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# Polysomnographic features of pregnancy: A systematic review

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## SUMMARY

Symptoms of sleep disturbances are common among pregnant women and generally worsen across gestation. Pregnancy-related sleep disorders are not only associated with a poor quality of life of the affected mothers, but also with adverse perinatal outcomes, including perinatal depression, gestational diabetes, preeclampsia, and preterm birth. The current knowledge about the impact of sleep disorders during pregnancy largely derives from the results of sleep surveys conducted in various populations. However, the number of studies examining changes in objective sleep variables during pregnancy via polysomnography has progressively increased in recent years.

Here we systematically reviewed the polysomnographic studies available in the literature with the aim to describe the sleep pattern and to identify possible markers of sleep disruption in pregnant women.

Based on our analysis, subjective worsening of sleep quality across gestation is related to objective changes in sleep macrostructure, which become particularly evident in the third trimester. Pregnancy per se does not represent an independent risk factor for developing major polysomnography-assessed sleep disorders in otherwise healthy women. However, in women presenting predisposing factors, such as obesity or hypertension, physiological changes occurring during pregnancy may contribute to the onset of pathological conditions, especially sleep-disordered breathing, which must be carefully considered. © 2019 Elsevier Ltd. All rights reserved.

Introduction

Pregnancy is a physiological condition of relatively short duration in a woman's life, but characterized by profound biological changes, which have a significant influence on sleep [1].

The typically increased secretion of several hormones across pregnancy considerably impacts on both the circadian and homeostatic components of sleep regulation, leading to modifications of sleep architecture [2]. In human studies, non-rapid eye movement sleep (NREM) has been shown to be enhanced by progesterone and prolactin [3,4], while rapid eye movement sleep (REM) is decreased by progesterone and increased by estrogens [5,6]. Oxytocin peaks during the night, promoting uterine contractions leading to sleep fragmentation [2]. Cortisol and growth hormone levels are also elevated, affecting sleep quality and inducing daytime sleepiness [2].

Besides hormones, other factors contribute to sleep disruption during pregnancy: gastroesophageal reflux, affecting up to 75% of pregnant women [7]; nocturnal micturition, due to an increase in overnight sodium excretion [8]; anatomical changes related to the growing uterus and increased body weight [9]. Moreover, iron and folate deficiency may play a role in the occurrence of sleep-related movement disorders in pregnant women [10,11].

Subjectively reported sleep disturbances are very common during pregnancy, with increasing rates from the first (13%), to the second (19%), and third (66%) trimester of gestation [12,13]. A recent meta-analysis showed that 46% of women experience poor sleep quality during pregnancy, with an average score of the Pittsburgh Sleep Quality Index (PSQI) of 6.4 (95% CI, 5.3–6.85) and with a worsening trend from the 2nd to the 3rd trimester by an average of 1.68 points (95% CI, 0.42–2.94) [14]. While at early gestational age women mainly attribute sleep problems to nausea/

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Abbrevia	tions	PaO <sub>2</sub> pf	Partial pressure of oxygen Preeclampsia
AHI	Apnea-hypopnea index	PLMS	Periodic leg movements during sleep
BMI	Body mass index	PLMSI	Periodic leg movements during sleep index
CHTN	Chronic hypertension	PSG	Polysomnography
CPAP	Continuous positive airway pressure	PSQI	Pittsburgh sleep quality index
EEG	Electroencephalography	RDI	Respiratory disturbance index
EMG	Electromyogram	REM	Rapid eye movement sleep
EOG	Electrooculogram	RLS	Restless legs syndrome
ESS	Epworth sleepiness scale	SaO <sub>2</sub>	Oxygen saturation
GA	Gestational age	SDB	Sleep-disordered breathing
GCT	Glucose challenge test	SE	Sleep efficiency
GDM	Gestational diabetes mellitus	SOL	Sleep onset latency
GHTN	Gestational hypertension	SWS	Slow wave sleep
HDP	Hypertensive disease of pregnancy	TCO <sub>2</sub>	Transcutaneous CO <sub>2</sub>
NREM	Non-rapid eye movement sleep	TIB	Time spent in bed
ODI	Oxygen desaturation index	TST	Total sleep time
OGTT	Oral glucose tolerance test	WASO	Wake after sleep onset
OSA	Obstructive sleep apnea		-

vomiting, urinary frequency, and backpain [15], in late gestation up to 69.9% of women report difficulty in maintaining sleep, 34.8% early morning awakenings, and 23.7% difficulty falling asleep [16], mainly due to fetal movements, heartburn, cramps or tingling in the legs, and shortness of breath [13,17–19]. By the end of pregnancy almost all women suffer from recurrent and long wake episodes during the night [17,20].

Self-reported sleep duration also declines across pregnancy [21]. Moreover, objectively assessed sleep duration and quality are related to age and ethnicity, with non-Hispanic black and Asian women having the shortest sleep duration, and younger pregnant women having the highest amount of wake after sleep onset (WASO), the lowest sleep efficiency (SE), and the latest sleep midpoint [22].

To date, the available literature on sleep during pregnancy is mostly based on subjective information from screening questionnaires or interviews [14,19]. However, in recent years, an increasing number of studies investigated sleep in pregnant women objectively, by using polysomnography (PSG) or actigraphy. Sleep parameters derived from actigraphy may significantly differ from those obtained by PSG recordings and should therefore be interpreted with caution [23]. Thus, PSG remains the gold standard for sleep depiction, being the only reliable tool to precisely describe sleep macro- and microstructure, correctly estimate respiratory and motor events, and permit an accurate identification of pregnancy-related sleep disorders.

We here present the first systematic review of polysomnographic studies conducted in pregnant women, with the aim to provide a detailed overview about the intrinsic, objective features of sleep in normal, healthy pregnancy, as well as in some typical pregnancy-related complications.

## Methods

We performed a systematic review of the literature by searching for studies reporting objective sleep parameters obtained by PSG in pregnant women until February 1, 2019. The review process followed the PRISMA statement guidelines [24]. The completed PRISMA checklist can be found in the Supplementary material section (Table S1).

## Search strategy

The terms 'pregnancy' OR 'gestation' AND 'polysomnography' OR 'PSG' were searched in the databases Medline, Scopus and

Embase. The search terms had to be included in the Title, Abstract or Keyword section of the articles. The first author reviewed the automatically generated list of items and classified every manuscript, based on its abstract, as "eligible", "not eligible" and "maybe eligible", according to the selection criteria described below. Articles considered "not eligible" were excluded from a further analysis. Afterward, the first and second authors independently examined the "eligible" and "maybe eligible" full-text articles in a blinded fashion, to determine whether they met the criteria to be included in the review. The inter-rater agreement calculated as Cohen's kappa coefficient ( $\kappa$ ) was 0.92. In case of disagreement, they consulted the senior author (MM) for a final decision.

