

Treatment of Cluster Headache in Pregnancy and Lactation

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Abstract Cluster headache (CH) is a neurovascular headache syndrome characterized by headache attacks that occur with a circadian and circannual periodicity. The calculated prevalence of CH in reproductive-aged women is 7.5 of 100,000 women. Although data suggest that CH during pregnancy is a relatively rare condition, when it does occur, attacks remain unchanged in character and severity in the majority of patients. Thus, treatment of CH in pregnant and lactating women may remain a significant therapeutic challenge. This manuscript briefly reviews the epidemiology of CH in women, and then focuses on treatment options for both acute and preventative management of CH in pregnant and lactating women.

Keywords Cluster headache · Cluster headache treatment · Pregnancy · Lactation

Introduction

Cluster headache (CH) is a neurovascular headache syndrome characterized by headache attacks that occur with a circadian and circannual periodicity. Typical attacks

are unilateral in location, of extreme intensity but short duration, and associated with autonomic dysfunction [1].

There is a relative paucity of information pertaining to CH in pregnancy and lactation, largely not without cause. CH is a relatively rare, primary headache disorder that affects an estimated 0.06% of the population, with an overall male:female ratio of approximately 2.5:1 [1, 2]. However, during reproductive years, the male preponderance is roughly 7:1 [2]. Thus, in reproductive-aged women, this results in a calculated prevalence of CH of only 7.5 of 100,000 women. To further reduce the population of interest, there are reports of relative hypofertility in women with CH [3, 4]. Specifically, when onset of attacks preceded a first pregnancy, women had significantly ($P < 0.01$) fewer children than those who were parous before their first attack [5].

Nevertheless, the strong male preponderance in CH has seen progressive decreases over recent decades, and varies in relationship to age of onset. The decline in the male:female ratio has been attributed to an increase in the number of female sufferers, an increase that has paralleled declines in the male:female ratios in smoking and in employment outside the home [6].

In addition, there is also variability in the gender ratio of CH based on the age of onset. When the onset of CH is between the ages of 30–49 years (when women are typically premenopausal), the gender ratio for episodic CH is 7.2:1 and an impressive 11:1 for chronic CH. After the age of 50 years, this gender disparity shrinks to only 2.3:1 for episodic CH cases and disappears altogether (0.6:1) for chronic CH [2].

Although the relative rarity of these headaches in premenopausal-aged women is suggestive of a possible protective effect of estrogen, the course of CH does not appear to be modified by the hormonal fluctuation of the menstrual

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cycle [3]. However, it is important to remember that even the lowest estrogen concentrations encountered in a normal menstrual cycle are many times higher than those found in postmenopausal women, when estrogen concentrations are typically lower than those of even age-matched males.

Data are conflicting as to whether CH improves in pregnancy or remains unchanged, with most studies limited by small numbers and retrospective design. To illustrate the issue, one review examined 249 patients with CH [4]. Only 34 patients were female, of whom only eight had experienced pregnancy since the onset of CH; six of those eight reported remission of cluster in the (very) high estrogen environment of pregnancy. In another study of 143 women with CH, 111 had been pregnant; only 19 of these patients reported CH attacks during a pregnancy, with the majority reporting no increase in severity or frequency of those attacks compared with attacks outside of pregnancy [5]. Another study found that only 5% of women with CH experienced attacks during pregnancy [1]. However, it is of note that pregnancy was associated with a change in the women's seasonal pattern of attacks, such that expected seasonal clusters did not occur when pregnant. Taken together, all of these studies suggest that CH during pregnancy is a relatively rare condition, but when it does occur, attacks remain unchanged in character and severity.

Nonpharmacologic Approaches

Nonpharmacologic approaches should always be considered first-line therapy, a practice that is particularly important in pregnancy and lactation. Specifically, pregnant women should be strongly encouraged to stop both smoking and excessive alcohol ingestion for a multitude of medical reasons, including potential injury to the fetus, but also because CH has been shown to have a close association with both smoking and alcohol ingestion [7].

