**Fibrosis-4 (FIB-4) Index, incident hepatobiliary disease and major adverse cardiovascular events in type 2 diabetes: The Fremantle Diabetes Study Phase 2**

**Aim:** To determine whether the Fibrosis-4 Index (FIB-4) is independently associated with incident hepatobiliary disease (HBD) and major adverse cardiovascular events (MACE; non-fatal myocardial infarction (MI), non-fatal stroke, cardiovascular disease (CVD) death) in type 2 diabetes after adjusting for conventional risk factors.

**Methods:** Participants with clinically-defined type 2 diabetes (n=1,551, mean age 65.7 years, 51.9% males) from the Fremantle Diabetes Study Phase II were followed from entry (2008-11) to end-2021 for first hospitalisations for/with, or death from/with, HBD and MACE. Baseline FIB-4 (calculated from age, serum transaminase concentrations, platelet count) was added to Cox and competing risk regression models of conventional predictors of both endpoints to assess its independent prognostic value.

**Results:** Of the 1,337 participants without prior HBD, 176 (13.2%) had a primary HBD hospitalisation. Independent predictors of incident HBD hospitalisation in Cox regression were A Body Shape Index (ABSI), Aboriginal background, eGFR <30 mL/min/1.73m², platelet count (inversely), and gamma glutamyl transferase (ƳGT) and α2 macroglobulin concentrations (*P*≤0.012), and, in competing risk analysis, ABSI, Aboriginal background, platelet count (inversely), and ƳGT (*P*≤0.010). FIB-4 was neither bivariably associated with incident HBD (*P*=0.158) nor a significant variable in Cox/competing risk models. Since admissions for/with Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD)/steatohepatitis represented only 10% of HBD hospitalisations, these data were not analysed further. Of 1,376 FDS2 participants without prior stroke/MI, 315 (22.9%) had a stroke/MI hospitalisation or died from CVD. Although an increased FIB-4 was bivariably associated with incident MACE (*P*<0.001), it was not a significant variable in Cox/competing risk models.

**Conclusions:** Although a recommended screening test for further investigation of MAFLD/fibrosis, the present data suggest that FIB-4 is not a significant predictor of HBD events warranting hospitalisation in type 2 diabetes. FIB-4 also appears to have limited prognostic value for MACE complicating type 2 diabetes.