

Impact of sleep disturbance on health-related quality of life in chronic obstructive pulmonary disease (COPD): What do we know so far?

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BACKGROUND

- Extra pulmonary impacts of chronic obstructive pulmonary disease (COPD) often include sleep disturbance, poor sleep quality, daytime sleepiness and fatigue resulting in detrimental impact on patients' health-related quality of life (HRQoL). Fragmented sleep further leads to irritability, decreased mood and cognitive impairment. (Agusti et al., 2011)
- Insomnia is one of the leading but underdiagnosed comorbidities of COPD, with reported prevalence in 27%–44% of patients with COPD. (Ban et al., 2018)
- While physiologic changes in COPD may contribute to nocturnal pulmonary symptoms, sleep quality is not necessarily related to physiologic disease severity. (Geiger-Brown et al., 2015)

OBJECTIVE

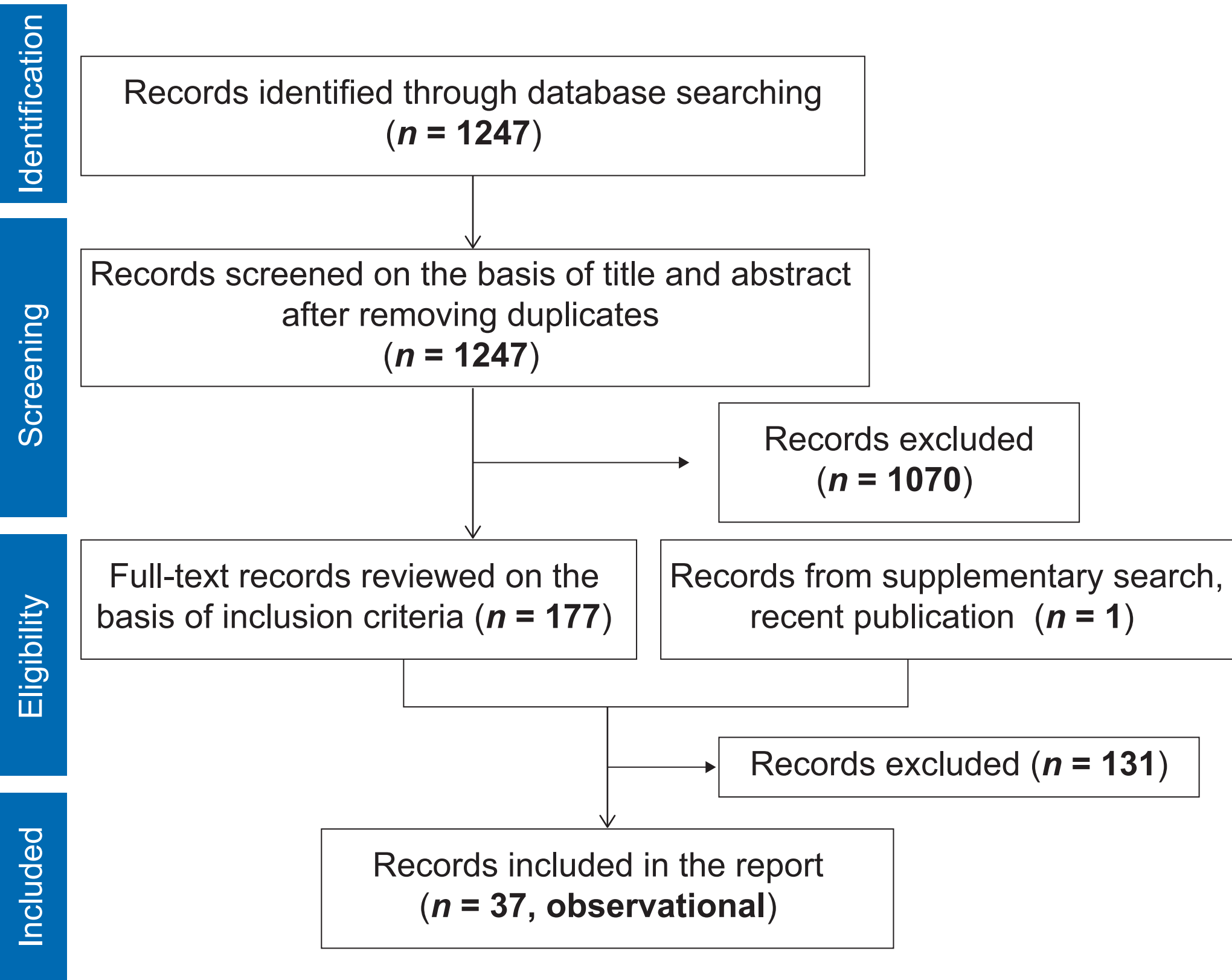
- This review aimed to evaluate the impact of sleep disturbance on HRQoL in patients with COPD

