

Supplementary Table 1. Features of NAFLD and MAFLD

	NAFLD	MAFLD
Diagnostic criteria	based on exclusion or “negative” criteria	uses “positive” and practical (simple) criteria
Pathogenesis	misunderstood as only “non-alcoholic”	highlights metabolic dysfunction
Disease severity	dichotomous stratification (steatohepatitis and non-steatohepatitis), too simple to capture the full spectrum of the disease course	based on grade of activity and stage of fibrosis, semiquantitative, better to capture histological changes
Metabolic dysregulation	often comorbid metabolic dysregulation (e.g. obesity and T2DM)	includes metabolic criteria: overweight or obesity, T2DM or metabolic dysregulation
Alcohol consumption	no history of drinking, or < 20 g/day for women; < 30 g/day for men	no limitation, maybe a new sub-phenotype
Other liver diseases	must be excluded	can coexist
Extra-hepatic complications	e.g. T2DM, CVD, CKD and extra-hepatic cancers	better identify metabolic dysregulation, CVD, CKD, etc.
Population	NAFLD without MAFLD: lean subjects without metabolic abnormalities or other etiologies of liver disease	MAFLD without NAFLD: subjects with metabolic abnormalities and other etiologies (e.g. alcohol and viral)
Specificity or Sensitivity	does exist numerous missed diagnosis of NAFLD	better for identifying high-risk patients or those with advanced liver fibrosis
Clinical trials	tend to heterogeneity, low statistical power and confounding biases	tend to homogeneity, increase the internal validity and possibility of “positive results”, but may decrease clinical effectiveness
Management	the word “non-alcoholic” is bewildering, bad for management of subjects	the word “metabolic” is naturally reminiscent of T2DM and dyslipidemia, etc., good for management of subjects

Abbreviations: NAFLD, non-alcoholic fatty liver disease; MAFLD, metabolic dysfunction-associated fatty liver disease; CKD, chronic kidney disease; CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus.