



PARIS MASH MEETING

11th edition

Organized by
Arun Sanyal & Lawrence Serfaty

September 11 & 12, 2025
Institut Pasteur, Paris





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Inclusion of cancer screening within MASLD treatment guidelines

Pr Jérôme Boursier
Angers, France

Disclosures

- **Consultant:** Novo Nordisk, Lilly
- **Board:** BMS, Intercept, Pfizer, Madrigal, MSD, Novo Nordisk
- **Speaker:** Abbvie, Gilead, Intercept, Novo Nordisk, Sanofi, Siemens
- **Funds for scientific research:** Diafir, Echosens, Gilead, Intercept, Inventiva, Ipsen, Siemens

What do the current guidelines tell us ?



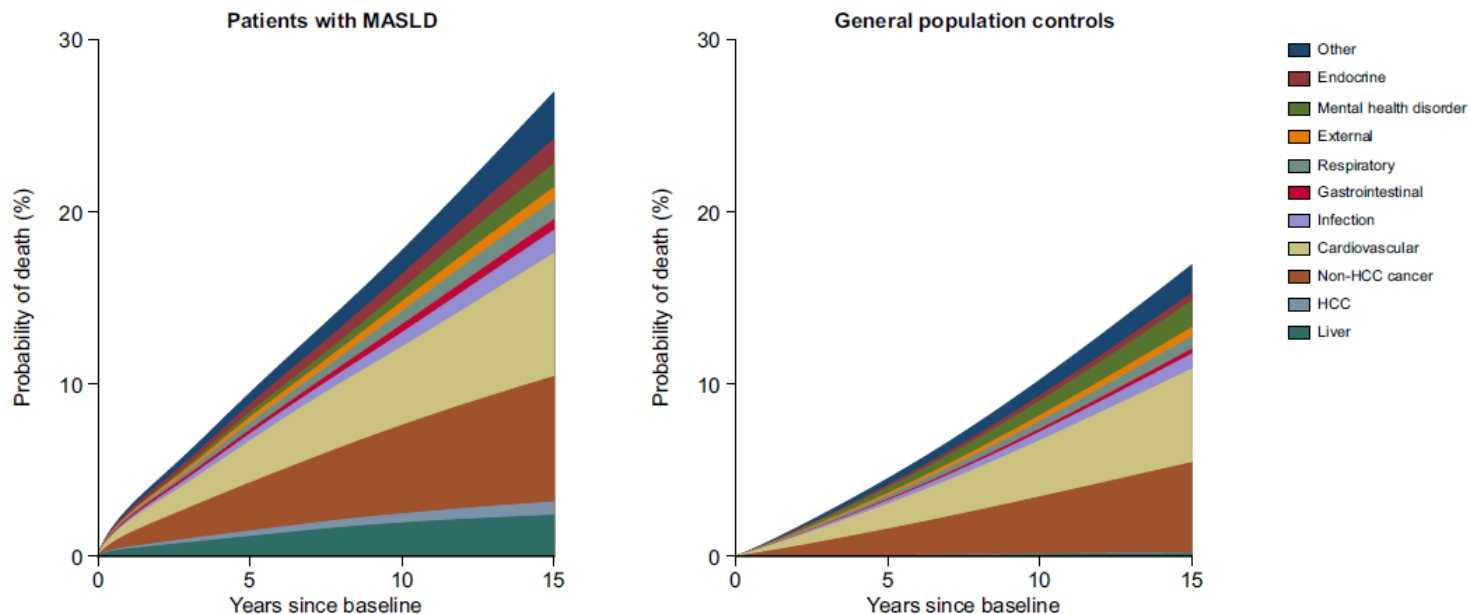
Adults with MASLD should be encouraged to participate in extrahepatic cancer screening according to current guidelines, based on their exposure to obesity and type 2 diabetes as risk factors for extrahepatic malignancies (LoE 3, strong recommendation).



Death from non hepatic malignancies is a common cause of death in patients with NAFLD, and thus, adherence to age-appropriate cancer screening has the potential to improve survival.

