treatment interventions, feasibility, and potential discomfort for the child and family.	63	2	0	5	21	73	94 (59)	Yes, 2 nd round
Q26R.2 ► Actigraphy is a non-invasive, generally well-tolerated, and accurate method for assessing and monitoring sleep disturbances over multiple days/nights in the PPC setting.	58	2	10	24	38	26	64 (37)	No
Q26R.3 ► Actigraphy is a non-invasive, generally well-tolerated, and accurate method for assessing and monitoring 24-hour sleep duration over multiple days/nights in the PPC setting.	58	2	9	22	41	26	67 (39)	No
Q27 Videosomnography is a new approach to better monitor the child during 24 hours in the crib or bed.	66	3	6	25	46	18	64 (43)	No
Q27R ► Videosomnography is a potentially useful non-invasive approach to monitor the child during 24 hours in a crib or bed.	57	0	7	28	47	18	65 (37)	No
Q28 Sleep disorder screening must be repeated following significant changes in the patient's location, medical status, and medications.	69	0	1	9	35	55	90 (62)	Yes
Q29 Children under long-term non-invasive ventilation at home must have at least one sleep assessment annually.	68	1	4	20	29	43	72 (50)	No
Q29R.1 ► Children treated with long-term non-invasive ventilation must be re-assessed routinely for changes in breathing sleep disorders necessitating treatment adjustments.	62	0	2	10	32	57	89 (55)	Yes, 2 nd round
Q29R.2 ► It is advisable that a pediatric sleep specialist or respirologist evaluate children treated with long-term non-invasive ventilation.	61	0	3	10	26	61	87 (53)	Yes, 2 nd round
Q30 Assessing the sleep routine and sleep schedule of the child with insomnia symptoms is important.	70	0	0	1	13	86	99 (69)	Yes
Q31 If there are problems in the child's sleep, it is also necessary to investigate their parents' sleep.	70	0	1	11	33	54	87 (61)	Yes

*Percentage results have been rounded up. Endorsed statements are reported in blue.
Q= question; n=number of voters.

- Consensus was reached on re-evaluating sleep disorders following significant **patient condition changes** (statement 28; 90% of agreement).
- Specifically, in children treated with **long-term non-invasive ventilation**, routine re-assessment is advised for changes in sleep disordered breathing to adjust treatment parameters, ideally by a pediatric **sleep specialist or respirologist** (statement 29R.1 and 29R.2; 89% and 87% of agreement, respectively).
- Notably, the panel also concurred on the necessity of **investigating the parents' sleep** whenever their child's sleep is altered and **raising awareness among professionals** about the likely impact of

sleep problems on caregivers (statements 31 and 20; 87% and 99% of agreement, respectively).

3.3.3. Treatment of sleep problems in PPC

- It was recommended that sleep problems in PPC should be **promptly** addressed through a **multidisciplinary approach**, including tailored non-pharmacological and pharmacological interventions (statements 32, 33, 34, 35; ≥88% of agreement overall).
- **Behavioral interventions and adjustments in sleep routines** were confirmed as the first-line treatment for insomnia, with the caveat

Table 3
Results of the Delphi survey on sleep problems in PPC - Treatment.

