RE06

Early Detection of Adverse Events Associated with Antihypertensive Medications: A Real-world Evidence Study Using FAERS Data

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Introduction

Randomized controlled trials (RCTs) are essential for establishing drug efficacy and initial safety but have limited ability to detect rare, delayed, or population-specific adverse events due to controlled settings and short follow-up.

Real-world evidence (RWE) complements RCTs by leveraging routinely collected healthcare data, including spontaneous adverse event reporting systems, to evaluate drug safety in routine clinical practice.

RWE plays an increasingly important role across therapeutic areas such as cardiology, oncology, endocrinology, and infectious diseases, where treatments are often long-term and patient populations are heterogeneous.

Antihypertensive medications, due to their widespread and chronic use, are well suited for RWE-based safety surveillance, as even infrequent adverse events may have significant public health impact.

This study evaluates post-marketing safety signals for five commonly prescribed antihypertensive agents using FAERS data, applying disproportionality analysis for early signal detection.

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Randomized Controlled Trials vs Real-world Evidence

Randomized Controlled Trials (RCTs)	Real-world Evidence (RWE)
Selected and homogeneous patient populations	Broad and heterogeneous patient populations
Strict inclusion and exclusion criteria	Routine clinical practice settings
Controlled and experimental environments	Real-world healthcare environments
Limited sample sizes	Large-scale patient populations
Short to moderate follow-up	Long-term treatment exposure
Focus on efficacy and initial safety	Focus on post-marketing safety and effectiveness
Limited detection of rare or delayed AEs	Enables detection of rare and delayed AEs

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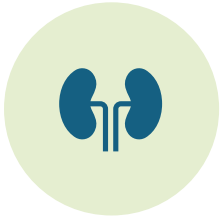
Why FAERS for Post-marketing Safety Surveillance



Randomized controlled trials are essential for establishing efficacy and initial safety but are not designed to detect rare, delayed, or population-specific adverse events.

Limited sample sizes, controlled study conditions, and relatively short follow-up durations restrict the ability of RCTs to fully characterize long-term drug safety.

Post-marketing surveillance is therefore critical to monitor medication safety once drugs are widely used in routine clinical practice.

The FDA Adverse Event Reporting System (FAERS) serves as a key real-world data source for ongoing pharmacovigilance by capturing spontaneous adverse event reports from diverse patient populations.

FAERS enables early identification of potential safety signals, supporting regulatory decision-making and continuous risk–benefit evaluation.

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Data Source & Study Design

Safety data were obtained from the FDA Adverse Event Reporting System (FAERS), including all quarterly releases from January 2018 to December 2023.

The analysis utilized FAERS Demographics, Drug, Reaction, Indication, Outcome, and Therapy datasets.

A retrospective observational study design was applied to evaluate post-marketing safety signals.

For each case, only the most recent version was retained to ensure accurate case identification.

The study focused on five commonly prescribed antihypertensive medications.

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Disproportionality Analysis

Disproportionality analysis was conducted to identify potential drug–adverse event associations.

Only drugs reported as Primary Suspect were included to reduce confounding.

Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR) were used to quantify disproportional reporting.

The chi-square statistic was applied to assess the statistical strength of observed associations.

Drug-adverse event pairs meeting predefined thresholds were considered potential safety signals.

Disproportionality Metrics and Signal Detection Criteria

METRIC	DESCRIPTION	THRESHOLD
PRR	Proportional Reporting Ratio; measures disproportionality in reporting	≥ 2
ROR	Reporting Odds Ratio; compares odds of AE reporting for a drug vs others	> 1 with 95% CI lower bound > 1
Chi-square	Statistical test for association strength	≥ 4
Minimum Reports	Ensures robustness of signal	≥ 3 case reports

Only drug–AE pairs meeting all criteria were considered valid safety signals.

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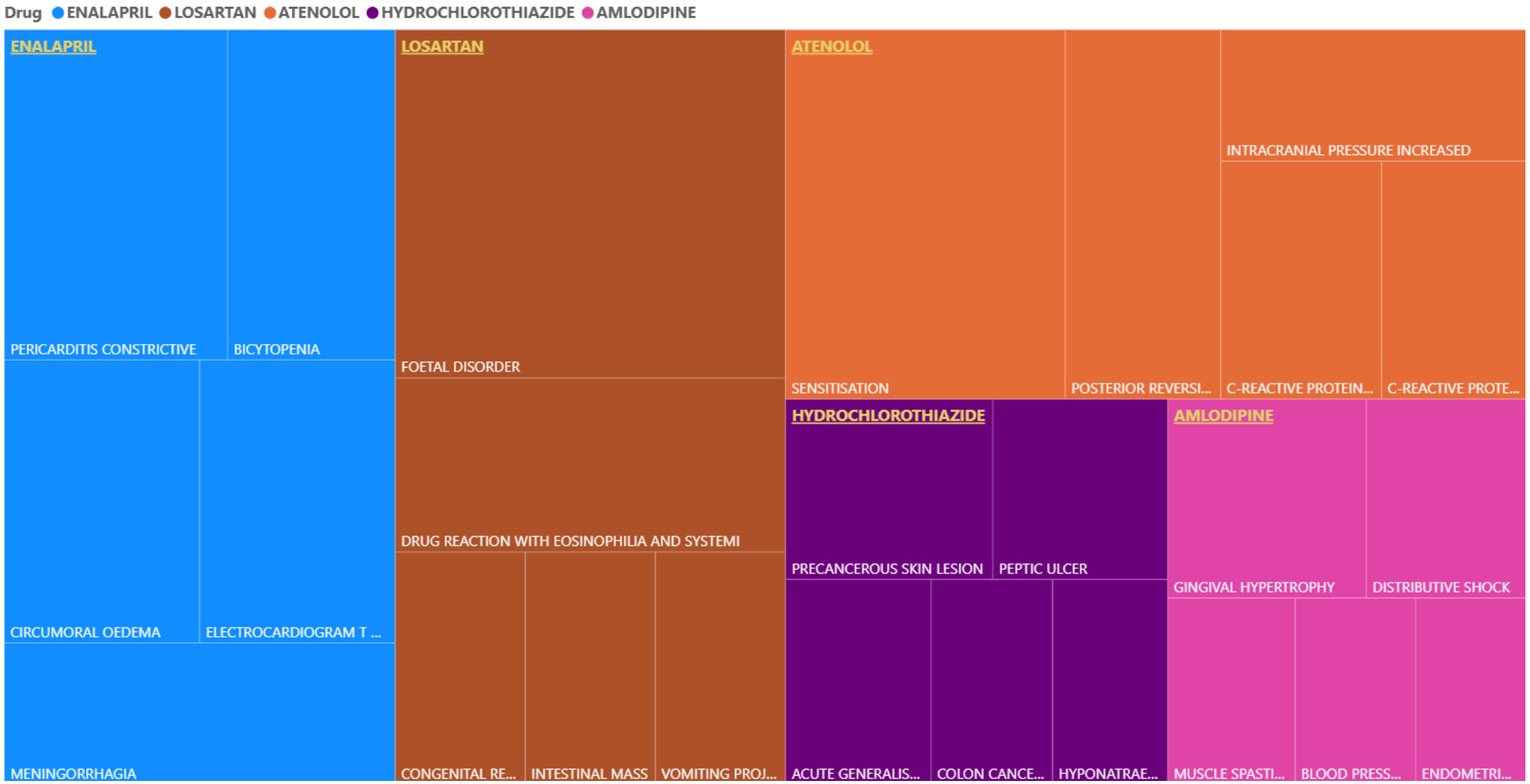
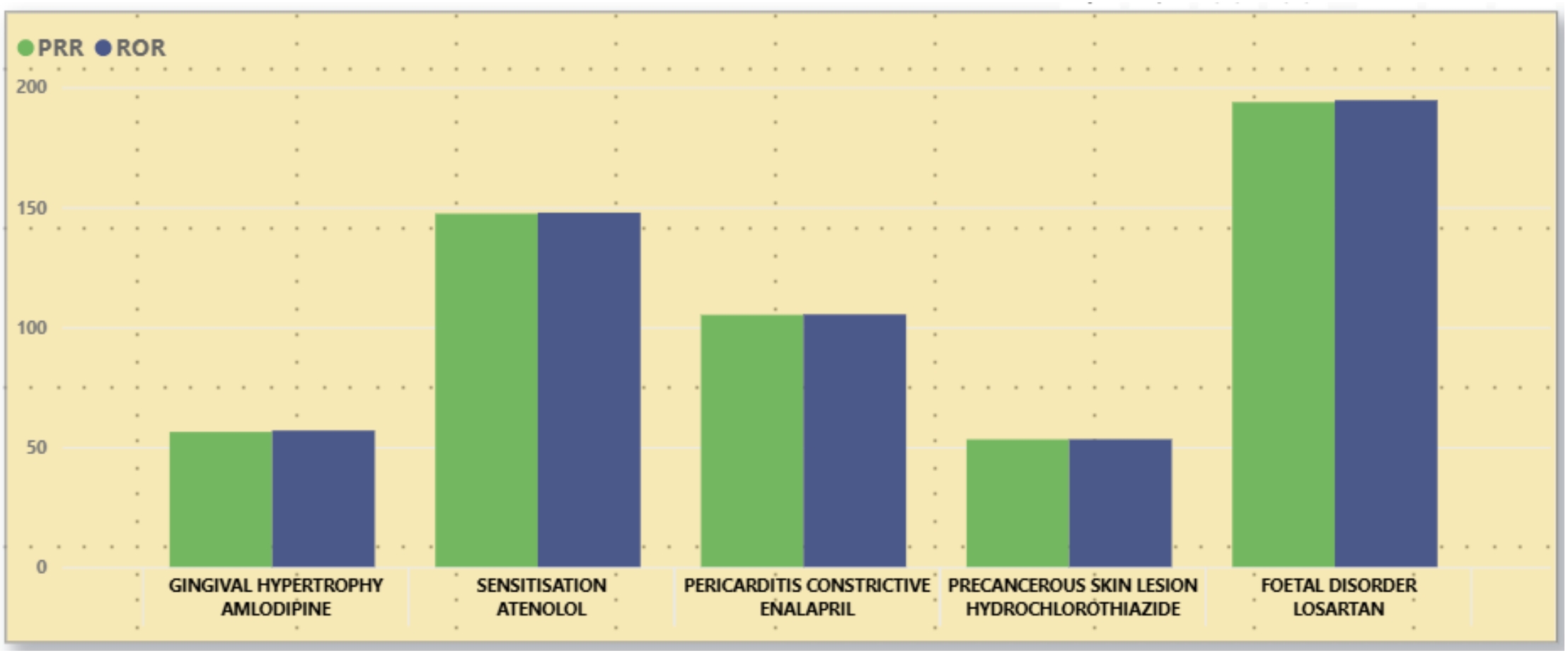
Results Visualization