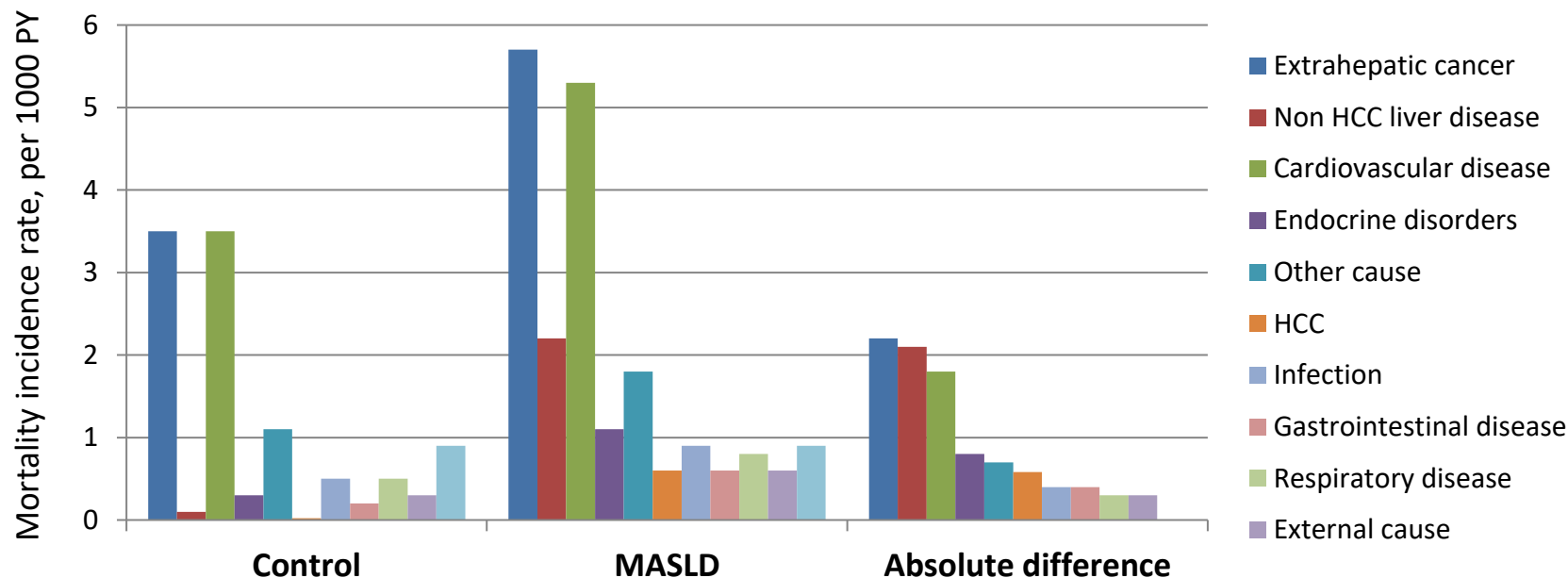
Cause of death in MASLD

Cause-specific mortality in 13,099 patients with MASLD and 118,884 matched controls (Swedish DELIVER cohort)
1,628 deaths in MASLD (median follow-up: 4.7 years [IQR: 2.0-9.2])
9,119 deaths in controls (median follow-up: 5.8 years [IQR: 2.7-10.5])



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Risk of extra-hepatic cancer in MASLD

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Studies (patients)	10 (182,202)	-	15 (7,454,208)	18 (16,699,438)
All	-	-	1,54 [1,35-1,76]	-

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Stomach	1,81 [1,19-2,75]	1,81 [1,19-2,75]	1,22 [1,05-1,40]	1,47 [1,07-2,01]
Pancreas	1,84 [1,23-2,74]	1,98 [1,47-2,65]	1,28 [0,90-1,83]	1,41 [1,11-1,79]
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* Respiratory tract cancer; § Male genital cancer

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+ 20-100%

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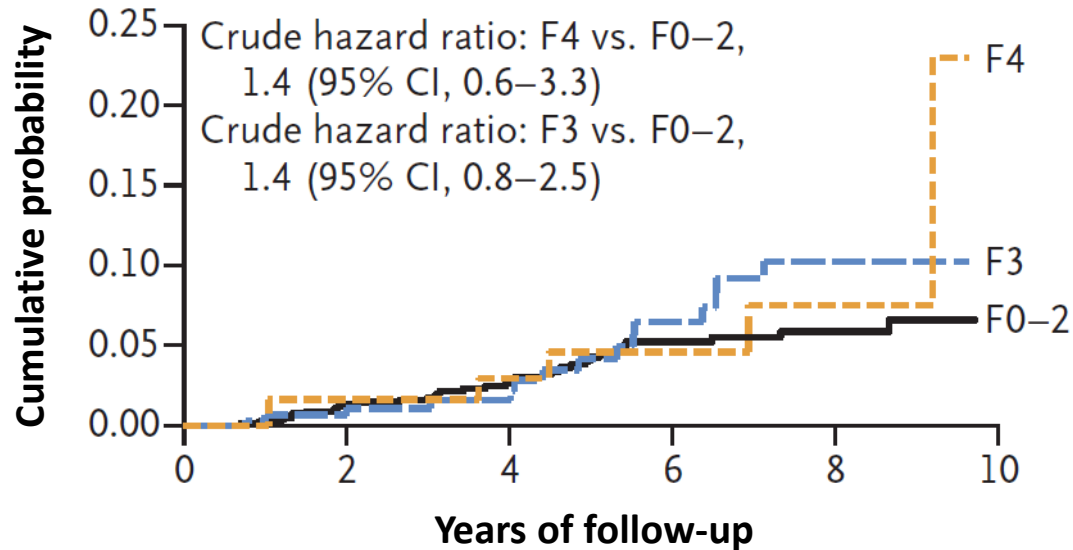
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Incidence of extrahepatic in patients with biopsy proven MASLD

Prospective cohort from the MASH-CRN including 1 773 patients with biopsy-proven MASLD
Mean follow-up: 4.0 years (IQR: 2.1-7.4)



Incidence of extrahepatic in patients with biopsy proven MASLD

8,892 biopsy-proven MASLD patients and 39,907 matched controls
1,691 incident cancers in MASLD and 6,733 in controls

Adjusted subdistribution hazard ratio for incident cancer in MASLD patients

	Simple steatosis	MASH w/o fibrosis	Non cirrhotic fibrosis	Cirrhosis
All cancers	1.0 (ref)	1.02 [0.88-1.19]	0.99 [0.86-1.14]	1.03 [0.85-1.25]
HCC	1.0 (ref)	1.45 [0.82-2.58]	2.31 [1.48-3.62]	3.56 [2.23-5.69]
No-HCC liver cancer	1.0 (ref)	0.75 [0.19-2.97]	1.76 [0.60-5.15]	1.33 [0.29-6.14]
- Extrahepatic cancers	1.0 (ref)	0.97 [0.82-1.15]	0.85 [0.72-1.00]	0.85 [0.67-1.08]
- Hematologic cancers	1.0 (ref)	1.32 [0.78-2.25]	1.27 [0.75-2.16]	0.26 [0.06-1.14]

