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RESEARCH ARTICLE

The screening and management of sleep disturbances in people living with HIV: Delphi consensus

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Summary

Sleep disturbances in people living with HIV (PLHIV) are frequent but their management remains insufficient. In the absence of specific recommendations, a DELPHI consensus research project was conducted in France to establish best practice. A multidisciplinary Steering Committee (STC) undertook a literature review and used it with clinical expertise to create statements that were voted on. Two profiles of healthcare professionals with significant experience in monitoring PLHIV were selected for the voting: physicians and nurses/psychologists. Votes were collected electronically, independently, and anonymously. The STC created 27 statements covering six areas: Screening of sleep disturbances, Investigation, First-line management, Referral to a specialist, Antiretroviral treatment (ARV), and Prevention. Two rounds of votes included 42 physicians and 32 nurses/psychologists. Consensus was reached for 24 out of 27 statements (89%) including: to assess quantity and quality of sleep among PLHIV at least annually, ideally using a common methodology within the medical department; to consider the temporary addition of a hypnotic treatment in cases of acute insomnia not improved by the rules of sleep hygiene, with full awareness of potential drug–drug interactions and risk of dependence; to correct ferritinaemia if <100 ng/mL before referral to a specialist when restless legs syndrome is suspected; to consider changing the time of ARV administration or an ARV switch within the same class when sleep disturbances are caused by an ARV. This DELPHI Consensus provides best practice for screening and managing sleep disturbances in PLHIV and optimising their quality of life.

KEYWORDS
comorbidities, Delphi consensus, HIV, quality of life, screening and management, sleep disturbances

1 | INTRODUCTION

Sleep disturbances lead to impaired overall health and have become a major public health issue (Léger & Bourdillon, 2019). Sleep and wake disorders, as defined by the International Classification of Sleep Disorders (ICSD-3), are associated with morbidity and mortality, such as accidental risk related to sleepiness, and cardiovascular, metabolic, and psychiatric morbidity (Gutierrez et al., 2019; Micoulaud-

Franchi, 2019). Sleep disturbances (in terms of quality or quantity of sleep) can also have an impact on activities of daily living, quality of life and compliance with treatments (Parish, 2009; Phillips et al., 2005; Robbins et al., 2004). In France, it is estimated that 10 million people suffer from sleep disorders (Léger & Bourdillon, 2019) and between 30% and 50% of adults have reported a sleep complaint (Chan-Chee et al., 2011). In patients suffering from chronic pathologies, sleep disturbances are more frequent than in the general population. Sleep is of lower quality (notably less restorative) and quantity (Parish, 2009). More specifically, among people living with HIV (PLHIV), around 58% have at least one sleep disturbance (Wu et al., 2015) and 68%–74% report poor quality of sleep (PSQI>5) (Faraut et al., 2018; Gutierrez et al., 2019; Wu et al., 2015). Subsequent manifestations are diverse and include: difficulty falling asleep, less restorative sleep, complaints of sleepiness (Allavena et al., 2016; Faraut et al., 2018; Phillips et al., 2005). However, despite the high prevalence and significant morbidity of sleep disorders in PLHIV, sleep disorders, and more generally sleep disturbances, remain largely underdiagnosed and insufficiently treated in this population (Gutierrez et al., 2019).

The high prevalence of insufficiently managed sleep disturbances should therefore be taken into account in clinical practice when monitoring PLHIV (Faraut et al., 2018). With the use in recent years of effective antiretroviral treatments (ART) with improved tolerability and safety profiles, the management of PLHIV has now evolved into a comprehensive care approach (Gutierrez et al., 2019). Thus, the management of HIV-associated comorbidities, such as sleep disturbances, should represent a key element to integrate into the management of PLHIV.

PLHIV should strive for optimal and prolonged adherence to medications to achieve effective viral suppression and to prevent disease progression (Allavena et al., 2016). Yet, adherence to ART may be impacted by sleep disturbances (Babson et al., 2013; Shubber et al., 2016). Addressing sleep disturbances to improve sleep quality and quantity could have a significant impact on the health and quality of life of PLHIV.

Because sleep disturbance associated manifestations and symptoms are often under-reported (Gutierrez et al., 2019), their screening and management, including at least a reminder of the sleep hygiene rules, should be part of HIV management (Faraut et al., 2018; Gutierrez et al., 2019).

Guidelines on sleep management in the general population do exist, but they do not include the particular characteristics of PLHIV and are not specifically adapted to HIV care teams (American Academy of Sleep Medicine, 2014; Gauld et al., 2022; Gauld et al., 2023; Riemann et al., 2017). To our knowledge, there are no recommendations for sleep disturbance screening and management in this particular population. The 2020 Recommendations of the International Antiviral Society – USA Panel is focussing on mental health and neurocognitive disorders through the section "ageing and HIV" (Gandhi et al., 2023; Saag et al., 2020). The 2022 guidelines from the European AIDS Clinical Society (EACS), included elements for comorbidity screening and management, such as major depressive disorder and anxiety disorders (EACS, 2021). Yet, mental health, depression and anxiety disorders are often associated with sleep disturbances (Gutierrez et al., 2019; Micoulaud-Franchi, 2019). Moreover, although the DHHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, and the European AIDS Clinical Society (EACS) (EACS, 2021; Gandhi et al., 2023; Saag et al., 2020) present sleep disturbance frequencies related to available ART agents, they do not establish practical recommendations on their management by physicians involved in HIV care.

Consequently, it is important to focus on the role of HIV care medical teams in the identification and first-line management of sleep disturbances in order to define and share best practice. In the absence of specific recommendations, a French national modified DELPHI consensus research project was conducted to establish best practice focussing on sleep alteration management as a broad definition and not only for sleep disorders with an original approach including a wide range of recommendations.

2 | MATERIALS AND METHODS

The Delphi method is an iterative consensus approach based on information collected from a panel of voters with expertise in the subject under consideration (Boulkedid et al., 2011; Dalkey, 1972; Diamond et al., 2014; Hasson et al., 2000; Hsu & Sandford, 2007; Humphrey-Murto et al., 2017; Kodjikian et al., 2022; Loblaw et al., 2012; Richard et al., 2022). In recent years, this approach has been used widely in many therapeutic areas and several times both in HIV care and in sleep medicine (Adegbehingbe et al., 2012; Berezin et al., 2021; Cummins et al., 2019; De Silva et al., 2021; Engler et al., 2019; Feyissa et al., 2018; Fredericksen et al., 2015; Geoffroy et al., 2023; Greacen et al., 2016; Johnson et al., 2017; Johnson et al., 2019; Maserati et al., 2014; O'Connell et al., 2020; Tsui et al., 2017; Uyei et al., 2015). Using this structured approach, voting experts give their opinion in an individual and anonymous way, and express their degree of agreement on statements in order to achieve consensus on a specific and well-defined subject.

In accordance with both French and international methodologies (Boulkedid et al., 2011; Diamond et al., 2014; Hasson et al., 2000; HAS (Haute Autorité de Santé), 2010; Letrilliart et al., 2009; Loblaw et al., 2012), our study was structured as a modified national Delphi consensus and conducted among full-time or part-time French hospital physicians, nurses, and psychologists between October 2021 and February 2022. The opinion of voting experts was collected during two assessment rounds using a questionnaire developed by a Steering Committee (STC) (Figure 1).

As recommended by the French National Authority for Health (HAS), voters specified their level of agreement with the statements using a 9-point Likert scale ranging from 1 "Strongly disagree" to 9 "Strongly agree" (HAS (Haute Autorité de Santé), 2010; Letrilliart et al., 2009; McMillan et al., 2016). The percentage of scores and the median were calculated for each statement separately in each voting round.