METHODS

Selection of relevant publications

- Literature searches were performed in MEDLINE and Embase (biomedical databases) via OvidSP platform until April 2019
- Specific search terms, such as “sleep,” “insomnia,” and “night-time awakening,” were used to identify studies on COPD that included sleep as a patient-reported outcome (PRO) endpoint
- The search had no restriction on timeframe and geographical boundaries; only full-text articles published in English were included
- Inclusion criteria:** Observational studies reporting sleep related PRO endpoints. These studies presented with results on correlations of impacted sleep on HRQoL in patients with COPD

Figure 1. Methods used in the review (selection process of relevant publications)



Instrument identification

- Sleep related PROs such as Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and COPD and Asthma Sleep Impact Scale (CASIS); as well HRQoL PROs such as the St George's Respiratory Questionnaire SGRQ, the COPD Assessment Test (CAT), the 36-Item Short Form Health Survey (SF-36), and the Nottingham Health Profile (NHP) were identified from the full-text articles

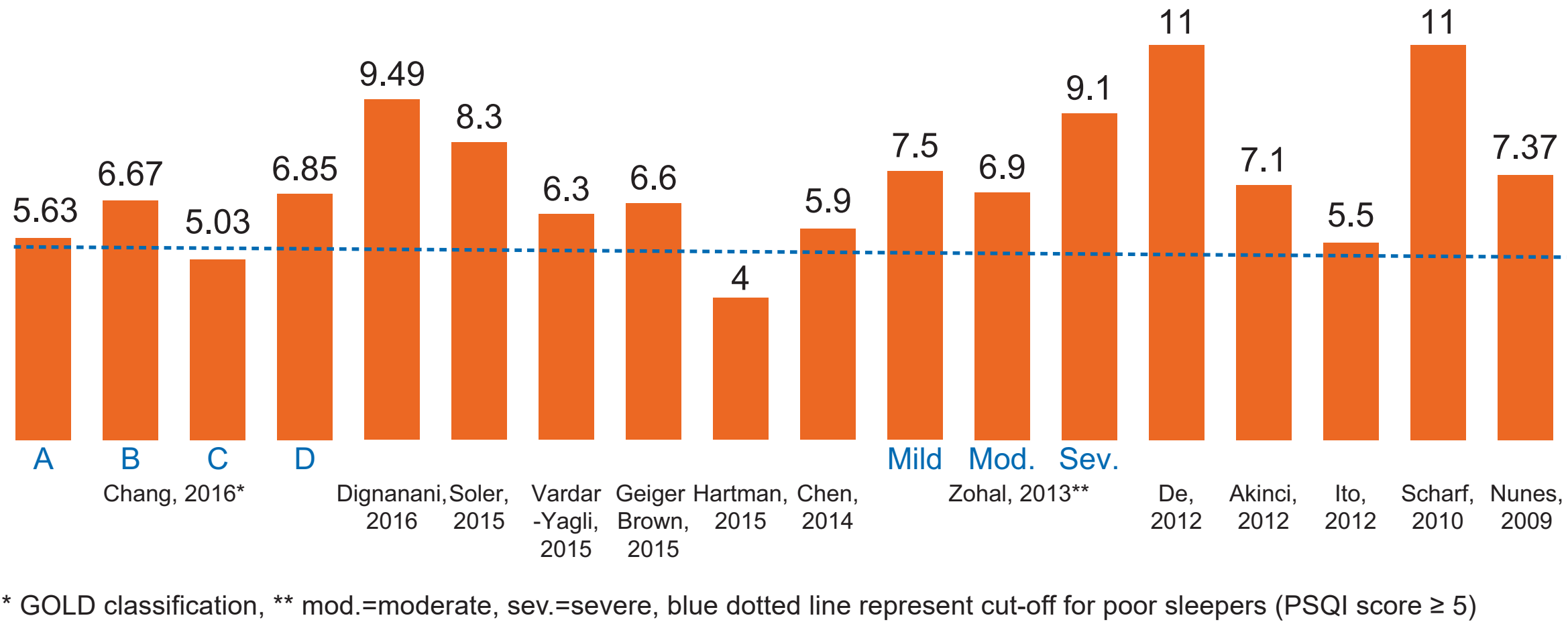
Analysis and Interpretation of results

- Results were included for assessment if they reported data on the correlations (Pearson's r or Spearman's ρ or univariate/ bivariate/ multivariate regression analysis) between any of the sleep related PRO measures, and HRQoL instruments
- Such correlations were analyzed for significance level and correlation values. Significant results are reported in this review