Incidence of extrahepatic cancer and MASLD severity

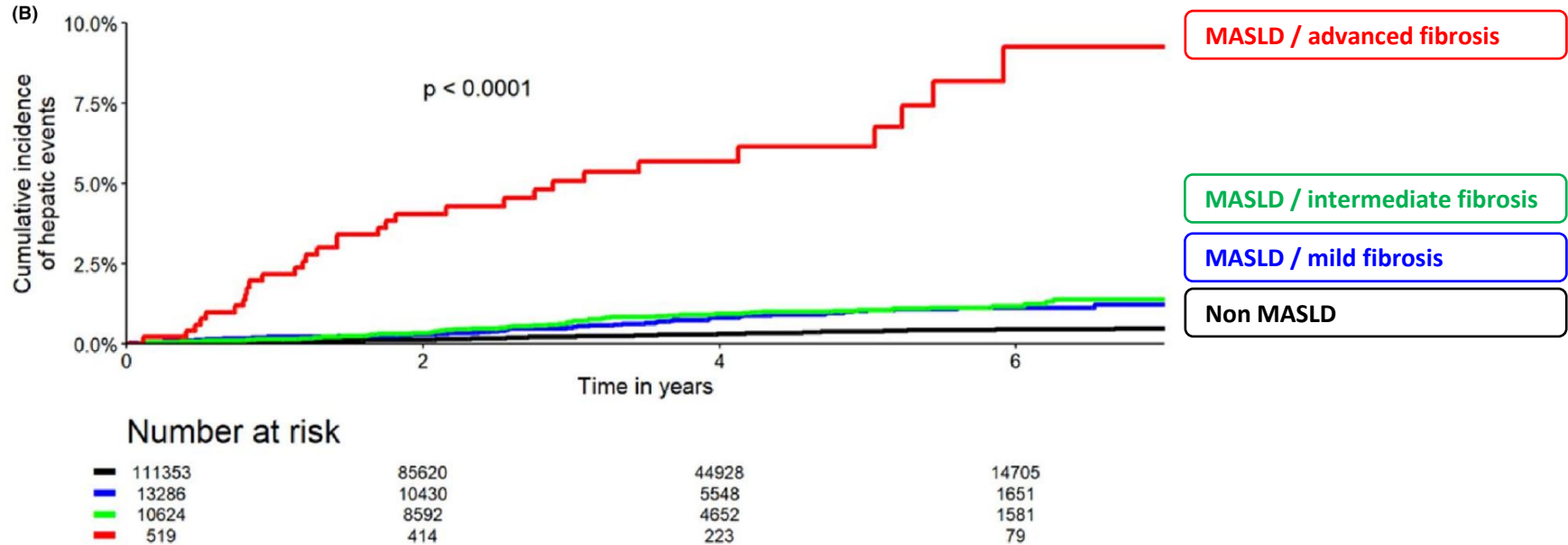
25,947 subjects who underwent a health check-up at a tertiary Korean center
8,721 subjects with MASLD (diagnosis based on presence of liver steatosis at ultrasound)

Table 5. Association between severity of NAFLD and cancer development.

Outcome	Univariate analysis		Multivariable analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
NFS: Low, <-1.455 (n = 6,562; reference), high and intermediate, ≥-1.455 (n = 2,159)				
All cancers	1.96 (1.62–2.37)	<0.001	1.87 (1.54–2.28)	<0.001
Hepatocellular carcinoma	9.61 (2.64–34.91)	0.001	5.64 (1.49–21.44)	0.01
Colon and rectum	1.45 (0.75–2.83)	0.27	1.40 (0.70–2.78)	0.34
Breast	0.79 (0.34–1.83)	0.58	0.76 (0.32–1.82)	0.54
FIB-4 score: Low, <1.45 (n = 7,007; reference), high and intermediate, ≥1.45 (n = 1,714)				
All cancers	1.88 (1.54–2.29)	<0.001	1.74 (1.42–2.13)	<0.001
Hepatocellular carcinoma	21.21 (4.70–95.68)	<0.001	13.99 (3.00–65.23)	0.001
Colon and rectum	1.72 (0.87–3.39)	0.12	1.64 (0.81–3.30)	0.17
Breast	1.69 (0.40–7.08)	0.48	1.80 (0.40–8.21)	0.45
Hepatic steatosis on ultrasound: Mild (n = 5,115; reference), moderate to severe (n = 3,606)				
All cancers	0.98 (0.81–1.19)	0.87	0.99 (0.82–1.20)	0.92
Hepatocellular carcinoma	3.18 (0.98–10.33)	0.054	3.39 (1.00–11.43)	0.049
Colon and rectum	0.99 (0.52–1.88)	0.98	1.15 (0.60–2.22)	0.67
Breast	1.61 (0.79–3.29)	0.19	1.76 (0.84–3.69)	0.14

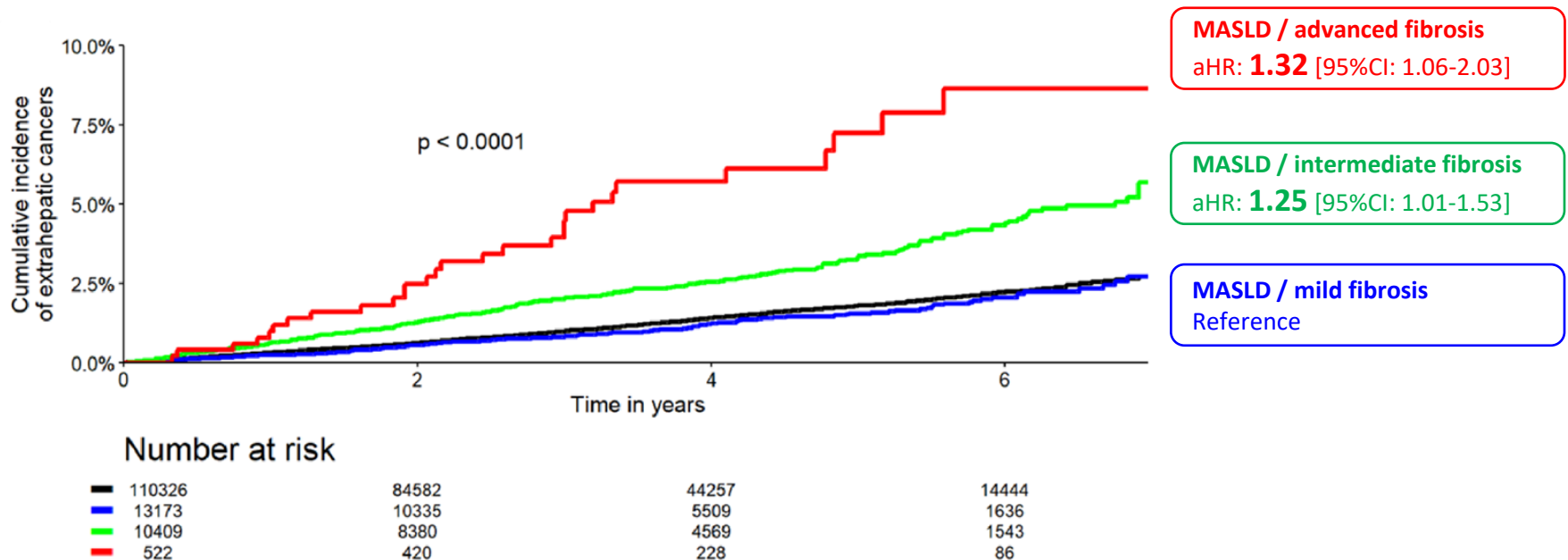
Incidence of extrahepatic cancer and MASLD severity

