Table 1. Principal cross-sectional and longitudinal studies of asymptomatic adult individuals undergoing screening colonoscopy that examined the association between NAFLD (diagnosed either by imaging or by histology) and the risk of colorectal tumours (ordered by the study design and publication year).

Author, Year [Ref.]	Study Design, Sample Size, Population Characteristics, Length of Follow-up (for longitudinal studies)	Diagnosis of NAFLD, Prevalence of NAFLD	Outcome Measures; Total number of colorectal adenomas or cancer; Percentage of adenomas or cancer in no-NAFLD vs. NAFLD group	Covariate Adjustments	Main Findings	NOS
			Cross-sectional studies (*n*= 8)			
Hwang ST *et al.* 2010 [19]	Cross-sectional study of 2,917 (mean age 47 years, 65% men, mean BMI 24 kg/m^2, mean waist circumference 82 cm) South Korean individuals undergoing screening colonoscopy	Ultrasonography; 32.3% with NAFLD	556 had colorectal adenomas/none had cancer; 16.8% adenomas in no-NAFLD vs. 24.5% in NAFLD group	Age, sex, smoking, hypertension, diabetes mellitus, metabolic syndrome	NAFLD was independently associated with increased risk of prevalent colorectal adenomas (aOR 1.28, 95% CI 1.03-1.60)	8
Stadlmayr A *et al.* 2011 [20]	Cross-sectional study of 1,211 (mean age 61 years, 50% men, mean BMI 27 kg/m^2, mean waist circumference 97 cm) Austrian individuals undergoing screening colonoscopy	Ultrasonography; 45.7% with NAFLD	341 had at least one colorectal tumours (280 adenomas, 54 advanced neoplasms and 8 cancers); 22.4% adenomas in no-NAFLD vs. 32.7% in NAFLD group	Age, sex, BMI, glucose intolerance status (impaired fasting glycaemia or diabetes mellitus)	NAFLD was independently associated with increased risk of prevalent colorectal adenomas (aOR 1.47, 95% CI 1.08-2.00)	9
Wong VW *et al.* 2011 [21]	Cross-sectional study of 380 (mean age 50 years; 47% men, mean BMI 25 kg/m^2; mean waist circumference 87 cm) Chinese individuals who were recruited from a community-based cohort (245 individuals) and a hospital-based cohort (135 consecutive patients with biopsy-proven NAFLD) undergoing screening colonoscopy	^{1}H-MRS in the community-based cohort; 26.1% with NAFLD. Liver biopsy in the hospital-based cohort; 36.3% with NASH	108 patients had colorectal adenomas, 47 had advanced neoplasms (defined as cancer (n=3) or adenomas with villous architecture or high-grade dysplasia); 21.5% adenomas in no-NAFLD vs. 34.7% in NAFLD group; 5.5% advanced neoplasms in no-NAFLD vs. 18.6% in NAFLD group. Among patients with biopsy-proven NAFLD, patients with NASH (n=49) had a higher prevalence of adenomas (51% vs. 25.6%)	Age, sex, BMI, smoking, family history of colorectal cancer, hypertension, diabetes mellitus	NAFLD (diagnosed by ^{1}H-MRS or biopsy) was independently associated with increased risk of prevalent advanced adenomas (aOR 3.04, 95% CI 1.29-7.20), but not of prevalent colorectal adenomas (aOR 1.61, 95% CI 0.90-2.90). In addition, among patients with biopsy-proven NAFLD (n=135), NASH was independently associated with increased risk of both prevalent adenomas	9