Another nonpharmacological consideration for management of CH during pregnancy and lactation is screening for sleep apnea. Sleep apnea prevalence has been reported as high as 80% in patients with episodic CH attacks [7, 8]. Reports have also suggested that obstructive sleep apnea (OSA) may be more common in pregnancy, particularly in the third trimester; it also may be associated with preeclampsia and harm to the fetus [8]. A reasonable approach would be to ask all cluster patients to complete a screener for OSA, such as the Berlin Questionnaire or the Pittsburgh Sleep Quality Index (See Appendix 1, 2 and 3), with referral for formal evaluation and treatment by a sleep specialist for those who screen positively or whose attacks worsen, especially in pregnancy [9]. Nasal continuous positive airway pressure or an appropriate dental device may then be appropriate considerations in those who do have OSA.

Treatment in Pregnancy

Many effective treatments exist for both abortive and preventive care of patients with CH. But when the patient is pregnant or lactating, collaboration among the headache specialist, obstetrician, and pediatrician is encouraged to ensure safety of both the mother and her developing baby.

Ideally, drugs would not be taken in pregnancy; however, circumstances often favor their judicious use. To illustrate current usage of drugs in pregnancy, a survey of 1,000 pregnant women in southwest France showed that 99% of the women received a prescription for at least one drug during pregnancy, with a mean of 13.6 medications per woman [10]. Drugs in Category X (fetal risk outweighs benefit) were prescribed to 1.6% of the women; 59% had a prescription from Category D (fetal risk exists, but benefits may be acceptable); and 79% were exposed to drugs for which information about safety in pregnancy was not available from animal or human studies.

The US Food and Drug Administration drug categories in pregnancy are reviewed in Table 1. Category A is almost nonexistent and includes products such as prenatal vitamins and thyroid hormone in physiologic replacement doses. In Categories B and C, harm has not been shown in humans, whereas in Categories D and X, harm has been shown in humans. In many cases, the difference between Categories B and C may hinge on how high the dose was pushed in laboratory animals.

Beyond these rating categories, treatment decisions may be guided by physiologic studies of drug transport, adverse events reporting, and experience collected from prospective pregnancy registries. In the absence of prospective drug treatment trials in pregnancy—which are rarely if ever conducted—product inserts generally do not recommend use in pregnancy. However, counterbalancing issues of relative safety, it is important to remember that the pain of CH is excruciating, even to the point of suicide, in patients with intractable or untreated CH [11].

As with pharmacologic treatment of any medical disorder in pregnancy, a detailed discussion of the risks and benefits of treatment of CH in pregnancy is essential. In general, the number of different medications as well as their dosage and frequency should be kept to a minimum.

The European Federation of Neurological Societies (EFNS) published evidence-based consensus recommendations for the treatment of CH in the general (nonpregnant) population [12]. The drugs of first choice were oxygen (100%, with a flow at least 7 L/min over 15 min) and sumatriptan (6 mg subcutaneous). Both of these may also be options in pregnancy for the treatment of CH.

Inhalation of pure oxygen via a non-rebreathing mask is the preferred first-line treatment due to the lack of obvious contraindications to either mother or fetus [13, 14]. Delivery of 100% oxygen during CH attacks results in cerebral

Table 1 FDA medication categories in pregnancy

Category	Interpretation
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities to the fetus in any trimester of pregnancy.
B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women. OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester.
C	Animal studies have shown an adverse effect, and there are no adequate and well-controlled studies in pregnant women. OR No animal studies have been conducted, and there are no adequate and well-controlled studies in pregnant women.
D	Adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective.
X	Adequate well-controlled or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities or risks. The use of the product is contraindicated in women who are or may become pregnant.

FDA US Food and Drug Administration

vasoconstriction and stimulates synthesis of serotonin in the central nervous system. A clinical trial of oxygen therapy in CH found complete resolution of pain within 20 min in six of the seven oxygen-treated subjects, whereas none of the six control subjects achieved pain resolution. It has also been suggested that higher flow oxygen rates up to 15 L per minute may be of benefit when lower rates have been unsuccessful [15].

If oxygen treatment is insufficient, injectable or intranasal sumatriptan may be considered. Sumatriptan has been widely used over the past decade and a half in CH. Among several mechanisms of actions, triptans have been shown to bind to serotonin (5-HT)_{1B/1D} receptors and inhibit the release of neuropeptides and inflammatory substrates at the trigeminal vascular junction. In addition, triptans act on central 5-HT_{1D} receptors to limit activation of the trigeminal nucleus caudalis and thus may aid in the prevention of central sensitization.

Like all triptans, sumatriptan is classified as Category C; however, its safety profile has been documented in pregnancy to a greater extent than other triptans, including exposure in first trimester [16, 17]. Its relative hydrophilicity makes it more difficult for sumatriptan (compared with more lipophilic triptans) to traverse the placental membrane. In physiologic testing, only about 15% of a dose crossed into the fetal compartment over 4 h. With an average elimination half-life of 2 h, it is evident that only very small amounts will cross from mother to fetus after a single dose of sumatriptan [18]. Due to significantly lower maternal serum concentration, the nasal spray formulation would be a logical first choice route of administration, with advancement to injection if needed for control of attacks.

Other acute options include intranasal installation of lidocaine (pregnancy Category B), which induces anesthesia

in the region of the pterygopalatine fossa and results in rapid relief with a low side-effect profile [12]. Intranasal dihydroergotamine, although effective in the general population of CH sufferers, would very rarely, if ever, be advocated in pregnancy, as it is Category X. Further, symptomatic treatment with metoclopramide (Category B) or prochlorperazine (Category C) could be employed when necessary.

Thus, in the pregnant patient, oxygen is the most appropriate first-line therapy for acute CH attacks, with the nasal spray formulation of sumatriptan (Category B) or nasal lidocaine (Category B) as appropriate second-line therapies when required (Table 2).

Both transitional and traditional preventative options may be required for the treatment of CH in pregnant women. Transitional preventives are those given to break cluster cycles. In this capacity, greater occipital nerve (GON) blockade has demonstrated efficacy in acute CH, and in some cases, will break a cluster cycle. In a small open-label study, 13 of 22 CH patients treated with GON blockade experienced complete or partial response, with partial responses lasting an average of 21 days [19]. Treatment was well tolerated with no adverse events. Although GON blockade has not been specifically tested in pregnancy, it is usually performed with lidocaine and betamethasone, drugs that are rated Categories B and C, respectively (Table 2).

The consensus choice of the EFNS for prevention of CH in the general (nonpregnant) population was verapamil (Category C) at a daily dose of at least 240 mg. In addition to verapamil, steroids are also generally accepted as effective in CH, despite the lack of evidence from class I or class II trials. The recommended dosage of methylprednisone (Category C) is an oral dose of at least 100 mg daily, or an intravenous dosage of up to 500 mg daily over 5 days before tapering.

Table 2 Pharmacologic recommendations for treatment of cluster headache in pregnant or lactating women

	FDA pregnancy category	AAP lactation category	Authors' recommendation	Note
Acute abortive therapy				
Oxygen	N/A	N/A	First line for both pregnancy and lactation	–
Sumatriptan (intranasal)	C	6: usually compatible	Second line for both pregnancy and lactation	If oxygen is not a choice or ineffective, sumatriptan would be an appropriate first-line consideration for both pregnancy and lactation.
Lidocaine (intranasal)	B	6: usually compatible	Second line for both pregnancy and lactation	If oxygen is not a choice or ineffective, lidocaine would be an appropriate first-line consideration for both pregnancy and lactation.
Metoclopramide	B	4: may be of concern	Third line during pregnancy and lactation	Metoclopramide has not been proven effective for CH and thus is listed as third line despite its relative safety in pregnancy; safety is of greater concern in lactation.
Bridge therapy				
GON blockade (using lidocaine and betamethasone)	B/C	6: usually compatible	First line for both pregnancy and lactation	Lidocaine is Category B, and betamethasone is Category C in pregnancy.
Steroids	C	6: usually compatible	Second line for both pregnancy and lactation	–
Preventive therapy				
Verapamil	C	6: usually compatible	First line for both pregnancy and lactation	–
Steroids	C	6: usually compatible	First line for both pregnancy and lactation	–
Topiramate	C	Has not been reviewed by the AAP	Second line for pregnancy; inadequate information to make recommendation for lactation	Studies, limited by open-label design or small numbers, suggest topiramate may be an effective preventive in CH; definitive trials are needed.
Lithium	D	5: caution	Third line for both pregnancy and lactation; should be used only when benefit clearly exceeds risk	–