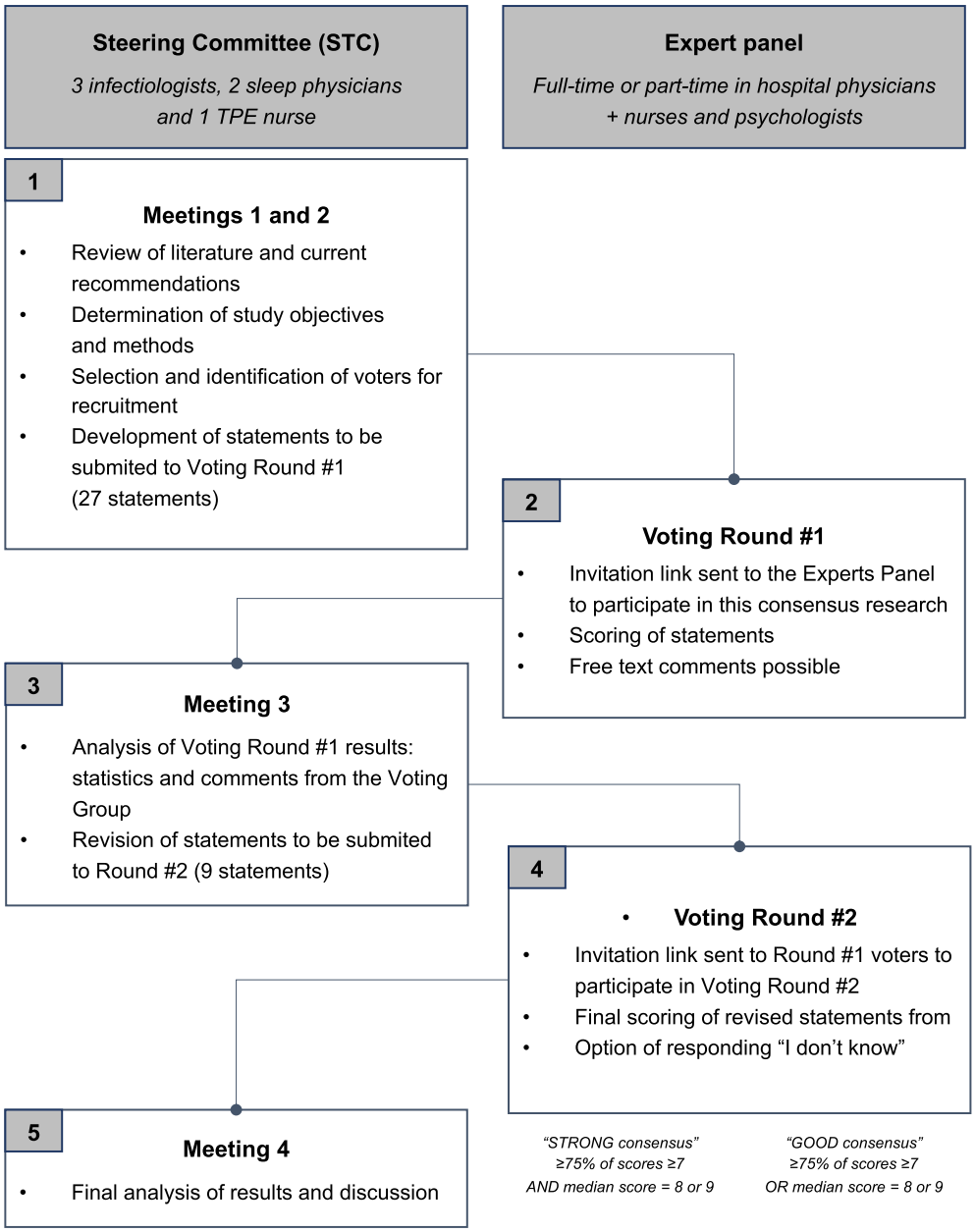

FIGURE 1 Modified Delphi process chart.

After analysing the literature, consensus for a statement was considered "strong" when >75% of the scores were ≥7 and the median score was ≥8 and considered "good" when only one of these two parameters was satisfied, or considered as "lacking" when none of the parameters was satisfied (Boulkedid et al., 2011; Koene et al., 2018; Loblaw et al., 2012).

2.1 | Steering committee (STC) and statements

The STC included six experts under the direction of the last author of this article: three infectiologists, two sleep specialist psychiatrists, and one therapeutic patient education (TPE) nurse. Two initial STC meetings were held in July and September 2021. Based on an analysis of the literature, existing recommendations, and their clinical experience, the STC developed 27 statements divided into six key areas of sleep disturbance management: Screening of sleep disturbances, Investigation, First-line management, Referral to a specialist, ARV treatment, and Prevention.

2.2 | Voting group

Two voter profiles were identified: firstly, physicians who practised full-time or part-time in hospital and secondly, nurses and psychologists. A list of voters was then compiled based on the following criteria: experience, acquired knowledge, and expertise in HIV care, presenting in national conferences or involvement in HIV care projects, with recruitment in the entire French territory and the inclusion of multiple medical specialties. The voters on this list were invited via

individual e-mails to participate in the online voting, with personalised access via a dedicated website. The anonymity of the Voting Group was guaranteed. Voters had no interaction with the STC. STC members did not take part in voting, in accordance with the current methodological recommendations (HAS (Haute Autorité de Santé), 2010).

2.3 | Voting round #1

During this first round of voting, a free text space for comments was made available enabling voters to develop or explain their opinion for each statement. At the end of the first round, scores and voter comments were summarised for each statement.

A third STC meeting took place in December 2021 to discuss the Round #1 results:

- Statements that achieved a "strong" consensus (i.e. >75% of scores ≥7 AND median ≥8) were validated in full and included in the final summary.
- Statements that achieved a "good" consensus (i.e. >75% of scores ≥7 OR median ≥8) were discussed and proposed for Voting Round #2 only when the STC was able to develop a revised version based on analysis of voter comments.
- Statements that did not achieve consensus were re-worded based on feedback from voters and submitted for Voting Round #2.

2.4 | Voting round #2

Only voters from Voting Round #1 were invited to participate in Voting Round #2 to assess the statements amended by the STC from Voting Round #1 results. The free text comment option was removed and replaced with an "I don't know" option. Choosing the "I do not know" option was then replacing the scoring response. Votes including this "I do not know" option were excluded from the analysis. Following the results of Voting Round #2, the STC closed the process.

2.5 | Ethical considerations

This research was conducted in accordance with the Declaration of Helsinki. All personal data transmitted for the study were separated from the results and anonymised, pursuant to the French data protection law (GDPR – General Data Protection Regulation).

3 | RESULTS

3.1 | Participation

Voters included 42 physicians and 32 nurses/psychologists. All voters in Round #1 actively voted in Round #2 (74/74, 100%).

TABLE 1 Characteristics of voters.

Characteristic	Physicians ($N = 42$)	Nurses/ Psychologists ($N = 32$)
Age, median [IQR], years	53 [42.5–58.75]	43.5 [36.75–51.25]
Gender F/M, *n* (%)		
Female	14 (33%)	29 (91%)
Male	28 (67%)	3 (9%)
Type of practice, *n* (%)	Full-time hospital workers: 35 (80%)	Nurses: 23 (72%)
	Part-time hospital workers: 7 (20%)	Psychologists: 4 (12%) Other: 5 (16%)
Number of PLHIV seen per year, median [IQR]	250 [120–300]	132.5 [30–300]
Years of experience in PLHIV management, median [IQR]	20 years [14.25–27.75]	7 years [4–11]
Experience in HIV care-related activities in the past 5 years, *n* (%)		
Conference abstract	35 (83%)	6 (19%)
Scientific article	30 (71%)	2 (6%)
Research project (not including this study)	41 (98%)	17 (53%)
Trainer	39 (93%)	15 (45%)
Professional or associate group or member	37 (88%)	19 (60%)
Speaker at scientific events	32 (76%)	10 (33%)

A summary of the characteristics of voters is shown in Table 1. The median experience in PLHIV management was 20 years (IQR [14.25–27.75]) for physicians and 7 years (IQR [4-11]) for nurses/psychologists. The distribution of physicians between full-time and part-time hospital work was respectively 80% ($n = 35$) and 20% ($n = 7$) and in the group of nurses/psychologists, 72% ($n = 23$) were nurses, and 12% ($n = 4$) psychologists.

