

# Lower-Intensity Versus Intensive Therapy in Older Adults with Newly Diagnosed AML: A Systematic Review and Meta-Analysis

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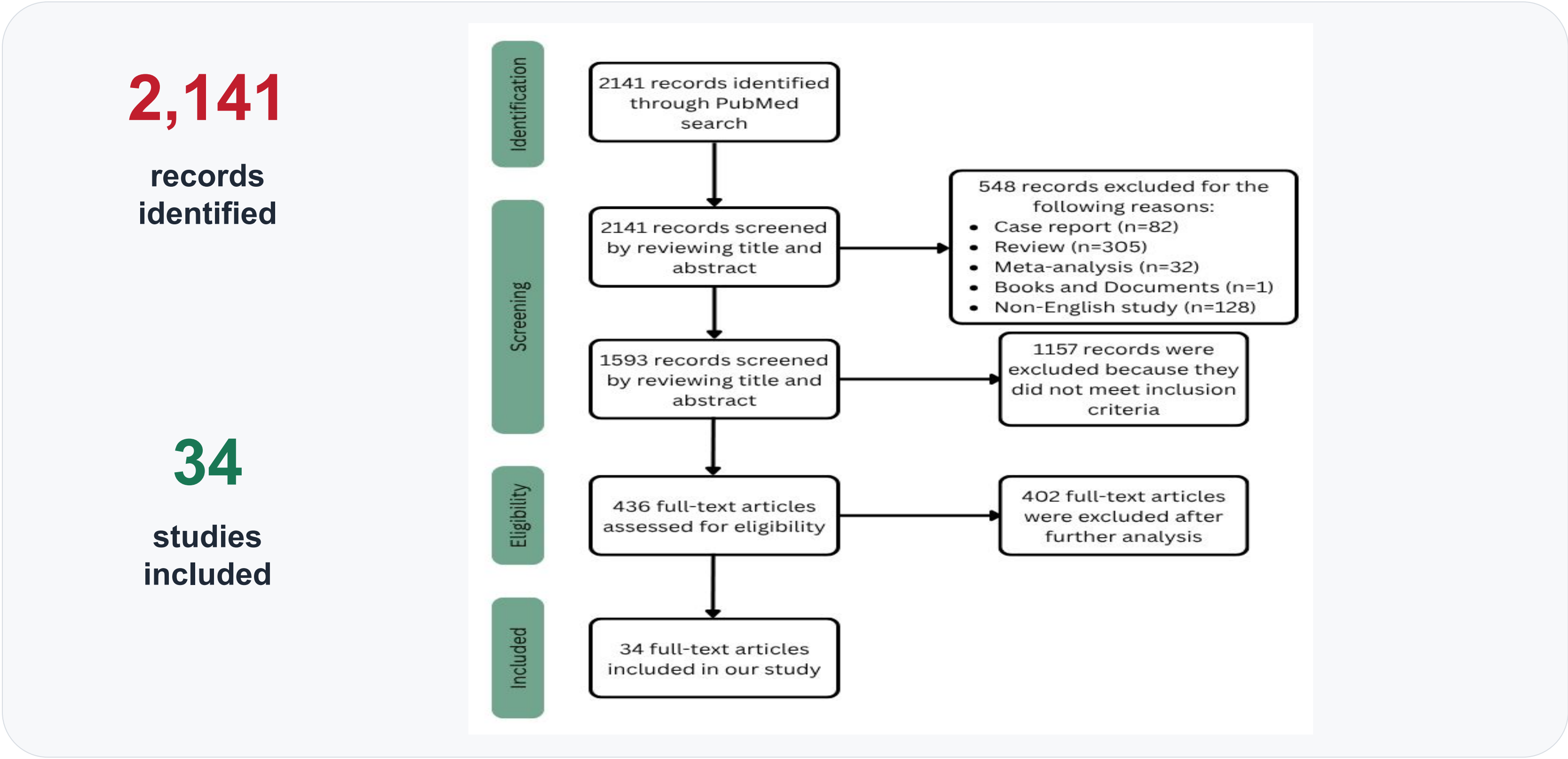
## BACKGROUND