- PSQI a widely reported PROM, is a generic instrument used in various indications including COPD to measure sleep quality. PSQI score ranges from 0 to 21, with higher scores denoting poorer sleep quality
- Included studies identified “good sleepers” as patients with PSQI score <5, and “poor sleepers” with score ≥5. (Geiger-Brown et al., 2015). Hence, a threshold score of five for the PSQI was used to identify poor sleep quality in patients with COPD in this review also
- Similarly, insomnia was determined by Insomnia Severity Index (ISI) frequently, which classifies patients into three groups based on the score—“clinical insomnia” (ISI ≥15), “subthreshold insomnia” (ISI: 8–15), and “non-insomnia” group (ISI <8; Ban et al., 2018)

RESULTS

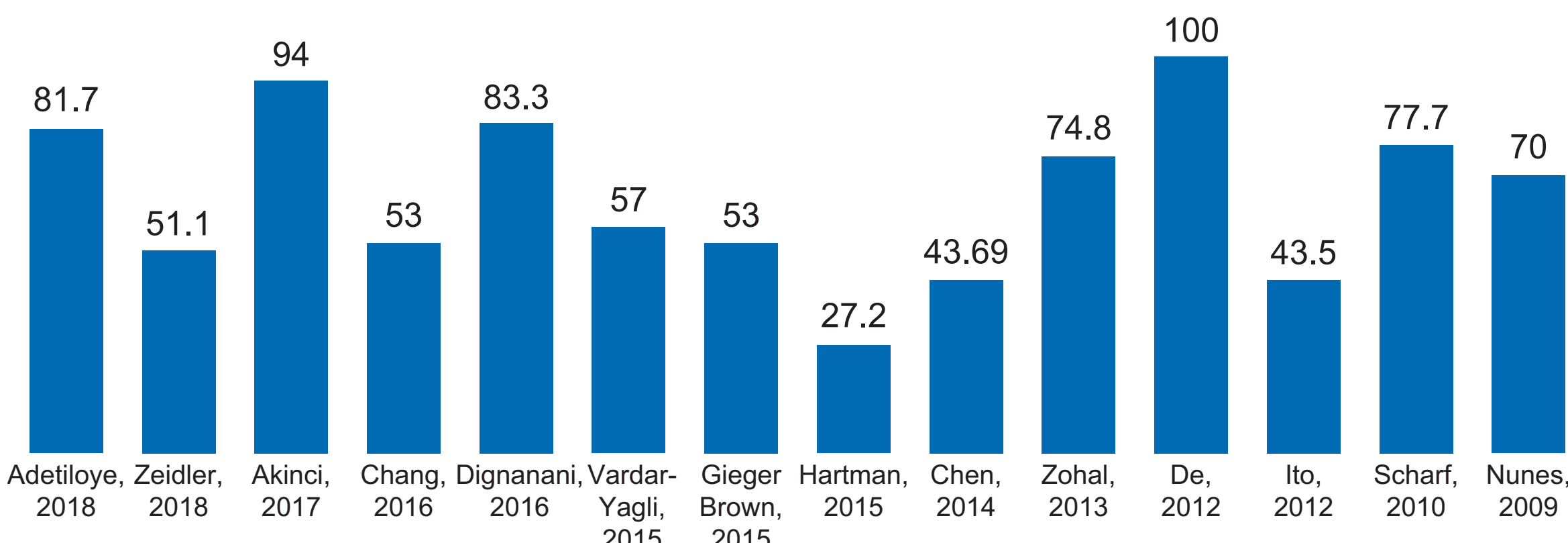
- A total of 1247 abstracts were identified, of which 177 were selected for full-text screening. Based on the inclusion criteria, 36 observational studies are reported in this review
- Of note, one recently published study was included from a desktop search. Hence, results of 37 studies are included in this review. (Figure 1)
- Thirteen studies reported mean PSQI scores. All except one study specified that mean PSQI scores were above the threshold (PSQI ≥5) indicating a poor sleep quality amongst patients with COPD. (Figure 2)
- Percentage of patients with poor sleep quality (PSQI≥5) from fourteen included studies are shown in Figure 3. Sleep disturbances and poor sleep quality was on average prevalent in more than one-third, ranging from 27%-100%, of patients with COPD

Figure 2. Mean PSQI scores at baseline from the included studies (poor sleepers have PSQI ≥ 5)



* GOLD classification, ** mod.=moderate, sev.=severe, blue dotted line represent cut-off for poor sleepers (PSQI score ≥ 5)

Figure 3. Percentage of patients with poor sleep quality (PSQI ≥ 5)



Prevalence of insomnia and association of insomnia with HRQoL

- The included studies showed that insomnia was present in 25%–48% of patients with COPD, which is consistent with literature on clinical studies on COPD.
- Six studies showed associations of insomnia with decreased HRQoL

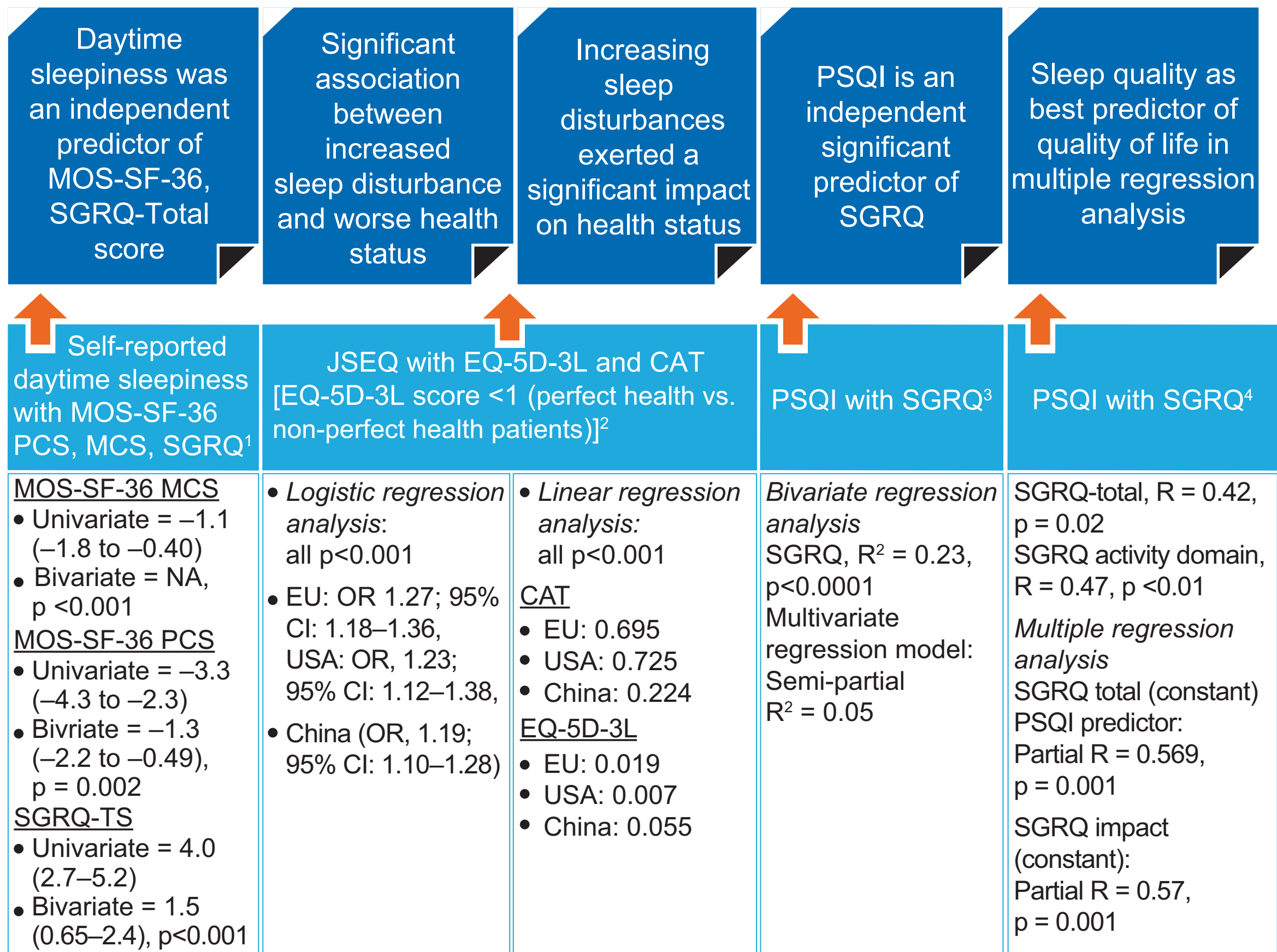
Correlations of sleep measures with HRQoL

