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## INTRODUCTION

- Xanomeline is a muscarinic agonist approved by the FDA for schizophrenia management.
- Xanomeline/trospium chloride is shown to reduce positive and negative symptom scale (PANSS) score by 5.9 – 17.4 points across trials.
- Clinical trials reported adverse events (AEs) include nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness and gastrointestinal reflux disease.
- Safety profile in routine clinical use remains inadequately evaluated.

## OBJECTIVE

We aimed to assess the real-world safety of Xanomeline/trospium chloride compared to an atypical antipsychotic (risperidone).

## METHODS

**Data source:** FDA Adverse Events Reporting System (FAERS) data from January 2024 to June 2025 and published clinical trials and case reports for both medications.

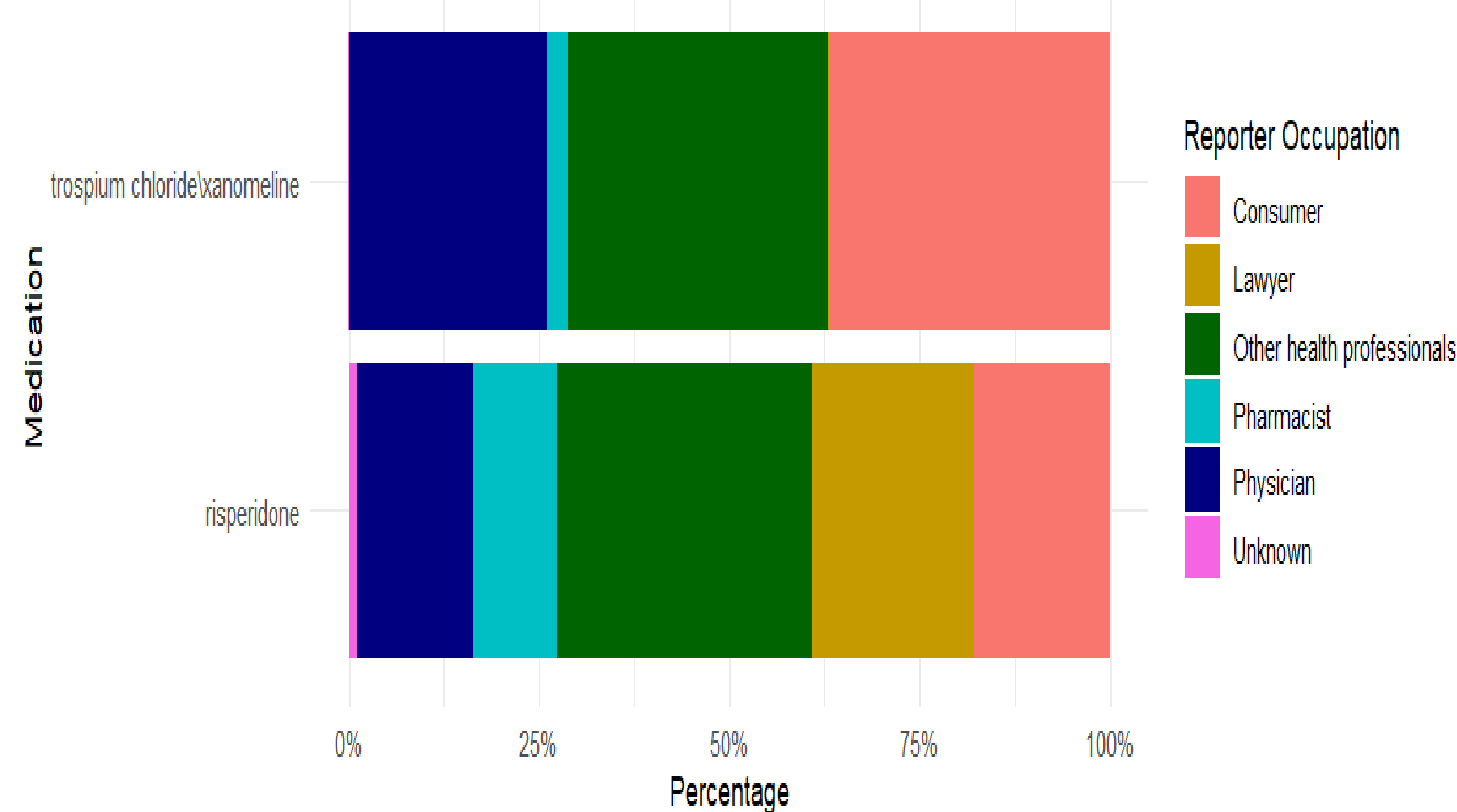
**Inclusion criteria:** Reports with Xanomeline/trospium chloride or risperidone as the primary suspect drug.

### Analysis:

- Potential adverse events (AEs) signals were detected by calculating reporting odds ratio (ROR), proportional reporting ratio (PRR), information component (IC) from Bayesian confidence propagation neural network, and empirical bayes geometric mean (EBGM) from multi-item gamma Poisson shrinker.
- A lexicon-based natural language processing pipeline was developed to detect clinical trials-published AE (5 publications) and compared to FAERS-reported AEs.

## RESULTS

**Figure 1: Adverse Events Reporter Occupation by Medication.**

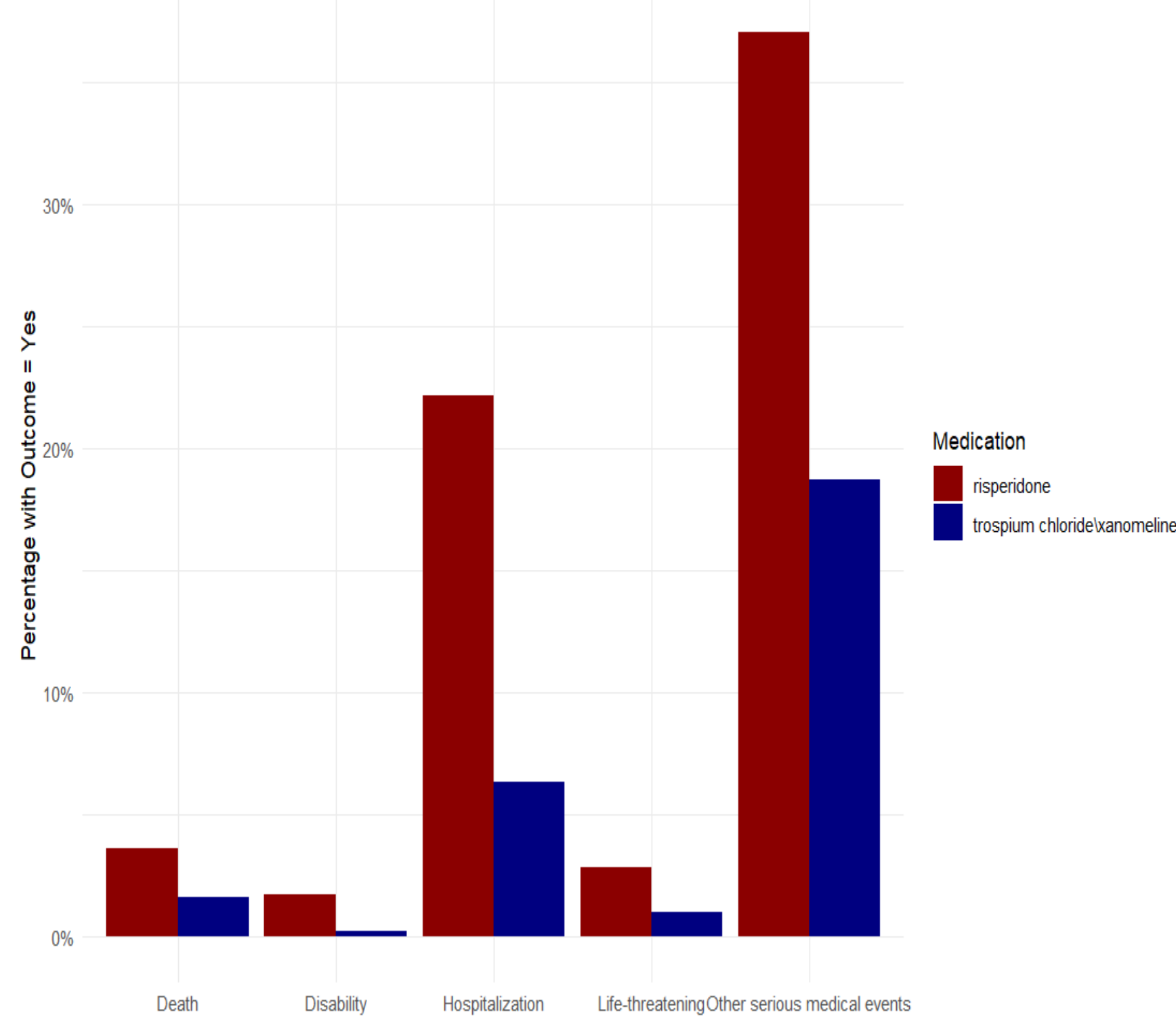


**Table 1: Demographic characteristics by Medication Type**

Variables	Xanomeline/trospium chloride n(%) N = 801	Risperidone n(%) N = 5,986	p-value*
<b>Sex</b>			<0.0001
Male	366 (45.70)	3566 (59.60)	
Female	263 (32.80)	1361 (22.70)	
