The prevalence of COAs and DHTs for studying sleep disorders in clinical trials

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Background

- "Insomnia" and "Obstructive Sleep Apnea," are the most prevalent sleep disorders according to Digital Health Measurement Collaborative Community[1].
- COAs capture how patients feel, function or survive[2] and DHTs provide continuous and real time data.
- COAs include patient-reported outcomes (PROs), observer-reported outcomes (ObsROs), clinician-reported outcomes (ClinROs), and performance outcomes (PerfOs).
- Clinical Outcome Assessments (COAs) and Digital Health Technologies (DHTs) enhance precision and patient-centricity in clinical trials.

➔ Objective: Aimed to look at the prevalence of COAs and DHTs in clinical trials for sleep disorders with drug interventions and regulatory recommendations for clinical research.

Methods

- PROINSIGHT™ database was searched in April 2025 to identify clinical guidelines with COA recommendations for sleep disorders. One guideline each from the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) were analyzed.
- ClinicalTrials.gov was searched in April 2025 for sleep studies from the last 10 years focusing on drug interventions. Primary outcome measures for 421 sleep trials were classified as COA, DHT, Biomarker, other or N/A.

A. Guidelines

Visited ePROVIDE[3] database

Filtered for PROINSIGHT and Therapeutic Indication Field for: "Sleep Apnea Syndromes" and "Sleep Initiation and Maintenance Disorders"

B. Clinical trials

Visited Clinical Trials.gov[4] website

Filtered Condition field for: "Sleep Initiation and Maintenance Disorders OR Insomnia OR Obstructive Sleep Apnea Syndrome"

Results

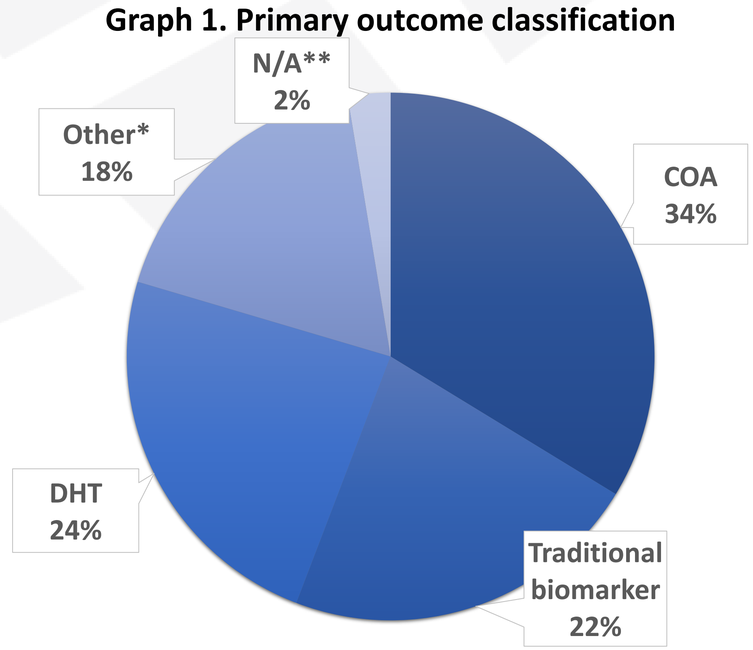
The recommendations regarding the use of outcome assessments shown in table 1 refer to efficacy studies for insomnia[5] by EMA and hypnotic drugs[6] by FDA, mention a variety of types of outcome assessments (OAs) including PROs, PerfOs and non-COAs. Endpoint positioning was not specified for any of these. FDA recommends evaluating sleep parameters with PRO and non-COA endpoints, whilst EMEA recommends the evaluation of a broader range of concept of interest (COI) including quality of sleep, HRQoL, daily functioning and cognitive performance using PRO, PerfO and non-COA measures.

COAs were used to measure 34% of primary endpoints in sleep trials, traditional biomarkers made up 22% and digital health technologies made up 24%.
The three most used COAs for primary endpoints shown in graph 2 were the ISI (n=29), the PSQI (n=24) and the ESS (n=10), which are all PROs. In graph 3 the three most used DHTs were polysomnography (n=69), actigraphy (n=10) and continuous positive airway pressure (CPAP) (n=6).

