

EXPLORING THE IMPACT OF PATIENT CHARACTERISTICS AND REPORTING PERIOD ON ADVERSE DRUG WITHDRAWAL EVENT SIGNALS IN THE FAERS DATABASE: A STRATIFIED DISPROPORTIONALITY ANALYSIS STUDY

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INTRODUCTION

Pharmacovigilance spontaneous reporting system databases play an important role in the post-marketing setting (1). The pharmacovigilance system is routinely used to detect new, rare, and severe adverse drug reactions (ADRs) (2).

Disproportionality analysis is a quantitative method that can be applied to such databases for signal detection (to identify new, rare, or previously under-recognised risks associated with drugs) (3,4).

Although the pharmacovigilance system has been used to advance our understanding of medication safety and ADRs caused by prescribing of medications, there appears to be limited use of this system for **adverse drug withdrawal events (ADWEs)** caused by discontinuation or deprescribing (reducing or stopping unnecessary or harmful medications).

RESULTS

Of 14,940,210 reports, **105,026** included drug-event pairs related to ADWEs (reports with relevant preferred terms containing "withdraw") (Table 1).

TABLE 1: Proportion of ADWEs reports (2014–2023)

Variables	FDA-FAERS n(%)
Sex	
Female	49,615 (47.2)
Male	45,554 (43.3)
Other/Unknown	9,857 (9.4)
Age group	
Adult (18–64 years)	27,074 (25.7)
Elderly (65+ years)	6,284 (5.9)
Other/Unknown	71,668 (68.2)
Reporting time	
2014–2015	10,680 (10.2)
2016–2017	15,535 (14.8)
2018–2019	14,383 (13.7)
2020–2021	34,277 (32.6)
2022–2023	30,151 (28.7)

Top signals for ADWEs by age group

Among top 50 drugs, baclofen, duloxetine and naloxegol were associated with positive signals for ADWEs in both elderly and adult populations. Thiothixene (n=7; IC=3.8; PRR=208.1; ROR=353.1), nefazodone (n=9; IC= 4.1; PRR= 146.8; ROR= 206.4) and buprenorphine/naloxone (n=59; IC= 5.7; PRR= 95.5; ROR = 117.2) showed a stronger signals in the elderly versus adults. Whereas, paroxetine (n=460; IC= 4.4; PRR= 22.7; ROR = 25.8) showed a stronger signal in adults versus elderly (n=42; IC= 3.5; PRR= 12.9; ROR = 13.1) (Figure 1).

Top signals for ADWEs by sex group

A sex-based difference was observed with betamethasone/fusidic acid and clobetasone followed by hydromorphone, duloxetine and oxycodone showing a larger positive signal in females than males (Figure 2). In males hydrocodone, morphine, naloxone and acetysalicylic acid/oxycodone had a stronger signal in males versus females (Figure 3). Moreover, buprenorphine/naloxone, baclofen and acetaminophen/propoxyphene were associated with positive signals for ADWEs in both sex group (Figure 4).

CONCLUSIONS

- ADWEs due to some medications have varied over time, and may differ based on age and sex.
- Elderly populations and female sex showed strong signals for ADWEs.
- Rare ADWEs were identified for tiotixene and nefazodone in elderly patients.

Implications: Monitor drugs with strong ADWE signals, consideration of age- and sex-based differences in clinical practice, implementation of continuous pharmacovigilance activities, and investigation of underlying mechanisms to develop safer, evidence-based deprescribing protocols.