			and advanced neoplasms (34.7% vs. 14.0%) than those with simple steatosis (n=86). Conversely, the prevalence of adenomas and advanced neoplasms was similar between patients with simple steatosis and control individuals		(aOR 4.89, 95% CI 2.04-11.7) and advanced neoplasms (aOR 5.34, 95% CI 1.92-14.8). Advanced neoplasms were found more commonly in the right sided colon	
Lin XF *et al.* 2014 [22]	Cross-sectional study of 2,315 (mean age 64 years; 59% men, mean BMI 22 kg/m^2) Chinese individuals undergoing screening colonoscopy	Ultrasonography; 11.4% with NAFLD	1,260 had colorectal adenomas and 446 had cancer; 55.7% adenomas in no-NAFLD vs. 44.5% in NAFLD group; 18% cancer in no-NAFLD vs. 29.3% in NAFLD group	Age, sex, BMI, hypertension, plasma triglycerides, uric acid, ALT, albumin, hemoglobin, platelet count	NAFLD was independently associated with increased risk of prevalent colorectal cancer (aOR 1.87, 95% CI 1.36-2.57), but not with risk of colorectal adenomas (unadjusted OR 0.85, 95% CI 0.61-1.20)	5
Lee T *et al.* 2016 [23]	Cross-sectional study of 44,220 (mean age 43 years, 71% men, mean BMI 24 kg/m^2) South Korean individuals undergoing screening colonoscopy in a health check-up program	Ultrasonography; 33.1% with NAFLD	2,824 had colorectal adenomas and 505 cancer; 5.7% adenomas in no-NAFLD vs. 7.8% in NAFLD group; 1.0% cancer in no-NAFLD vs. 1.5% in NAFLD group	Age, sex, BMI, smoking, family history of colorectal cancer, aspirin use, hypertension, diabetes mellitus	NAFLD was independently associated with increased risk of prevalent colorectal adenomas (unadjusted OR 1.39; 95% CI 1.29-1.51) and cancer (1.50, 95% CI 1.26-1.79). Compared to those without NAFLD, the risks of colorectal adenomas according to ultrasonographic NAFLD severity were: 1.12 (95% CI 1.01-1.23) for mild, 1.10 (95% CI 0.91-1.33) for moderate, and 1.65 (95% CI 1.02-2.67) for severe NAFLD. The risks of colorectal cancer according to NAFLD severity were: 1.22 (95 % CI 0.98-1.53) for mild, 1.21 (95 % CI 0.78-1.89) for moderate, and 0.96	10

					(95 % CI 0.23-3.98) for severe NAFLD, respectively	
Ahn JS *et al.* 2017 [24]	Cross-sectional study of 26,540 (mean age 51 years, 65% men, mean BMI 24 kg/m^2) South Korean individuals undergoing screening colonoscopy in a health check-up program	Ultrasonography; 36.8% with NAFLD	8,529 had any colorectal tumours and 569 had advanced neoplasms; 28.9% any colorectal tumours in no-NAFLD vs. 38.0% in NAFLD group; 1.9% advanced neoplasms in no-NAFLD vs. 2.8% in NAFLD group	Age, sex, BMI, smoking, alcohol intake, first-degree family history of colorectal cancer, aspirin use, fasting plasma glucose, total cholesterol, triglycerides, systolic blood pressure, use of any hypoglycemic, anti-hypertensive drugs or use of statins	NAFLD was independently associated with increased risk of any prevalent colorectal tumours (aOR 1.10, 95% CI 1.03-1.17), but not with increased risk of advanced neoplasms (aOR 1.21, 95% CI 0.99-1.47). In addition, advanced NAFLD fibrosis (as detected by NFS ≥1.455) was independently associated with increased risk of any prevalent colorectal tumours (aOR 1.66, 95% CI 1.51-1.82) and advanced neoplasms (aOR 2.26, 95% CI 1.75-2.92). Similar findings were observed using other non-invasive markers of fibrosis (such as FIB4 score ≥1.45 and APRI score ≥0.5)	10
Chen QF *et al.* 2017 [25]	Cross-sectional study of 3,686 (mean age 43 years, 66% men, mean BMI 24 kg/m^2) Chinese individuals undergoing screening colonoscopy in a health check-up program	Ultrasonography; 13.3% with NAFLD	498 had adenomas, no cancer was found; 17.9% of adenomas in no-NAFLD vs. 27.4% in NAFLD group	Age, sex, smoking, alcohol intake, metabolic syndrome	NAFLD was independently associated with increased risk of prevalent colorectal adenomas (aOR 1.28, 95%CI 1.05-1.51). After stratification by sex, this association remained significant only in men (aOR 1.53, 95%CI: 1.18-2.0), but not in women. In addition, NAFLD was associated with multiple (≥3) adenomas (OR 1.82, 95%CI 1.29-2.55), distal	8