Table 1. Comparison of guidelines

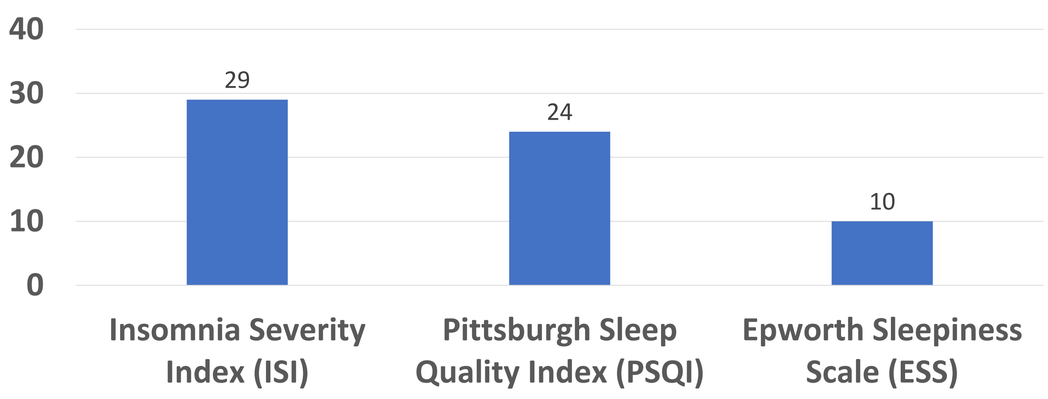
Agency	Title	Endpoint positioning	Types of Outcome Assessment (TOA)	Concept of Interest (COI)
EMA	Guideline on medicinal products for the treatment of insomnia	Not mentioned	PRO	Quality of sleep
		Not mentioned	PerfO	Cognitive performance
		Not mentioned	Non-COA	Sleep parameters
		Not mentioned	PRO	Health-Related Quality of Life (HRQOL)
		Not mentioned	PRO	Daily function
FDA	Guideline for the clinical evaluation of hypnotic drugs	Not mentioned	PRO	Sleep parameters
		Not mentioned	Non-COA	Sleep parameters

Graph 1. Primary outcome classification

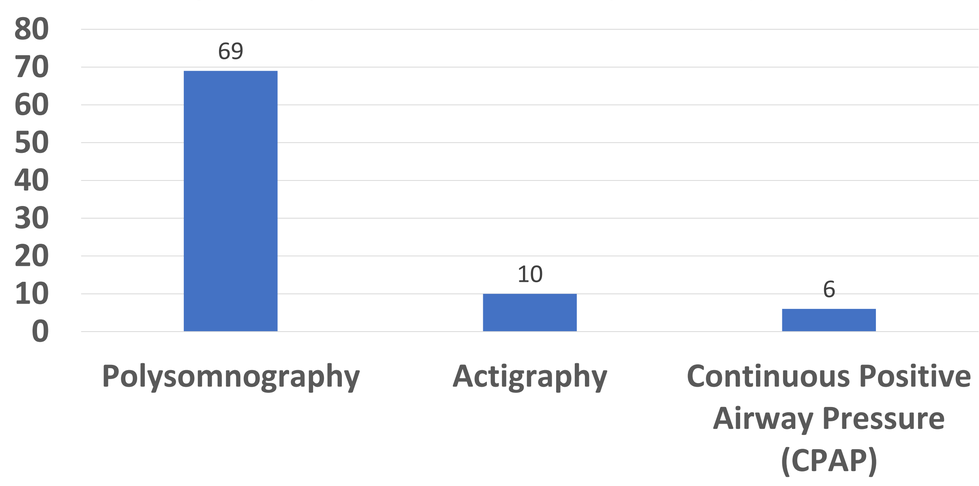


*Includes examples such as adverse events and clinical judgements
**Capturing studies that weren't evidently classified as drug intervention

Graph 2. Top 3 COAs used in sleep studies (n=421)



Graph 3. Top 3 DHTs used in sleep studies (n=421)



Discussion

- The three most used COAs and DHTs address the COIs "HRQOL", "sleep parameters" and "quality of sleep" as recommended in the EMA and FDA guidelines. "Cognitive performance" and "daily function" are not covered and the guidelines did not provide recommendations for their endpoint positioning. Additionally, only primary endpoints were analyzed in sleep studies.
- According to Izmailova et al., 2023, DHTs being under utilised in clinical trials reflects a transitional phase. Reasons for this are: regulatory ambiguity, challenges in validation, and lack of standardisation[7]. Clearer definitions and further validation are needed for digital biomarkers and digital COAs as well as collaboration between regulators, sponsors and technology developers to create frameworks and standards to facilitate the wider use[7].

References

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