Heatmap of Statistically Significant Drug-AE Signals



Results Visualization

Top AE Signals per Antihypertensive Agent



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Key Safety Signals Identified

Amlodipine showed strong disproportionality signals involving gingival, musculoskeletal, and hemodynamic adverse events, consistent with calcium channel blocker pharmacology.

Losartan demonstrated notable signals related to foetal, congenital, and hypersensitivity-associated adverse events, reflecting established safety considerations for angiotensin receptor blockers.

Atenolol was associated with neurological and cardiovascular-related safety signals, aligned with beta-blocker pharmacologic effects.

Enalapril exhibited signals involving cardiovascular, hematologic, and edema-related adverse events, consistent with ACE inhibitor safety profiles.

Hydrochlorothiazide showed significant signals for dermatologic, gastrointestinal, oncologic, and electrolyte-related adverse events, reflecting known thiazide-associated risks.

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Summary

Disproportionality analysis of FAERS data revealed consistent safety signals for commonly used antihypertensives. Sensitisation with Atenolol and Foetal disorder with Losartan were among the prominent findings, aligning with known safety profiles.

The application of real-world evidence enabled early detection and quantification of adverse event patterns across a large post-marketing population. These insights complement traditional clinical trial findings and support the ongoing use of pharmacovigilance tools to monitor drug safety in broader clinical settings.

This analysis reinforces the value of integrating RWE into regulatory science and lays the groundwork for further exploration using additional real-world data sources.

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QUESTIONS?

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