



# Translating the Role of Vitamin D Supplementation in Chronic Liver Disease:

## SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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### Introduction

Vitamin D (VD) deficiency is highly prevalent in chronic liver disease (CLD). Although international societies recommend supplementation in cases of proven deficiency, its impact on CLD remains uncertain. Our aim was to evaluate the effect of VD supplementation in CLD by conducting a systematic review and meta-analysis of randomized controlled trials (RCTs).

### Methods

We systematically searched three databases on 8th November 2022 (PROSPERO: CRD42022370312). Our outcomes involved survival, controlled attenuation parameter (CAP), liver stiffness measurement (LSM), changes in liver enzymes and homeostasis model assessment of insulin resistance (HOMA-IR), among others. Pooled risk ratio (RR), mean difference (MD), and 95% confidence intervals (CI) were calculated using the random-effects model.

### Results

Forty-one RCTs were included, comprising 3,562 patients. When comparing the VD group with the control, the overall survival RR was 1.14 (CI: 0.85; 1.54; 4 RCTs) at 6 months and 0.99 (CI:0.83;1.17; 4 RCTs) at 12 months. VD resulted in non-significant lower CAP (3 RCTs, MD:-23.50 dB/m; CI:-81.72, 34.72) and LSM (3 RCTs, MD:-0.65 kPa; CI:-1.98;0.68). A significant reduction in HOMA-IR was observed in the VD group (12 RCTs; MD:-0.44; CI:-0.87;-0.01). Alanine aminotransferase (20 RCTs; MD:-3.26 IU/L; CI:-6.37,-0.16) and gamma glutamyl transferase (10 RCTs; MD:-5.15 IU/L; CI:-9.05;-1.25) were significantly reduced.

### Conclusion

Our results showed significant differences for ALT, GGT, and HOMA-IR in the VD group. In addition, there were no differences in survival, CAP, and LSM. Further RCTs with adequate power are warranted to clarify the results.

