

Distributed Autonomic-Type Symptom Burden Across Rule-Based Symptom Patterns

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BACKGROUND

Autonomic symptoms are frequently reported during benzodiazepine withdrawal. It remains unclear whether autonomic-type symptom burden is concentrated in a small group of patients or distributed across broader symptom patterns.

OBJECTIVE

To determine whether autonomic-type symptoms were concentrated in a small high-burden subgroup or distributed across multiple rule-based symptom patterns.

METHODS

- Baseline observational data from **39** patients enrolled in a specialty benzodiazepine withdrawal program.
- Structured **233-item** symptom questionnaire (0–10 severity scale).
- Symptoms mapped to five predefined symptom domains informed by proposed regulatory mechanisms: CRH/adrenergic, ENI, autonomic, BG/Cer, and MCAS-overlap.
- Rule-based symptom patterns were assigned using severe symptom tallies ($\geq 7/10$).
- Autonomic-type symptom burden across the rule-based patterns was evaluated using representative autonomic symptom constructs.
- Study caution:** Symptom data were patient-reported. Formal dysautonomia diagnosis, objective autonomic testing, and causal inference were beyond the scope of this observational study.

RESULTS

Autonomic-type symptoms were present across the CRH-heavy, ENI-heavy, and high-autonomic groups, with the greatest concentration in the high-autonomic group. (Figure 1).

ENI patients demonstrated broad moderate-to-severe autonomic involvement, while CRH-heavy patients also showed overlapping autonomic-type symptoms.

Across the full cohort, autonomic-type symptoms were commonly reported, whereas severe autonomic symptom burden occurred in a smaller subset of patients (Figure 2).

Together, these findings suggest autonomic-type symptoms are distributed across the rule-based symptom patterns, with the greatest concentration in the high-autonomic group (Figure 3).

FIGURE 1 Distributed Autonomic-Type Symptom Burden Across Rule-Based Symptom Patterns