199,341 adult participants from the French national CONSTANCE cohort
Stratification of MASLD severity with non-invasive tests (FLI, Forns index); MASLD: 18.3%



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Association between MASLD and early-onset cancer

2,877,245 young adults (20-39 years) from the Korea National Health Insurance Service (NHIS)

Exclusion of history of cancer and underlying liver diseases other than MASLD

46,729 early-onset cancers (before 50 years of age)

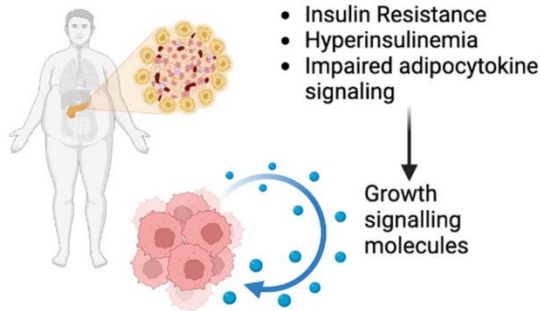
Cancer site	aHR (95% CI)
Uterine corpus	3,78 [3,22-4,44]
Liver	2,02 [1,61-2,53]
Biliary	1,79 [1,20-2,68]
Pancreatic	1,36 [1,07-1,72]
Renal	1,36 [1,19-1,56]
Thyroid	1,36 [1,31-1,42]
Colorectal	1,19 [1,10-1,30]
Breast cancer	0,89 [0,81-0,96]

No significant association with :

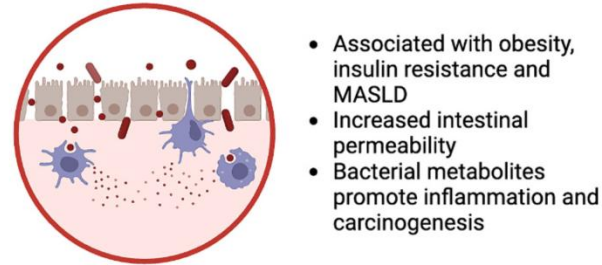
- Gastric
- NH lymphoma
- Uterine cervical
- Oral cavity & pharyngeal
- Laryngeal
- Oesophageal
- Lung
- Bladder
- Prostate
- Testicular
- Ovarian
- Skin melanoma
- Central nervous system
- Leukemia
- Multiple melanoma

Why MASLD is associated with increased extrahepatic cancers?

