

**Supplementary Table S1.** Eligible observational cohort studies examining the association between NAFLD and incidence of different types of extra-hepatic tumours.

Author, Year, Ref.	PMID	Study characteristics (median or mean follow-up duration)	Study country	Sample size (n)	NAFLD Individuals (n)	Modality of NAFLD diagnosis	Mean Age (years)	Male sex (n)	Mean BMI (kg/m <sup>2</sup> )	Current smokers (n)	Patients with established diabetes (n)	Incident cases of extra-hepatic cancers at different sites (n)	Ascertainment of outcomes	Main results	Covariate adjustment(s)
Longitudinal cohort studies (n=10)															
Lee et al. 2012	21679251	Retrospective cohort study (by health examination check-up program) (mean follow-up: 4.5 years)	South Korea	5,517	831	Ultrasound	47	0	23	161	143 with type 2 diabetes	65 female patients developed colorectal adenomas; 15 female patients developed colorectal cancer	ICD-10 codes	Women with NAFLD had a higher risk of incident colorectal adenomas (aHR 1.94, 95%CI 1.11-3.40) and colorectal cancer (aHR 3.08, 95%CI 1.02-9.34)	Age, BMI, smoking, hypertension, dyslipidemia, impaired fasting glucose/diabetes
Huang et al. 2013	23398678	Retrospective cohort study (by health examination check-up program) (mean follow-up: 2.6 years)	Taiwan	1,522	619	Ultrasound	54	913	24	219	94 with type 2 diabetes	216 patients developed colorectal adenomas (of whom 13 had advanced adenomas)	Asymptomatic individuals with negative baseline colonoscopy who received consecutive self-paid health examinations and colonoscopy between 2003 and 2010	Patients with NAFLD had a higher risk of incident colorectal adenomas (aHR 1.45, 95%CI 1.07-1.98)	Age, sex, BMI, smoking, hypertension, diabetes, MetS
Sun et al. 2015	26656334	Retrospective cohort study (by national health Insurance program) (mean follow-up: 3.6 years)	Taiwan	10,545	2,109	ICD-9 codes	61	6,565	NR (149 with obesity)	NR	1,699 with type 2 diabetes	15 patients developed uterine cancer; 9 patients developed thyroid cancer; 43 patients developed stomach cancer; 55 patients developed prostate cancer; 19 patients developed pancreas cancer; 102 patients developed	ICD-9 codes	Patients with non-alcoholic cirrhosis had a higher risk of incident esophagus cancer (aHR 7.25, 95%CI 2.44-21.6), stomach cancer (aHR 5.50, 95%CI 2.78-10.9), colorectal cancer (aHR 2.58, 95%CI 1.59-4.18), but not a higher risk of incident thyroid cancer (aHR 1.97, 95%CI 0.34-11.5), lung cancer (aHR 1.54, 95%CI 0.85-2.80), uterine cancer (aHR 2.03, 95%CI 0.60-6.80), prostate cancer (aHR 1.58, 95%CI 0.73-3.44), urinary system cancers (aHR 1.60, 95%CI 0.69-3.72) and	Age, sex, obesity, hypertension, diabetes, dyslipidemia, viral hepatitis, and colon polyps, and diagnostic procedures of esophagogastroduodenoscopy, colonoscopy, abdomen CT, or ultrasonography

												lung cancer; 16 patients developed esophagus cancer; 105 patients developed colorectal cancer; 46 patients developed urinary system cancers		haematologic cancers (aHR 3.12, 95%CI 1.34-7.25)	
Yang et al. 2017	28777831	Retrospective hospital-based cohort study (follow-up: up to 5 years)	South Korea	1,023	441	Ultrasound or CT	55	522	25	226	127 with type 2 diabetes	298 developed colorectal adenomas	Occurrence of colorectal tumours at 3 and 5 years after index colonoscopy	Patients with NAFLD had a higher risk of incident colorectal adenomas (aHR 1.31, 95%CI 1.01-1.71)	Propensity score matching analysis Age, sex, BMI, smoking, hypertension, diabetes, use of aspirin, lipid-lowering agents and imaging for NAFLD diagnosis
Kim GA et al. 2017	29150142	Retrospective cohort study (by health examination check-up program) (median follow-up: 7.4 years)	South Korea	25,947	8,721	Ultrasound	48	13,966	24,5	5,067	2,174 with type 2 diabetes	162 patients developed stomach cancer; 24 patients developed pancreas cancer; 118 patients developed male genital organ cancer; 83 patients developed lung cancer; 22 patients developed female genital organ cancer; 8 patients developed esophagus cancer; 76 patients developed colorectal cancer; 91	Pathological and/or radiological confirmation	Patients with NAFLD had a higher risk of incident breast cancer (aHR 1.92, 95%CI 1.15-3.20), but not a higher risk of incident stomach cancer (aHR 0.98, 95%CI 0.69-1.38), esophagus cancer (aHR 1.93, 95%CI 0.48-7.72), colorectal cancer (aHR 1.45, 95%CI 0.88-2.38), pancreas cancer (aHR 1.16, 95%CI 0.51-2.65), male genital organ cancer (aHR 0.91, 95%CI 0.63-1.31), female genital organ cancer (aHR 2.06, 95%CI 0.86-4.91), lung cancer (aHR 1.34, 95%CI 0.87-2.07), kidney cancer (aHR 1.76, 95%CI 0.96-3.22), bladder cancer (aHR 1.93, 95%CI 0.94-3.95), non-Hodgkin lymphomas (aHR 0.94,	Age, sex, smoking hypertension, diabetes, lipids, GGT levels

												patients developed breast cancer; 42 patients developed kidney cancer; 30 patients developed bladder cancer; 49 patients developed non-Hodgkin lymphoma; 16 patients developed leukemias		95%CI 0.52-1.70), and leukemias (1.16, 95%CI 0.42-3.19)	
Hamaguchi et al. 2019	31275587	The NAGALA cohort study (by health examination check-up program) (mean follow-up: 6.5 years)	Japan	27,944	3,211	Ultrasound	45	8,585	25	3,457	299 with type 2 diabetes	48 patients developed stomach cancer; 52 patients developed colorectal cancer	ICD-10 codes (subjects undergoing health check-ups for gastric cancer or colorectal cancers)	Patients with NAFLD had higher risk of incident stomach cancer (aHR 3.3, 95%CI 1.57-6.90) and colorectal cancer (aHR 3.04, 95%CI 1.47-6.30)	Age, sex, obesity, smoking, diabetes, physical activity, alcohol consumption
Allen et al. 2019	31470068	Retrospective hospital-based matched cohort study (median follow-up: 8 years)	USA	19,163 (4,722 with NAFLD and 14,441 individuals matched for age, and sex)	4,722	ICD-9/10 codes	54	8,959	31	1,946	2,895 with type 2 diabetes	202 patients developed uterine cancer; 30 patients developed stomach cancer; 581 patients developed prostate cancer; 72 patients developed pancreas cancer; 69 patients developed ovary cancer; 238 patients developed lung cancer; 29 patients developed	ICD-9/10 codes	Patients with NAFLD had higher risk of incident uterine cancer (aHR 2.40, 95%CI 1.40-4.10), stomach cancer (aHR 2.30, 95%CI 1.30-4.10), prostate cancer (aHR 1.60, 95%CI 1.00-2.50), pancreas cancer (aHR 2.00, 95%CI 1.20-3.30), ovary cancer (aHR 1.70, 95%CI 1.05-3.00), colorectal cancer (aHR 1.80, 95%CI 1.10-2.80) and breast cancer (aHR 1.60, 95%CI 1.05-2.60), but not higher risk of incident lung cancer (aHR 1.40, 95%CI 0.50-2.40) and esophagus cancer (aHR 1.70, 95%CI 0.80-2.70)	Age, sex, and obesity