Unknown	172 (21.50)	1059 (17.70)	
<b>Age group</b>			<0.0001
Neonates	0 (0.00)	9 (0.20)	
Infants	0 (0.00)	7 (0.10)	
Children	1 (0.10)	648 (10.80)	
Adolescents	3 (0.40)	464 (7.80)	
Adults	371 (46.30)	1022 (17.10)	
Elderly	32 (4.00)	238 (4.00)	
Unknown	394 (49.20)	3598 (60.10)	
<b>Indications/Reason for Use</b>			<0.0001
Schizophrenia, schizoaffective disorders, & psychotic disorders	479 (59.80)	1195 (20.00)	
Other mental health disorders	6 (0.70)	1447 (24.20)	
Neurodevelopmental/neurocognitive disorder	0 (0.00)	285 (4.80)	
Accidental use/medication error	0 (0.00)	49 (0.80)	
Intentional misuse	0 (0.00)	49 (0.80)	
Other indications	0 (0.00)	52 (0.90)	
Unknown	316 (39.50)	2902 (48.60)	

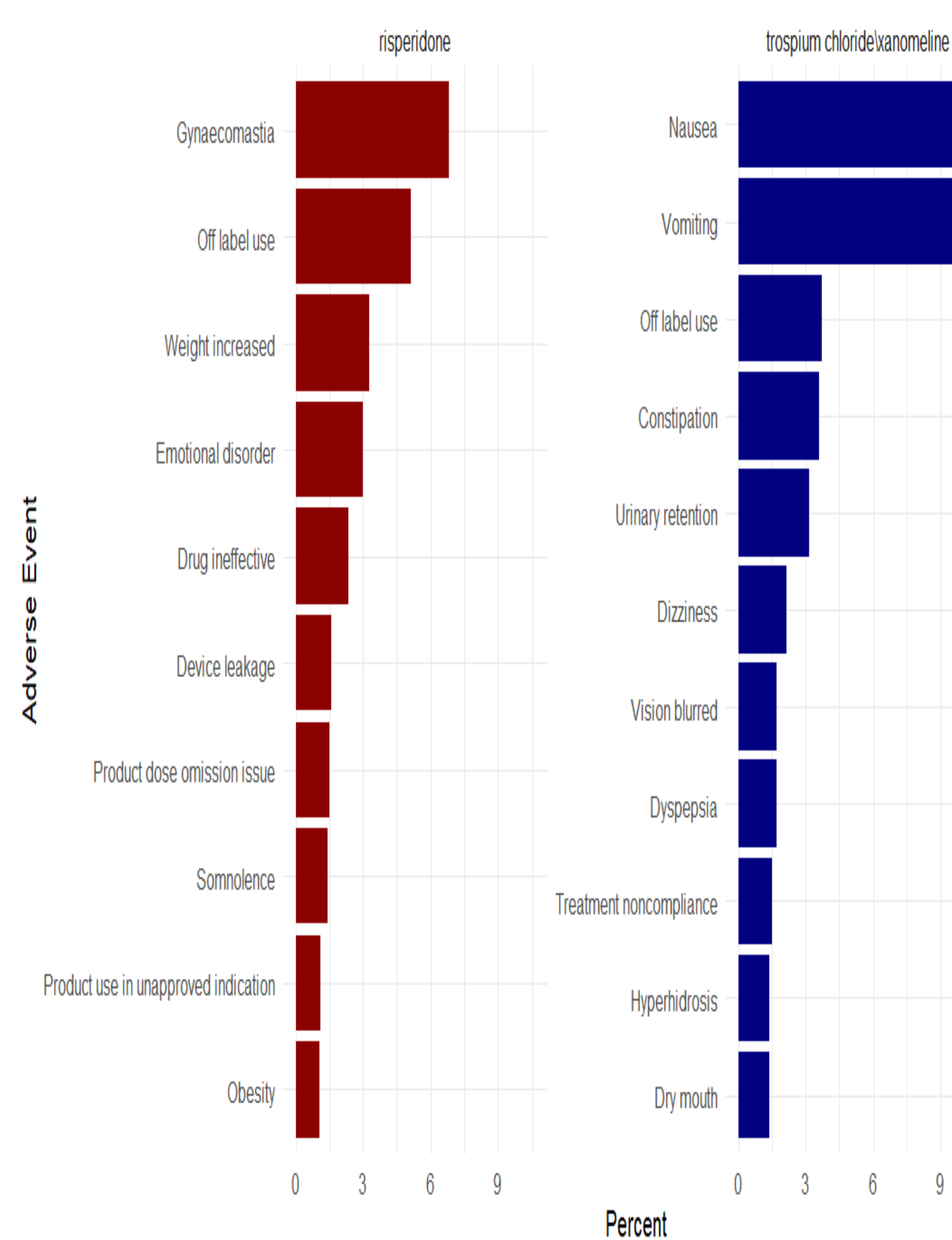
\*Pearson's Chi-square test without continuity correction was conducted.

**Figure 2: Reported Case Outcomes by Medication**

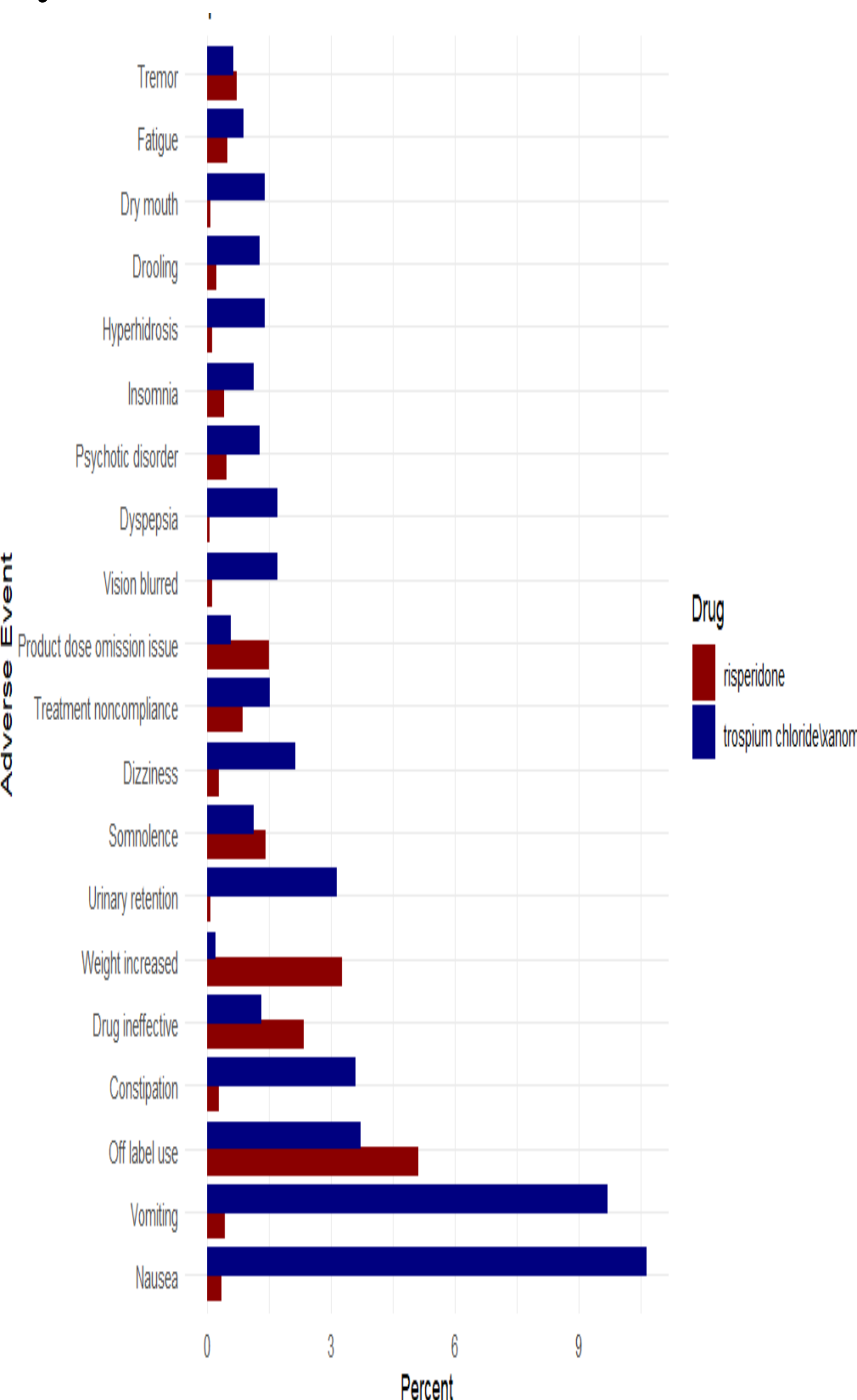


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