

Adherence to Mineralocorticoid Receptor Antagonists for Uncontrolled and Treatment–Resistant Hypertension: A Targeted Literature Review and Meta–Analysis

Robert T. Olender¹, Zarmina Khankhel¹, Grace Goldsmith-Martin¹, Aaron Crowley¹, Siwei Zhu¹, Kay Sadik²
¹Genesis Research Group, Hoboken, NJ, USA, ²Mineralys Therapeutics, Inc., Radnor, PA, USA

INTRODUCTION

- Hypertension affects approximately 120 million adults in the US, including ~33 million treated adults who may require treatment intensification to achieve blood pressure (BP) control.¹
- Uncontrolled hypertension (uHTN) and treatment-resistant hypertension (rHTN) are associated with considerable cardiovascular morbidity and healthcare burden.^{2,3}
- Dysregulated aldosterone is associated with increased cardiorenal risk and is an important therapeutic target in uHTN and rHTN.⁴
- Mineralocorticoid receptor antagonists (MRAs), particularly spironolactone, are recommended for rHTN; however, tolerability concerns and poor adherence may limit their effectiveness in clinical practice.⁵⁻⁷

OBJECTIVES

To synthesize observational evidence on real-world MRA adherence among adults with uHTN or rHTN and explore potential sources of variation in reported adherence.

METHODS

Study Design and Search Strategy

- A targeted literature review (TLR) and meta-analysis were conducted to identify and synthesize observational evidence on MRA adherence in adults with uHTN or rHTN.
- A structured electronic literature search of Embase (Ovid) was conducted on December 8, 2025, covering database inception (1974) to the search date.
- The search combined terms relating to uHTN/rHTN, MRAs, and adherence/non-adherence.
- Records were screened according to prespecified population, intervention, comparator, outcomes, and study design (PICOS) criteria by one reviewer, with quality assurance by a second reviewer.

Eligibility and Outcomes

- Eligible observational studies included adults with uHTN or rHTN and reported adherence to spironolactone specifically or MRAs at the class level, or reasons for non-adherence.
- Study characteristics, including evaluable population, MRA category, adherence definition and assessment method, were extracted.
- The primary outcome was the proportion of patients classified as adherent among those evaluable for MRA adherence.
- Secondary outcomes included reasons for adherence and factors associated with adherence/non-adherence, and were summarized narratively.

Statistical Analysis

- Adherence proportions were pooled using a random-effects meta-analysis, with a logit transformation applied to the adherence proportions.
- Robustness was assessed using a Freeman-Tukey double-arcsine sensitivity analysis.
- Between-study heterogeneity was assessed using τ^2 , I^2 , and Cochran Q.
- Exploratory subgroup analyses examined hypertension population (uHTN vs rHTN), MRA category (spironolactone-specific vs class-level), and adherence assessment method.

RESULTS

Study Selection

Of 384 records screened, 93 full texts were retrieved, and 12 studies met the eligibility criteria and were included in the adherence evidence base.

Study Characteristics (Figure 1)

Of the 12 included studies:

- Publication:** 10 (83%) full-text; 2 (17%) conference abstracts
- Geography:** 9 (75%) Europe; 1 (8%) US; 1 (8%) multi-regional; 1 (8%) unclear
- Population:** 9 (75%) rHTN; 3 (25%) uHTN. No studies combined both rHTN and uHTN.
- MRA:** 7 (58%) class-level; 5 (42%) spironolactone-specific
- Adherence assessment:** 10 (83%) biochemical/combined biochemical; 2 (17%) pharmacy-based

Primary Meta-Analysis (Figure 2)

- Study level-adherence ranged from 5.2% to 85.2%; 9 of 12 studies reported adherence below 60%.
- In the primary random-effects meta-analysis using a logit transformation, the pooled adherence proportion was 39.1% (95% CI, 19.5%-63.1%).
- Between-study heterogeneity was $\tau^2=2.2422$; $I^2=98.5\%$; $Q(11)=711.98$; $P<.001$.
- The variability in estimates indicates that the magnitude of MRA adherence differed considerably across the populations and settings represented in the available evidence.

Figure 3. Sensitivity Analysis

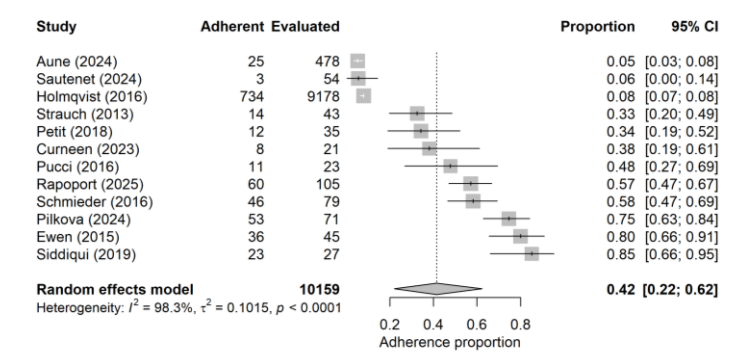


Figure 1. Characteristics of Included Studies (N = 12)