In addition to their clinical practice experience, all physicians and a significant proportion of nurses/psychologists had extensive experience in HIV care-related activities over the previous 5 years, such as research projects (98% and 53%, respectively), writing scientific publications (71% and 6%), presenting at conferences (83% and 19%), training (93% and 45%), belonging to a professional or associated group (88% and 60%), and presenting at scientific events (76% and 33%).

Voters were spread across the French territory: 40% of physicians and 34% of nurses/psychologists were from the Paris region, 55% and 57% from the provinces and 5% and 9%, respectively, worked in the French Overseas Territories (Figure 2).

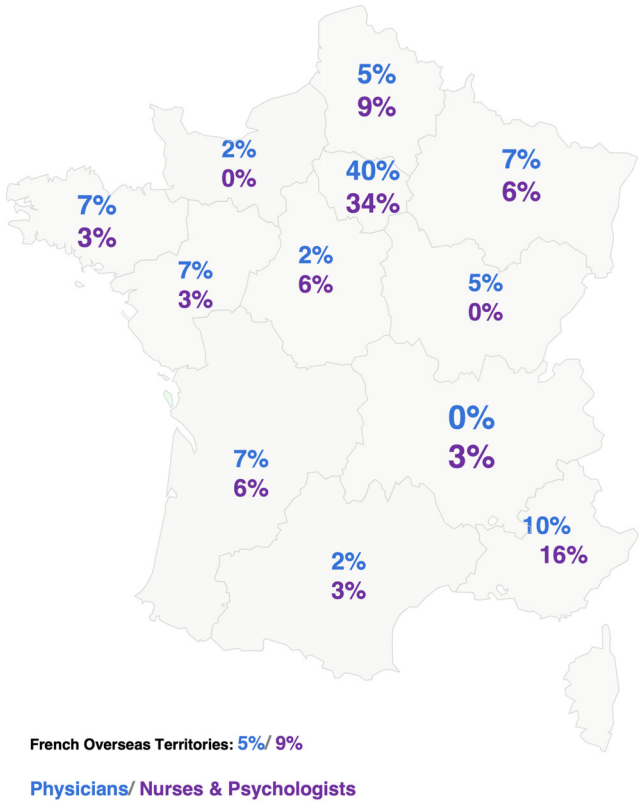

FIGURE 2 Geographic distribution of voters.

3.2 | Statements

After Voting Round #1, 16/27 statements achieved a "strong" consensus (≥75% votes ≥7 and median ≥8); 1/27 statements achieved a "good" consensus (≥75% votes ≥7 or median ≥8), and 10 statements lacked a consensus: nine were revised by the STC for Voting Round #2, and one was not revised. After Voting Round #2, 7/9 revised statements achieved a "strong" consensus, and two statements did not achieve a consensus. In total, 24/27 statements (89%) achieved consensus. The distribution of votes, medians, and results are provided in Table 2.

3.3 | Screening of sleep disturbances

Voters recognised the need to provide a warning about the high frequency of sleep disturbances among PLHIV and their impact on quality of life and health (strong consensus) (Table 2). They recommended an assessment of the quantity and quality of sleep at least once a year (strong consensus) by HIV care physicians or nurses or someone working in TPE (good consensus). It was felt that this should be achieved using a common method within the same HIV care team (scale, questionnaire), which would ideally be an approved assessment tool (strong consensus). Voters also strongly agreed on elements that should be included in this assessment (statement 4), and on the need to file this assessment of sleep quantity and quality in patient's records.

Depending on the voter profile (physicians or nurses/psychologists), three statements achieved differing consensus. Votes relating to performance of such an assessment by HIV care physicians or nurses or someone working in TPE strongly diverged: nurses/psychologists approved it with a strong consensus, while there was no consensus among physicians. Votes relating to the use of a common method within the same HIV care team and on filing the assessment in the patient's records showed a slight difference between voter profiles: good consensus for physicians and strong consensus for nurses/psychologists.

3.4 | Investigation

With strong consensus, voters approved that causal elements be sought in the event of sleep disturbances (quantity or quality) (Table 2). According to them, four types of causal elements should be investigated (statements 8 to 11) relating to: the patient's environment and lifestyle (impacting sleep behaviour), an obstructive sleep apnea–hypopnea syndrome (OSAS), patient health or ARV treatment.

3.5 | First-line care

Concerning first-line care by HIV care teams, if sleep disturbances are linked to the patient's environment and lifestyle, voters approved with strong consensus a reminder of the rules of sleep hygiene for PLHIV in order to modify these sleep behaviours (statement 12) (Table 2).

In the event of acute insomnia not improved by the application of sleep hygiene rules, voters agreed on the temporary addition of a hypnotic, taking into account the ARV treatment (risk of drug–drug interactions (DDIs) with pharmacokinetic potentiators (boosters) and risk of dependence (strong consensus). However, the stimulus control rule used in cognitive behavioural therapy for insomnia (CBTi): "stay in bed for a limited time and, if not sleeping, get out of bed after 20–30 minutes" did not achieve consensus. Among physicians, these rules achieved a good consensus, excluding 8/42 (19%) who answered "I don't know"; among nurses/psychologists, there was no consensus, excluding 5/32 (16%) who answered "I do not know".