## Selection criteria

The following criteria were applied:

- Sleep assessment: only studies reporting PSG data recorded during pregnancy and using a minimal montage of at least one EEG channel either in mono- or bipolar, electrooculogram (EOG), chin electromyogram (EMG) were included. Studies based on other objective sleep assessment methods than PSG (e.g., actigraphy or polygraphy) or using subjective tools (e.g., questionnaires) were excluded;
- 2) Number of nights recorded: at least one full night PSG recording
- 3) Sample size: only studies with a sample size of >10 women
- 4) Language: English;
- Type of study: original studies on human subjects; no single case reports, reviews, commentaries/letters, editorial, conference abstracts;
- 6) Control group: studies including either a control group (healthy pregnant or non-pregnant women) or without a control group were included.

Additionally, the authors went through the reference lists of the selected articles to identify further studies. Unpublished manuscripts were not included.

## Quality assessment

The quality assessment of the studies included in the systematic review was performed using the Newcastle-Ottawa scale (NOS) adapted for cross-sectional studies (according to Herzog et al. [25]), cohort studies, and case—control studies (available at http://www. ohri.ca/programs/clinical\_epidemiology/oxford.asp). The NOS consists of several items included in three domains (selection of the study groups, comparability of the groups, and outcome/exposure assessment). Each item is evaluated based on a 'star system'. Trials included in our review were evaluated using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials [26] and the Cochrane Collaboration's risk of bias in non-randomized studies (ROBINS-I) [27]. The results of the quality assessment of all included studies are summarized in Table S2 (supplementary material).

## Statistical analysis

Mean and standard deviation of longitudinal studies reporting total sleep time (TST) and SE were pooled in order to evaluate changes in these sleep variables from the first to the third trimester of gestation. Weighted mean difference (WMD) with 95% confidence interval (95% CI) was used to estimate absolute differences of continuous outcomes. I<sup>2</sup>-statistics was adopted to measure the percentage of variance attributable to study heterogeneity

 $(I^2>50\%)$ . The Egger's weighted regression test was used to detect publication bias. Statistical analysis was performed using StatsDirect software version 3.0 (Cambridge, UK).

## Results

## Literature search

A detailed flowchart of the results of the literature search process is presented in Fig. 1. Finally, 40 studies were considered for the qualitative analysis (systematic review). Twenty-four of them were cross-sectional studies (n = 24), ten prospective cohort studies (n = 10), five clinical trials (n = 5), and one case–control study (n = 1). Out of 40 studies, n = 27 included a control group, while n = 13 were not controlled. Regarding the country of origin, most studies were performed in the USA (n = 20), followed by Australia (n = 9) and Canada (n = 4). Sample sizes examined ranged between 10 and 234 women. A detailed overview of the main study characteristics is provided in Tables S3 and S4 (supplementary material). Main findings of the reviewed studies are highlighted in Table 1.



Fig. 1. Flowchart of study selection according to systematic review process.

## Table 1

Changes in sleep variables in pregnancy and pregnancy-related complications.

Authors	Year	Type of patients evaluated	GA (in weeks)	Chang	e in slee	p variabl	es in cas	es in respe	ect to conti	rols/contr	ol conditio	ons	
				TST	SE	AI	SL	REM	SWS	RDI	AHI	ODI	OSA%
Healthy pregnancy													
Izci-Balserak et al. [34]	2018	Healthy pregnant women in the first (controls)	12.05 ± 1.80 (controls)	$\downarrow$	Ļ	$\leftrightarrow$	$\leftrightarrow$	$\downarrow$	$\downarrow$		<b>↑</b>		<b>↑</b>
		compared to the third trimester (cases).	33.61 ± 2.56 (cases)										
El-Helbawy et al. [39]	2017	Healthy pregnant women (cases) and healthy	23.03 ± 8.88 (cases)								1	1	
D: 117 - 1 [00]	2017	non-pregnant women (controls).	22 4										
Rimpila et al. [29]	2017	Healthy pregnant women (cases) and healthy	$33 \pm 1$	Ļ	Ļ		$\leftrightarrow$	Ļ	Ļ		$\leftrightarrow$	$\leftrightarrow$	
Wilcon et al [20]	2011	Don-pregnant women in the first and third trimester	Controls and first trimoster $(0, 14)$ vs			*							*
	2011	of pregnancy (cases) and healthy non-pregnant	third trimester $(30-38)$		$\leftrightarrow$	I	$\rightarrow$	$\leftrightarrow$	$\leftrightarrow$				I
		controls (controls)	Controls vs third trimester $(30-38)$		1		$\leftrightarrow$	1	1				↑
Trakada et al. [43]	2003	Healthy pregnant women pre- (cases) and	36 (cases)	$\leftrightarrow$	* ↔	$\leftrightarrow$		* ↔	* ↔				I
		postpartum (controls).	4–6 mo PP (controls)										
Lee et al. [32]	2000	Healthy women pre-, during and after	Pre-pregnancy (controls)	<b>↑</b>	↓		$\leftrightarrow$	$\leftrightarrow$	Ļ				
		pregnancy.	11-12 (cases)										
			35-36 (cases)	<b>↑</b>	<b>↑</b>		$\leftrightarrow$	$\leftrightarrow$	$\downarrow$				
			3–4 wk PP (controls)										
Hertz et al. [28]	1992	Healthy pregnant women (cases) and non-	30–38	$\leftrightarrow$	Ļ		$\leftrightarrow$	$\downarrow$	$\leftrightarrow$				
		pregnant healthy women (controls).											
Hypertensive disorders	of preg	nancy											
Suri et al. [59]	2018	Pregnant women with PE and/or GH (cases) and	$34.9 \pm 1.7$ (cases)			1					1		↑
		healthy pregnant women (controls).	$35.7 \pm 2.0$ (controls)										
Wilson et al. [56]	2018	Pregnant women with GH/PE (cases) and	$33.5 \pm 3.4$ (cases)	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	Ļ	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	↑
		healthy pregnant women (BMI and GA match, controls)	$33.1 \pm 2.4$ (controls)										
Reid et al. [55]	2016	Pregnant women with GH (cases) and healthy	$34.2 \pm 3.3$ (cases)	Ţ	$\leftrightarrow$	$\leftrightarrow$		Ţ		<b>↑</b>	$\leftrightarrow$		
		pregnant women (controls).	$34.5 \pm 3.2$ (controls)	•				·					
O'Brien et al. [52]	2014	Pregnant women with CHTN, GHT and PE	24.6 ± 8.1 (cases, cHT)	$\leftrightarrow$							$\leftrightarrow$		↑
		(cases) and healthy pregnant women (controls).	$33.0 \pm 2.9$ (cases, GHT)										
			$30.1 \pm 4.2$ (cases, PE)										
			$33.8 \pm 3.8$ (controls)										
Blyton et al. [69]	2013	Pregnant women with PE (cases) and healthy	$33.3 \pm 3.5$ (cases)	$\leftrightarrow$		$\leftrightarrow$		$\leftrightarrow$	Î		Î	$\leftrightarrow$	
Poid at al [52]	2011	pregnant women (controls).	$33.9 \pm 2.0$ (controls)							*	*		•
Reid et al. [53]	2011	program women (age and CA match, controls)	$34.7 \pm 3.2$ (cases) $24.7 \pm 3.6$ (controls)	Ļ	Ļ	$\leftrightarrow$		Ļ	$\leftrightarrow$	Т	T	$\leftrightarrow$	T
Blyton et al. [68]	2004	Pregnant women with PF (cases) 50% with	$33 \pm 4$ (cases)	⇔						$\leftrightarrow$			
biyton et al. [00]	2004	CPAP and healthy pregnant women (controls)	$34 \pm 2$ (controls)					÷					
Edwards et al. [54]	2001	Pregnant women with OSAS and PE (cases) and	34 + 1 (cases)	$\leftrightarrow$		$\leftrightarrow$		$\leftrightarrow$		$\leftrightarrow$			
		normotensive pregnant women with OSA	$32 \pm 2$ (controls)										
		(controls).											
Edwards et al. [57]	2000	Pregnant women with PE (cases) and	$33 \pm 1$ (cases)	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\downarrow$	<b>↑</b>	$\leftrightarrow$			
		normotensive healthy pregnant women	$34 \pm 1$ (controls)										
		(controls).											
Gestational diabetes me	ellitus												
Bisson et al. [61]	2014	Pregnant women with newly diagnosed GDM	$31.6 \pm 1.4$ (cases)	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$		$\leftrightarrow$	$\leftrightarrow$	$\leftrightarrow$
		and BMI $\leq$ 35 (cases) and healthy pregnant	32.3 ± 1.0 (controls)										
		women matched for GA, BMI and age (controls).											
Izci Balserak et al. [62]	2013	Healthy pregnant women stratified for the	$12 \pm 2.1$	$\leftrightarrow$		$\leftrightarrow$					$\leftrightarrow$		
		presence (cases) and absence (controls) of GDM,	3ra trimester	$\leftrightarrow$		$\leftrightarrow$					$\leftrightarrow$		
		rog in first triffester and tillru triffester.											

