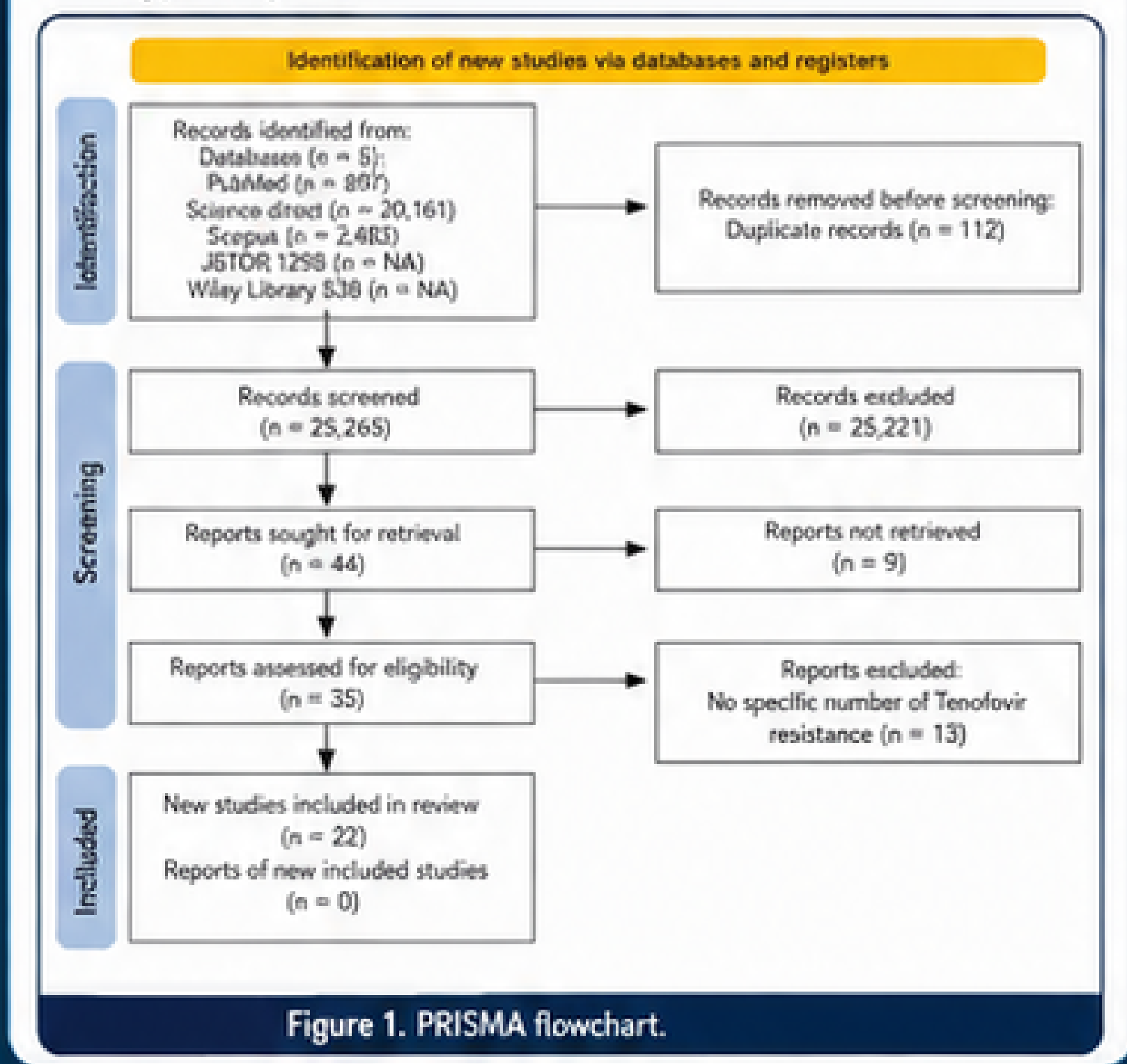


INTRODUCTION

Hepatitis B virus (HBV) remains a major global health problem, with an estimated 254 million people living with chronic infection worldwide. Tenofovir is a first-line nucleos(t)ide analogue with potent antiviral activity and a high genetic barrier to resistance. However, the true global burden of tenofovir resistance—including its prevalence, associated mutations, HBV genotypes, and geographic distribution—remains poorly characterized. This study aimed to comprehensively assess global tenofovir resistance in HBV patients.

- ## METHODS
- Design:** Systematic review and proportional meta-analysis following PRISMA.
 - Registration:** PROSPERO CRD420261446657.
 - Databases:** PubMed, ScienceDirect, Scopus, JSTOR, and Wiley (inception to July 2026).
 - Population:** Adult HBV-infected patients receiving tenofovir.
 - Outcome:** Confirmed tenofovir resistance.
 - Analysis:** Random-effects proportional meta-analysis in R 4.6.0 with univariable meta-regression.
 - Additional analyses:** Geospatial mapping and Moran's I spatial autocorrelation.
 - Risk of bias:** ROBINS-E. Publication bias: funnel plot and Egger's regression.



DISCUSSION

Our findings indicate that tenofovir resistance is no longer a theoretical concern, but a real-world clinical entity. Although the pooled prevalence appears modest, its implications are substantial when extrapolated to the global chronic HBV population. Resistance seems to emerge independently across dispersed regions, likely driven by chronic therapeutic exposure and universal clinical pressures rather than geographic clustering. These findings support the need for routine surveillance and stronger treatment monitoring, particularly in patients with long-term therapy or virologic breakthrough.

CONCLUSION

Tenofovir resistance in chronic hepatitis B is a clinically meaningful global problem, with a pooled prevalence of 3%. Chronic HBV status is the most important identified predictor. Standardized resistance testing, global surveillance, and prospective registries are essential to preserve the long-term effectiveness of hepatitis B antiviral therapy.