OBJECTIVE

To perform disproportionality analysis to compare how reporting signals for adverse drug withdrawal events (ADWEs) differ based on patient characteristics (age, sex) and over time

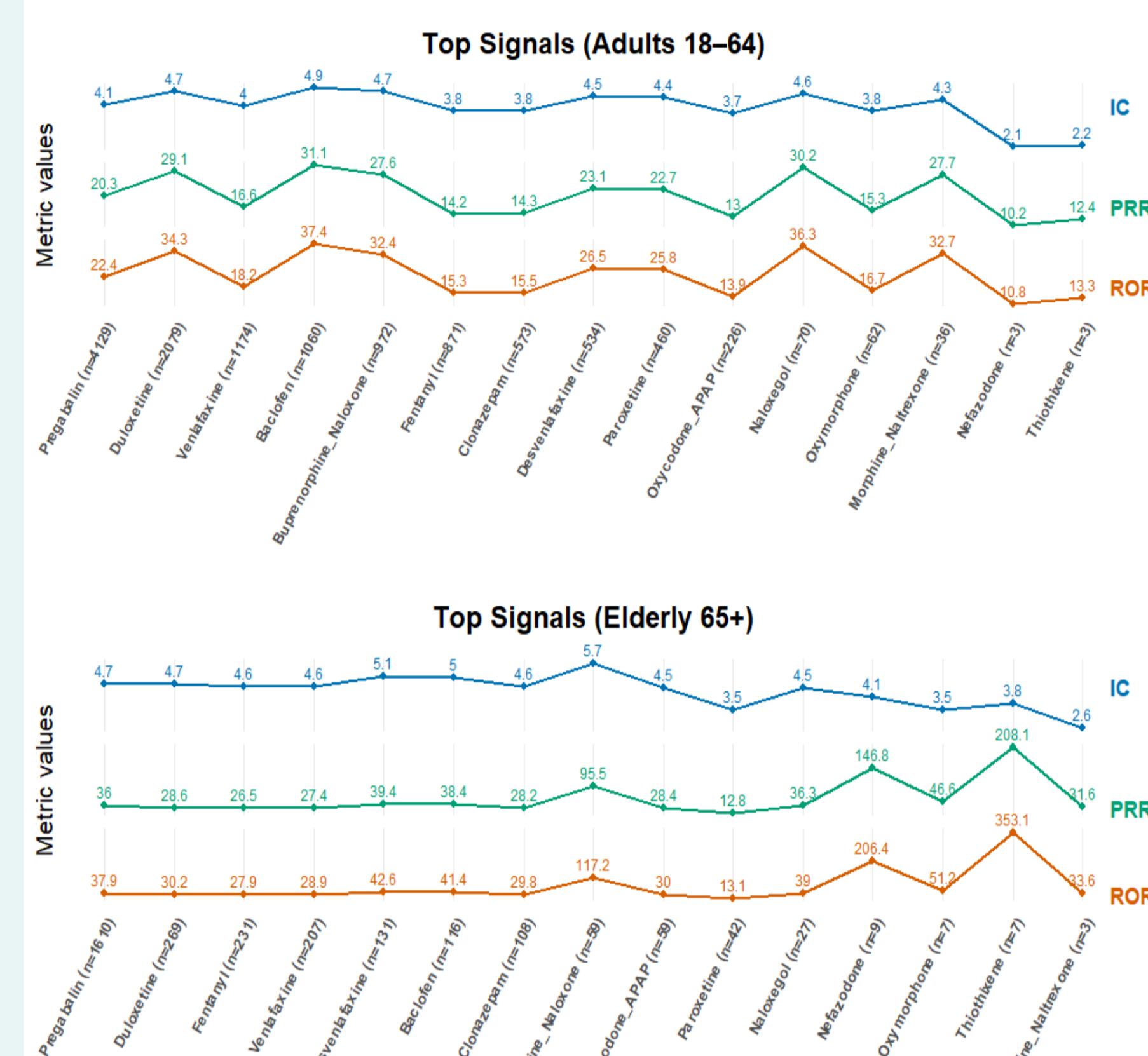