					adenomas (OR 1.63, 95%CI: 1.11-2.39) and bilateral adenomas (OR 1.89, 95%CI 1.23-2.91)	
Pan S *et al.* 2017 [26]	Cross-sectional study of 1,793 (mean age 50 years 64% men, mean BMI 23 kg/m^2) Chinese individuals undergoing screening colonoscopy in a health check-up program	Ultrasonography; 31.9% with NAFLD	341 had colorectal tumours and 27 had cancer; 16.1% of colorectal tumours in no-NAFLD vs. 25.2% in NAFLD group; 1.1% cancer in no-NAFLD vs. 2.5% in NAFLD group	Age, sex, ALT, uric acid, metabolic syndrome	NAFLD was independently associated with increased risk of prevalent colorectal adenomas (aOR 2.11, 95% CI 1.35-2.87) and cancer (aOR 2.16, 95% CI 1.29-3.21)	9
Longitudinal studies (*n*= 3)						
Lee YI *et al.* 2012 [27]	Longitudinal (retrospective) study of 5,517 (mean age 47 years, mean BMI 23 kg/m^2) South Korean women undergoing screening colonoscopy. Mean follow-up: 4.5 years	Ultrasonography; 15.1% with NAFLD	65 developed incident colorectal adenomas and 15 developed incident colorectal cancer over follow-up; overall, 185 x 10^5 persons/year for adenomas in no-NAFLD vs. 628 x 10^5 persons/year in NAFLD group; 27 x 10^5 persons/year for cancer in no-NAFLD vs. 234 x 10^5 persons/year in NAFLD group	Age, BMI, smoking, hypertension, dyslipidemia, fasting glucose levels	NAFLD was independently associated with increased risk of incident colorectal adenomas (aHR 1.94, 95% CI 1.11-3.40) and cancer (aHR 3.08, 95% CI 1.02-9.34) in women	4
Huang KW *et al.* 2013 [28]	Longitudinal (retrospective) study of 1,522 (mean age 54 years, 60% men, mean BMI 24 kg/m^2, mean waist circumference 84 cm) Taiwanese individuals who underwent two consecutive colonoscopies at Taipei Veterans General Hospital. Follow-up: 2.6 years	Ultrasonography; 40.7% with NAFLD	216 individuals developed incident colorectal adenomas and 13 incident advanced neoplasms or cancer; overall, 10.6% incident adenomas in no-NAFLD vs. 19.3% in NAFLD group	Age, sex, BMI, smoking, hypertension, diabetes mellitus, metabolic syndrome	NAFLD was independently associated with increased risk of incident colorectal adenomas (aOR 1.45, 95% CI 1.07-1.98). No separate statistical analyses were available for advanced neoplasms or cancer	6
Yang YJ *et al.* 2017 [29]	Longitudinal (retrospective) study of 1,023 (mean age 55 years; 51% men, mean BMI 25 kg/m^2) South Korean individuals undergoing	Ultrasonography (or computed tomography); 43.1% with NAFLD	After propensity score matching 234 individuals developed incident colorectal adenomas or cancer during the follow-up. Overall, 22.4% incident	Age, sex, smoking, hypertension, diabetes mellitus, use of aspirin or lipid-lowering agents; imaging for diagnosis of NAFLD	NAFLD was independently associated with increased risk of overall colorectal tumours (aHR 1.31, 95% CI 1.01-1.71). NAFLD was independently associated	6

	screening colonoscopy. After propensity score matching analysis, 441 patients in the NAFLD group and 441 patients in the control group were identified. Follow-up: up to 5 years	colorectal tumours in no-NAFLD vs. 30.6% in NAFLD group. Cumulative incidence rates of overall colorectal tumours at 3 and 5 years of follow-up in the NAFLD group were 9.1% and 35.2% vs. 5.0% and 25.3% in no-NAFLD groups	with development of three or more adenomas (aHR 2.49, 95% CI 1.20-5.20). No separate statistical analyses were available for colorectal adenomas and cancer

Abbreviations: ^{1}H-MRS, proton magnetic resonance spectroscopy; aHR, adjusted hazard ratio; aOR, adjusted odds ratio; ALT, alanine aminotransferase; AST, aspartate aminotransferase; APRI, AST platelet ratio index; BMI, body mass index; CI, confidence interval; FIB4, fibrosis-4 score; NFS, NAFLD fibrosis score.

Note: With regards to the cut-offs used for defining excessive alcohol consumption, five studies have excluded subjects who drank more than 20 g/day for both sexes [19,20,25,26,28]; four studies have excluded subjects who drank more than 30 g/day for men and 20 g/day for women, respectively [21,22,24,29]; one study has excluded subjects who drank more or equal than 40 g/day [23], and another study has excluded subjects, who drank more than 5 g/day (only women were included in such study) [27].