Where restless legs syndrome is suspected, performing a ferritinaemia and correcting it if it was <100 ng/mL was recommended before referral to a sleep specialist (strong consensus).

If OSAS is strongly suspected or associated with excessive daytime sleepiness or a high cardiovascular risk, voters considered that the physician should recommend an objective assessment of sleep by polysomnography or respiratory polygraphy and should ensure that it is performed (strong consensus).

However, in patients with anxiety and/or major depressive disorder, the statement proposing that HIV care physicians initiate a specific treatment and reserve referral to the specialist only if there are signs of severity or gravity did not achieve consensus.

TABLE 2 Statements and voting results

	Statements	Validity 1-2-3 (n)	Validity 4-5-6 (n)	Validity 7-8-9 (n)	Median	Results
Screening of disturbances						
1	All clinicians should be alerted to the significant frequency of sleep disturbances in PLHIV and their impact on quality of life and health	0% (0)	9.5% (7)	90.5% (67)	8	**Strong consensus**
2	As part of the monitoring process, each PLHIV must have an assessment of the quantity and quality of their sleep at least once a year	0% (0)	9.9% (7)	90.1% (64)	8	**Strong consensus**
3	The evaluation of sleep quantity and quality is to be carried out by the physician responsible for HIV care, or a nurse or someone working in TPE	7.7% (4)	26.1% (21)	66.2% (49)	8	Good consensus
4	The evaluation of sleep quantity and quality must examine the following elements: • *Sleep satisfaction/Feeling on waking up* • *Bedtimes and wake-up times* • *Duration and regularity of sleep* • *Environmental conditions* • *Ease of falling asleep* • *Difficulty staying asleep/nocturnal awakenings* • *Waking up before the desired time in the morning* • *Nightmares, restlessness* • *Snoring* • *Daytime sleepiness, nap* • *Daytime effects: fatigue, difficulty concentrating, irritability* • *Taking a hypnotic treatment* • *Length of time the disorder has existed*	1.4% (1)	14.8% (11)	83.8% (62)	8	**Strong consensus**
5	Within the same HIV care team, a common method should be used to assess sleep quantity and quality in PLHIV	4.1% (3)	17.5% (13)	78.4% (58)	8	**Strong consensus**
6	Investigation of sleep quantity and quality by HIV teams should ideally be performed using an approved assessment tool (scale, questionnaire)	2.7% (2)	16.2% (12)	81.1% (60)	8	**Strong consensus**
7	The evaluation of sleep quantity and quality should be filed in the patient's record	4.1% (3)	16.2% (12)	79.7% (59)	8	**Strong consensus**
Investigation						
8	Should one or more sleep disturbances be present (quantity or quality), the causal elements related to the patient's environment and lifestyle should be investigated: • *Environmental setting unsuitable for sleep (noise, light*, etc.*)* • *Napping too long* • *Evening physical activities* • *Substances: caffeine, alcohol*, etc. *at the end of the day* • *Excessive stress, overwork* • *Increasing time spent in bed without sleep*	1.4% (1)	8.1% (6)	90.5% (67)	8	**Strong consensus**

TABLE 2 (Continued)

	Statements	Validity 1-2-3 (n)	Validity 4-5-6 (n)	Validity 7-8-9 (n)	Median	Results
9	Should one or more sleep disturbances be present (quantity or quality), the causal elements related to an obstructive sleep apnea-hypopnea syndrome (OSAS) should be investigated: • *Snoring, feeling of nocturnal suffocation, breathing pauses noted by family members/partners*	1.4% (1)	10.8% (8)	87.8% (65)	8	**Strong consensus**
10	Should one or more sleep disturbances be present (quantity or quality), the causal elements related to the patient's health should be investigated: • *Depressive symptoms* • *Anxiety symptoms* • *Restless legs syndrome: the urge to move the legs ("restlessness") often in the evening, increasing with inactivity, forcing legs to move, relieved by movement* • *Digestive disorders: GERD, abdominal cramps, diarrhoea*, etc. • *Obesity* • *Other somatic disorders: heart disease, pain*, etc.	0% (0)	5.4% (4)	94.6% (70)	9	**Strong consensus**
11	Should one or more sleep disturbances be present (quantity or quality), the causal elements related to ARV treatment should be investigated: • *Complaints of insomnia, unusual dreams, nightmares or sleep disturbances occurring concomitantly with the introduction of a new treatment*	0% (0)	0% (0)	100% (74)	9	**Strong consensus**
First-line care						
12	Should the sleep disturbances be related to the patient's environment and lifestyle, the PLHIV should be reminded of the following sleep hygiene rules: • *Maintain regular wake-up times and bedtimes, even on weekends* • *Establish a bedtime ritual* • *Exposure to daylight, especially in the morning, to help regulate the biological clock* • *Limit naps and their duration* • *Practise regular physical activity and stop it preferably 3 to 4 h before bedtime* • *Prioritise quiet activity in the evening* • *Avoid stimulants (coffee, tea, alcohol, tobacco) after noon* • *Switch off screens at least 1 hour before bedtime and leave them off until the next morning* • *Arrange the bedroom so that it is conducive to sleep: noise, light, temperature between 18° and 20°. Place the alarm clock/clock well out of sight.* • *Keep the bedroom for sleep: avoid television, work and meals in bed*	0% (0)	13.5% (10)	86.5% (66)	8.5	**Strong consensus**