Reutrakul et al. [60]	2013	Pregnant women with GDM (cases), healthy	$33.3 \pm 3.5 (cases)$	$\rightarrow$	Ţ	•	\$	¢		\$	¢	
		pregnant women (controls). Healthy pregnant women (cases) and healthy non-pregnant women (controls).	33.9 ± 2.0 (controls) 33.9 ± 2.0 (cases)	\$	Ļ		$\rightarrow$	\$		Ļ	\$	
Clinically suspected OSA	S or ris	k factors for OSAS										
Bourjeily et al. [40]	2014	Pregnant women with suspected OSAS (cases) and healthy non-pregnant women matched for	26.6 ± 7.6 (cases)	$\rightarrow$	↓ ¢	\$	\$	$\rightarrow$	\$	\$		
		age, bivit and AHI (controls).										
Edwards et al. [44]	2005	Pregnant women with suspected OSAS (cases)	33 ± 2 (cases)	\$	←	¢	$\rightarrow$	←		←		
		and postpartum (controls).	$4 \pm 2$ mo PP (controls)									
Maasilta et al. [42]	2001	Obese pregnant women (cases) and normal-	≥12	\$	← ¢	\$	\$	\$	←	Ļ	÷	
		weight healthy pregnant women (controls).	≥30	\$	← ¢	\$	\$	\$	←	←	←	
Guilleminault et al. [38]	2000	Pregnant women with chronic snoring and/or	24	\$				¢		\$		
		SaO2 drop $\geq$ 5% in a screening examination (cases), and healthy pregnant women matched for age and BMI (controls).										
Restless legs syndrome												
Dzaja et al. [45]	2009	Pregnant women with RLS (cases) and healthy pregnant women (controls).	$35.9 \pm 1.9$ (cases and controls)	\$		\$	\$	¢				
AHI – apnea/hypopnea indu	ex, AI – â	arousal index, BMI – body mass index, CHTN – chro	onic hypertension, CPAP – continuous po	ositive airwa	y pressure	, GA – gesta	ttional age,	GHTN – ges	stational h	ypertensic	n, GDM –	gestational

diabetes mellitus, ODI – oxygen desaturation index, OSA – obstructive sleep apnea, PE – pre-eclampsia, RDI – respiratory disturbance index, REM – rapid-eye-movement sleep, RLS – restless legs syndrome, TST – total sleep time, SE – sleep efficiency, SL – sleep latency, SWS – slow-wave sleep, PP-post partum, mo- months, wk- weeks.

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## Polysomnographic findings

## Sleep structure

Subjective perception of poor sleep quality reported by women across gestation is related to objective changes in sleep structure. We found three cross-sectional studies investigating the differences in sleep parameters of pregnant women vs. non-pregnant controls.

Hertz et al. reported a significantly decrease in SE, due to a substantial increase in WASO and number of awakenings in 12 women during late pregnancy compared to 10 age-matched nonpregnant controls [28]. NREM sleep stage S1 was also increased in the pregnant group with, in turn, a decrease of both REM sleep and SWS. Rimpilä et al. obtained similar results studying 18 healthy pregnant in the third trimester, compared to 12 non-pregnant controls [29].

In a larger PSG investigation (27 women in the first trimester of gestation, 21 in the third trimester, and in 24 healthy non-pregnant controls), Wilson et al. [30] confirmed women during the third trimester having poorer SE, more awakenings, less stage 4 sleep, more stage 1 sleep and fewer minutes spent in REM sleep compared to control group. Interestingly, higher progesterone levels within third-trimester women were associated with an increase in WASO and arousals.

Three studies assessed changes in sleep parameters in the same individuals across the perinatal period in a longitudinal setting. Coble et al. [31] performed PSG at three time points during pregnancy and two during the postpartum, comparing pregnant women with (n = 13, in remission) vs. without (n = 20) a history of affective disorders. They found that women with a previous depression have a longer TIB and TST in early pregnancy, an earlier onset and more pronounced sleep disruption, as well as a reduced REM-latency in late pregnancy, compared to control women.