Statements	n	Response (%) [*]					Consensus score, % (n)	Final result
		1	2	3	4	5		
Q32 Sleep problems in palliative care must be promptly addressed.	69	0	0	3	32	65	97 (67)	Yes
Q33 The treatment of sleep disorders in PPC requires a multidisciplinary approach.	69	0	0	4	22	74	96 (66)	Yes
Q34 Sleep problems in PPC must be addressed by combining pharmacological and non-pharmacological interventions.	68	0	1	10	18	71	88 (60)	Yes
Q35 Shared and personalized setting strategies must be adopted when treating sleep problems in inpatient and home settings.	67	1	0	1	20	76	96 (65)	Yes
Q36 Pharmacotherapy is the primary treatment option for sleep-wake problems in PPC.	67	16	40	31	9	3	12 (8)	No
Q36R.1 ▶ Behavioral interventions and adjustments of sleep practices are the first-line treatment for sleep onset and maintenance issues for children in PPC.	63	0	0	14	34	52	86 (54)	Yes, 2 nd round
Q36R.2 ▶ Pharmacotherapy may be necessary in addition to behavioral interventions and adjustments of sleep practices to treat insomnia in these patients adequately.	63	0	0	3	32	65	97 (61)	Yes, 2 nd round
Q37 Benzodiazepines and antihistamines are the first-line therapy as hypnotics in PPC.	66	22	26	28	16	5	21 (14)	No
Q37R.1 ▶ While commonly used in the PPC setting, benzodiazepines and antihistamines have little empirical evidence to support their use as first-line therapy hypnotics.	60	0	7	20	40	33	73 (44)	No
Q37R.2 ▶ Benzodiazepines and antihistamines may have significant associated side effects that limit their utility.	62	0	2	15	42	42	84 (52)	Yes, 2 nd round
Q38 When using melatonin, it is advisable to consider a combination of immediate-acting and long-acting formulations to increase total sleep duration.	67	4	12	40	34	9	43 (29)	No
Q38R.1 ▶ It is advisable to consider individual sleep patterns and available administration routes when recommending immediate-acting, long-acting, or combined formulations to decrease sleep onset latency, reduce night awakenings, and increase total sleep duration.	63	0	2	2	30	67	97 (61)	Yes, 2 nd round
Q38R.2 ▶ For melatonin products manufactured in the US, only those verified by the United States Pharmacopeia should be used; for products from other countries, guidance from the respective drug oversight organizations should be considered.**	57	2	2	21	30	45	75 (43)	Yes, 2 nd round
Q39 In children with severe neurological impairment and neuro-irritability, gabapentin improves sleep, mood, and general well-being.	63	0	5	26	47	18	65 (43)	No
Q39R ▶ In children with severe neurological impairment and irritability due to chronic pain or neuropathic pain, gabapentin may improve sleep.	61	0	2	11	51	36	87 (53)	Yes, 2 nd round
Q40 The side effect of inducing sleepiness caused by some medications is helpful for children with insomnia when the medication is given at nighttime.	68	0	0	15	50	35	85 (58)	Yes
Q41 Using long-acting medications to manage symptoms overnight is helpful to limit sleep interruptions.	68	1	3	20	45	29	74 (51)	No
Q41R ▶ When possible, using long-acting formulations to manage symptoms overnight helps limit sleep interruptions.	63	2	2	11	51	35	86 (54)	Yes, 2 nd round
Q42 Improving analgesia generally improves sleep problems in patients with chronic pain conditions.	68	0	0	4	40	56	96 (65)	Yes
Q43 Treatment for anxiety is suitable for disrupted sleep related to anxiety and fear.	69	0	1	6	48	45	93 (64)	Yes
Q44 Control of respiratory distress and pain facilitates reducing nocturnal awakenings and regulating the sleep-wake rhythm.	69	0	0	1	35	63	98 (68)	Yes
Q45 Optimizing meals, drug administration, and timing of rehabilitation sessions according to the sleep-wake routine improves sleep quality.	68	0	0	3	22	75	97 (66)	Yes
Q46 Developing a pre-sleep routine is important for the pharmacotherapy of insomnia.	69	0	1	3	28	68	96 (66)	Yes
Q47 Complementary and alternative therapies (such as music therapy, reiki, and hypnosis) performed by accredited therapists are effective additional interventions to improve sleep.	69	6	6	29	27	32	59 (41)	No
Q47R ▶ Complementary and alternative therapies (such as music therapy, reiki, and hypnosis) performed by accredited therapists should be considered as additional therapeutic strategies to address insomnia.	63	2	10	11	40	38	78 (49)	Yes, 2 nd round
Q48 Physical and cognitive stimulation during the daytime helps counteract daytime sleepiness, where applicable.	68	0	1	13	49	37	85 (58)	Yes
Q49 Parent-led behavioral sleep interventions can potentially improve insomnia in the home setting.	69	0	0	10	39	51	90 (62)	Yes
Q50 Children's sleep and mood improve with mobile apps for relaxation (e.g., white or pink noise) and distraction.	67	1	9	41	34	13	47 (32)	No
Q50R ▶ In chosen cases and if used correctly, verified digital tools for relaxation (e.g., white or pink noise) and distraction may help manage insomnia symptoms.	61	0	8	16	49	26	75 (46)	Yes, 2 nd round
Q51 Environmental strategies, such as noise and light control and room privacy, help reduce sleep problems at home and in hospital settings.	69	0	0	1	38	61	99 (68)	Yes
Q52 It is important to concomitantly treat parent/caregiver sleep problems when present.	69	0	1	7	35	57	91 (63)	Yes