FIGURE 1: Top drugs associated with positive signal by age

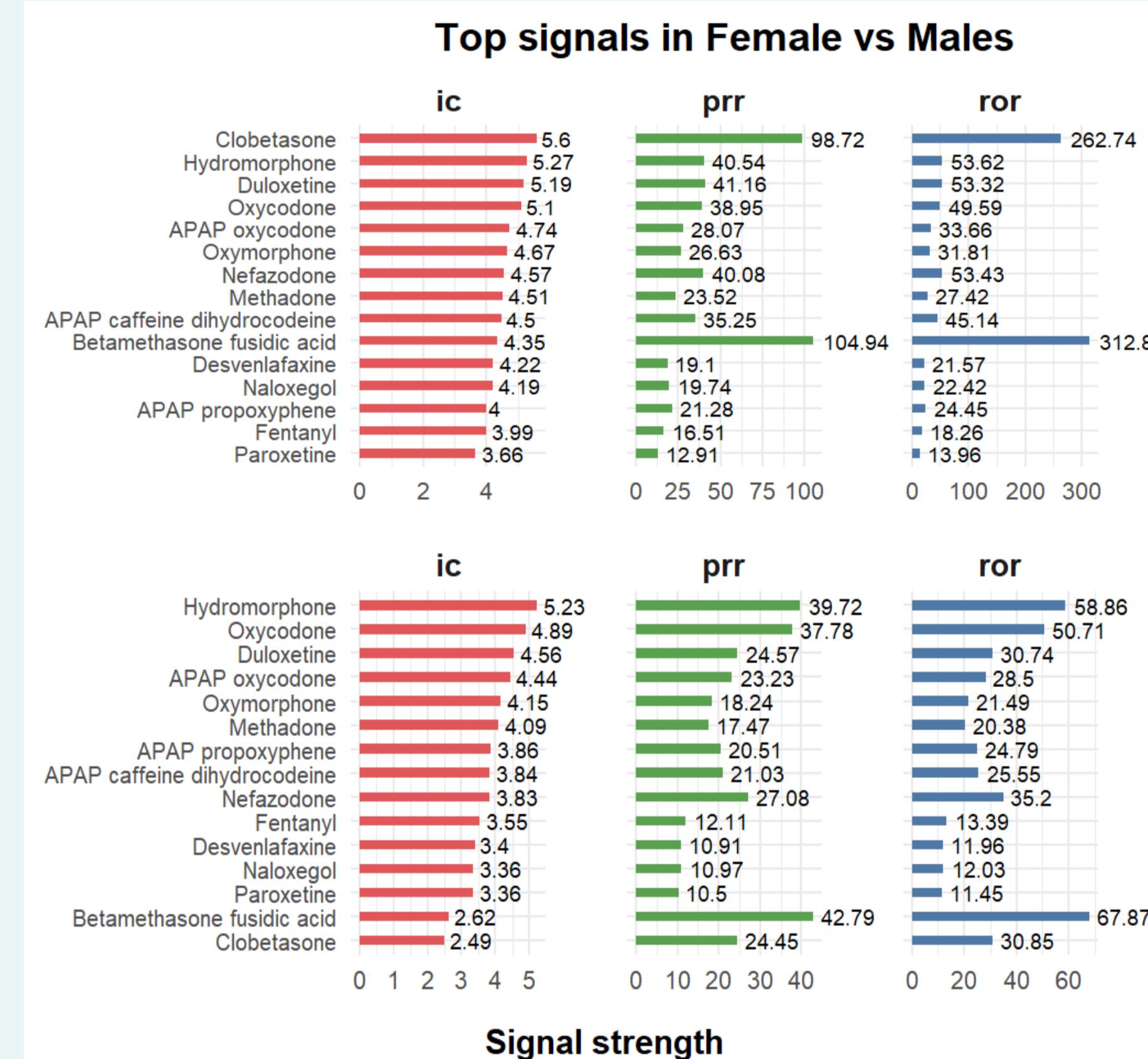