Lee et al. [32] examined women during the follicular phase (n = 33), the first (n = 33) and third trimester of pregnancy (n = 29), as well as postpartum (n = 29). Changes were already evident in the first trimester, with an increase of TST, decrease of SE and a marked reduction of SWS during pregnancy, compared to pre-pregnancy baseline. No variation in REM sleep was noted. These changes remained relatively stable in the course of pregnancy and improved after delivery.

In a secondary analysis of their 2013 dataset [33], Izci-Balserak et al. [34] evaluated changes in sleep architecture and spectral EEG bands during pregnancy in 123 women who underwent PSG in early pregnancy and in 97 of them also in late pregnancy. They found a shorter sleep duration, poorer SE, more awakenings, more stage N2 sleep, less SWS and REM sleep in late compared to early pregnancy, thus partially replicating the results from one of the first longitudinal studies on PSG-assessed sleep across pregnancy [35].

In summary, changes in sleep structure during pregnancy seem to mainly affect the third trimester of gestation, which is generally characterized by a shorter sleep duration and a more disrupted sleep, with an increased number of awakenings and superficial sleep stages, as well as a reduction of SWS and REM sleep. These findings are more evident when comparing pregnant women with non-pregnant controls, but they have also been recently confirmed in the same individuals recorded at early and late GA [34].

## Breathing pattern

Sleep-disordered breathing (SDB), is estimated to affect 10-32% of pregnant women, depending on its definition [36]. Obstructive sleep apnea (OSA), in particular, is estimated to be a frequent condition during pregnancy, with a pooled worldwide prevalence of 15% (95% CI 12-18%), and it has been associated with gestational hypertension, gestational diabetes, pre-eclampsia, C-section, postoperative wound complication, and pulmonary edema [37]. Moreover, OSA is related to an increased risk for preterm birth (aOR = 1.62) and neonatal intensive care unit admission (aOR = 1.28) [37]. Based on these findings, the analysis of respiratory parameters in pregnant women has become the main target of sleep research studies.

Guilleminaut et al. [38] screened 267 healthy pregnant women with a normal BMI ( $23.7 \pm 0.8 \text{ kg/m}^2$  at study entry) regarding the presence of daytime sleepiness and snoring. A selected subgroup based on stratified questionnaire results (n = 26) underwent overnight PSG. None of the subjects showed an apnea-hypopnea index (AHI) > 5/h but chronic snorers presented breathing abnormalities such as esophageal pressure crescendos in S1 and S2 and abnormal sustained effort during SWS, which were associated with higher systolic and diastolic blood pressure increases, as well as a non-dipper profile in the 24-hour blood pressure (24 h-BP) recordings (six out of 13 snorers).

Small cross-sectional studies in pregnant women compared to non-pregnant controls also reported slightly decreased mean and minimum oxygen saturation (SaO<sub>2</sub>) values but no differences in AHI and/or oxigen desaturation index (ODI) or transcutaneous carbon dioxide (TcCO<sub>2</sub>) levels [28,29].

However, El-Helbawy et al. [39], examining 30 primiparous pregnant women vs. 30 age-matched non-pregnant controls found a higher mean AHI ( $4.38/h \pm 4.45$  vs.  $1.77/h \pm 1.2$ ), ODI ( $3.72/h \pm 4.03$  vs.  $2.27/h \pm 1.11$ ), and snoring index ( $8.19/h \pm 6.87$  vs.  $1.08/h \pm 1.75$ ) in the pregnant group. Among pregnant women, 36.7% had a mild OSA and 53.3% were snorers. Patients with OSA had a significantly higher GA, BMI, a larger neck circumference, a higher ODI, flow limitation index, snoring index, and Epworth sleepiness scale (ESS) score compared to healthy subjects. GA and BMI, in particular, emerged as independent risk factors for OSA during pregnancy, with odds ratio of 2.23 and 4.99 respectively.

Izci-Balserak et al. [34], by applying a longitudinal design, found a statistically significant increase in AHI (2.09/h  $\pm$  3.17 vs. 3.41/h  $\pm$  4.60, p < 0.002) and OSA cases [AHI>5 events/h; n = 14 (11.38%) vs. n = 26 (26.80%), p < 0.004] during late compared to early pregnancy.

An elevated BMI has been often associated with a higher risk for developing SDB during gestation. To assess pregnancy as an independent risk factor for SDB, Bourjeily et al. performed a third trimester PSG in obese pregnant women (BMI 44.1  $\pm$  6.9) compared to BMI- and age-matched non-pregnant controls [40,41]. AHI and oxygen desaturation showed no differences between groups, with 8/25 within the case group qualifying as OSA (AHI $\geq$ 5/h). However, pregnant women had significantly more flow limitations during TST and in each sleep stage compared to controls.

Maasilta et al. [42], compared obese with normal weight women, during early and late pregnancy. They found no difference in sleep structure, but an increase in AHI (1.7/h vs. 0.2/h; p < 0.05), RDI (7.4/h vs. 0.8/h; p < 0.001), ODI (5.3/h vs. 0.3/h p < 0.005) and snoring time (32% vs. 1%, p < 0.001), as well as a worsening in sleep-related breathing parameters in the obese group.

Pien et al. [33] studied 105 women (mean BMI  $33.4 \pm 6.4$ ) during the first and third trimester of pregnancy. The mean AHI increased across gestation from 2.07 events/h to 3.74 events/h. BMI and maternal age at the beginning of pregnancy positively correlated with the occurrence of OSA in late pregnancy. Moreover, in a secondary analysis of the same cohort [34], including 123 women recorded in early and 97 also in late pregnancy, the authors reported a higher AHI (3.41/h  $\pm$  4.6 vs. 2.09/h  $\pm$  3.17) and a higher periodic leg movements during sleep index (PLMSI) index (5.62/ h  $\pm$  12.65 vs. 2.47/h  $\pm$  6.23) in late compared to early pregnancy. Also in this cohort, the increase in AHI was conceivably related to the increase in BMI, with values of  $30.56 \pm 7.22 \text{ kg/m}^2$  in early vs.  $33.3 \pm 6.25 \text{ kg/m}^2$  in late pregnancy (p < 0.001).