^{*}Percentage results have been rounded up;

^{**}In areas such as the USA, where melatonin is available as an 'over-the-counter' medication, the labeled melatonin content may not reflect the actual melatonin content, compromising efficacy and safety. Endorsed statements are reported in blue.

Q=question; n=number of voters.

Table 4
Quantitative results of the two-round Delphi voting.

First round	n (%)
Total consensus agreement	35/52 (67)
• Definition	11/16 (69)
• Assessment/Monitoring	10/15 (67)
• Treatment	14/21 (67)
Second round	
Total consensus agreement	19/26 (73)
• Definition	3/7 (43)
• Assessment/Monitoring	6/9 (67)
• Treatment	10/11 (91)
Both rounds	
Total consensus agreement	53/61 ^a (87)
• Definition	14/16 (87)
• Assessment/Monitoring	16/19 (84)
• Treatment	23/24 (96)

^a Of the statements not approved in Round 1, nine were reformulated, seven split into two new statements, and one into three.

- that adding pharmacotherapy may be beneficial in many cases (statements 36R.1 and 36R.2; 86% and 97% of agreement, respectively).
- Furthermore, consensus was obtained on the potential value of **complementary and alternative therapies** as additional strategies when administered by accredited therapists (statement 47R; 78% of agreement).
 - The limited utility of **benzodiazepines and antihistamines** was agreed upon because of the significant associated side effects (statement 37R.2; 84% of agreement), while consensus was not reached on avoiding them as first-line therapy hypnotics, given the limited empirical evidence available.
 - According to the Panel, the choice between immediate-acting, long-acting, or combined **melatonin** formulations should consider individual sleep patterns and available administration routes (statements 38R.1; 97% of agreement).
 - It was also agreed that the use of melatonin products manufactured in the United States should be limited to those **verified** by the United States Pharmacopeia; for other countries, it is advisable to refer to licensed medications or guidance from the national regulatory agencies (statements 38R.2; 75% of agreement).
 - Interestingly, **gabapentin** was proposed as a therapeutic option to possibly improve sleep in neuro-irritability (statement 39R; 87% of agreement).
 - Several other potentially useful non-pharmacological and pharmacological **interventions** were provided with varying levels of agreement (Table 5).
 - Similar to the previous sections, the importance of treating **care-givers'** sleep problems was confirmed (statement 52; 91% of agreement).

Table 5
Non-pharmacological and pharmacological approved interventions to improve sleep problems in PPC.

Statement	Suggested interventions	Level of agreement
Q40	Use of medications causing sleepiness at nighttime	85%
Q41R	Use of long-acting formulations to manage symptoms overnight	86%
Q42	Improvement of analgesia in chronic pain conditions	96%
Q43	Treatment for anxiety	93%
Q44	Control of respiratory distress	98%
Q45	Optimization of meals, drug administration, and timing of rehabilitation sessions	97%
Q46	Development of a pre-sleep routine	96%
Q48	Physical and cognitive stimulation during the daytime	85%
Q49	Parent-led behavioral sleep interventions	90%
Q50R	Use of relaxation and distraction (verified) digital tools	75%
Q51	Environmental control (noise and light control, room privacy)	99%

4. Discussion

The dearth of published evidence and limited clinical knowledge about sleep in PPC presented both a challenge and an opportunity for developing recommendations, as well as for designing and implementing interventions for this unique pediatric population. The overall level of agreement in the Panel was significant despite the variation in the members' professional and cultural backgrounds and experiences.

PPC and sleep medicine experts agreed that disrupted, reduced, and poor-quality sleep is an important clinical issue. Prompt and accurate identification and management of children's sleep problems were defined as an essential component of gold-standard PPC because of the significant potential impact of poor sleep on both children and care-givers [4,5].