AAP American Academy of Pediatrics, CH cluster headache, FDA US Food and Drug Administration, GON greater occipital nerve

Topiramate may be an acceptable alternative to verapamil for CH prevention in pregnancy. Although not well established (primarily due to small sample sizes and design limitations), several studies have suggested that topiramate may be an effective CH preventive therapy, with headache remission in 50% to 70% of those with episodic or chronic CH. As it is pregnancy Category C, topiramate may be of consideration in pregnant CH sufferers when prevention is required (Table 2) [20•].

Although methysergide (which is no longer available in the United States and is Category D) and lithium (also Category D) are recommended as alternative treatments in the general population, they are not generally used in pregnancy unless the benefit to the mother “clearly exceeds the risk to the fetus,” as harm has been shown in human pregnancies. Finally, surgical procedures for CH exist, and

although promising, require further scientific scrutiny before formal recommendations can be made.

Thus, in the pregnant patient, verapamil (pregnancy Category C) and steroids (Category C) remain the preferred options when preventive treatment is required (Table 2).

Treatment in Lactation

Virtually all drugs taken by the mother will be present to some extent in breast milk. Membrane transport is achieved primarily by passive diffusion, with the classic factors of concentration gradient, lipophilicity, protein binding, and degree of ionization determining transport kinetics [21••].

The extent of drug transfer into breast milk is most commonly described quantitatively using the milk:plasma

Table 3 The American Academy of Pediatrics Committee tables on drugs compatible with breastfeeding^a

1. Cytotoxic drugs that may interfere with cellular metabolism of the nursing infant
2. Drugs of abuse for which adverse effects on the infant during breastfeeding have been demonstrated
3. Radioactive compounds that require temporary cessation of breastfeeding
4. Drugs for which the effect on nursing infants is unknown, but may be of concern
5. Drugs that have been associated with significant effects on some nursing infants and should be given to nursing mothers with caution
6. Maternal medication usually compatible with breastfeeding
7. Food and environmental agents

^a The American Academy of Pediatrics lists these seven points or categories as “tables” of drugs

concentration ratio. The infant dose can thus be calculated and expressed as a percentage of the maternal dose. For most drugs, an arbitrary cutoff of 10% has been accepted as a guide to the safe use of drugs in lactation; however, for drugs with greater inherent toxicity, such as cytotoxic agents, that cutoff would not apply. Rather, breastfeeding would be contraindicated in their presence. Premature infants have a severely limited ability to clear drugs, but, in general, if the infant dose—as a percentage of the maternal dose (corrected for weight)—is close to 1%, the drug can be considered safe regardless of infant age [21••].

The route of administration is also a factor. Topical creams, nasal sprays, or inhalers usually convey less exposure to the breastfed infant than oral drugs due to lower maternal concentrations. Drugs that are poorly absorbed or have high maternal first-pass metabolism are also less likely to be a concern in lactation, along with very hydrophilic drugs that have difficulty crossing physiologic membranes into breast milk. Timing breastfeeding to occur immediately prior to a maternal drug dose may also help to minimize infant exposure, as drug concentrations in milk tend to be lowest at the end of the dosing interval.

The American Academy of Pediatrics (AAP) Committee on Drugs divides medication usage in lactation into seven “tables” (To limit confusion we describe what the AAP terms as “tables” as “categories” of medications in lactation in Table 3.) [22].

The AAP lists sumatriptan as compatible with breastfeeding [22]. Other triptans, many of which are lipophilic, have not yet been reviewed or received this categorization. Also, among compatible medications are lidocaine, prednisone, prednisolone, and verapamil.