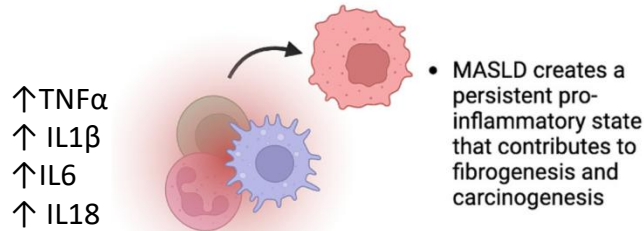
A Metabolic Dysregulation



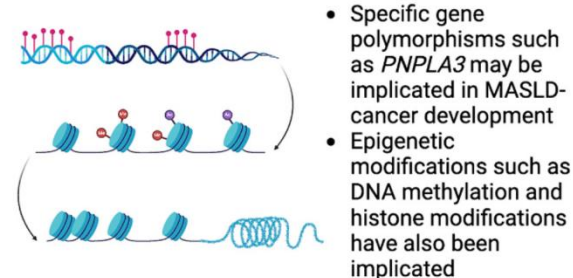
B Gut dysbiosis



C Chronic Inflammation



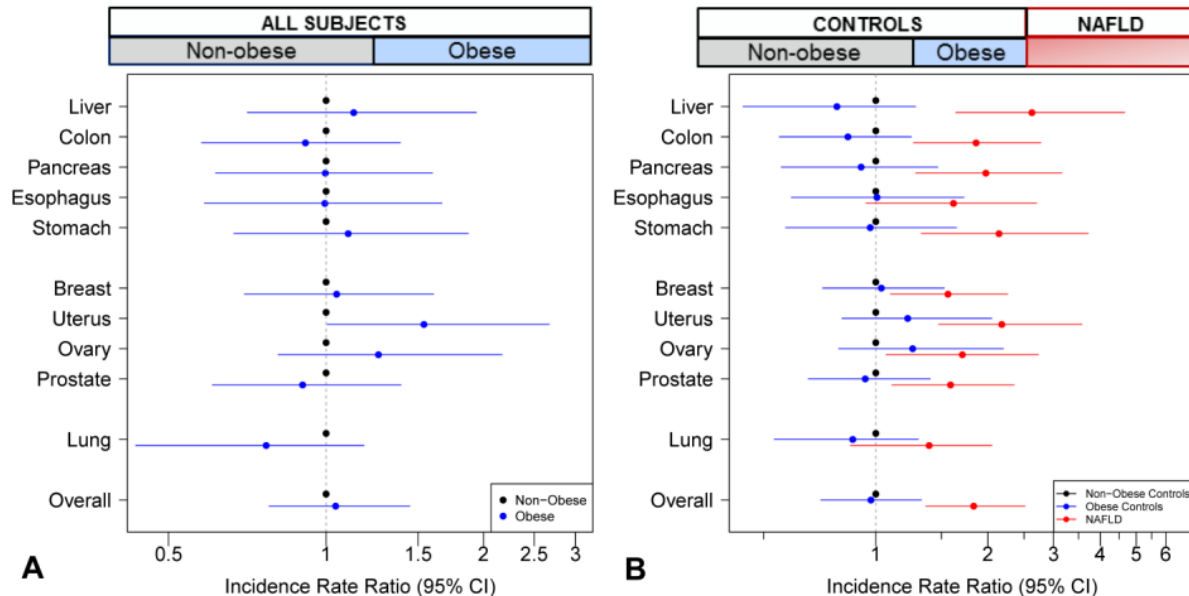
D Genetic and Epigenetic factors



Obesity, MASLD and incidence of extrahepatic cancer

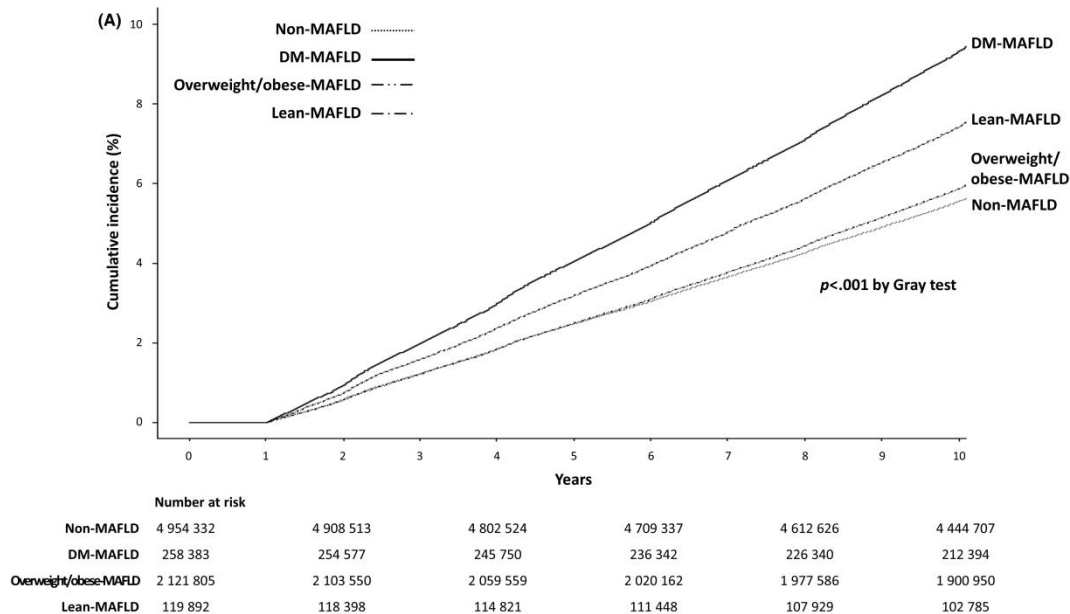
4,722 individuals with NAFLD matched by age and sex to referent individuals from the same population (1:3) on the index diagnosis date

Adjusted
by age, sex
and diabetes



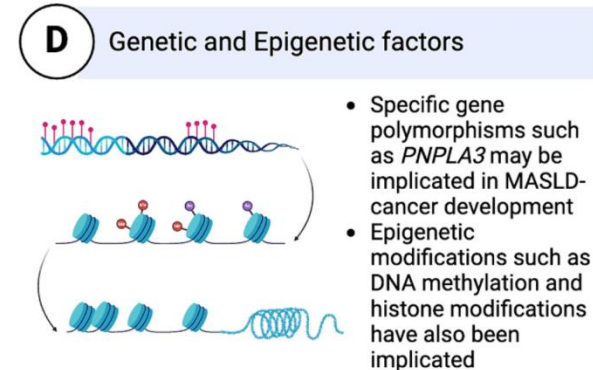
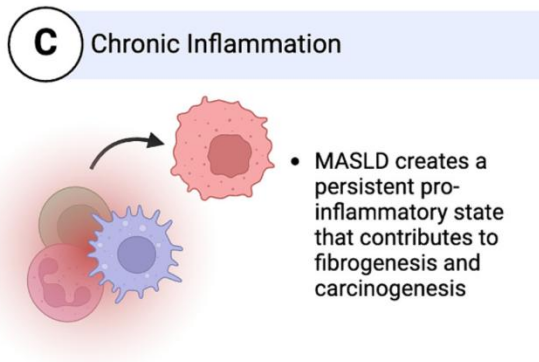
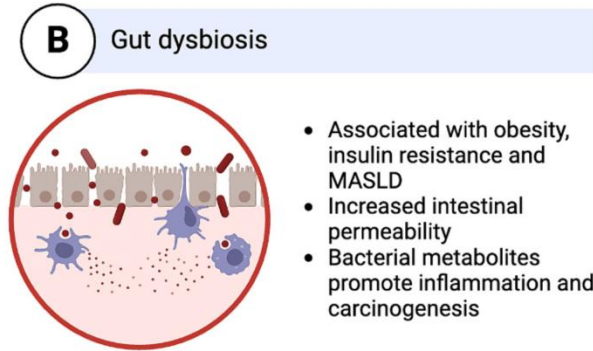
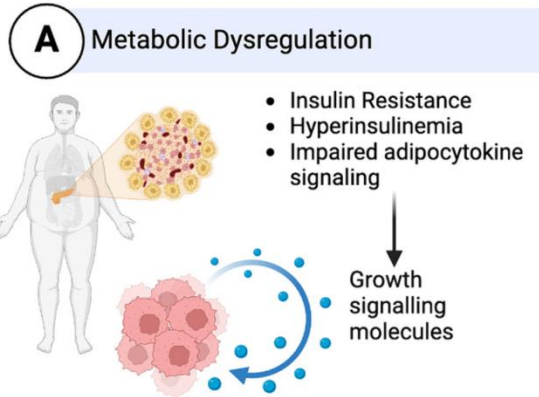
T2DM and incidence of extrahepatic cancer

Retrospective cohort from the National Health Insurance Service (NHIS) database of Korea
7,454,412 patients with 33.5% of them having MASLD followed during a median 10.3 years (IQR: 10,1-10,6)



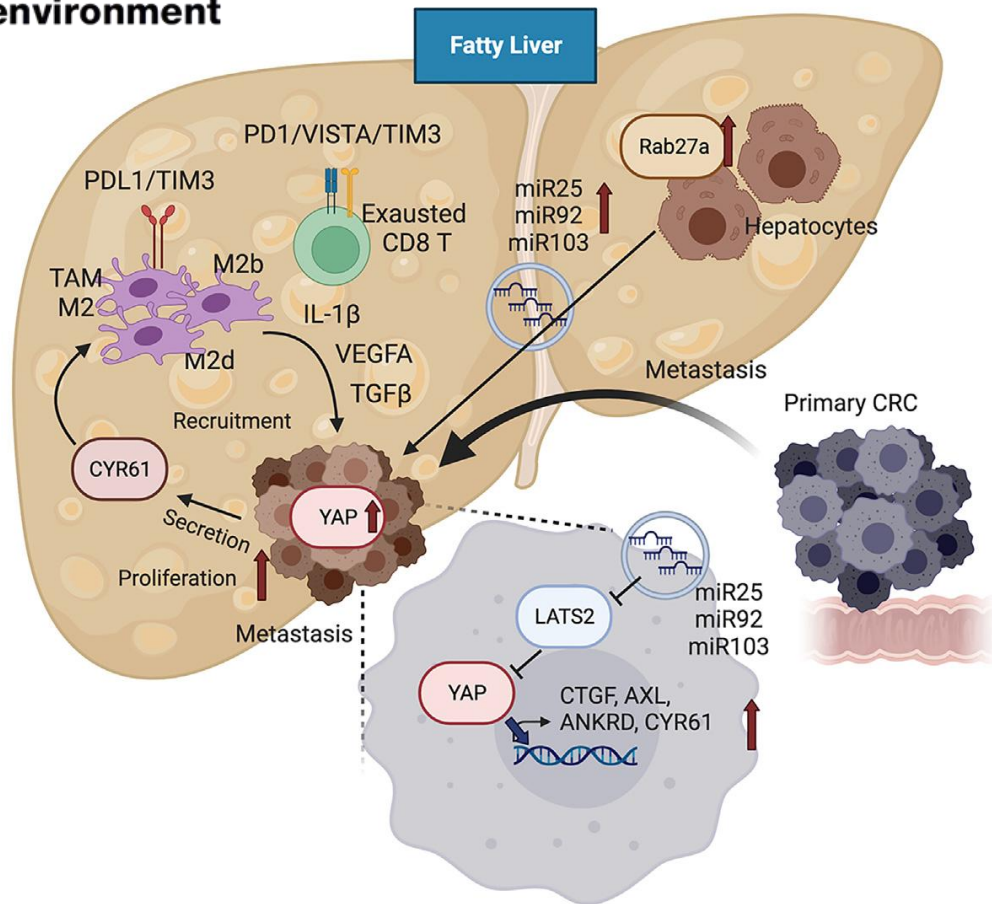
	Model 2 ^b	
	aSHR (95% CI)	p
Extrahepatic malignancies		
No MAFLD	1 (Reference)	
DM-MAFLD	1.13 (1.11-1.14)	<.001
Overweight/obese-MAFLD	1.00 (.99-1.00)	.419
Lean-MAFLD	1.12 (1.10-1.14)	<.001
No MAFLD	1 (Reference)	
MAFLD	1.02 (1.02-1.03)	<.001

Why MASLD is associated with increased extrahepatic cancers?



Cell Metabolism

Extracellular vesicles in fatty liver promote a metastatic tumor microenvironment



Should we update the guidelines on extrahepatic cancer in MASLD?

- **Screening programs for extrahepatic cancer should be strictly followed in patients with MASLD**

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- **Screening programs for extrahepatic cancer should be strictly followed in patients with MASLD**
- Adopt a mediterranean diet, increase physical activity, achieve weight loss.

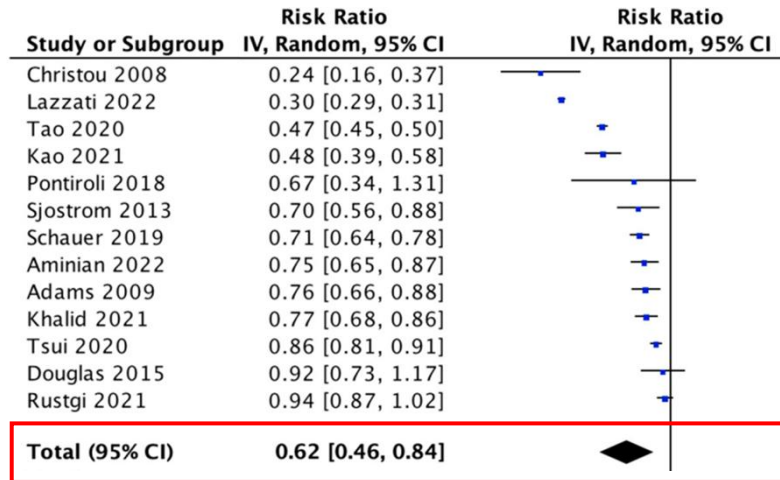
Physical activity and cancer-specific mortality risk in MASLD

5,211 participants of the NHANES 1999-2004
Association between physical activity and cancer-specific mortality risk

	Age-sex-race adjusted model		Multivariable model 1		Multivariable model 2	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Total physical activity						
By PA Guideline						
<150 min per week	Reference		Reference		Reference	
≥150 min per week	0.77 (0.46–1.27)	0.2958	0.78 (0.41–1.5)	0.4478	0.81 (0.41–1.58)	0.5281
By amount of total PA						
0 min per week	Reference		Reference		Reference	
1–149 min per week	1.17 (0.59–2.35)	0.6448	1.70 (0.80–3.63)	0.1635	1.72 (0.8–3.67)	0.1612
150–299 min per week	0.56 (0.25–1.26)	0.1587	0.84 (0.32–2.2)	0.7204	0.88 (0.33–2.32)	0.7916
≥300 min per week	0.99 (0.55–1.77)	0.9638	1.34 (0.56–3.2)	0.5092	1.39 (0.57–3.37)	0.462
By Vigorous LTPA ^a						
No LTPA	Reference		Reference		Reference	
0% vigorous LTPA	0.84 (0.52–1.35)	0.458	1.05 (0.61–1.82)	0.8595	1.06 (0.59–1.91)	0.8541
1%–49% vigorous LTPA	0.57 (0.21–1.51)	0.2512	0.6 (0.15–2.4)	0.4647	0.63 (0.15–2.61)	0.5159
≥50% vigorous LTPA	0.21 (0.07–0.64)	0.0074	0.19 (0.06–0.61)	0.0061	0.21 (0.06–0.66)	0.0091

Impact of bariatric surgery on extrahepatic cancer

Meta-analysis including 13 studies
511 585 patients who underwent bariatric surgery
1 889 746 controls



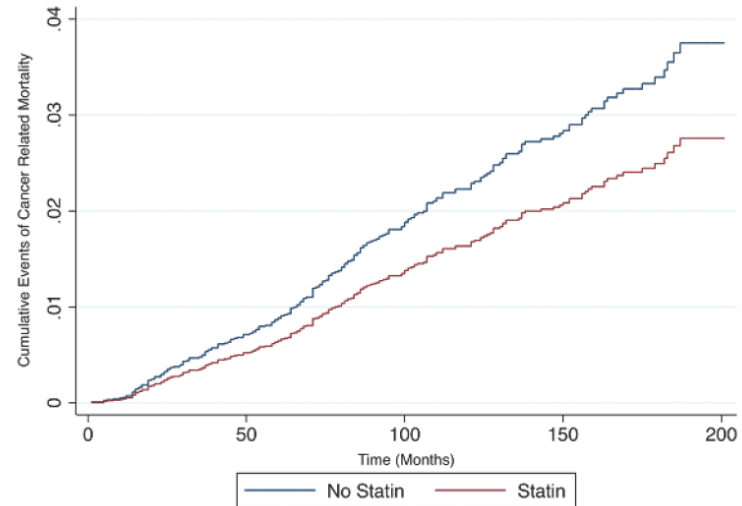
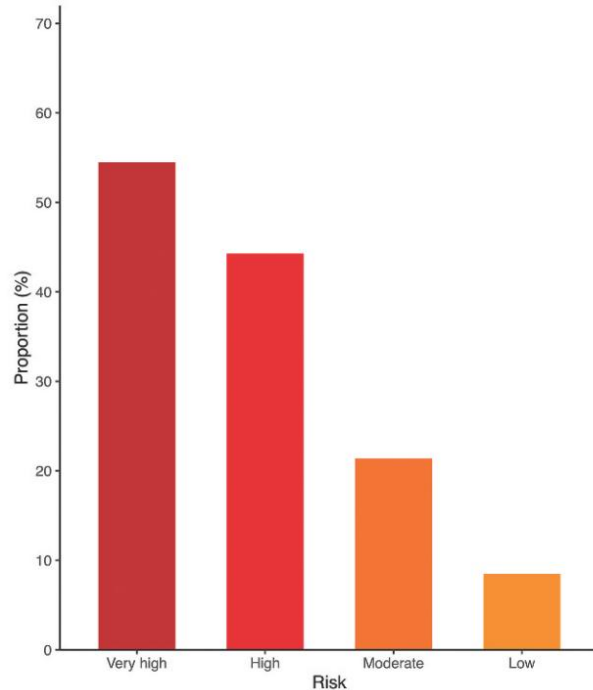
Cancer	Etudes (n)	patients (n)	RR (95%CI)
Hepatocarcinoma	8	619 870 / 17 239 239	0,35 (0,22-0,55)
Gallbladder	6	439 621 / 1 653 119	0,41 (0,18-0,96)
Pancreas	7	440 656 / 1 658 865	0,52 (0,29-0,93)
Œsophageal	9	487 825 / 1 797 407	0,66 (0,34-1,30)
Colorectal	13	382 686 / 3 143 652	0,69 (0,53-0,88)
Endometrial	8	346 460 / 1 075 024	0,38 (0,26-0,55)
Ovarian	6	317 977 / 753 595	0,45 (0,31-0,64)
Breast	13	425 846 / 1 757 986	0,56 (0,44-0,71)
Kidney	9	776 444 / 4 626 529	0,69 (0,47-0,99)
Multiple myeloma	7	440 656 / 1 658 865	0,54 (0,26-1,11)
Thyroid	6	439 621 / 1 652 759	0,84 (0,66-1,08)
Stomac	5	390 525 / 1 219 643	0,60 (0,21-1,71)
Prostate	4	58 749 / 391 040	0,78 (0,22-2,70)

Should we update the guidelines on extrahepatic cancer in MASLD?