FIGURE 2: Top drugs with positive signals in females

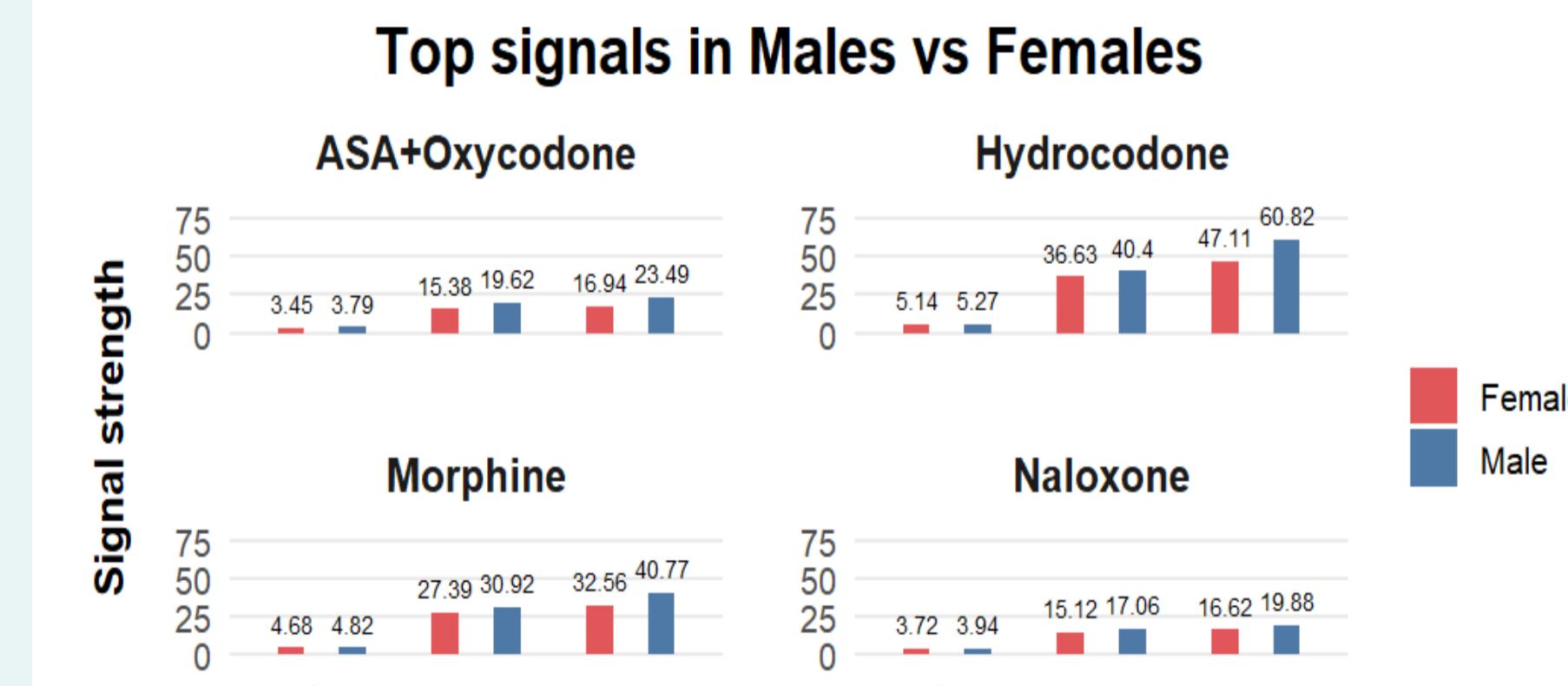


FIGURE 3: Top drugs