Trakada et al. [43] studied 11 healthy pregnant women at 36 wk of gestation and again at 4-6 mo postpartum with measurement of Partial pressure of oxygen (PaO<sub>2</sub>) every two hours. The AHI was significantly lower during late pregnancy compared to postpartum (5.81/h + 2.1 vs. 12.1/h + 2.7, p < 0.05) with a longer mean duration of apneas/hypopneas in the postpartum period. The overall mean SaO2 (%) did not differ between the two time-points, but the mean PaO2 (%) in supine position was significantly lower in the antenatal period compared to the one in postnatal period (90.1  $\pm$  0.6 vs.  $99.2 \pm 0.4$ , p < 0.001). Edwards et al. [43] investigated 10 pregnant women (BMI 30  $\pm$  3 kg/m<sup>2</sup>) with OSA diagnosed in the third trimester with a second PSG 4 mo after delivery (BMI  $27 \pm 3 \text{ kg/m}^2$ ). Women were treated with CPAP until delivery. The postnatal recordings showed consistent improvement of both AHI (63/h  $\pm$  15 vs.  $18/h \pm 4$ , p = 0.03) and minimum SaO2 ( $86\% \pm 2\%$  vs.  $91\% \pm 1\%$ , p = 0.01) with reduced severity of blood pressure responses to apneas (170-180 mmHg vs. 130-140 mmHg), contrasting results of previous studies [43]. No significant relationship between changes in either weight or BMI from the antenatal to the postnatal sleep studies and changes in AHI were found.

## Periodic limb movements during sleep (PLMS)

Few studies reported data on PLMS [28–30,34]. Most of them found no [28–30] or only a clinically non-significant increase [34] of the PLMS-Index measured across normal gestation or compared to non-pregnant controls.

Dzaja et al. [45] studied 10 pregnant women with RLS and 9 without RLS around the 36th wk of gestation and 12 wk postpartum. Women with RLS showed more PLMS before ( $F_{1,13} = 6.11$ , p < 0.05) and after delivery ( $F_{1,13} = 3.21$ , p < 0.1) than controls. In particular, during pregnancy, PLMS were significantly more frequent in the RLS group in wake ( $F_{1,13} = 7.19$ , p < 0.05), S1 ( $F_{1,13} = 11.72$ , p = 0.005), and S2 ( $F_{1,13} = 4.87$ , p < 0.05) sleep stage. Interestingly, subjects affected by RLS also had higher blood estradiol levels during pregnancy compared to controls. However, there was no correlation between PLMS index and RLS severity within the RLS group. Overall, PLM activity showed a negative correlation with estradiol levels in RLS patients (r = -0.66, p < 0.05), but not in the control group (r = 0.03, ns).

# Subjective and other objective sleep assessment vs. polysomnography

Zhu et al. [23] analyzed the agreement between actigraphy and PSG in estimating basic key sleep parameters (TST, SE, WASO and sleep onset latency (SOL)) of 38 healthy pregnant women during the third trimester. The best correspondence to PSG-derived parameters was obtained by using the 10 immobile/mobile minutes for sleep onset/end with an activity threshold of 10 (10-by-10), while the default scoring setting (10-by-40) provided significantly different results from the PSG (p < 0.01).

By examining possible discrepancies between subjectively reported and objective PSG parameters in 33 women in the third trimester of gestation, 16 in the first trimester, and 15 non-pregnant women, Wilson et al. [46] found that the first group slightly overestimated TST, whereas the second and third groups tended to underestimate TST. Sleep latency was overestimated by all groups and corresponded closest to the first epoch of 10 min uninterrupted sleep or first epoch of SWS.

The same group later screened 380 pregnant women during the second trimester by means of the Berlin Questionnaire (BQ) and the Multivariable Apnea Risk Index (MAP-Index) [47]. Forty-three participants repeated the questionnaires and additionally underwent PSG at 37 wk of gestation, which in 15 cases (35%) showed an

RDI>5/h. Overall, both the BQ and the MAP-index had low to moderate predictive value and were judged inadequate as screening instruments for SDB in pregnancy.

In a recent secondary analysis of their previous longitudinal study [33], Balserak et al. [48] tested the predictive value for OSA of the Sleep Apnea Symptom Score (SASS) vs. a combined model incorporating questionnaire data with clinical measures, in 94 women not meeting the diagnostic criteria for OSA according to PSG in the first trimester of gestation. In the third trimester, 17 women (15.98%) had incident OSA (AHI≥5 events/h). The mean SASS administered in the first trimester showed acceptable validity and reliability to predict OSA. However, when adding maternal age, BMI, and bedpartner-reported information, the combined model performed better than the SASS alone in predicting OSA.

Finally, Sharkey et al. [49] and O'Brien et al. [50] tested the validity of two portable devices, compared to PSG, for the assessment of SDB during pregnancy. Both the Apnea Risk Evaluation System (ARES) [49] and the Watch-PAT-200 wrist-worn screening device [50] showed good sensitivity and specificity in the identification of SDB among pregnant women.

## Polysomnographic findings in pregnancy-related complications

It is estimated that about 5% of all pregnancies are affected by the occurrence of gestational complications, ranging from minor diseases to potentially life-threatening conditions for both mother and fetus [51].

Sleep disorders during pregnancy may play a role in inducing or exacerbating gestational complications, but these, in turn, may also deteriorate sleep. Few PSG studies addressed the topic of sleep in women affected by typical pregnancy-related complications, such as gestational hypertension (GHTN), preeclampsia (PE), and gestational diabetes (GDM), with the aim to shed more light on the bidirectional relationship between sleep and health problems occurring during pregnancy.

#### Hypertensive disease of pregnancy (HDP)

Three studies examined sleep in HDP. O'Brien et al. [52] studied 51 pregnant hypertensive women, of which 59% with chronic hypertension (CHTN), 23% GHTN and 18% PE, compared to 16 pregnant healthy women. Subjects belonging to the hypertensive group had a mean BMI>30 kg/m<sup>2</sup> vs. 28.1  $\pm$  4.7 of the control subjects. Snoring was significantly more reported by hypertensive women (n = 31; 61%) compared to controls (n = 3; 19%). Snoring hypertensive women had a significantly higher AHI (19.9/h  $\pm$  34.1 vs. 3.4/h  $\pm$  3.1, p = 0.013), a significantly lower SpO2% nadir (86.4%  $\pm$  6.6 vs. 90.2%  $\pm$  3.5, p = 0.021) and were significantly more likely to have undiagnosed OSA (AHI $\geq$ 5; 53% vs. 24%, p = 0.03), than non-snoring hypertensive women. Thus, the authors pointed out that pregnant women presenting with a combination of hypertension and snoring are at risk of developing OSA with clinically significant oxyhemoglobin desaturation.

Reid et al. [53] investigated 34 obese pregnant women with GHTN, compared to 26 healthy pregnant women. Sleep-disordered breathing (SDB) was significantly more frequent in the cases compared to the controls (53% and 12% respectively, p < 0.001). Nocturnal blood-pressure monitoring showed no group specific differences in hemodynamic response to respiratory events including flow limitations, contrasting the results from another recent study by Edwards et al. [54]. However, in both groups, upper airway obstructive events of any severity were associated with a substantial transient blood pressure response, as shown by a later secondary analysis of the dataset [55].