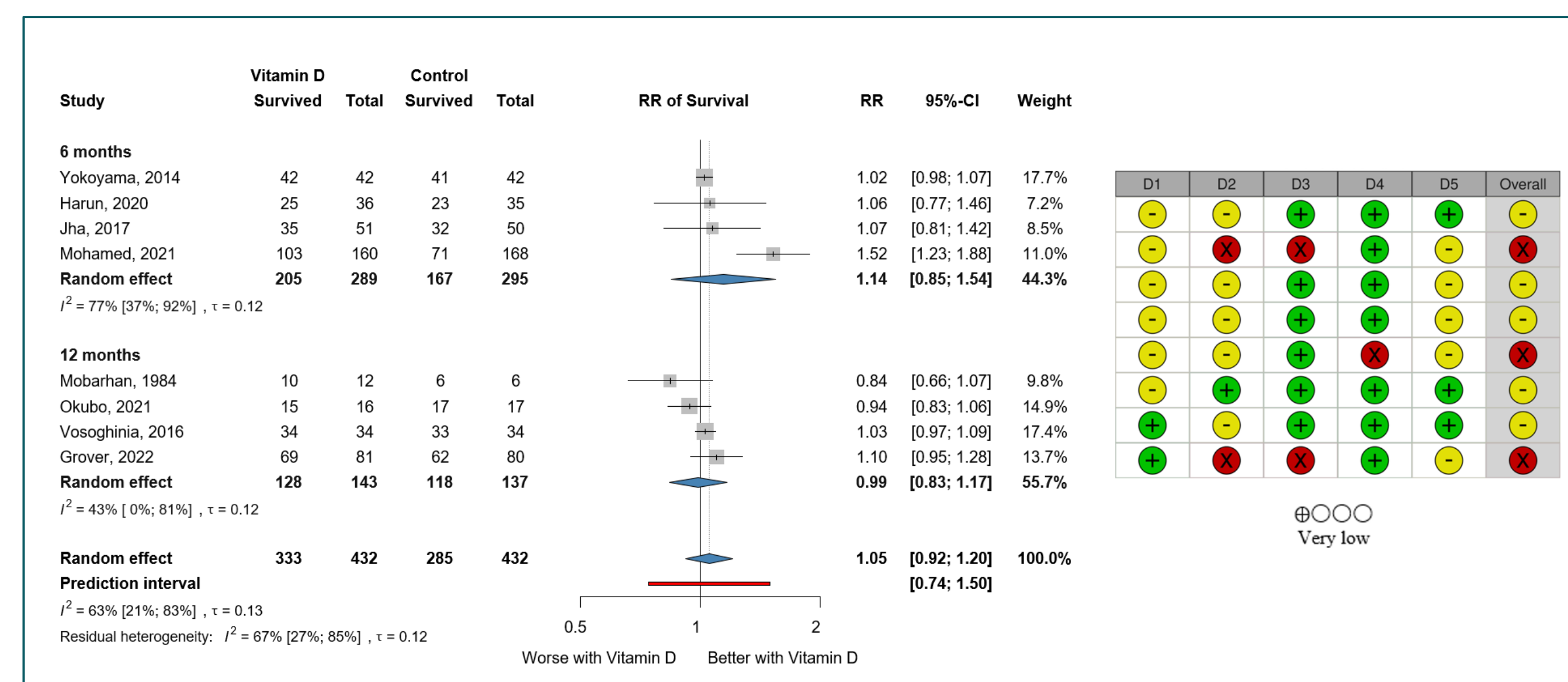


Figure 1. Forest plot showing survival in vitamin D and control groups at 6 and 12 months. CI: confidence interval; RR: risk ratio