with positive signals in males

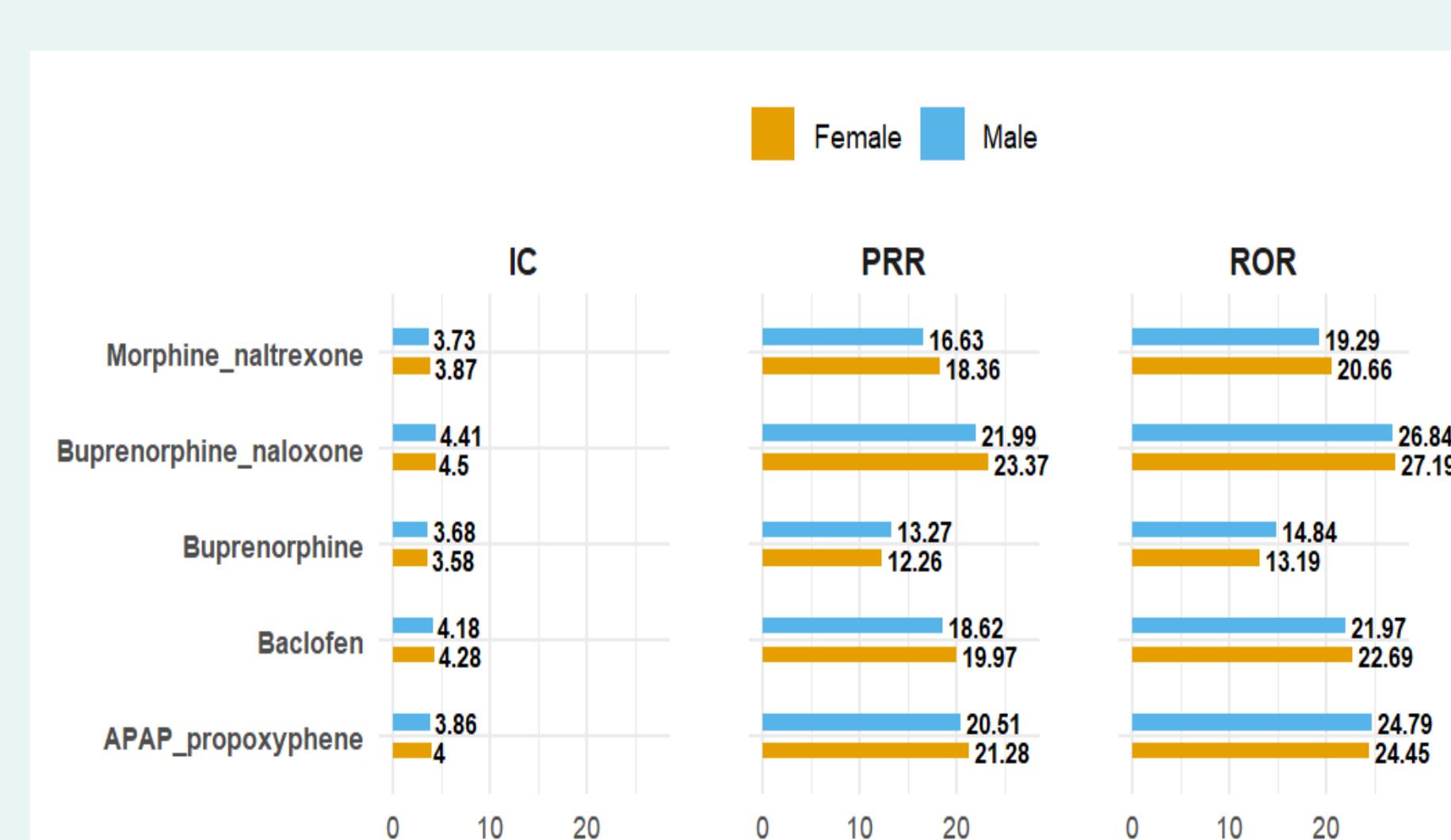
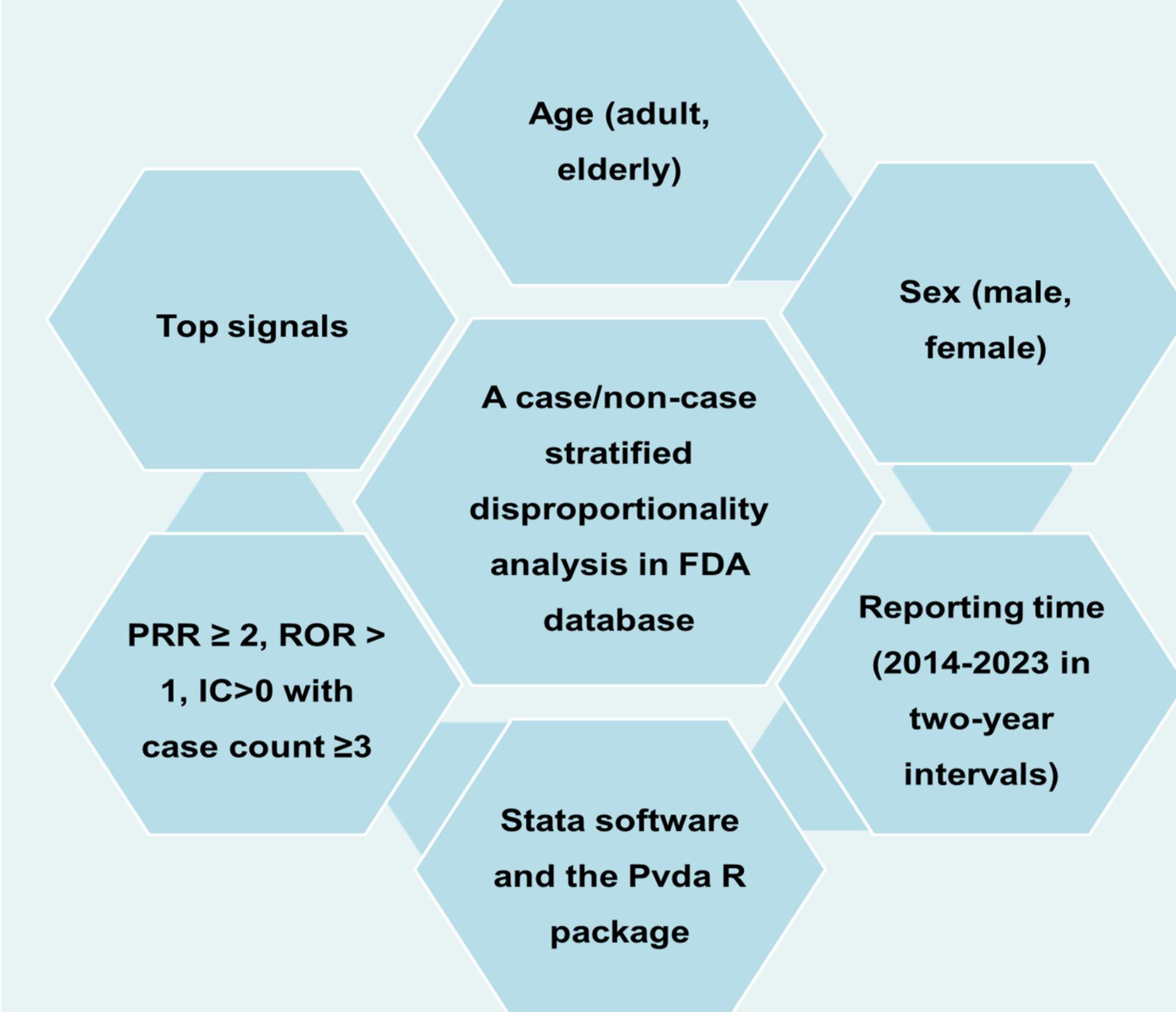