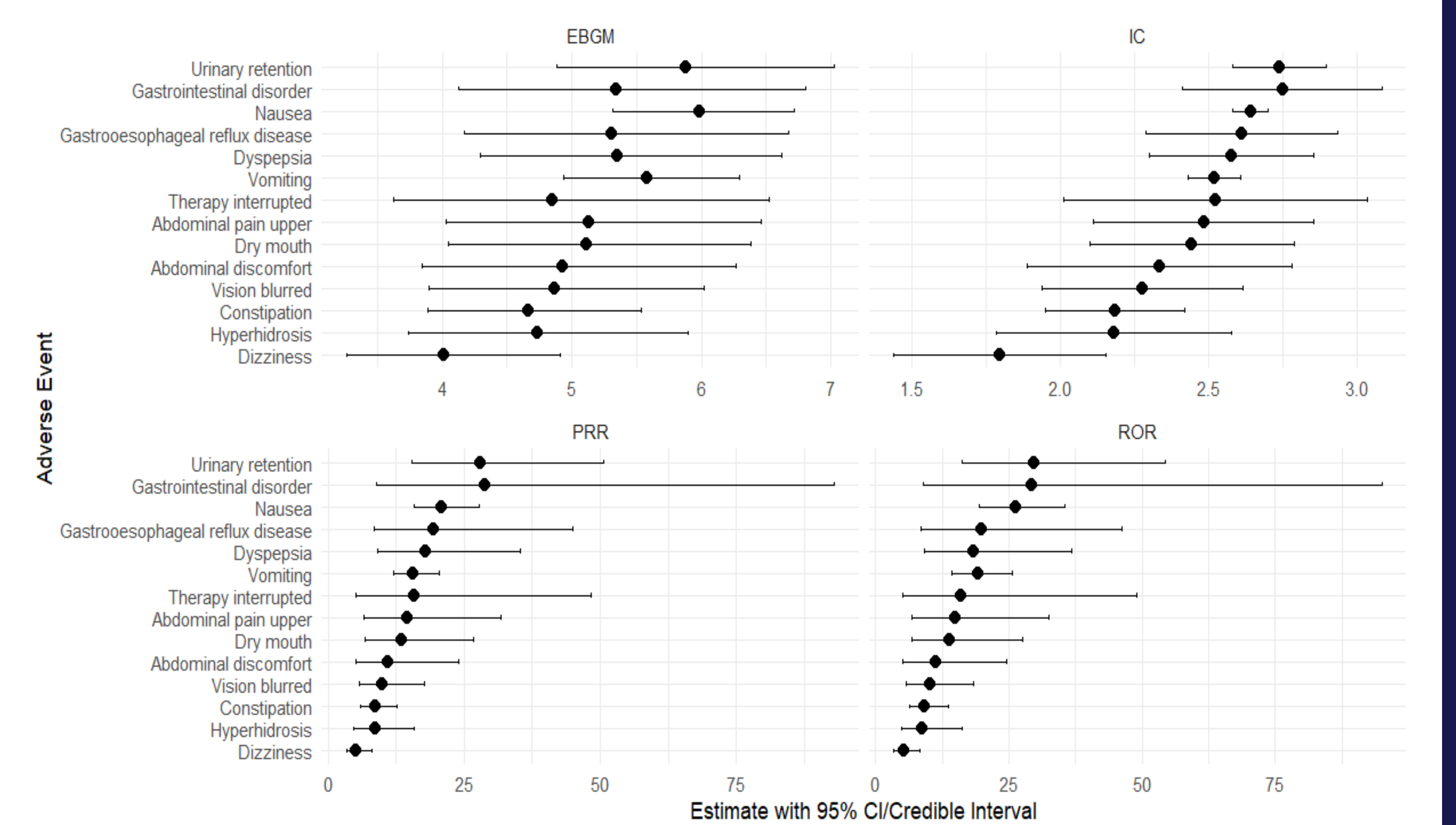
**Figure 3: Top 10 Adverse Events per Medication.**