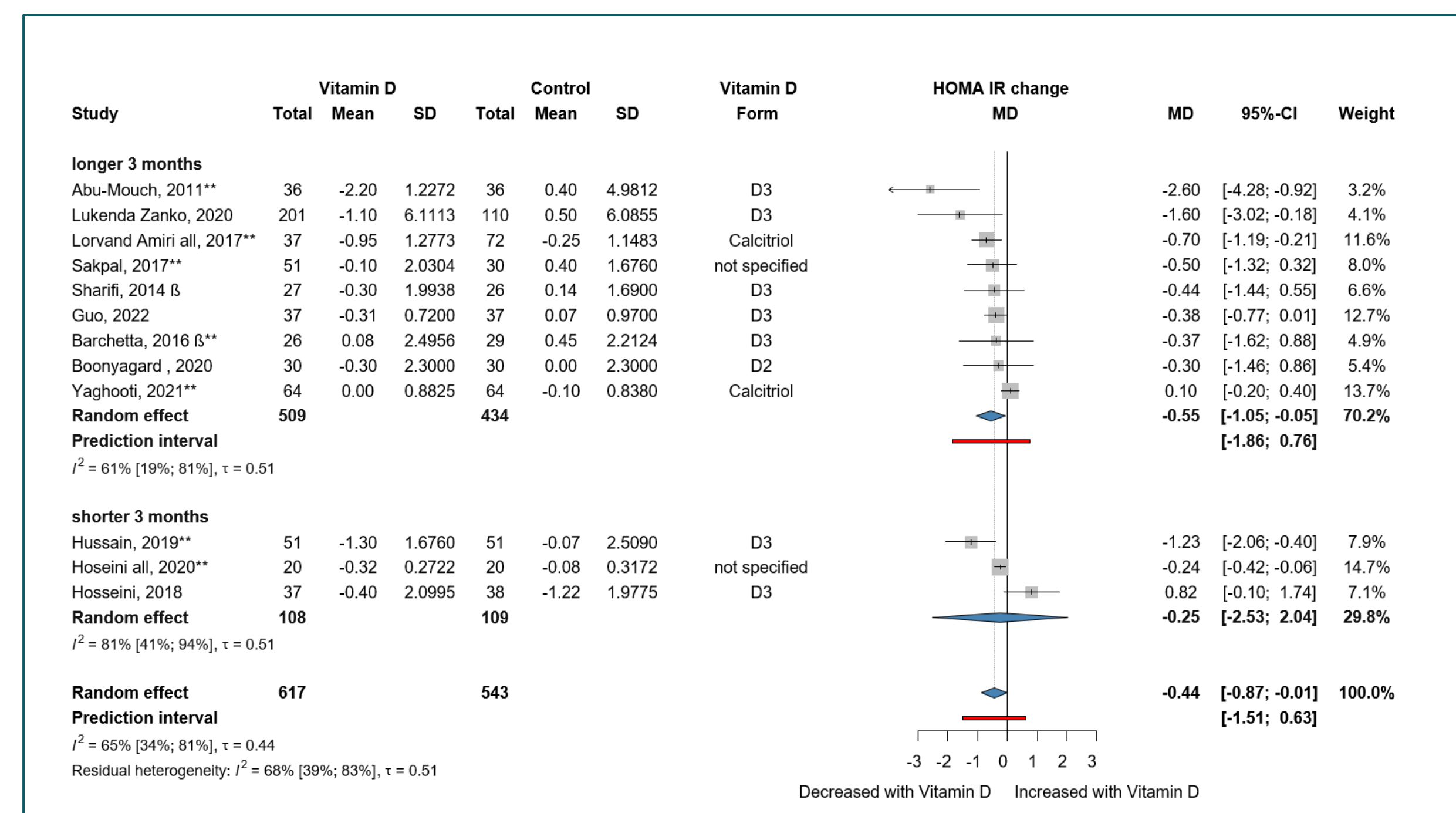


Figure 2. Forest plot showing HOMA-IR change in vitamin D and control groups by length of intervention. CI: confidence interval; MD: mean difference; SD: standard deviation.