Additional points of note include the following: 1) Although the AAP has not issued a position statement for the use of dihydroergotamine in lactation, it considers the use of the related compound ergotamine to be cause for “caution.” Ergotamine exposure has resulted in convulsions in the nursing infant. 2) Although metoclopramide is considered relatively safe in pregnancy (Category B) it is of more concern in lactation, where it is concentrated in breast milk relative to the maternal serum concentration, and according to the AAP,

“may be of concern.” Prochlorperazine, as all phenothiazines, are similarly categorized as “may be of concern” (Table 3). 3) Finally, particular caution should be exercised with lithium, as it crosses readily into breast milk at levels considerably higher than the referenced 10% cutoff figure—in some cases up to 50% of the maternal dose [22]. The long-term outcome is unknown, and prescription of lithium to lactating women is controversial [23]. Although there is no absolute contraindication, it is known that the kidney is particularly sensitive to lithium just after birth, and cases of renal toxicity have been reported.

Thus, the preferred agents for acute treatment of CH during lactation would include oxygen, sumatriptan, and lidocaine; for prevention, prednisone/prednisolone and verapamil would be appropriate first options when required (Table 2) [24].

Conclusions

Cluster headache (CH) is a relatively uncommon neurovascular headache syndrome characterized by headache attacks that occur with a regular periodicity. Although CH during pregnancy is a relatively rare condition, the data suggest that when it does occur, attacks remain unchanged in character and severity in the majority of patients. Thus, treatment of CH in pregnant and lactating women may present a significant therapeutic challenge. Nevertheless, when non-pharmacological agents are not sufficient, it is reassuring that many of our standard first-line therapies for treatment of CH remain viable options in the pregnant and lactating woman who suffers from these debilitating attacks.

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Appendix 1 Berlin questionnaire

Subject's Initials _____ ID# _____ Date _____ Time _____ AM
 _____ PM

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?
 BED TIME _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
 NUMBER OF MINUTES _____
3. During the past month, what time have you usually gotten up in the morning?
 GETTING UP TIME _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)
 HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .
 - a) Cannot get to sleep within 30 minutes

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - b) Wake up in the middle of the night or early morning

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - c) Have to get up to use the bathroom

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - d) Cannot breathe comfortably

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - e) Cough or snore loudly

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - f) Feel too cold

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - g) Feel too hot

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - h) Had bad dreams

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------
 - i) Have pain

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____
------------------------------------	--------------------------------	-------------------------------	-------------------------------------

j) Other reason(s), please describe _____

How often during the past month have you had trouble sleeping because of this?

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

6. During the past month, how would you rate your sleep quality overall?

Very good _____

Fairly good _____

Fairly bad _____

Very bad _____

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all _____

Only a very slight problem _____

Somewhat of a problem _____

A very big problem _____

10. Do you have a bed partner or room mate?

No bed partner or room mate _____

Partner/room mate in other room _____

Partner in same room, but not same bed _____

Partner in same bed _____

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

b) Long pauses between breaths while asleep

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

c) Legs twitching or jerking while you sleep

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

d) Episodes of disorientation or confusion during sleep

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

e) Other restlessness while you sleep; please describe _____

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

Appendix 2 Pittsburgh sleep quality index

Pittsburgh Sleep Quality Index (PSQI)

References and Scoring

Reference

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28:193-213, 1989.

Notes on data entry

The range of values for questions 5 through 10 are all 0 to 3.

Questions 1 through 9 are not allowed to be missing except as noted below. If these questions are missing then any scores calculated using missing questions are also missing. Thus it is important to make sure that all questions 1 through 9 have been answered.

In the event that a range is given for an answer (for example, '30 to 60' is written as the answer to Q2, minutes to fall asleep), split the difference and enter 45.

Scores – reportable in publications

On May 20, 2005, on the instruction of Dr. Daniel J. Buysse, the scoring of the PSQI was changed to set the score for Q5J to 0 if either the comment or the value was missing. This may reduce the DURAT score by 1 point and the PSQI Total Score by 1 point.