Wilson et al. [56] compared obese women with HDP with normotensive pregnant controls matched for BMI, age and gestational age. SDB was found to be more common (52.5% vs. 37.5%) and more severe (35% vs. 15% of subjects with RDI>10/h, p = 0.039) in the HDP vs. control group, although RDI did not differ (p = 0.20) between groups.

## Pre-eclampsia (PE)

Four studies examined the sleep pattern of women with PE. Edwards et al. [57] performed third trimester PSG in 25 women suffering from PE and 17 healthy pregnant control subjects. Preeclamptic patients showed an increase in SWS ( $43 \pm 3\%$  vs.  $21 \pm 2\%$ , p < 0.001), a longer REM sleep latency ( $205 \pm 23$  vs.  $92 \pm 11$  min, p < 0.001) and a reduced REM-sleep percentage ( $10 \pm 2\%$  vs.  $18 \pm 1\%$ , p < 0.001). REM-related sleep changes were possibly due to clonidine medication in the patient group.

In a later study, the same authors performed PSG in pregnant women in the third trimester suffering from OSA (n = 10) or both OSA and PE (n = 10) [54]. Blood-pressure responses to obstructive respiratory events during sleep were significantly increased in patients affected by both conditions, compared to normotensive OSA patients. No significant difference between groups in heart rate response was found, but, as compared to control OSA patients, heart rate did not show any modification during sleep and wakefulness in PE patients, suggesting a possible alteration in the normal pattern of reduced sympathetic tone during NREM sleep in this group.

Guilleminaut et al. [58] performed PSG in 12 women with risk factors for PE (hypertension, obesity and prior PE). None of them had oxygen desaturations >3% but all participants showed significant SDB (mean RDI 8.5/h  $\pm$  2.6). All women received nasal CPAP treatment for the remainder of pregnancy, which was effective in alleviating SDB symptoms and ameliorating blood pressure control in patients with pre-existing hypertension, but did not prevent negative pregnancy outcomes associated with obesity and PE.

Suri et al. [59] conducted a prospective PSG study in 40 patients with PE or GHTN aged  $25.3 \pm 3.9$  y (mean GA  $34.9 \pm 1.7$  wk) and 60 healthy pregnant controls aged  $25 \pm 3.5$  y (mean GA  $35.7 \pm 2.0$  wk). Pre-pregnancy and present BMI, as well as AHI, snoring, systolic (SBP), diastolic (DBP), and mean (MBP) blood pressures were significantly higher in cases than in controls. SDB was more frequent (p = 0.018; OR 13.1) and more severe (p = 0.001; OR 1.8) in hypertensive pregnant women vs. healthy pregnant women, even after controlling for pre-pregnancy BMI. AHI was significantly associated with blood pressure, even after adjustment for BMI. Therefore, the authors concluded that not only obesity may play a role in the causation of hypertension and SDB, but also SDB may be implicated in the development of hypertension (r = 0.612; p = 0.01).

## Hyperglycemia and gestational diabetes mellitus (GDM)

Three studies examined sleep in women with GDM. Reutrakul et al. [60] analyzed PSG features of healthy pregnant women, pregnant women with GDM and non-pregnant healthy controls (n = 15 individuals for each group). When comparing pregnant women with and without GDM, the first group showed a lower TST (median 397 vs. 464 min, p < 0.02), a higher AHI (median 8.2 vs. 2.0, p < 0.05) and a higher prevalence of OSA (73% vs. 27%, p < 0.01). In multivariate analysis, after adjusting for pre-pregnancy BMI, the diagnosis of OSA was associated with GDM (OR 6.60). In pregnant women, a higher AI was significantly associated with higher HbA1c and fasting glucose levels, which, in turn, were positively associated with ODI.

By contrast, Bisson et al. [61], evaluating sleep characteristics of pregnant women with and without GDM, found no statistically significant differences between groups regarding sleep structure, breathing variables, and movement parameters.

In their large prospective PSG study, Izci Balserak et al. [62] examined the correlation between SDB and glucose tolerance (measured with Oral glucose tolerance test (OGTT) at enrollment) in a cohort of 104 pregnant women, recorded in the first and third trimester (83 women). No differences in sleep structure and breathing parameters were found between the hyperglycemia (Glucose challenge test (GCT) $\geq$ 135, n = 11) and normoglycemia (GCT<135, n = 93) groups. Although RDI and flow-limitations were not reported, symptoms of SDB (snoring 9.3% vs. 45.5%, p < 0.01; daytime nap duration 1.49 ± 1.3 h vs. 2.27 ± 1.4, p = 0.07; MAP-index 0.52 ± 0.8 vs. 1.53 ± 1.1, p < 0.01) rather than objective breathing parameters were associated with maternal impaired glucose tolerance.

## Adverse fetal outcomes

Sahin et al. [63] performed third trimester PSG in 35 healthy pregnant women who reported frequent snoring. Among the four women, who were found to suffer from OSA (mean BMI 37.5  $\pm$  8.4, mean AHI 13.5  $\pm$  5.5), two also had GDM and one cardiovascular disease. Three of them showed fetal heart deceleration accompanying maternal desaturation and their neonates had lower APGAR scores, as well as birth weights compared to those from women without OSA.

More recently, Pamidi et al. [64] explored the relationship between PSG-diagnosed SDB in the third trimester of pregnancy and delivery of small for GA infants (SGA, defined as growth <10th percentile for the corresponding GA) in a prospective cohort study of 234 women. Twenty-seven (12%) women delivered a SGA infant. SDB symptoms in the third trimester were found to be not predictive of delivering an SGA infant and their overall sensitivity and specificity for predicting a PSG-based diagnosis of SDB was also poor. By contrast, a PSG-based diagnosis of SDB in the third gestational trimester was associated with a significantly increased odds of delivering an SGA baby (using a AHI cut-off of 10 events/h, OR 2.65).

In their prospective study, Fung et al. [65] investigated the effects of maternal OSA on fetal growth. Of 371 screened women, 41 patients (n = 26 high-risk and n = 15 low-risk) underwent PSG during the second trimester and subsequent fetal growth assessment in the third trimester. Fourteen women received a PSG-confirmed diagnosis of OSA (RDI>5/h). The remaining 27 subjects represented the control group. Impaired fetal growth was observed in 43% of cases, vs. 11% of non-OSA controls (RR 2.67; 1.25–5.7; p = 0.04). Logistic regression analysis identified OSA (OR 6; 1.2–29.7, p = 0.03) and BMI (OR 2.52; 1.09–5.80, p = 0.03) as significant predictor of fetal growth restriction. However, when adjusting for BMI in multivariate analysis, the association did not reach statistical significance (OR 5.3; 0.93–30.34, p = 0.06).