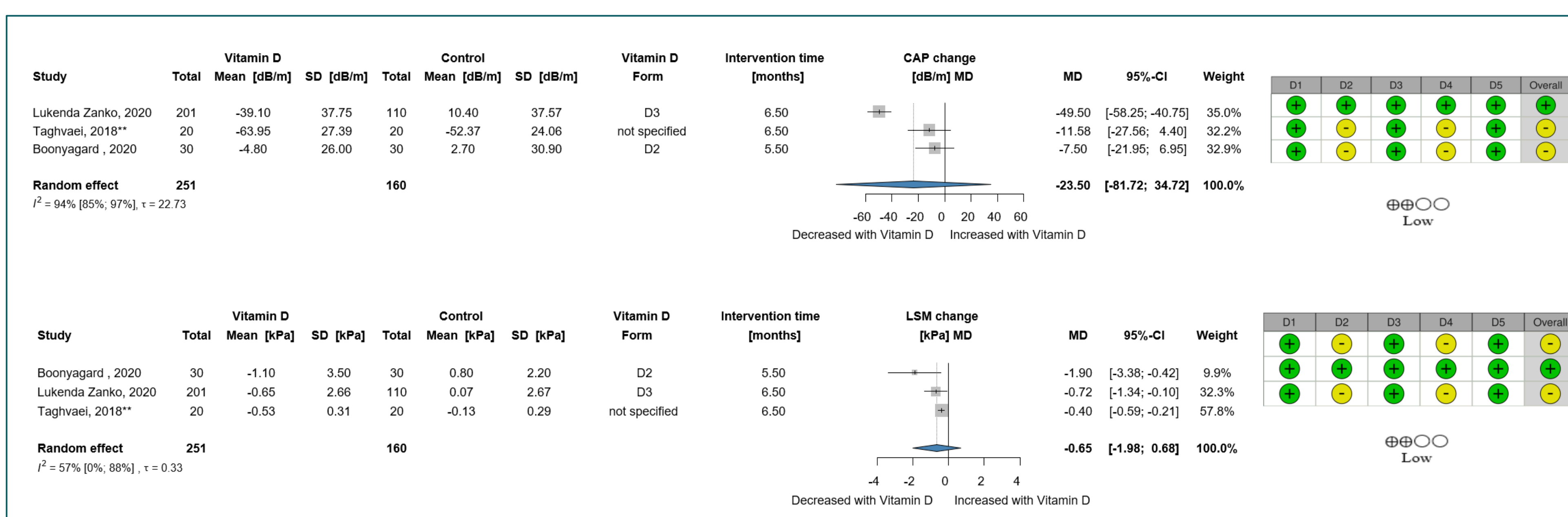


Figure 3: (A) Forest plot showing the change in the controlled attenuated parameter (CAP) representing liver steatosis and (B) Forest plot showing the change in the liver stiffness measurement (LSM) representing liver fibrosis. CI: confidence interval; MD: mean difference; SD: standard deviation.

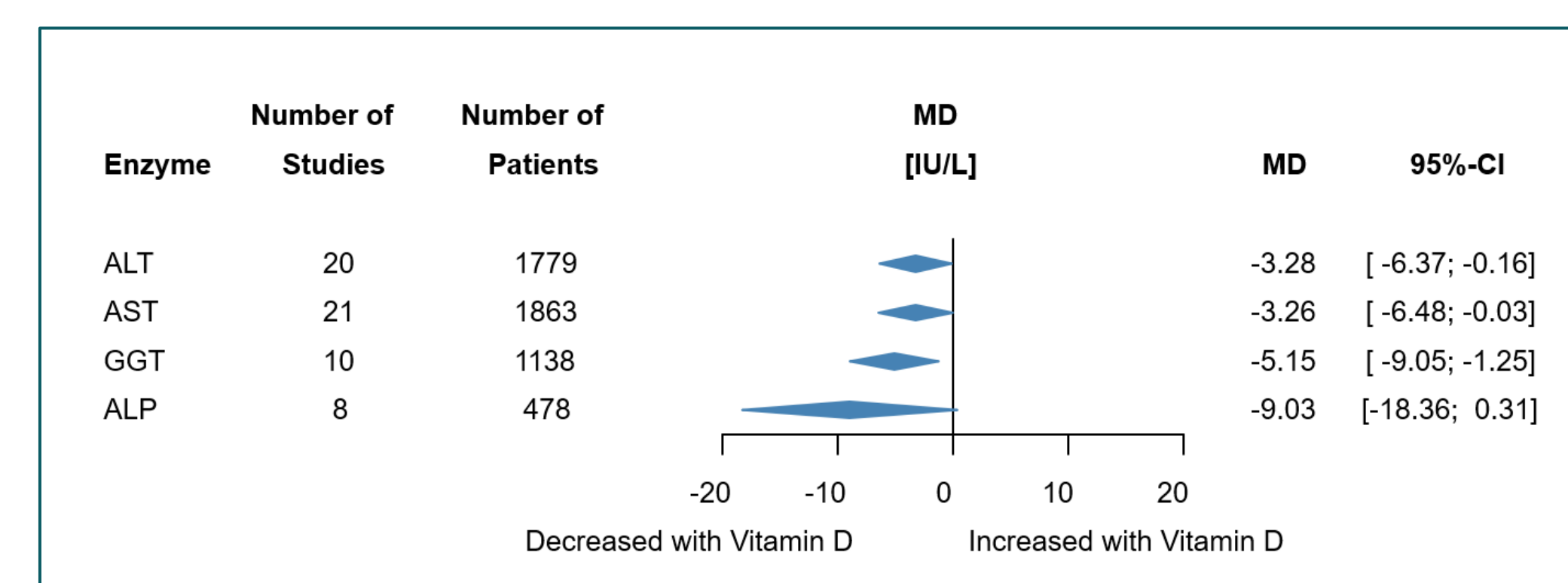


Figure 4. Summary Forest plot showing changes in alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) in vitamin D and control groups. CI: confidence interval; MD: mean difference.