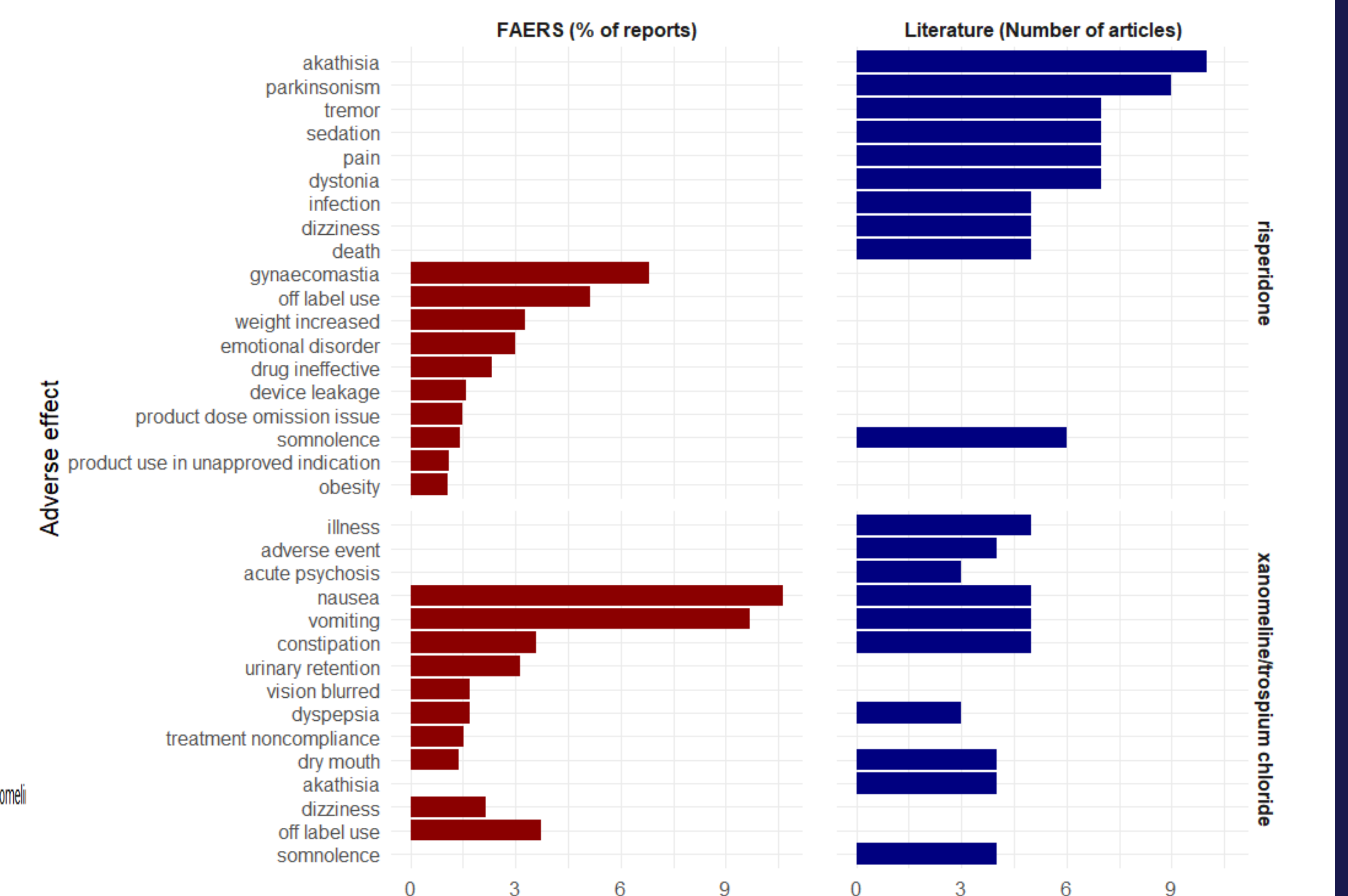
**Figure 4: Top 20 Common Adverse Events by Medication.**



**Figure 5: Potential adverse events signal detection for Xanomeline/trospium chloride.**



**Figure 6: Comparison of FAERS- Vs. Published Literature-reported Adverse Events.**



## DISCUSSION

Real-world safety profile of xanomeline/trospium chloride differed from risperidone. There was concordance between FAERS- and trial-reported AEs for xanomeline/trospium chloride. However, the FAERS analysis revealed additional AEs which were not detected the NLP analysis.

## FUTURE DIRECTION

- Longitudinal studies using EHR data.
- Large language models based natural language processing pipeline.