- AML disproportionately affects older adults, in whom comorbidities and reduced physiologic reserves complicate treatment selection
- Intensive chemotherapy can achieve deeper remission but carries substantial treatment-related toxicity
- Lower-intensity strategies are increasingly used, yet their comparative efficacy and early safety remain uncertain

## METHODS

- PRISMA-concordant systematic review of studies published from 2010-2025
- Population: adults ≥65 years with newly diagnosed AML
- Interventions: azacitidine/decitabine, LDAC, VEN-based combinations; comparators included intensive chemotherapy and other conventional strategies
- Randomized trials and prospective/retrospective cohorts were eligible
- Random-effects meta-analysis; pooled RR with 95% CI
- RoB 2 for randomized trials; Newcastle-Ottawa Scale for observational cohorts.

## STUDY SELECTION

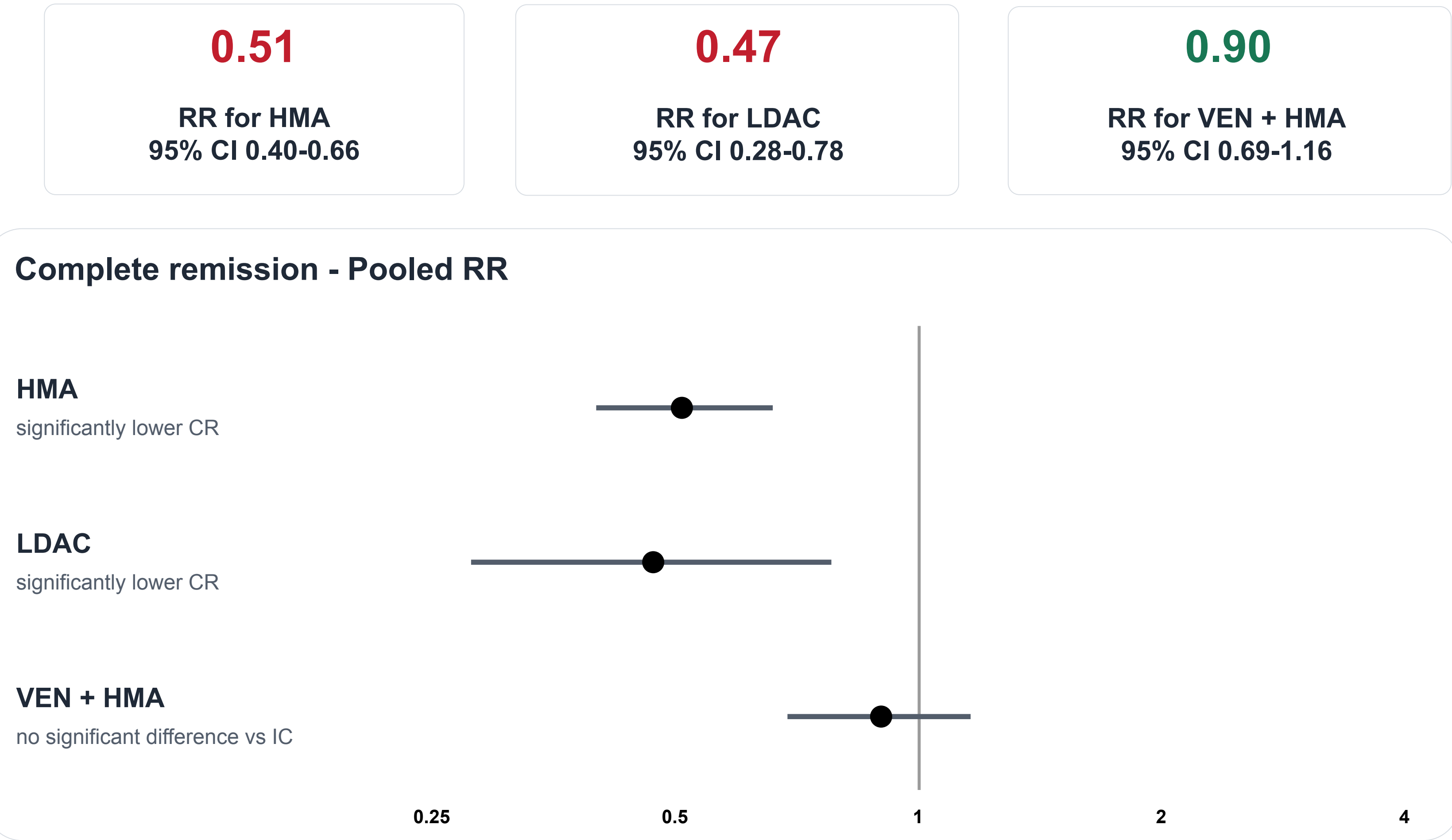


## ROBUSTNESS & LIMITATIONS

- Leave-one-out sensitivity analyses did not materially change pooled estimates
- Publication-bias testing suggested asymmetry for HMA complete remission; several other funnel plots were qualitatively asymmetric
- Overall survival and event-free survival could not be pooled because survival reporting was heterogeneous
- Molecular and cytogenetic risk were not reported consistently enough for NPM1, TP53, IDH1, FLT3, CBF AML, or ELN-stratified analyses
- Grade ≥3 infections, time to count recovery, and time to response were not consistently available

