THE ASSOCIATION OF CARDIOVASCULAR DISEASE WITH THE T3111C POLYMORPHISM IN THE *CLOCK* GENE

Ivana Škrlec [1], Jasminka Talapko [1], Snježana Džijan [1,2], Hrvoje Lepeduš [1,3]

[1] Faculty of Dental Medicine and Health Osijek, J. J. Strossmayer University of Osijek, Croatia
[2] Genos Ltd., DNA Laboratory, Zagreb, Croatia
[3] Faculty of Humanities and Social Sciences Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia

INTRODUCTION

Cardiovascular diseases (CVDs) are among the leading causes of death worldwide, although CVDs mortality has decreased in developed countries. Numerous pathophysiological processes lead to the development of CVDs. The circadian rhythm coordinates many physiological processes, and its disruption can lead to many pathophysiological changes. One of the significant circadian rhythm genes is the CLOCK gene, whose polymorphisms are associated with CVD risk factors. Research findings of the association between CLOCK gene polymorphism and CVDs and its comorbidities are not consistent. This meta-analysis was performed to quantify the relationships between T3111C polymorphism and the risk of CVDs.

Faculty of Dental Medicine and Health, Osijek Croatia – iskrlec@fdmz.hr

METHODS

The PubMed and Scopus databases were searched for studies reporting on the association between T3111C (rs1801260) in the circadian *CLOCK* gene and cardiovascular disease and its comorbidities such as obesity, hypertension, insulin resistance, and coronary artery disease **(Figure 1)**. A fixed-effect model was used to calculate the pooled odds ratio and 95% confidence interval by comprehensive meta-analysis software.