- Sleep measures such as the PSQI, PROMIS-sleep disturbance domain, ESS, ISI, and CASIS showed significant correlations (all p<0.05) with HRQoL (determined by the CAT, the SF-36, the NHP, and the SGRQ)

Univariate, bivariate and multivariate analyses

- Seven studies presented with correlations between sleep quality and HRQoL
- Four studies showed sleep quality (evaluated by PSQI), sleep disturbance (evaluated by JSEQ) and daytime sleepiness as an important determinant for HRQoL in COPD, as shown in Figure 4a

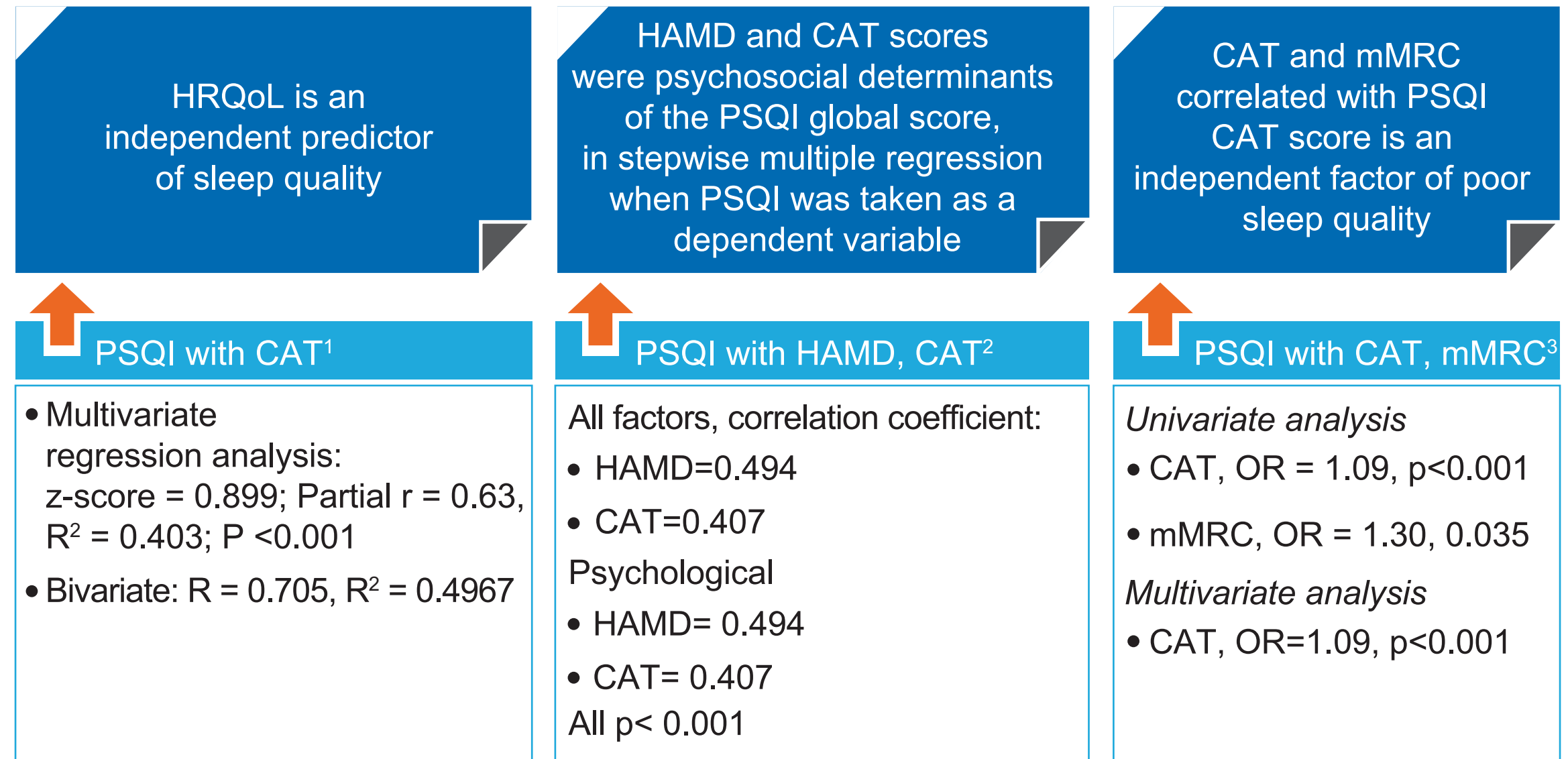
Figure 4a. Studies (n = 4) showing sleep disturbance, sleep quality and daytime sleepiness as predictor of HRQoL



Source: ¹Moy et al., 2009, ²Ding et al., 2017, ³Scharf et al., 2011, ⁴Nunes et al., 2009
CAT: COPD Assessment Test; EU: European Union; EQ-5D-3L: Euro QoL 5 Dimension 3 Level; JSEQ: Jenkins Sleep Evaluation Questionnaire; MOS-SF-36: Medical Outcomes Study 36-Item Short Form; MCS: Mental Component Summary; OR: Odds Ratio; PCS: Physical component summary; PSQI: Pittsburgh Sleep Quality Index; SGRQ: St George's Respiratory Questionnaire; USA: United States of America

- Furthermore, three studies showed that HRQoL was an important predictor of sleep quality, thereby suggestive of a bidirectional relationship between sleep and HRQoL
- Figure 4b presents correlation values of regression analyses, along with the interpretation of these results

Figure 4b. Studies (n = 3) showing HRQoL as predictor of sleep quality



Source: ¹Adetloye et al., 2018, ²Chen et al., 2016, ³Chang et al., 2016
CAT: COPD Assessment Test; HAMD: Hamilton Depression Scale; OR: Odds Ratio; PCS: Physical component summary; mMRC: Modified Medical Research Council; PSQI: Pittsburgh Sleep Quality Index; SGRQ: St George's Respiratory Questionnaire