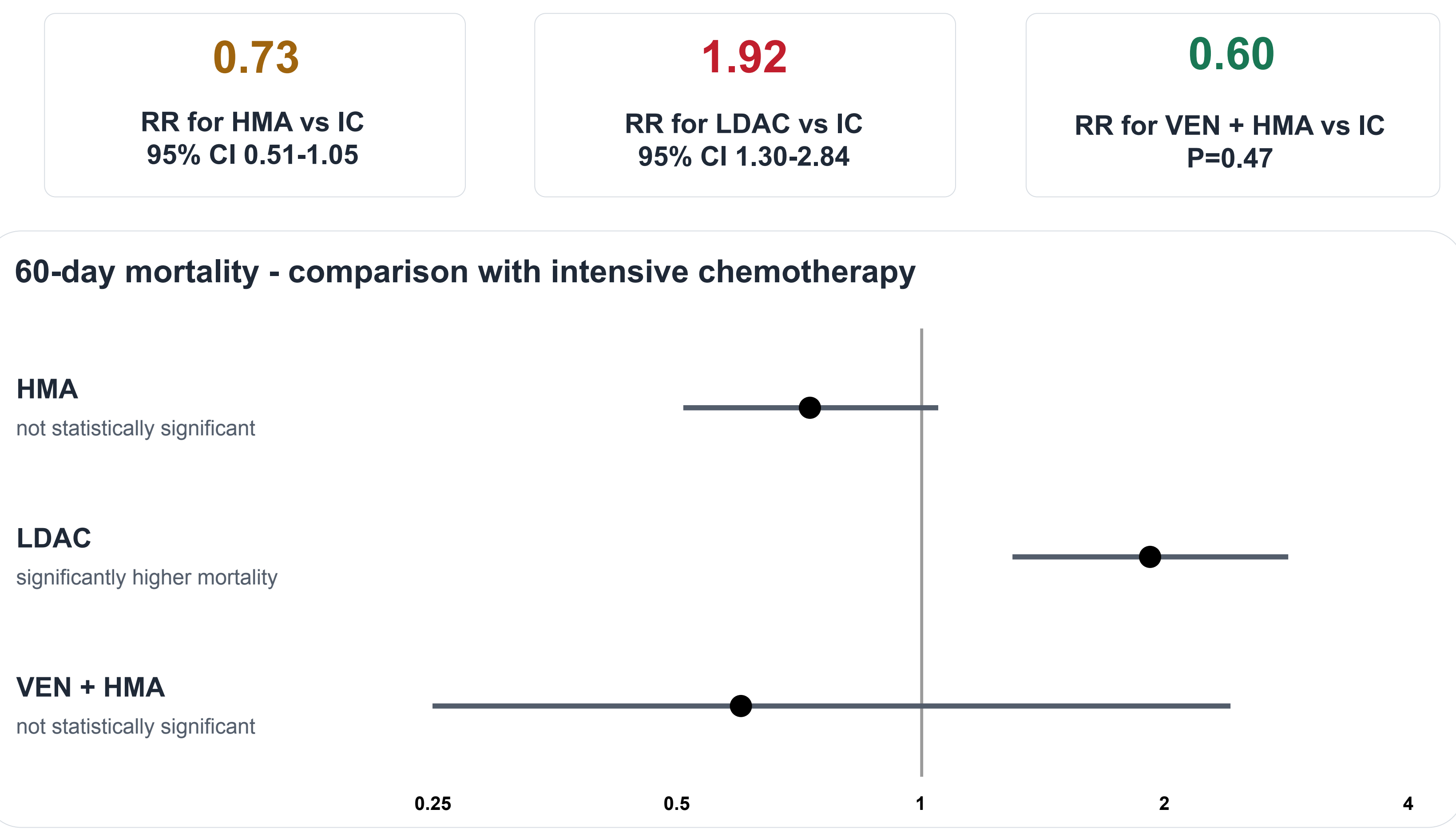
## EFFICACY: COMPLETE REMISSION

HMA and LDAC achieved fewer complete remissions; VEN + HMA was comparable with intensive chemotherapy



## EARLY MORTALITY

Thirty-day mortality was similar across strategies; clinically important separation emerged by 60 days