(Continues)

TABLE 2 (Continued)

	Statements	Validity 1-2-3 (n)	Validity 4-5-6 (n)	Validity 7-8-9 (n)	Median	Results
13	In the case of insomnia, the following two rules should be reinforced: stay in bed for a limited time and, if you are not sleeping, get out of bed after 20–30 min	3.3% (2)	29.5% (18)	67.2% (41)	7	No consensus
14	In the case of acute insomnia, if not improved by applying the sleep hygiene rules, the temporary addition of a hypnotic drug can be considered	5% (2)	15% (6)	80% (32)	8	**Strong consensus**
15	The prescription of hypnotic drugs in PLHIV must take into account the ARV treatment (risk of drug–drug interactions (DDIs) with boosted ARVs) and the risk of dependence	4.8% (2)	2.3% (1)	92.9% (39)	9	**Strong consensus**
16	In the event of an anxiety and/or depressive disorder, HIV care physicians should initiate a specific treatment (anxiolytic, anti-depressant, other); referral to a specialist is only required should there be signs of severity or gravity (persistence of symptoms under treatment, risk of suicide, etc.)	38.1% (16)	40.5% (17)	21.4% (9)	4.5	No consensus
17	Should restless legs syndrome be suspected, HIV care physicians should measure ferritinaemia levels and correct it if necessary (< 100 ng/mL) before considering referral of the PLHIV to a sleep specialist	2.7% (1)	13.5% (5)	83.8% (31)	8	**Strong consensus**
18	Should there be a strong suspicion of OSAS or suspicion associated with excessive daytime sleepiness or a high cardiovascular risk, HIV care physicians should strongly recommend an objective sleep assessment to the patient and ensure that it is performed: polysomnography or respiratory polygraphy (which will be carried out by a sleep specialist or a pulmonologist)	0% (0)	11.9% (5)	88.1% (37)	9	**Strong consensus**
Referral to a specialist						
19	Specialist advice should be considered in the following situations: • *Sleep specialist: Insomnia that is severe or resistant to sleep hygiene measures and/or treatments* • *Sleep specialist: Severe restless legs syndrome or syndrome with high ferritin levels* • *Sleep specialist or pulmonologist: Strong suspicion of OSAS or suspicion associated with excessive daytime sleepiness or high CV risk* • *Psychiatrist: Anxiety and/or depressive disorders that are moderate to severe or resistant to treatment or have a risk of suicide*	0% (0)	4.8% (2)	95.2% (40)	8	**Strong consensus**
Antiretrovirals (ARV) and sleep						

TABLE 2 (Continued)

	Statements	Validity 1-2-3 (n)	Validity 4-5-6 (n)	Validity 7-8-9 (n)	Median	Results
20	When faced with sleep-related complaints, before considering an ARV switch, it is advisable to carry out an in-depth assessment with the PLHIV as to the quantity and quality of sleep	0% (0)	14.3% (6)	85.7% (36)	9	**Strong consensus**
21	When faced with sleep disturbances, any possible cause other than the ARV treatment should be investigated and managed before switching the ARV treatment	7.1% (3)	16.7% (7)	76.2% (32)	8	**Strong consensus**
22	Before considering a change in ARV treatment for sleep-related adverse effects, a change in the timing of ARV treatment intake may be considered	0% (0)	14.3% (6)	85.7% (36)	8	**Strong consensus**
23	Sleep disturbances are more common with the following classes of ARVs: non-nucleoside inhibitors and integrase inhibitors (NNRTIs and InSTIs)	3.3% (2)	15% (9)	81.7% (49)	8	**Strong consensus**
24	Sleep disturbances at the initiation of ARV treatment therapy may lessen or disappear after a few weeks. A reminder of the rules of sleep hygiene may be useful during this period	1.4% (1)	8.2% (6)	90.4% (66)	8	**Strong consensus**
25	Within the same therapeutic class, some ARVs being more frequently associated with sleep disturbances than others, it is possible switch to an ARV in the same therapeutic class	0% (0)	14.3% (6)	85.7% (36)	8	**Strong consensus**
26	Should there be a sleep disturbance or disturbances, a special note should be made of ARV treatment compliance	6.7% (5)	17.6% (13)	75.7% (56)	8	**Strong consensus**
Prevention						
27	Even if there is no sleep disturbance, as part of overall care, all PLHIV should be reminded once a year of the rules of sleep hygiene	11% (8)	32.8% (24)	56.2% (41)	7	No consensus

Note: For each statement, a total number of voters equaling 42 indicates that only physicians were invited to vote and a total number of voters different from 42 or 74 indicates the use of the "I don't know" option by voters.

3.6 | Referral to a specialist

Voters considered, with a strong consensus, that referral to a specialist be recommended in the following situations: to a sleep specialist in the event of insomnia that is severe or resistant to sleep hygiene measures and/or treatments, and in the case of severe restless legs syndrome or syndrome with high ferritin levels; to a sleep specialist or pulmonologist where there is strong suspicion of OSAS or suspicion of OSAS associated with excessive daytime sleepiness or high CV risk; to a psychiatrist in patients presenting with anxiety and/or major depressive disorders that are moderate to severe or resistant to treatment or with a risk of suicide (Table 2).