												esophagus cancer; 276 patients developed colorectal cancer; 676 patients developed breast cancer			
Wang et al. 2020	32407969	Retrospective cohort study (by health examination check-up program) (follow-up: up to 10 years)	China	54,187	17,528	Ultrasound	53	54,187	NR (3,385 with obesity)	17,117	5,597 with type 2 diabetes	58 male patients developed stomach cancer; 8 male patients developed small intestine cancer; 29 male patients developed prostate cancer; 208 male patients developed lung cancer; 29 developed esophagus cancer; 95 male patients developed colorectal cancer; 114 male patients developed kidney cancer, 96 male patients developed bladder cancer	Self-reported information through questionnaires in the every 2-year routine follow-up and by linkage with the provincial vital statistics data	Men with NAFLD had higher risk of incident lung cancer (aHR 1.23, 95%CI 1.02-1.49), but not stomach cancer (aHR 1.01, 95%CI 0.71-1.43), small intestine cancer (aHR 1.68, 95%CI 0.73-3.84), esophagus cancer (aHR 1.45, 95%CI 0.77-2.73), colorectal cancer (aHR 1.22, 95%CI 0.91-1.64), kidney cancer (aHR 1.46, 95%CI 0.96-2.21), and bladder cancer (aHR 1.04, 95%CI 0.61-1.75)	Age, BMI, physical activity, smoking, diabetes, hypertension, alcohol consumption, education level, serum ALT, lipids, C-reactive protein
Yamamoto et al. 2020	33201570	Retrospective cohort study (by health examination check-up program) (follow-up: up to 14 years)	Japan	30,172	4,394	Ultrasound	44	9,517	22	3,415	663 with type 2 diabetes	226 patients developed stomach cancer; 15 patients developed small intestine cancer; 13 patients developed	ICD-10 codes and/or participant questionnaires	Patients with NAFLD had higher risk of incident stomach cancer (aHR 1.40, 95%CI 1.02-1.94), and lung cancer (aHR 1.34, 95%CI 1.07-1.67), but not small intestine cancer (aHR 2.80, 95%CI 0.87-8.96), rectum cancer (aHR	Age, sex, BMI, smoking, dyslipidemia, diabetes, thyroid dysfunction, hypertension, sleep apnea, chronic kidney disease, cardiovascular disease

												rectum cancer; 219 patients developed male genital organ cancer; 206 patients developed lung cancer; 250 patients developed female genital organ cancer; 43 patients developed esophagus cancer; 560 patients developed breast cancer; 86 patients developed urinary system cancers		0.69, 95%CI 0.15-3.30), male genital organ cancer (aHR 0.75, 95%CI 0.52-1.07), female genital organ cancer (aHR 1.03, 95%CI 0.69-1.54), esophagus cancer (aHR 1.40, 95%CI 0.71-2.78), breast cancer (aHR 1.22, 95%CI 0.94-1.59), and urinary system cancers (aHR 0.86, 95%CI 0.50-1.47)	
Kim NH et al. 2020	32630984	Retrospective hospital-based cohort study (mean follow-up: 3.5 years)	South Korea	6,182	2,642	Ultrasound	44	4,659	24	3,051	NR	1,999 patients developed cancer or any adenoma; 144 patients developed cancer or advanced adenoma	Colonoscopy	Patients with NAFLD had a higher risk of developing metachronous colorectal cancer or any adenoma (men: aHR 1.17, 95%CI 1.06-1.29; women: aHR 1.63, 95%CI 1.27-2.07). In addition, NAFLD was an independent predictor for metachronous colorectal cancer or advanced adenoma in women (aHR 2.61, 95%CI 1.27-5.37), but not in men (aHR 0.97, 95%CI 0.66-1.42)	Age, sex, smoking family history of colorectal cancer, regular exercise, baseline adenoma characteristics, medications

**Abbreviations:** ALT, alanine aminotransferase; aHR, adjusted hazard ratio; aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; CT, computed tomography; GGT, gamma-glutamyltransferase; ICD, international classification of diseases; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; NR, not reported.