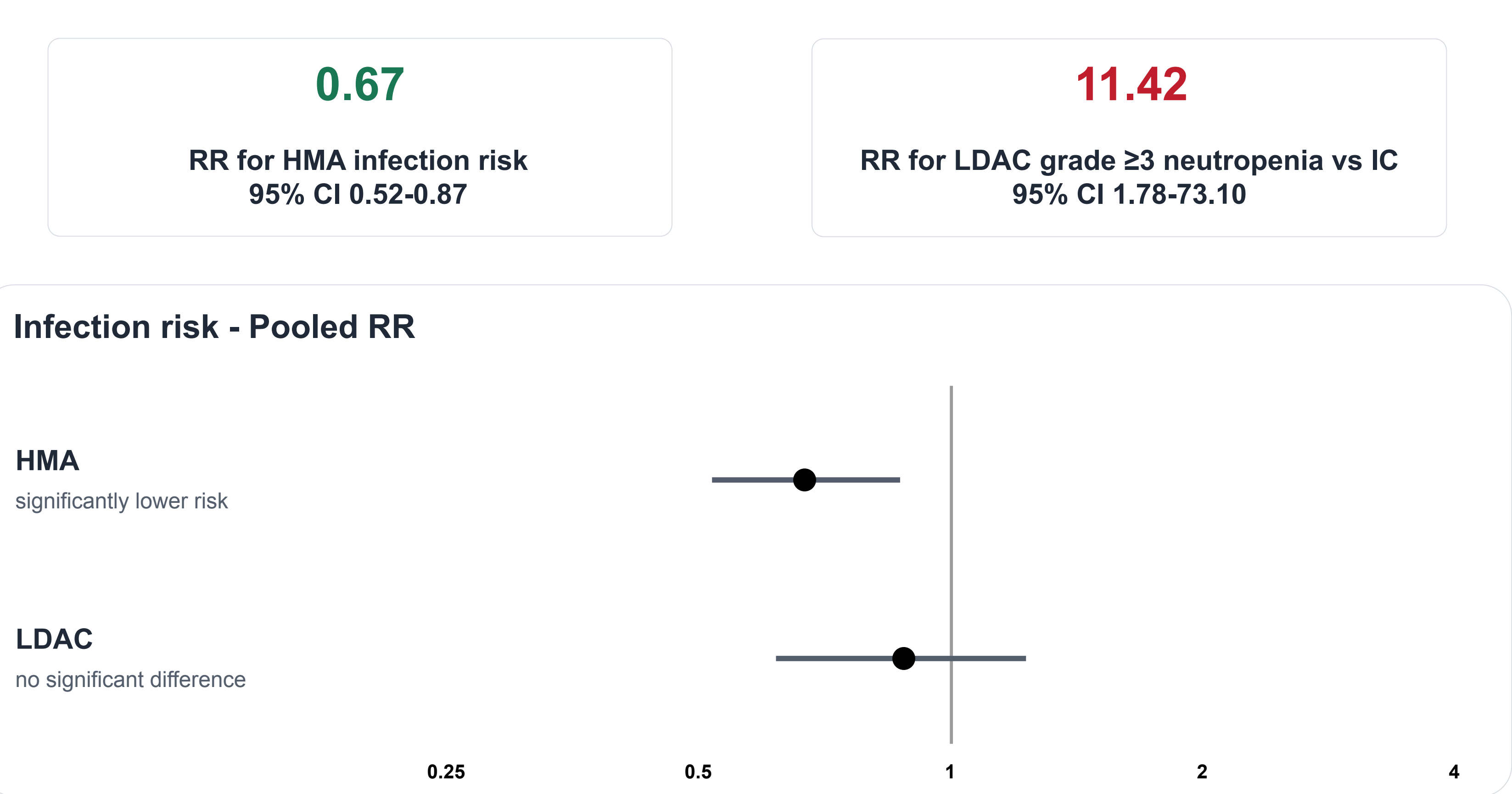


## META-REGRESSION

- In HMA-treated cohorts, increasing median age and a higher proportion of male participants were associated with lower remission rates
- No significant moderators were identified for LDAC outcomes; VEN analyses were insufficient for meta-regression

## SAFETY & TOXICITY

HMA reduced infection risk; LDAC did not demonstrate a consistent safety advantage



## HOW TO READ THESE RESULTS

- HMA: improved early tolerability comes at the cost of lower remission
- LDAC: lower remission plus higher 60-day mortality versus intensive chemotherapy argues against viewing LDAC as simply a safer alternative
- VEN + HMA: the most balanced lower-intensity profile in this analysis, with remission and early mortality comparable to intensive chemotherapy

## CLINICAL CONTEXT

- Treatment selection in older AML should incorporate fitness, comorbidity, disease biology, patient goals, and anticipated toxicity - not chronologic age alone
- These pooled data support the contemporary movement toward VEN-based lower-intensity therapy while underscoring the need for molecularly informed comparisons

## REFERENCES

- Döhner H, Estey E, Grimwade D, et al. Diagnosis and management of acute myeloid leukemia in adults 2017 recommendations from an international expert panel. *Blood*. 2017;129(4):424-447. doi:10.1182/blood-2016-08-733196
- Appelbaum FR, Gundacker H, Head DR, et al. Age and acute myeloid leukemia. *Blood*. 2006;107(9):3481-3485. doi:10.1182/blood-2005-09-3724

## CONCLUSION

*In older adults with newly diagnosed AML, lower intensity treatments do not uniformly mean safer or equally effective. HMA reduced infection risk but produced fewer remissions; LDAC had inferior remission and higher 60-day mortality versus intensive chemotherapy. VEN + HMA achieved comparable remission and early mortality, supporting its role as the most compelling lower-intensity strategy in this meta-analysis and systematic review.*