Narcolepsy Type I Risk Screening at Scale with Multi-Night Home Sleep Testing

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Introduction

Narcolepsy Type 1 (NT1) is a chronic neurological disorder characterized by excessive daytime sleepiness (EDS), cataplexy, and disrupted sleep architecture. It remains significantly underdiagnosed due to the high cost and patient burden of standard in-lab diagnostics including a nap-based protocol called a Multiple Sleep Latency Test (MSLT).

The International Classification of Sleep Disorders (ICSD-3-TR) defines one of the diagnostic pathways for NT1 as :

- Cataplexy, AND
- Mean Sleep Latency (MSL) ≤ 8 min on MSLT, AND
- ≥2 Sleep-Onset REM Periods (SOREMPs) on MSLT

Where SOREMP is defined as REM onset < 15 min from first non-wake epoch

MSLT limitations: controlled in-lab setting, full-day protocol, medication washout, high cost, and limited access, creating substantial delays to diagnosis (often 8–10 years).

Device used: EnsoHST (FDA-cleared, K231355) is a PPG-based HSAT that enables automated sleep staging across consecutive nights in the patient's home environment, at a fraction of in-lab cost.

Hypothesis: Multi-night PPG home sleep testing can screen for NT1 by applying MSLT-analogous criteria (MSL ≤ 8 min AND ≥2 SOREMPs) across sequential home recordings.

Objectives:

- Characterize NT1 screening rates in a large real-world HSAT cohort
- Determine the minimum nights needed to satisfy screening criteria
- Investigate whether Obstructive Sleep Apnea (OSA) co-morbidity suppresses NT1 biomarker signals

Materials & Methodology

Study Population:

- N = 44,176 patients with ≥3 completed EnsoHST studies
- 3–7 recording nights per patient
- All nights within a 10-day recording window
- Minimum per-night inclusion: TST ≥ 4 hours

NT1 Screening Criteria (MSLT analog):

- MSL ≤ 8 min AND
- ≥2 SOREMPs across recorded nights

Data Processing:

- EnsoHST scoring generated 4-stage (wake, light, deep, REM) hypnograms, as well as respiratory events
- Hypnograms were used to compute: Sleep latency, REM Latency, TST, and a SOREMP flag for each nights
- Respiratory events and TST were used to compute: Apnea-Hypopnea Index (AHI) and OSA severity (Normal < 5, Mild 5–14, Moderate 15–29, Severe ≥ 30)

Results

Patient Demographics:

The cohort reflects a typical clinical HSAT-referred population: predominantly male, middle-aged, and overweight, with a mean AHI indicating mild-to-moderate sleep-disordered breathing on average. The majority of patients completed exactly 3 nights, meaning most findings are driven by the minimum recording length, which makes the multi-night efficiency results conservative.

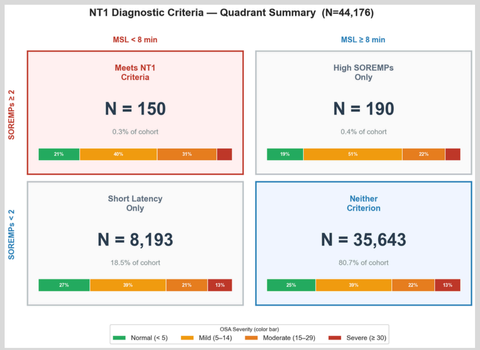
Variable	Value
Total Patients (N)	44,176
Sex	
Female	16,789 (38.0%)
Male	26,712 (60.5%)
Age (mean ± SD)	49.6 ± 14.2 years
BMI (mean ± SD)	31.6 ± 6.8 kg/m²
AHI (mean ± SD)	15.3 ± 15.7 events/hr
OSA Severity	
Normal (AHI < 5)	11,276 (25.5%)
Mild (AHI 5–14)	17,340 (39.3%)
Moderate (AHI 15–29)	9,753 (22.1%)
Severe (AHI ≥ 30)	5,807 (13.1%)
Mean TST (mean ± SD)	6.5 ± 0.9 hr
Number of Nights (mean ± SD)	3.4 ± 0.9
Night Distribution	
3 Nights	34,773 (78.7%)
4 Nights	4,912 (11.1%)
5 Nights	2,029 (4.6%)
6 Nights	1,603 (3.6%)
7 Nights	859 (1.9%)

NT1 Diagnostic Criteria: Quadrant Summary

The MSLT criteria applied to multi-night EnsoHST patients revealed a scree-positive rate of 0.3%, consistent with the expected NT1 prevalence of a sleep test referral population.