PSQIDURAT	DURATION OF SLEEP IF Q4 \geq 7, THEN set value to 0 IF Q4 < 7 and \geq 6, THEN set value to 1 IF Q4 < 6 and \geq 5, THEN set value to 2 IF Q4 < 5, THEN set value to 3 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQIDISTB	SLEEP DISTURBANCE IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) = 0, THEN set value to 0 IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) \geq 1 and \leq 9, THEN set value to 1 IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 9 and \leq 18, THEN set value to 2 IF Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 18, THEN set value to 3 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQILATEN	SLEEP LATENCY First, recode Q2 into Q2new thusly: IF Q2 \geq 0 and \leq 15, THEN set value of Q2new to 0 IF Q2 > 15 and \leq 30, THEN set value of Q2new to 1 IF Q2 > 30 and \leq 60, THEN set value of Q2new to 2 IF Q2 > 60, THEN set value of Q2new to 3 Next IF Q5a + Q2new = 0, THEN set value to 0 IF Q5a + Q2new \geq 1 and \leq 2, THEN set value to 1 IF Q5a + Q2new \geq 3 and \leq 4, THEN set value to 2 IF Q5a + Q2new \geq 5 and \leq 6, THEN set value to 3 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQIDAYDYS	DAY DYSFUNCTION DUE TO SLEEPINESS IF Q8 + Q9 = 0, THEN set value to 0 IF Q8 + Q9 \geq 1 and \leq 2, THEN set value to 1 IF Q8 + Q9 \geq 3 and \leq 4, THEN set value to 2 IF Q8 + Q9 \geq 5 and \leq 6, THEN set value to 3 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQIHSE	SLEEP EFFICIENCY Diffsec = Difference in seconds between day and time of day Q1 and day Q3 Diffhour = Absolute value of diffsec / 3600 newtib = IF diffhour > 24, then newtib = diffhour - 24 IF diffhour \leq 24, THEN newtib = diffhour (NOTE, THE ABOVE JUST CALCULATES THE HOURS BETWEEN GNT (Q1) AND GMT (Q3)) tmphse = (Q4 / newtib) * 100 IF tmphse \geq 85, THEN set value to 0 IF tmphse < 85 and \geq 75, THEN set value to 1 IF tmphse < 75 and \geq 65, THEN set value to 2 IF tmphse < 65, THEN set value to 3 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQISLPQUAL	OVERALL SLEEP QUALITY Q6 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQIMEDS	NEED MEDS TO SLEEP Q7 Minimum Score = 0 (better); Maximum Score = 3 (worse)
PSQI	TOTAL DURAT + DISTB + LATEN + DAYDYS + HSE + SLPQUAL + MEDS Minimum Score = 0 (better); Maximum Score = 21 (worse)

Appendix 3 Pittsburgh sleep quality index references and scoring

Berlin questionnaire

SLEEP EVALUATION

1 Complete the following:

height _____ age _____
weight _____ male, female _____

2 Do you snore?

- yes
 no
 don't know

If you snore:

3 Your snoring is?

- slightly louder than breathing as loud as talking
 louder than talking
 very loud. Can be heard in adjacent rooms.

4 How often do you snore?

- nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

5 Has your snoring ever bothered other people?

- yes
 no

6 Has anyone noticed that you quit breathing during your sleep?

- nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

Scoring Questions: Any answer with a box outline is a positive response.

Scoring Categories: Category 1 is positive with 2 or more positive responses to questions 2-6.

Category 2 is positive with 2 or more positive responses to questions 7-9.

Category 3 is positive with 1 or more positive responses and/or a BMI > 30.

Final Results: 2 or more positive categories indicates a high likelihood of sleep disordered breathing.

EDWARD GILLY

Name _____

Address _____

CATEGORY 2

7 How often do you feel tired or fatigued after your sleep?

- nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

9 During your wake time, do you feel tired, fatigued or not wake up to par?

- nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

8 Have you ever nodded off or fallen asleep while driving a vehicle?

- yes
 no

If yes, how often does it occur?

- nearly every day
 3-4 times a week
 1-2 times a week
 1-2 times a month
 never or nearly never

CATEGORY 3

10 Do you have high blood pressure?

- yes
 no
 don't know

BMI = _____

EDWARD

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

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