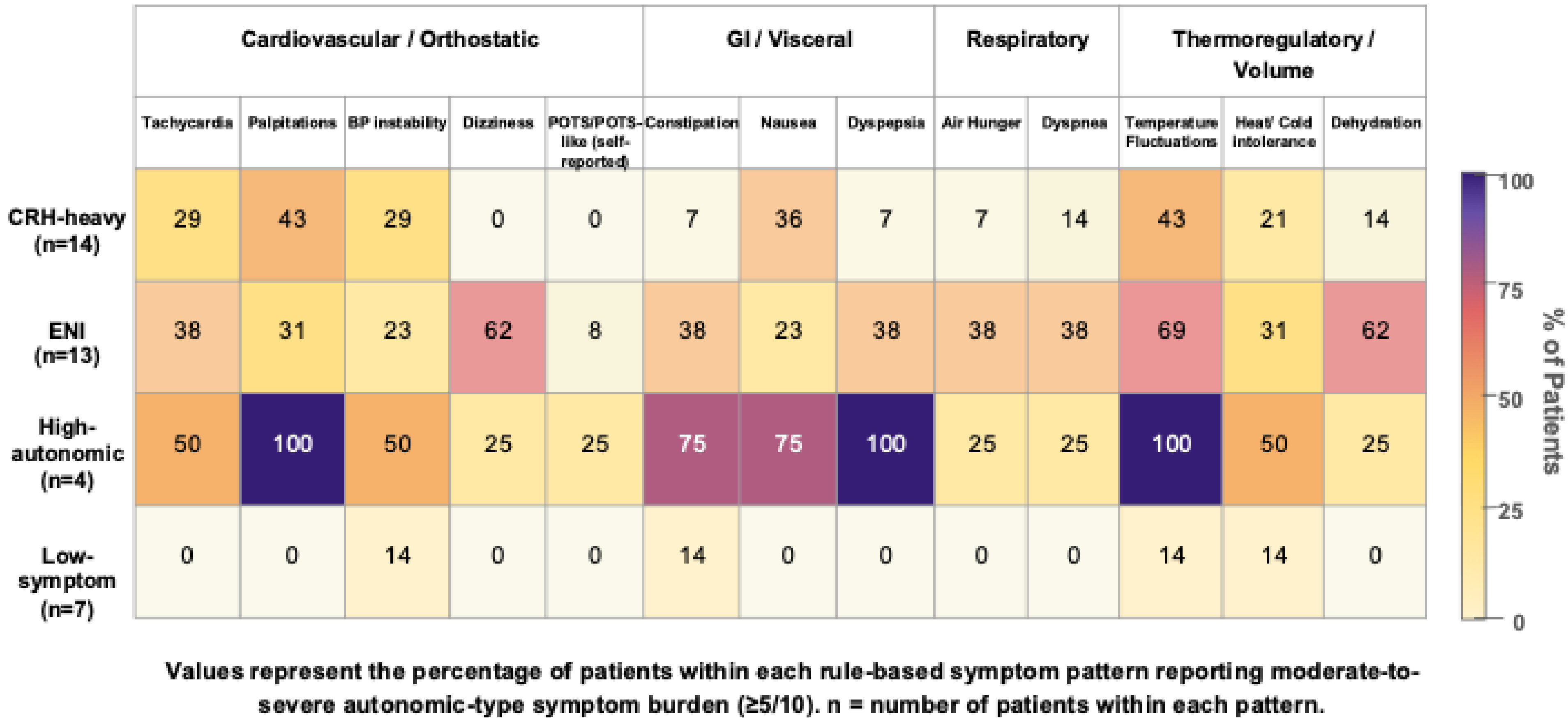
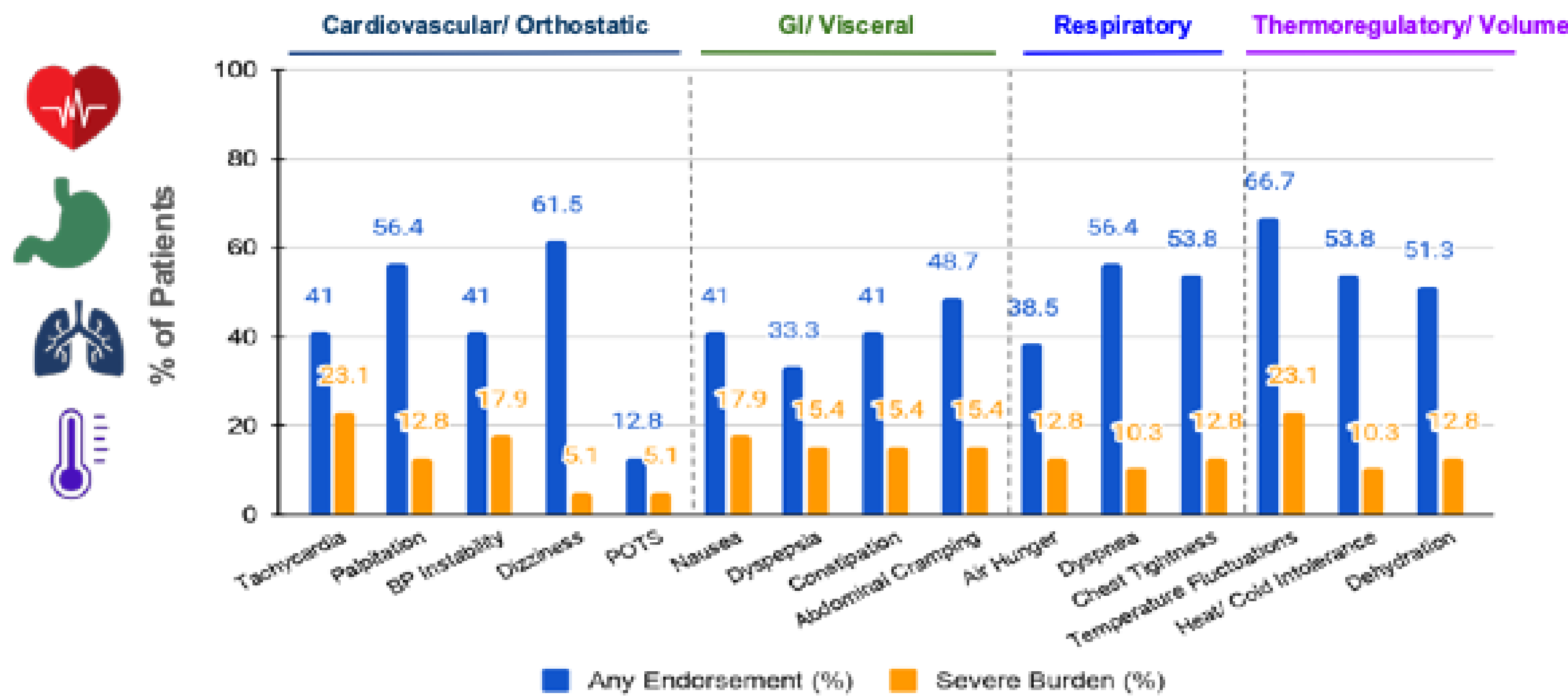


FIGURE 2 Autonomic Symptoms: Any Endorsement vs Severe Burden
Full Cohort (N= 39)