3.7 | Antiretrovirals (ARV) and sleep

When faced with sleep complaints or disturbances, before considering an ARV switch, voters recommended, with strong consensus, an in-depth assessment of sleep quantity and quality, to look for any possible cause other than the ARV treatment and to manage it before switching ARV (Table 2).

Voters acknowledged that sleep disturbances are more common with the following classes of ARVs: non-nucleoside reverse transcriptase inhibitors (NNRTIs) and integrase inhibitors (InSTIs).

At initiation of ARV therapy, sleep disturbances may lessen or disappear after a few weeks; the patient should be reminded of sleep hygiene rules during this period (strong consensus).

Should an adverse effect on sleep be attributed to an ARV, voters agreed that a change in administration time could first be considered (strong consensus). Moreover, voters agreed that, within the same therapeutic class some ARVs being more frequently associated with sleep disturbances than others, it is possible to switch to an ARV in the same therapeutic class (strong consensus).

Finally, in the event of sleep disturbances, particular vigilance in ARV treatment compliance is recommended (strong consensus). According to the voter profile, this recommendation achieved a strong consensus among physicians and a good consensus among nurses/psychologists.

3.8 | Prevention

Voters disagreed on the statement that, as part of overall patient care, all PLHIV should be reminded once a year of the rules of sleep hygiene, even if there is no sleep disturbance (Table 2).

4 | DISCUSSION

Our study is the first consensus research using the DELPHI method aimed at establishing recommendations for best practice in the management of sleep disturbances in PLHIV.

4.1 | Screening, investigation, and prevention

The consensus achieved from statements on the screening and investigation of sleep disturbances, the majority from Voting Round #1, appear consistent with the observation made by the STC on the current clinical management of PLHIV. This consensus reflects awareness and concern that already exists among experts in HIV care on the emerging realisation of the impact of sleep disturbances among PLHIV. Indeed, the high prevalence of sleep disturbances is explained by potentially deprived socio-demographic conditions, frequent anxiety-depressive disorders, lifestyles favouring aspects such as drug substance use like chemsex, as well as iatrogenic causes. While some first-generation non-nucleoside reverse transcriptase inhibitors (NNRTIs) have frequent adverse effects on sleep, they are less used today in favour of integrase strand transfer inhibitors (InSTIs), particularly second-generation ones which are now very widely prescribed and may also be responsible for sleep disturbances, albeit at lower frequencies. Furthermore, the strong consensus on the use of an approved assessment tool demonstrates that sleep disturbances are indeed of concern in HIV care teams; it also testifies to the need for information dissemination on the screening and management of these disturbances.

However, the non-achievement of consensus on the recommendation to remind all PLHIV of the rules of sleep hygiene once a year as a preventive measure as part of overall care, even if there are no sleep disturbances, shows the need to continue to focus on this issue, even if the median of voter scores was 7, with a trend in favour of this preventive action.

Knowledge of sleep hygiene rules is important for overall health and is part of primary prevention on health behaviours (diet, physical activity, sleep) (Buysse, 2014; HAS (Haute Autorité de Santé), 2006; Leah et al., 2015). Populations at risk of sleep disturbances, such as PLHIV, should therefore be reminded of these rules. Health education measures have notably demonstrated benefits in terms of improving sleep behaviours and sleep health (Buysse, 2014; Leah et al., 2015; Murawski et al., 2018).

4.2 | Care and referral to a specialist

4.2.1 | Insomnia

Insomnia is a comorbidity that should be managed. According to the International Classification of Sleep Disorders (ISCD3), insomnia disorder is defined by a disturbance of nocturnal sleep, at least three nights a week for a period of 3 months and an associated diurnal change (Riemann et al., 2017). The non-achievement of consensus on reminding patients with an insomnia disorder of the rules (stay in bed for a limited time and get out of bed) in our study shows the voters' lack of appreciation of these rules, despite them having been approved by several teams (Edinger et al., 2021; HAS (Haute Autorité de Santé), 2006; Maurer et al., 2021; Riemann et al., 2017). This may be because HIV care physicians, nurses, and psychologists are not aware

of these recommendations and so do not adopt them. Training on insomnia disorder management practices and awareness-raising measures should be encouraged.

4.2.2 | Depressive and anxiety disorders

The non-achievement of consensus among voters about the possible management of anxiety or depressive disorders by infectious disease specialists likely reveals a lack of knowledge or lack of training on first-line management of these disorders. Also, a lack of knowledge of signs that would require referral to a psychiatrist, and the possible feeling that it is not their expertise. Furthermore, the lack of time and the difficulties in accessing psychiatric care and sleep centres should also be taken into account. Reflection on the optimisation and coordination of patient pathways, with involvement of the attending physician, could also be considered in this context.

4.2.3 | Obstructive sleep apnea syndrome (**OSAS**)

In the context of suspicion of OSAS, there was a strong consensus on the role of the HIV care physician recommending objective assessment of sleep by polysomnography or respiratory polygraphy and referring to a specialist if needed. This shows the well-known importance of OSAS management in the HIV population, who are frequently at high cardiovascular risk.