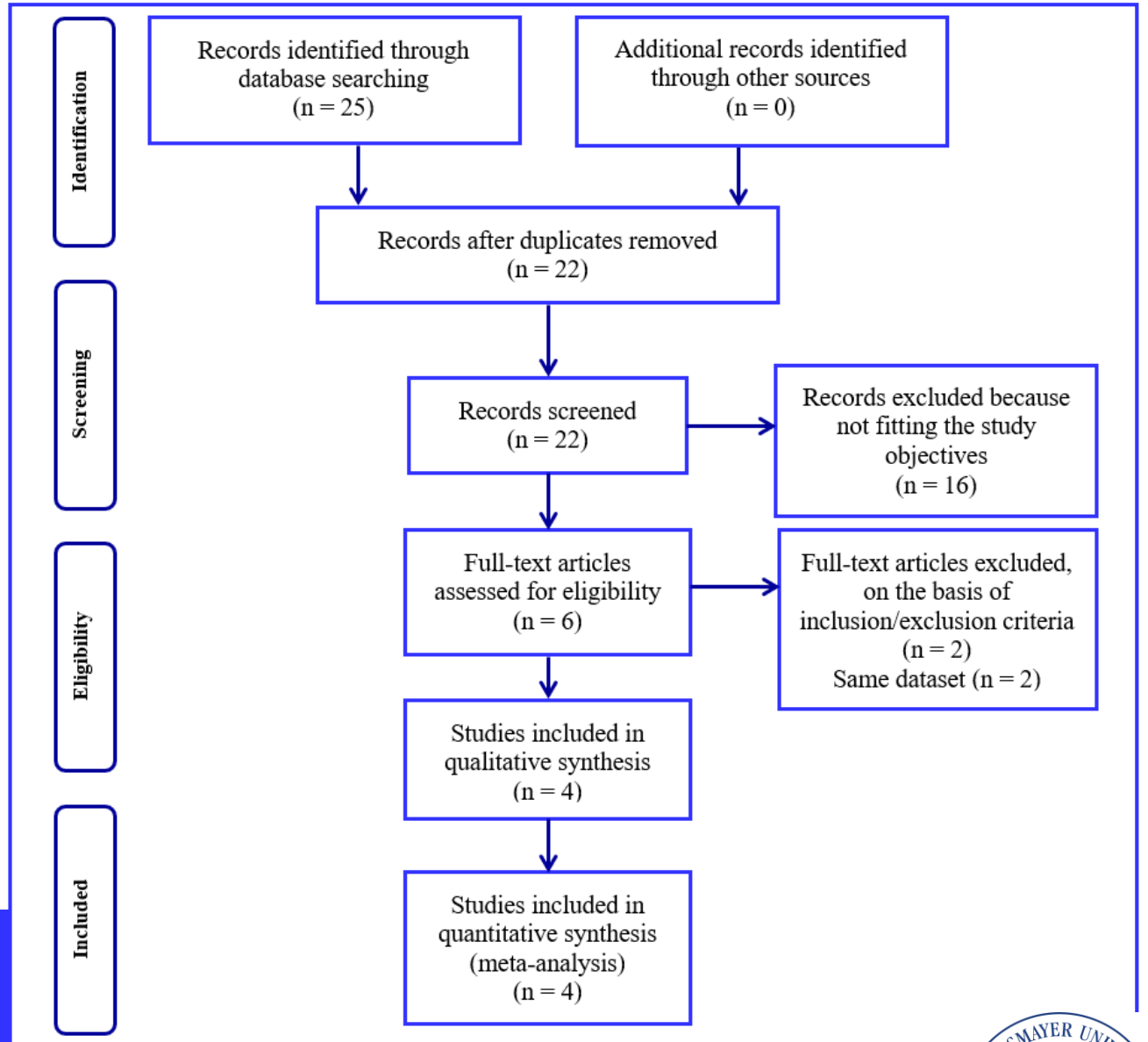

Figure 1. PRISMA flow diagram detailing the inclusion and exclusion criteria, and the number of studies included and excluded at each step of the literature search.

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RESULTS

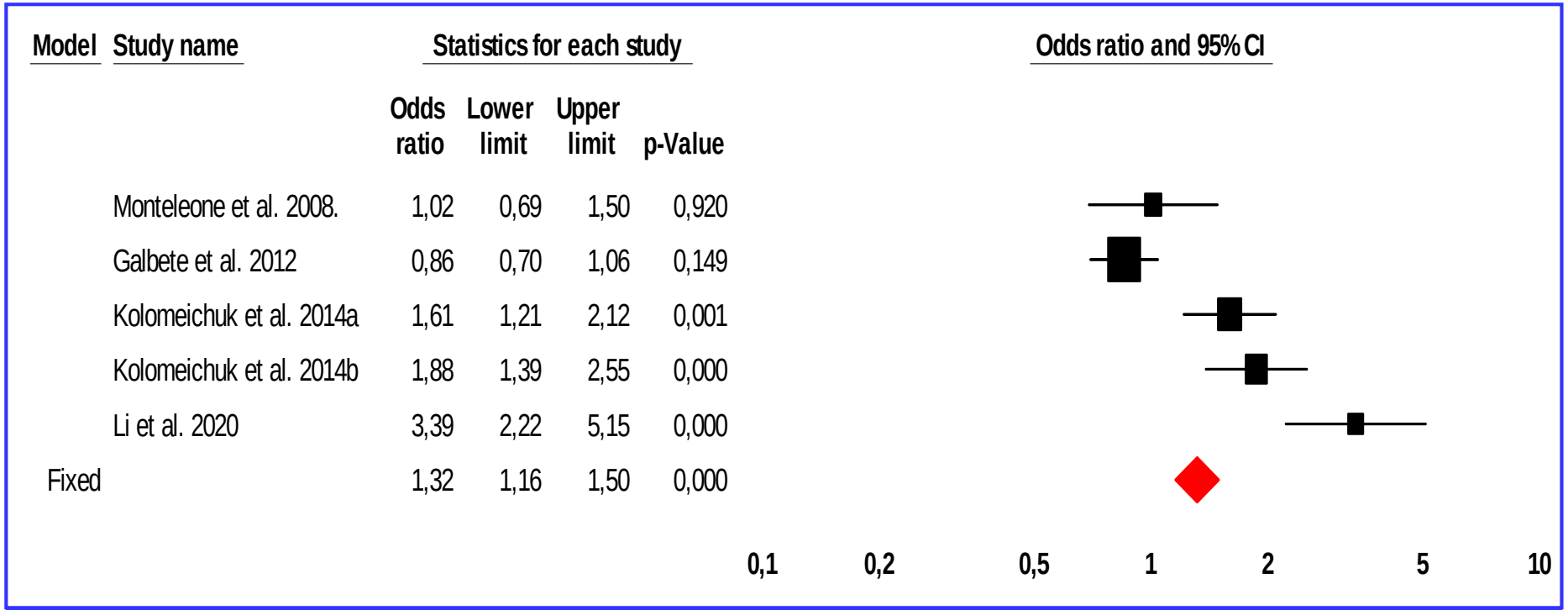

Figure 2. Forest plots for the association between T3111C polymorphism and cardiovascular diseases.

Five independent studies, including case-control, cross-sectional, and cohort research methods, were analyzed with 3,123 subjects in total. The meta-analysis revealed a significant association between T3111C polymorphism and cardiovascular disease (OR = 1.32, 95% CI: 1.16–1.50, $p < 0.001$, **Figure 2**) with significant heterogeneity ($I^2 = 91.1\%$, $p < 0.001$) and no publication bias.

The subgroup analysis on comorbidity related to CVDs revealed that hypertension was associated with T3111C polymorphism (OR = 2.02, 95% CI: 1.60–2.54, p < 0.001, **Figure 3A**), while there was any association of T3111C with obesity as a risk factor for CVDs (**Figure 3B**).

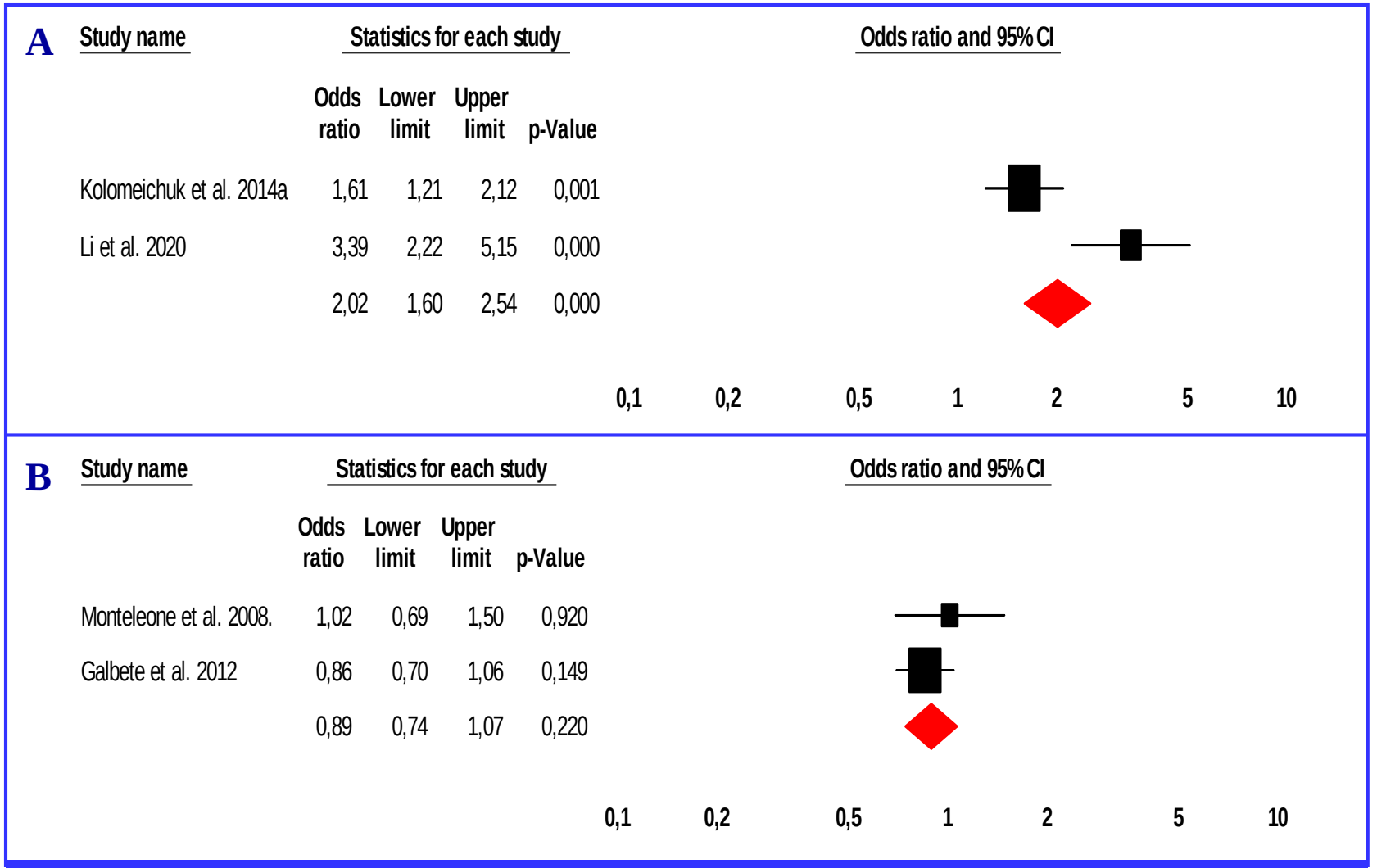

Figure 3. Forest plots for the association between T3111C polymorphism and **A)** hypertension risk, and **B)** obesity risk.

CONCLUSION

Our meta-analysis based on available studies using a fixed model shows that T3111C polymorphism in the *CLOCK* gene is associated with CVDs susceptibility. Further studies are warranted to elucidate the mechanistic link between T3111C polymorphism and cardiovascular diseases.

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