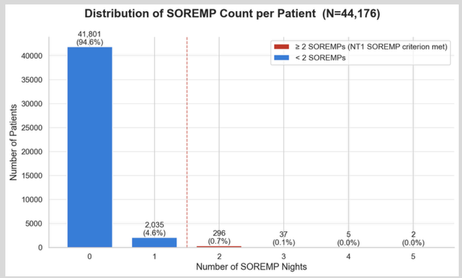
The NT1 screen group carries a notably higher moderate OSA burden than the Neither group, yet these patients still meet both criteria. This directly challenges the assumption that OSA comorbidity would suppress or obscure NT1 markers.

The High SOREMPs Only group warrants particular attention. While they do not meet the formal screening threshold, these 190 patients may include genuine NT1 cases.



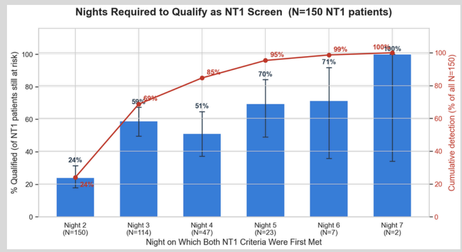
Distribution of SOREMP Count per Patient:

The extreme right-skew of this distribution establishes that SOREMPs are rare events in a real-world home sleep testing population and not a commonly observed artifact. The steep drop-off at the NT1 criterion threshold (≥2) means the classification has inherent selectivity. The sizeable group with exactly 1 SOREMP represents patients who demonstrated the signal at least once but did not accumulate the required count which is a direct illustration of why single-night recording is insufficient for SOREMP-based NT1 screening.



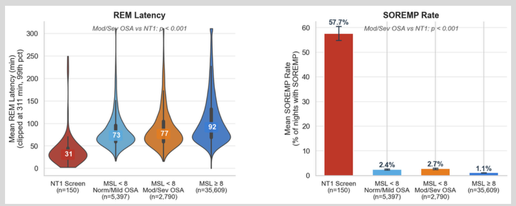
Nights Required to Qualify as NT1 Screen

MSL typically confirms early, the bottleneck for meeting both criteria simultaneously is almost always the second SOREMP. The practical implication is that a standard 5-night prescription captures the majority of NT1 screen patients, which is aligned with the 5 naps minimum requirement for an MSLT.



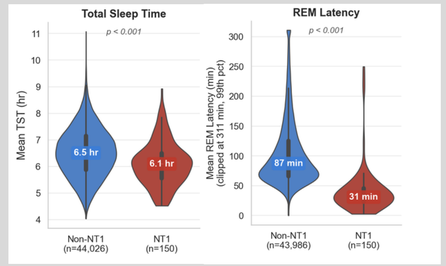
OSA-Masked NT1

This analysis directly tests whether moderate-to-severe OSA suppress NT1 markers. On both independent metrics, their profiles are statistically indistinguishable from the general non-NT1 population and clearly distinct from confirmed NT1 screen patients.



Independent Biomarker Validation: REM Latency & TST

NT1 patients entered REM ~56 min earlier on average, consistent with the hypersomnolent REM dysregulation hallmark of narcolepsy. NT1 patients show modestly reduced TST, reflecting fragmented nocturnal sleep architecture. These findings replicate known NT1 PSG signatures using EnsoHST data, providing independent support that the multi-night screening criteria are capturing a biologically coherent phenotype.



Conclusions

Multi-night PPG home sleep testing replicates the logical structure of the MSLT by repeated sampling of sleep latencies and identification of SOREMPs in a real-world ambulatory setting at scale. This study provides the first large-cohort evidence that MSLT-analogous criteria are applicable outside a controlled lab environment.

A standard 4-5 night HSAT prescription captures the majority of screen-positive patients. NT1 screening does not require a new protocol, it can be embedded within existing home sleep testing workflows without modification.

The true prevalence of NT1-related phenotypes in this cohort is likely underestimated by the 0.3% full-criteria rate. Patients with ≥2 SOREMPs but borderline MSL show REM latency profiles far closer to confirmed NT1 than to controls, suggesting that some genuine cases fall just outside the current threshold. The combined rate of 0.7% may be a more accurate reflection of NT1 and NT1-spectrum disease in an HSAT-referred population.

OSA comorbidity was present at clinically significant levels in a substantial portion of this cohort, however, it was not found to suppress NT1 signals. The screening approach is applicable across the full spectrum of sleep-disordered patients, not just those with clean presentations.

Finally, validity from independent biomarkers (REM latency, TST) confirmed that the criteria are capturing a recognizable NT1 sleep phenotype, not a statistical artifact of threshold selection.