The bi-directional relationship between sleep problems and a host of negative consequences, including impaired functioning and exacerbation of other critical symptoms and global distress, was further clarified. This establishes some new and crucial implications, diverging from the current practice of palliative care, where sleep disturbances are often underdiagnosed and/or under-treated [12].

The recognition of a sleep problem's multifactorial nature in the PPC setting reflects its multidimensional complexity and calls for a thorough and repeated assessment of sleep disorders, keeping in mind the possibility of their co-occurrence in the same child, and for the active involvement of the pediatric sleep specialist in the care plan, when needed.

Inadequate pain control was confirmed as a major risk factor for sleep disturbances. As previously suggested, addressing sleep problems without addressing concomitant pain may not be effective [17]. Therefore, pain must be assessed whenever a sleep problem is identified. If treatment is started, follow-up is warranted to ensure its efficacy.

Although a growing number of studies have focused on the impact of environment-related contributors on sleep [18,19], their consequences on children with life-threatening and life-limiting illnesses have not been extensively investigated [5]. We recognized the importance of considering environmental exposures when diagnosing sleep problems in PPC conditions and applying appropriate strategies to counteract them. The hospital environment often presents disturbing levels of sound and light; in the PPC setting, these are likely to include devices essential for care and support and those needed at home. Concomitantly, caring for these children may require several nighttime interventions, such as changing the patient's position, aspiration, feeding, and administering medications, resulting in frequent sleep disruptions. Control-stimuli strategies should be applied to reduce negative influences and optimize the care plan by conveniently scheduling medical and nursing procedures.

Unexpectedly, there was no agreement on the relative role of drug interactions in hypersomnia and psychological factors in insomnia. The panelists may have perceived that both the use of different medications to treat various medical issues and patient apprehension are unavoidable and, therefore, less amenable to intervention. However, it is

common in palliative care to use multiple medications that, singly or in combination, can alter sleep, such as sedating medications to relieve pain, reduce muscle tone, or inhibit central nervous system activity [10]. Moreover, the Panel almost unanimously agreed on the importance of considering concomitant drugs when evaluating sleep disorders. Similarly, the contribution of anxiety and depression in disturbing sleep is well-known [20,21]. Therefore, even if not consensus-wise, these factors are likely to contribute to sleep problems.

The availability of appropriate instruments to investigate sleep becomes even more important in children and adolescents with PPC needs, as many of them are unable to express themselves due to severe neurological impairment [5]. To date, only a few tools have been specifically designed and validated in this setting [8,22]. During voting, several assessment and monitoring aspects were deemed both helpful and feasible.

Exploring sleep routines and schedules when insomnia is present found a solid agreement, requiring further change in the current PPC approach. In these children, sleep problems are primarily linked to impaired sleep-regulating processes due to underlying disease, comorbidities, or external causes; however, it seems reasonable that they may also be fostered by inadequate sleep hygiene [5]. This etiology appears particularly relevant in the home setting, where the goal of healthy sleep habits should be pursued as best as possible.

The overall lack of a rationale for referring these patients for an in-lab sleep study was firmly established; this may represent an impractical option and may not align with the overall non-invasive treatment goals. Moreover, access to such expertise may not be commonly available.

The Panel was less certain that objective measures such as actigraphy, videosomnography, and polysomnography offer a significant advantage in this setting over less invasive approaches, such as surveys and sleep diaries. Even if not widely accepted, the potential of actigraphy in PPC seems unquestionable based on the literature, which suggests that it effectively provides reliable monitoring data [23,24]. Besides studying sleep in the natural, domestic setting, it complements costly and burdensome laboratory examinations [23]. Videosomnography has also shown promise in measuring multidimensional aspects of pediatric sleep [25]. Thus, these methods appear to play a role in clinics and research, but they have limitations in providing important parameters such as sleep stages or breathing problems.

Most panelists endorsed behavioral interventions as the first-line treatment, with the caveat that simultaneous pharmacologic treatment may be needed. Other approaches, such as music therapy, reiki, and hypnosis, were supported.