Finally, Kneitel et al. [66] compared women without OSA or treated with PAP-therapy in a retrospective case—control setting. There was no difference between the percentage of infants with growth restriction (SGA, <10th percentile) from women with or without OSA, although in logistic models the presence of OSA was predictive of slowing fetal growth in the third trimester.

## Interventional approaches in pregnancy

#### CPAP during pregnancy

As for non-pregnant women, CPAP is generally considered the first-line therapy for pregnant women affected by OSA. Three studies objectively assessed the effects of CPAP on sleep during pregnancy.

Guilleminaut et al. [67] treated 12 women with OSA with nasal CPAP (mean AHI 21 events/h, mean RDI 33 events/h). Full PSG was performed at study entry, during CPAP titration, and repeated at 6 mo of GA. An additional home monitoring of cardio-respiratory variables was conducted at 8 mo GA. From the first to the second PSG recording, a moderate worsening of PLM score and snoring was noted in three women, and CPAP pressure had to be increased in six cases. Subjective measures of sleepiness, fatigue and snoring improved significantly compared to study entry and CPAP showed overall a good compliance and safety.

Blyton et al. [68] studied the effect of CPAP treatment on blood pressure, heart rate and cardiac stroke volume in 24 women with severe PE, who were randomly assigned to either receive nasal CPAP (n = 12) or no treatment (n = 12). PSG was performed on two consecutive nights (baseline and treatment). Objective sleep features were compared between groups and to a healthy pregnant control group (n = 15). The amount of REM sleep (%) was reduced in PE women regardless of treatment status compared to control subjects  $(23 \pm 3, 12 \pm 6, \text{ and } 12 \pm 7\% \text{ of TST in control, no-CPAP, and}$ CPAP subjects, respectively, p < 0.001). The RDI was slightly increased in both PE groups compared to control subjects (9  $\pm$  4 events/h,  $19 \pm 10$  events/h, and  $22 \pm 23$  events/h in control, non-CPAP, and CPAP subjects, respectively, p = 0.10) and all cases showed upper-airway flow limitations. Pre-eclamptic women had increased daytime BP, a reversed nocturnal BP decrement and a significantly lower heart rate in NREM, as well as a significant decrease of cardiac stroke volume during sleep compared to control cases. Furthermore, total peripheral vascular resistance was heightened, and cardiac output reduced. All the above-mentioned variables improved or normalized with CPAP treatment.

The same authors [69] also performed third trimester PSG in 20 women with PE and 20 healthy pregnant women (BMI 31.9  $\pm$  3.2 vs. 30.6  $\pm$  2.5 kg/m<sup>2</sup>, p = 0.15). Preeclamptic patients showed significantly more flow limitations, higher AHI and increased number of oxygen desaturation especially during REM sleep, compared to controls. Fetal wellbeing, measured by movement pattern and hiccups, was also significantly reduced in PE patients and responded to CPAP.

#### Positional therapy

In the third trimester, the majority of pregnant women spend up to 25% of TST in supine position [70–72], which is considered to be a risk factor for still births (SB), with an attributable risk between 3.7% and 37% [73,74]. Avoiding supine position during sleep in pregnant women could therefore significantly reduce the occurrence of late SB.

Kember et al. [75] performed a two-night, in-lab, PSG study with a cross-over design in 20 pregnant women in the third trimester, in order to evaluate the effect of a positional therapy device (Pre-naBelt), compared to a sham device, in discouraging healthy pregnant women to sleep in supine position. Considering all available recordings (n = 40 nights), the median percentage of sleep time spent in supine position was reduced from comparable low baseline values of 16.4% on the sham night to 3.5% on the PrenaBelt night (p = 0.03), with overall good compliance and tolerability. Sleep macrostructure and sleep-related breathing and movement parameters did not significantly differ between groups and remained within the normal range, as expected in this low-risk population.

## Quantitative analysis (meta-analysis)

Five studies reporting TST and six reporting SE were selected for inclusion in the meta-analysis. Results are presented as forest plots in Figs. 2 and 3. TST was overall significantly reduced from the first to the third trimester of pregnancy by 26.8 min (pooled WMD, 95% CI = 12.14-41.56). Similarly, SE was reduced between first and third trimester by 4% (pooled WMD, 95% CI = 1.50-6.65). A significant statistical heterogeneity between studies was found for both sleep parameters evaluated (I<sup>2</sup>>50%). Egger's test detected no significant



26.857772 (95% CI = 12.148938 to 41.566606), Z = 3.57882, P = 0.0003 Heterogeneity: Cochran's Q = 11,006579 (df = 4) P = 0,0265,  $I^2 = 63,7\%$ 

Fig. 2. Forest plot of studies reporting TST included in meta-analysis.

-20

-10

10

20

30

40

50

60

70



Fig. 3. Forest plot of studies reporting SE included in meta-analysis.

publication bias for studies reporting TST (p > 0.1), but a possible publication bias for studies reporting SE (p = 0.072).

## Discussion

Changes in sleep structure during pregnancy, as objectively measured by PSG, mainly consist in a reduction of sleep duration (TST), due to an increase of WASO, and in a transition from N3 and REM sleep to more superficial NREM sleep stages (N1, N2) [28,29]. As a result, mean SE is diminished and sleep is perceived as non-restorative across gestation [30].

These findings become particularly evident in the third trimester and are confirmed both by studies comparing pregnant with age-matched non-pregnant women, and by a recent large analysis of PSG data collected among the same mothers during early and late pregnancy [34].

Hormonal variations can only partially explain these alterations, which should instead be ascribed to a series of concurrent factors, including anatomical/mechanical changes and psychological variables [31]. Objective sleep alterations occurring during pregnancy are precisely detected by PSG and might be relevant in guiding appropriate therapeutic strategies for women reporting poor sleep quality and insomnia symptoms across gestation. Previous research has shown that, in untreated women, actigraphyassessed sleep variables tend to worsen from pregnancy to postpartum [76] and that cognitive behavioral therapy for insomnia (CBT-I) can significantly reduce insomnia symptoms and improve objectively measured sleep variables, such as SE, SOL, and TIB in pregnant women [77]. However, since objective TST seems to be not significantly modified by CBT-I [77], the benefits of using this treatment during pregnancy need to be further studied and evaluated.