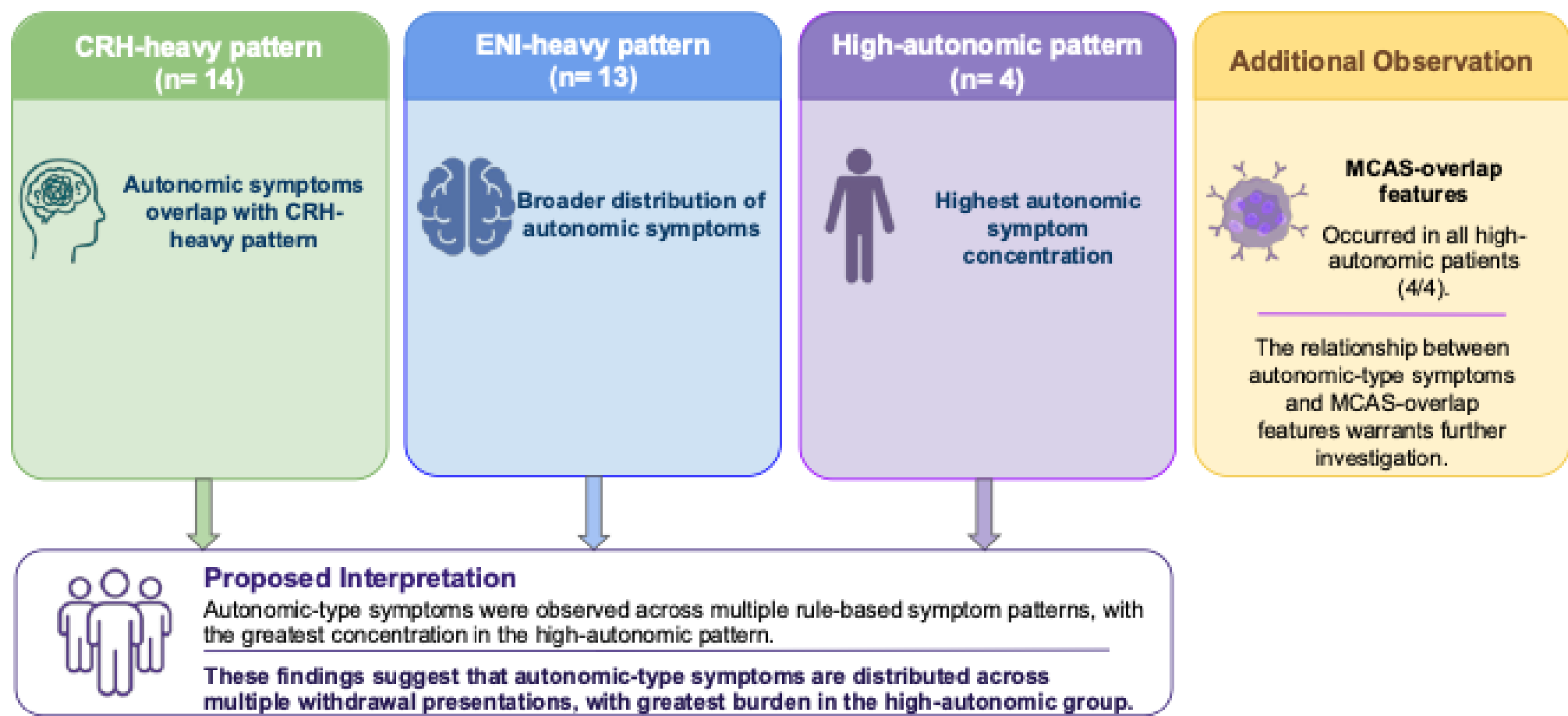
Any endorsement: symptom rated $\geq 1/10$ severity. Severe burden: symptom rated $\geq 7/10$ severity. Percentages represent the proportion of the full cohort (N = 39) reporting each representative autonomic symptom construct.

Key Finding: Autonomic-type symptoms were commonly endorsed across the cohort, but severe burden was lower for most symptoms. Temperature dysregulation was among the most frequently severe autonomic-type symptoms.

KEY FINDING

Autonomic-type symptoms were not confined to the group with the highest autonomic burden. Instead, autonomic-type symptom burden extended across the rule-based symptom patterns, with the greatest concentration in the high-autonomic group.

FIGURE 3 Clinical Interpretation of Autonomic-Type Symptom Burden



INTERPRETATION

Autonomic-type symptoms were distributed across multiple withdrawal groups, suggesting that autonomic symptom burden is not confined to patients in the high-autonomic group.

These findings suggest autonomic-type symptoms may be a cross-cutting feature of benzodiazepine withdrawal rather than an isolated subgroup.

CONCLUSIONS

- Autonomic symptoms were not limited to patients with high autonomic burden and should be considered across multiple withdrawal presentations.
- Symptom mapping may help identify patients for whom targeted autonomic evaluation could be considered.
- Future studies should compare symptom-derived autonomic patterns with objective autonomic testing

CONTACT / DISCLOSURES/PREPRINT

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Preprint:
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Distinct Phenotypes with Treatment Implications.
DOI:10.1101/2025.10.07.25336923

Note: This poster was updated in late July 2026 to reflect our current interpretation of the data, which emphasizes overlapping symptom organization rather than discrete phenotypes.