- **Screening programs for extrahepatic cancer should be strictly followed in patients with MASLD**
- Adopt a mediterranean diet, increase physical activity, achieve weight loss.
- Screen and treat metabolic comorbidities

Statins and cancer-specific mortality risk in MASLD

12,538 participants of the NHANES 1999-2018
Association between statins and cancer-specific mortality risk



Impact of GLP1RA on extrahepatic cancer

Meta-analysis of 90 randomized controlled trials (80 for T2DM; 10 for obesity)
> 24 weeks follow-up; > 100 participants

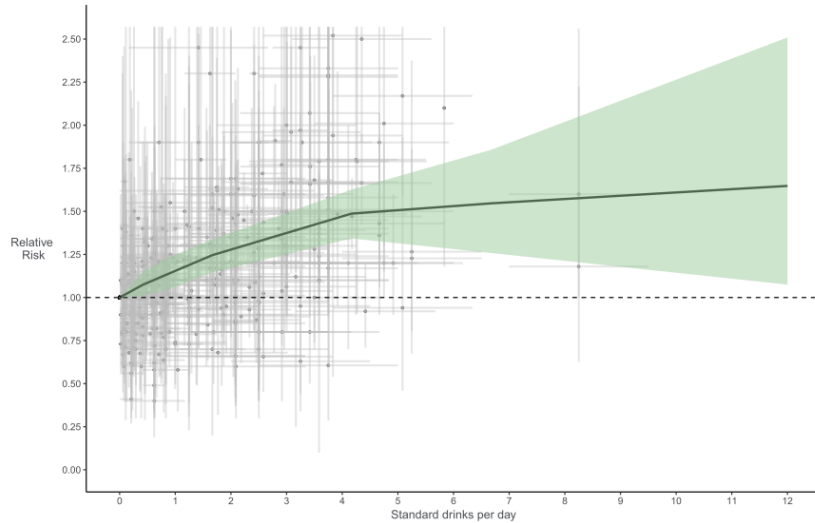
Cancer	Patients (n)	Studies (n)	Odd ratio	I ²
Biliary tract	61,724	14	0.98 [0.54 - 1.78]	0%
Colorectal	101,654	56	1.13 [0.92 - 1.39]	0%
Anal	33,993	3	0.63 [0.14 - 2.76]	0%
Colon	88,268	39	1.18 [0.91 - 1.52]	0%
Rectum	80,421	30	1.13 [0.74 - 1.72]	0%
Gallbladder	45,997	8	1.32 [0.43 - 4.00]	0%
Stomach	68,747	24	0.88 [0.58 - 1.33]	0%
Liver	68,867	21	0.79 [0.51 - 1.21]	0%
Oesophageal	53,490	12	0.70 [0.38 - 1.28]	0%
Pancreas	94,279	49	1.05 [0.77 - 1.43]	0%
Small intestine	41,877	5	0.78 [0.20 - 3.04]	0%
All	124,791	90	0.99 [0.86 - 1.13]	0%

Should we update the guidelines on extrahepatic cancer in MASLD?

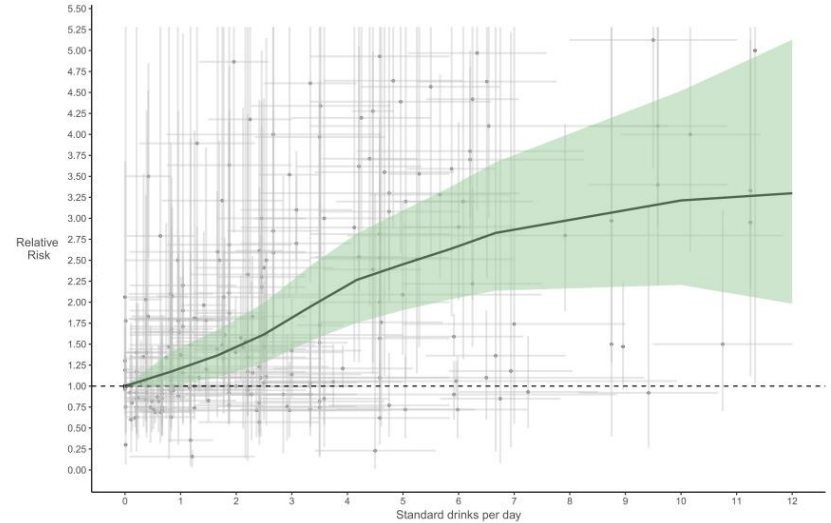
- **Screening programs for extrahepatic cancer should be strictly followed in patients with MASLD**
- Adopt a mediterranean diet, increase physical activity, achieve weight loss.
- Screen and treat metabolic comorbidities
- Reduce modifiable risk factors, especially smoking and alcohol consumption

Alcohol consumption and risk of cancer

Breast cancer



Oesophageal cancer



Should we update the guidelines on extrahepatic cancer in MASLD?

- **Screening programs for extrahepatic cancer should be strictly followed in patients with MASLD**
- Adopt a mediterranean diet, increase physical activity, achieve weight loss.
- Screen and treat metabolic comorbidities
- Reduce modifiable risk factors, especially smoking and alcohol consumption
- Improve the understanding of the links between MASLD and extrahepatic cancer
- Tailor MASLD treatment and cancer screening according to risk



PARIS MASH MEETING

11th edition