FIGURE 4: Positive signals in both males and females

METHOD



Top signals for ADWEs by time period

Analysis over time showed that among the drugs with strongest signals were duloxetine peaking in 2016-2017, hydrocodone and hydromorphone in 2022-2023, oxycodone in 2020-2021, and baclofen in 2018-2019 (Figure 5).

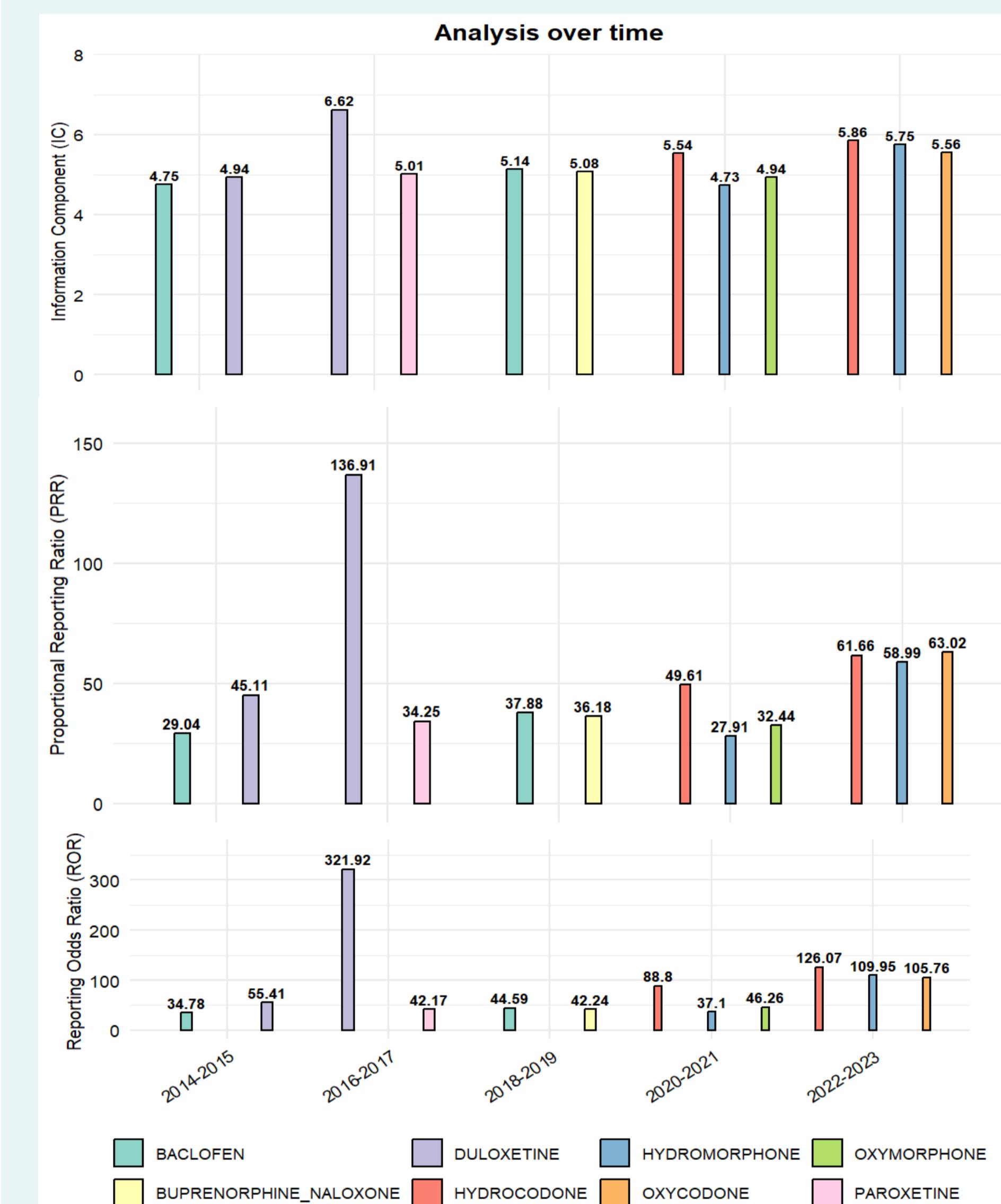


FIGURE 5: Top signal over time in FDA database

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