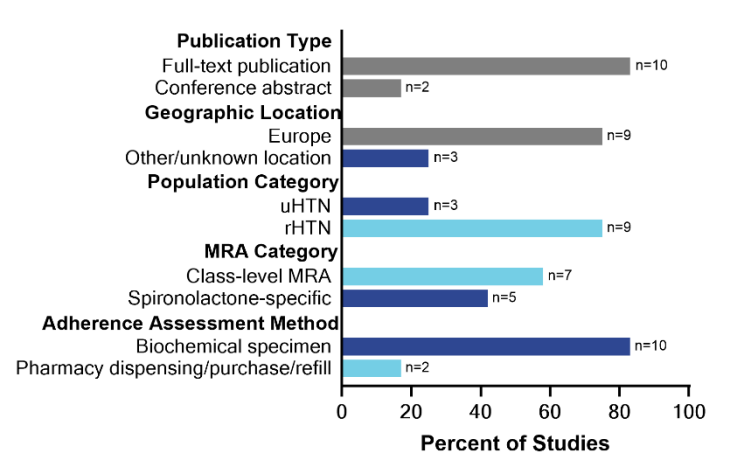
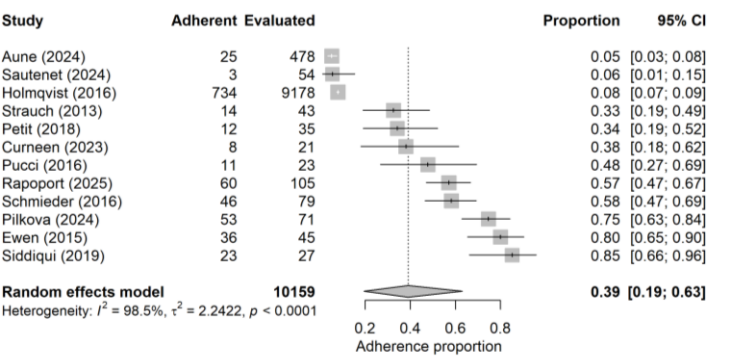


Figure 2. Primary Random-effects Meta-analysis of Pooled Adherence



Sensitivity Analysis (Figure 3)

- The Freeman-Tukey double-arcsine sensitivity analysis produced a similar pooled estimate of 41.5% (95% CI, 22.1%-62.4%),
- Sensitivity analysis produced a similar pooled adherence estimate to the primary analysis (41.5% vs 39.1% in the primary analysis) with substantial between-study heterogeneity ($I^2=98.2\%$); $P<.0001$
- The overall numerical result was therefore not affected by the transformation used.

Acknowledgements

- Medical writing and editorial assistance were provided by Kate Rogers of Genesis Research Group (Hoboken, NJ).
- This study was funded by Mineralys Therapeutics.

Exploratory Subgroup Analyses (Figure 4)

- Exploratory subgroup analyses showed no statistically significant differences in pooled adherence according to hypertension population, MRA category, or adherence assessment method (all $P>0.05$).
- Subgroup findings should be interpreted cautiously given the small number of studies within some groups.

Reasons for Non-adherence

- Evidence on reasons for and factors associated with non-adherence was narratively summarized from individual studies and was not included in the meta-analysis.
- One included study evaluated antihypertensive treatment broadly rather than MRAs specifically. Among 25 patients who acknowledged non-adherence, the most frequently reported reasons were adverse effects (36%; n=9) and forgetfulness (32%; n=8).⁸
- In the same study, no reason was documented for 6 patients; other reported reasons included running out of medication, misunderstanding instructions, prescription cost, and apathy.⁸

Factors Associated with Adherence/Non-adherence

- Three studies reported potential associations between lower adherence and younger age, shorter hypertension duration, greater medication burden, and outpatient care; however, findings were sparse and not consistently demonstrated across studies.

Limitations

- Reasons for non-adherence and associated factors were sparsely reported across the literature identified and, when reported, were generally not MRA-specific.
- Given the targeted nature of the literature review, the search may not have captured all relevant evidence, although the limited evidence base is consistent with previous literature reviews of MRA adherence.⁹

CONCLUSIONS

- Across the available real-world evidence, adherence to MRA therapy was frequently suboptimal among patients with uHTN and rHTN.
- Adherence estimates varied substantially across studies, and considerable between-study heterogeneity was observed in the primary and subgroup analyses.
- Tolerability concerns associated with MRAs may represent a barrier to sustained treatment. However, evidence directly evaluating reasons for MRA non-adherence was limited in this review, highlighting an important evidence gap.
- Together, these findings highlight the need to address barriers to antihypertensive treatment adherence and identify strategies to support long-term BP control in patients with uHTN and rHTN.



References

- Million Hearts. Accessed September 2026. [URL:<https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html>]
- Carey et al. Hypertension. 2018;72(5):e53–e90.
- McEvoy et al. European Heart Journal. 2024;45(38):3912–4018.
- Acelajado et al. Int J Hypertens. 2011;2011:837817.
- Lee et al. J Am Heart Assoc. 2022;11(17):e026582.
- Choudhry et al. Hypertension. 2022;79(1):e1–e14.
- Williams et al. Lancet. 2015;386(10008):2059–2068.
- Pucci et al. J Hum Hypertens. 2017;31(4):253–257.
- Taylor et al. J Hypertens. 2025;43(Suppl 1):e224.

Disclosures

- RTO, ZK, GGM, AC, and SZ are employees of Genesis Research Group, which received funding from Mineralys Therapeutics to conduct this study.
- KS: Employee of Mineralys Therapeutics