Medication specifications were less harmonized, with a consensus on limiting the use of benzodiazepines and sedating antihistamines, as well as on the potential side effects of opioids and corticosteroids on sleep and daily QoL as previously put in evidence [26,27]. Support for melatonin was strong, with some cautions. Manufacturing and sales are regulated differently worldwide, and over-the-counter formula contents can also differ greatly from the label [28], jeopardizing its efficacy and safety. Since many medications, mostly unregulated, are now available for international purchase online in countries where melatonin is prescription-only, this acknowledgment is of particular importance for their clinical applications, with implications beyond the PPC field.

Gabapentin emerged anew as a treatment option for sleep problems in recurrent irritability/agitation in children with disorders of the central nervous system.

Remarkably, considering caregivers' sleep quality was deemed essential throughout each section, as caring for a child with PPC needs can impact sleep and threaten QoL, daytime function, and long-term care ability. Unlike the current clinical approach, caregivers deserve to be screened for sleep disorders and the development of novel sleep-promoting interventions.

4.1. Limitations

This study has some limitations. First, the wide and diverse spectrum of conditions requiring palliative care represents a heterogeneous population in terms of age, disease progression, comorbidities, and needs, for which our recommendations may not always be suitable.

Second, the definition of 'problematic' sleep is not univocal and may depend greatly on the child, parenting style, family dynamics, and cultural beliefs, with differences in how they are valued and reported.

Third, our sample was less representative of developing countries, where clinical practice and research priorities may differ due to the diverse challenges in the healthcare systems. Even in developed countries, applying some recommendations may be limited by the divergent resources and policies (availability and accessibility to specific healthcare services, tools, and medications) and the organization of PPC services.

5. Future directions

This international consensus is intended to raise awareness of sleep health and advance sleep medicine for children and adolescents requiring palliative care and their families.

The literature review highlighted critical gaps in efforts and knowledge about sleep problems in PPC. Based on this process, specific areas can be recommended for future research consideration.

It is imperative to begin a systematic and rigorous assessment of sleep-wake disorders in this population by implementing non-invasive and reliable tools. Research should allow for defining the nature of problematic sleep in this population and identifying aspects amenable to prevention and treatment, including pharmacological and non-pharmacological interventional studies.

Knowledge about the possible sleep alterations that characterize different diseases should be deepened to enable accurate diagnosis and interpretation and to help distinguish from changes that are purely associated with corresponding sleep disorders. Given the wide heterogeneity and trajectories, an initial distinction between malignant and non-malignant conditions may be useful.

Specific sleep assessment measures are needed, favoring non-self reports and considering also the impact of sleep on different aspects of QoL. The psychometric properties of existing assessments should be examined, including whether such measures can capture the singular sleep-related changes of this setting.

Likewise, grant funding programs and clinical research are needed to increase our understanding of the mediators and moderators of sleep issues in PPC and to develop novel and effective treatment strategies. A 'one-size-fits-all' approach fails to acknowledge the reality of children with PPC needs and their parents. In particular, developing tailored and effective non-pharmacological interventions and protocols is urgent, given the pharmacological burden (and potential complications) to which these patients are already exposed, as well as strategies to create a sleep-conducive environment both at home and hospital admission.

6. Conclusion

The importance of sleep in palliative care has been underappreciated. There is a clear need for global guidance for the assessment and management of sleep concerns in children and adolescents with palliative care needs and their caregivers to reduce the associated physical and emotional burden. Based on the information gathered from this study, guidelines are currently being developed to promote sleep health and improve the quality of care in PPC. In addition to demanding a more proactive approach from sleep medicine and research in addressing the unique challenges of the PPC dimension, this effort represents a call to action for governments and institutions worldwide serving this population to incorporate sleep into their care plans.

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Ethics approval

Not required.

7. Target journal

Sleep medicine.

CRediT authorship contribution statement

Anna Mercante: Writing – review & editing, Writing – original draft, Investigation, Data curation, Conceptualization. **Judith Owens:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Oliviero Bruni:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Magda L. Nunes:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Paul Gringras:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Shirley Xin Li:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Simonetta Papa:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Ulrika Kreicbergs:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Joanne Wolfe:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Boris Zernikow:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Ana Lacerda:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Franca Benini:** Writing – review & editing, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

None.

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