According to the PSG studies published so far, there is poor evidence of an increased occurrence of SDB among healthy, normal-weight pregnant women without risk factors, suggesting that pregnancy per se does not necessarily predispose to major changes in sleep-related respiratory parameters. However, a deterioration of the respiratory pattern during pregnancy, with a higher AHI, ODI, snoring time and incidence of OSA, particularly in the third trimester, is generally a common finding in studies analyzing SDB in at-risk pregnant women. Besides gestational age, some preexisting conditions, such as a BMI in the range of obesity, a larger neck circumference, as well as higher maternal age at pregnancy onset, should be carefully considered as possible risk factors for the development of OSA during pregnancy [33,34,75].

Also, in most studies, the classical PSG parameters considered for diagnosing OSA in the non-pregnant population, such as AHI and ODI, show no significant differences or are only slightly increased, without reaching a pathological threshold (i.e., AHI≥5) in pregnant women [38]. This raises the question whether the current diagnostic criteria for OSA also apply to pregnancy, and whether other respiratory markers, such as airflow limitations and snoring, may be more reliable in identifying possible borderline pathological conditions, which may predispose to pregnancyrelated adverse cardiovascular or other health outcomes [40]. Future research should be therefore focused on better defining normative PSG values for SDB during pregnancy based on large datasets.

The frequency and characteristics of PLMS during pregnancy are clearly underinvestigated, but the available studies did not show a relevant increase of PLMS-Index in women across gestation or compared to non-pregnant controls. This is a surprising finding, considering the high prevalence of RLS during pregnancy [78] and that up to 80% of patients with RLS also have increased PLMS [79]. In fact, the only small PSG study examining pregnant women with RLS confirmed these to have more PLMS before and after delivery than healthy pregnant controls [45].

Subjective tools to evaluate sleep characteristics or to screen for SDB in pregnant women must be carefully interpreted, due to their generally lower accuracy compared to PSG. Some of these instruments may be implemented by adding information provided by the women themselves or their bed partners, which may critically improve the sensibility of the tools [47,48]. This suggests that the creation and validation of new questionnaires specifically targeting the pregnant population are recommended for future research studies.

Actigraphy represents a valid objective alternative to PSG for assessing some fundamental sleep parameters, such as TST, SE or WASO. However, its accuracy in comparison to PSG seems to be clearly influenced by the basic settings of the devices used, which would require to be validated during pregnancy [23], paying particular attention to the late GA, when mobility is reduced.

Single validation studies of a few portable devices for detecting SDB in pregnant women have shown a good diagnostic sensibility of these instruments with respect to PSG [49,50].

Hypertensive disorder of pregnancy (HDP), independently from its nature, is associated with snoring, and women affected by both conditions are more likely to have a higher AHI and to suffer from OSA [52]. Moreover, obesity may play a significant role in predisposing pregnant women with HDP to develop SDB and BMI should be therefore carefully accounted for when evaluating pregnant hypertensive individuals.

Pregnant women affected by PE not only show alterations of sleep structure, with increased SWS and REM sleep latency, as well as reduced REM sleep percentage, but are also more likely to suffer from snoring and SDB. In particular, PE patients have a higher AHI, AI, and a lower minimum oxygen desaturation, which all positively correlate with blood pressure parameters, even after adjustment for BMI, and predispose to poor maternal and fetal outcomes [58].

Data regarding the association between gestational diabetes and altered sleep pattern or SDB are scarce and not consistent. However, the largest study on maternal hyperglycemia conducted so far showed that, also in this case, the traditional parameters used to diagnose SDB may not differ between patients and healthy control subjects, even if symptoms of respiratory disturbances during sleep may be significantly more frequent in patients with impaired glucose tolerance [62].

A few studies examined the association between OSA and severe perinatal outcomes, such as impaired fetal growth or the delivery of SGA newborns. In particular, a PSG-based diagnosis of SDB in the third gestational trimester was associated with a significantly increased odds of delivering an SGA baby [64]. However, BMI seems, once again, to critically influence the value of OSA as predictor of fetal growth restriction [80]. In general, further evidence especially regarding the role of mild OSA as risk factor for pregnancy-related complication, as well as the efficacy of CPAP therapy in preventing such complications is warranted.

To date, interventional studies evaluating the effects of CPAP on pregnancy-related OSA and PE by using PSG are lacking, but overall supporting the use of this type of non-invasive ventilation, which is generally well tolerated and remarkably contributes to improve subjective sleep quality and daytime symptoms, as well as objective sleep and hemodynamic parameters [67,68].

Some limitations of the present analysis should be considered. First, some studies only report parts of their polysomnographic results, generally those addressing the specific research question, or possibly only the positive ones. Also, main characteristics considerably differ between studies, e.g., regarding design, population, sample size, time of pregnancy and criteria used for PSG scoring. This large heterogeneity makes it difficult to draw definitive conclusions about most outcome parameters and to pool the data in order to perform a meta-analysis.

Finally, articles reporting PSG results from a sample <10 women, as well as reduced montage polygraphic studies (without EEG, EMG and EOC derivations) were excluded from the present review. Although PSG is the most accurate method for sleep depiction, its use in the clinical setting may be complicated by the limited availability, the necessary technical equipment, and the elevated costs. Also, it must be considered that PSG data obtained from a single recording might be biased by an habituation effect (also called "first night effect"), especially if the sleep study was not performed in the home environment [81].

In conclusion, a growing number of PSG studies are providing further knowledge on the intrinsic features of sleep during pregnancy, thus contributing to better describe changes in objective sleep variables occurring in pregnant women beyond subjective reports. Portable devices will help to collect large-scale data in future research, but efforts are needed in designing more homogenous and comparable studies, in order to maximize the information gained from the results and to better understand the clinical value of using PSG during pregnancy.

## **Practice points**

Sleep disturbances during pregnancy are common and may sometimes require a full polysomnographic assessment in order to:

- 1. correctly identify pregnancy-related sleep disorders according to current diagnostic criteria
- 2. avoid under- or overestimation of self-reported sleep problems
- establish an early treatment of pathological conditions, which represent a risk factor for the health of the fetus and the mother

## **Research agenda**

Future research studies using polysomnography in pregnant women should be preferably aimed at:

- evaluating changes in sleep variables within the same women at different time points before, during, and after pregnancy by adopting longitudinal study designs
- establishing an expert consensus on the minimal polysomnographic parameters to be reported in studies on pregnancy and on the sleep scoring criteria to be adopted
- 3. creating large datasets in order to define normative polysomnographic values per each trimester of pregnancy
- developing algorithms based on combined information from PSG and questionnaires, in order to better predict pregnancy-related clinical outcomes
- 5. further validating the accuracy of portable polygraphy devices vs standard polysomnography
- 6. evaluating the efficacy of CBT-I and CPAP during pregnancy for the treatment of insomnia and sleep-disordered breathing, respectively

## **Conflicts of interest**

The authors have no conflicts of interest to disclose.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.smrv.2019.101249.

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