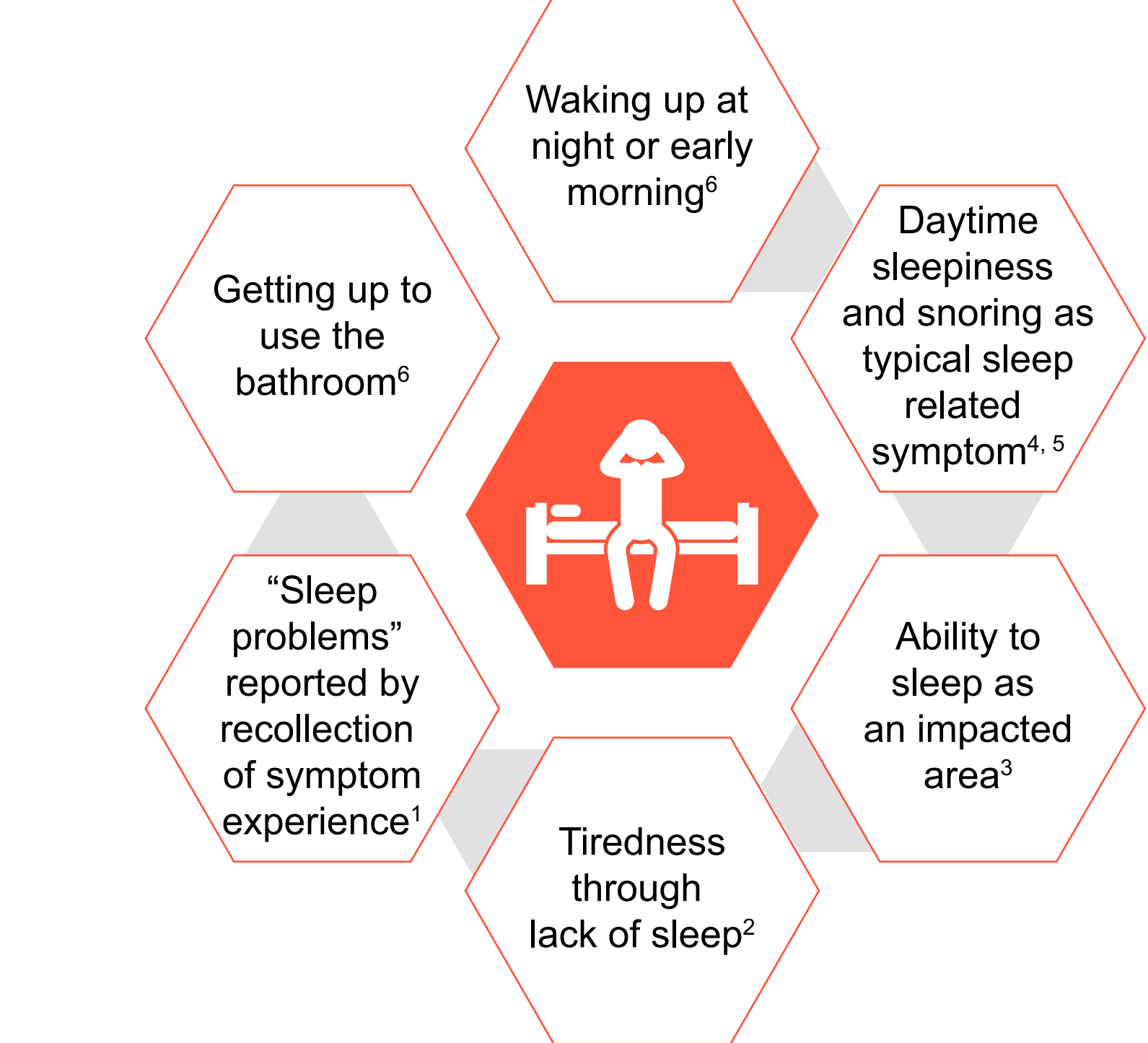
Important associations of sleep with HRQoL

- “Good sleepers” (PSQI<5) have a better HRQoL compared to “poor sleepers” (PSQI≥5)
- Increased sleep disturbance was associated with increased emotional impact, mainly anxiety and depression
- Furthermore, higher PSQI scores were associated with greater exacerbation risks, including risk of death
- Patients with COPD reporting concomitant obstructive sleep apnea (OSA) had worse HRQoL
- Both significant (all p<0.05; n = 8) and non-significant (all p>0.05; n = 4) correlations were observed for the association of disease severity and symptoms on sleep

Qualitative data identified from six studies

- Qualitative data on sleep related problems was identified from six studies and presented in Figure 5
- This data refers to phrases and quotes from qualitative studies (e.g., Focus group discussion in Doward et al., 2017) and also information generated by individual item level analyses of PROMs (e.g., individual item on “getting up to use the bathroom” from PSQI in Chang et al., 2016)

Figure 5. Phrases related to sleep problems as voiced by patients with COPD



Sources: ¹Doward, et al., 2017; ²Ding et al., 2017; ³Svedater et al., 2017; ⁴Akinci et al., 2018; ⁵Hartman et al., 2015; ⁶Chang et al., 2016

CONCLUSIONS

- Sleep disturbance has a detrimental impact on overall HRQoL of patients with COPD, including substantial emotional impacts. However, sleep quality was not necessarily dependent on the disease severity
- A bidirectional relationship of sleep quality and HRQoL was reported in the studies analyzed for this review. Sleep quality is an independent significant predictor of HRQoL in patients with COPD
- As a consequence, sleep needs to be considered as an important HRQoL component when evaluating the health status of patients with COPD. Sleep quality is highly impacted in patients with COPD but has not been studied extensively in clinical trials, hence it warrants attention from sponsors considering sleep as endpoints in clinical studies

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Disclosures

Christel Naujoks, Francesco Patalano and Florian Gutzwiller are employees of Novartis Pharma AG, Basel, Switzerland. Nuzhat Afroz is an employee of Novartis Healthcare Private Limited, Hyderabad, India

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