4.2.4 | Restless legs syndrome

There was strong consensus for performing a ferritinaemia level and correcting it if <100 ng/mL before considering referral to a sleep specialist. Nevertheless, five voters answered "I don't know" during Voting Round #2: this indicates a need to disseminate this information more widely to HIV care physicians.

4.3 | **Antiretrovirals** (ARV) **and sleep**

There was strong consensus on ensuring that sleep disturbances are not simply attributed to ARV treatment. Knowledge of ARV classes most frequently associated with sleep disturbances – as well as options to be considered depending on the clinical situation with regard to ARV treatment associated with sleep disturbances – were approved, including changing the time at which an ARV treatment is administered, the impact of which has been documented by Capetti et al. (Capetti et al., 2018); also, the possibility of switching to an ARV in the same therapeutic class since some ARVs are more associated with sleep disturbances than others within the same class. A summary description of the adverse effects of ARVs in each class, including mention of sleep disorders, is available, in particular, in the EACS recommendations, which are updated in each new version (Gauld et al., 2023).

4.4 | Adaptation of future recommendations

The population of PLHIV is more exposed than the general population to the risk of sleep disturbances and is likely frequently of multifactorial origin (Wu et al., 2015). Reference to this risk should be specifically developed in recommendations for the management of PLHIV, with particular attention to individuals who may present an increased risk, for example through the use of psychoactive substances (Ogunbajo et al., 2020).

Sleep hygiene rules are relevant to all PLHIV in most clinical situations, including management during pregnancy, ageing, substance abuse.

Finally, recommendations for the therapeutic management of insomnia, and depressive or anxiety disorders should be adapted in individuals with an increased risk of dependence on hypnotic drugs, in particular psychoactive drug users.

4.5 | Limitations

Although the Delphi method is known and followed as a structured procedure, this approach has some limitations associated with voter profiles, statement development, and criteria considered to achieve the consensus (Skinner et al., 2015). Our research sought to limit these potential biases as much as possible in order to guarantee maximum objectivity.

Although the voters were only recruited in France, they were selected on objective criteria based on their experience and expertise in HIV care. These criteria made it possible to obtain a sample with reassuring characteristics: a median of 20 years of experience in HIV in the physicians group and 7 years in the nurses/psychologists group, with 98% and 53%, respectively, with recent active participation in a research project in HIV. The absence of any remuneration or attrition between Voting Rounds #1 and #2 also testifies to their commitment.

Concerning the statements, a preliminary analysis of literature enabled the identification of the main questions raised in clinical practice and offered precise wording. As for the threshold used to achieve the consensus, our study was based on a rigorous approach with two criteria. This strict and demanding definition gives our results high credibility. Finally, our research took place with a continuous and complete separation between voters who voted completely anonymously, and members of the STC, who neither participated in voting nor interacted directly with voters. The constraint inherent in this separation was the absence of direct exchange between voters or members of the STC and voters: such exchanges could have been useful when revising statements being addressed in Voting Round #2.

This research is in addition to a more general approach to improving overall care of PLHIV. Additionally, as with all Delphi consensuses, this aims only to provide a daily guide to practitioners, who remain in control of their practice and adapt it to patients, according to individual circumstances.

5 | CONCLUSIONS

During this consensus research using the Delphi method, 24/27 (89%) statements achieved a consensus from 74 voters with a strong clinical experience of HIV management in France. This result constitutes a solid basis for implementation of more uniform practices in sleep disturbance management in PLHIV, whose overall care is a major issue as sleep disturbance prevalence is higher than in the general population (Wu et al., 2015). Among PLHIV – a potentially vulnerable population – the promotion of sleep hygiene and behaviour rules seems essential. Similarly, training HIV care teams and disseminating recommendations for insomnia disorder management appear necessary (Baglioni et al., 2020). Finally, there should be promotion of care networks between centres, with coordination channels involving multidisciplinary care between HIV caregivers, sleep specialists, respiratory physicians, and psychiatrists.

In the absence of established recommendations on sleep disturbance management in PLHIV, this expert consensus enables formalisation of best practice for physicians and HIV care teams. Ultimately, it is hoped that this consensus research will drive improved screening and investigation of sleep disturbances, improved management of their consequences for the daily lives of PLHIV and thus contribute to optimising the quality of life for PLHIV.

AUTHOR CONTRIBUTIONS

Clotilde ALLAVENA: Conceptualization; methodology; validation; formal analysis; writing – original draft; writing – review and editing. **Frédéric BASTIDES:** Conceptualization; methodology; validation; formal analysis; writing – review and editing. **Anne MOROY:** Conceptualization; methodology; validation; formal analysis; writing – review and editing. **Stéphanie OCCHIPINTI:** Conceptualization; methodology; validation; formal analysis; writing – review and editing. **François DURAND:** Conceptualization; validation; funding acquisition; resources. **Guillaume BARRIERE:** Conceptualization; validation; funding acquisition; project administration; resources. **Jean-Arthur MICOULAUD-FRANCHI:** Conceptualization; methodology; validation; formal analysis; writing – original draft; writing – review and editing. **Jade GHOSN:** Conceptualization; methodology; validation; formal analysis; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The agregated data report that support the findings of this study is available on request to Gilead authors. The raw data are not publicly available due to third party restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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