

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



Early onset pancreatic cancer

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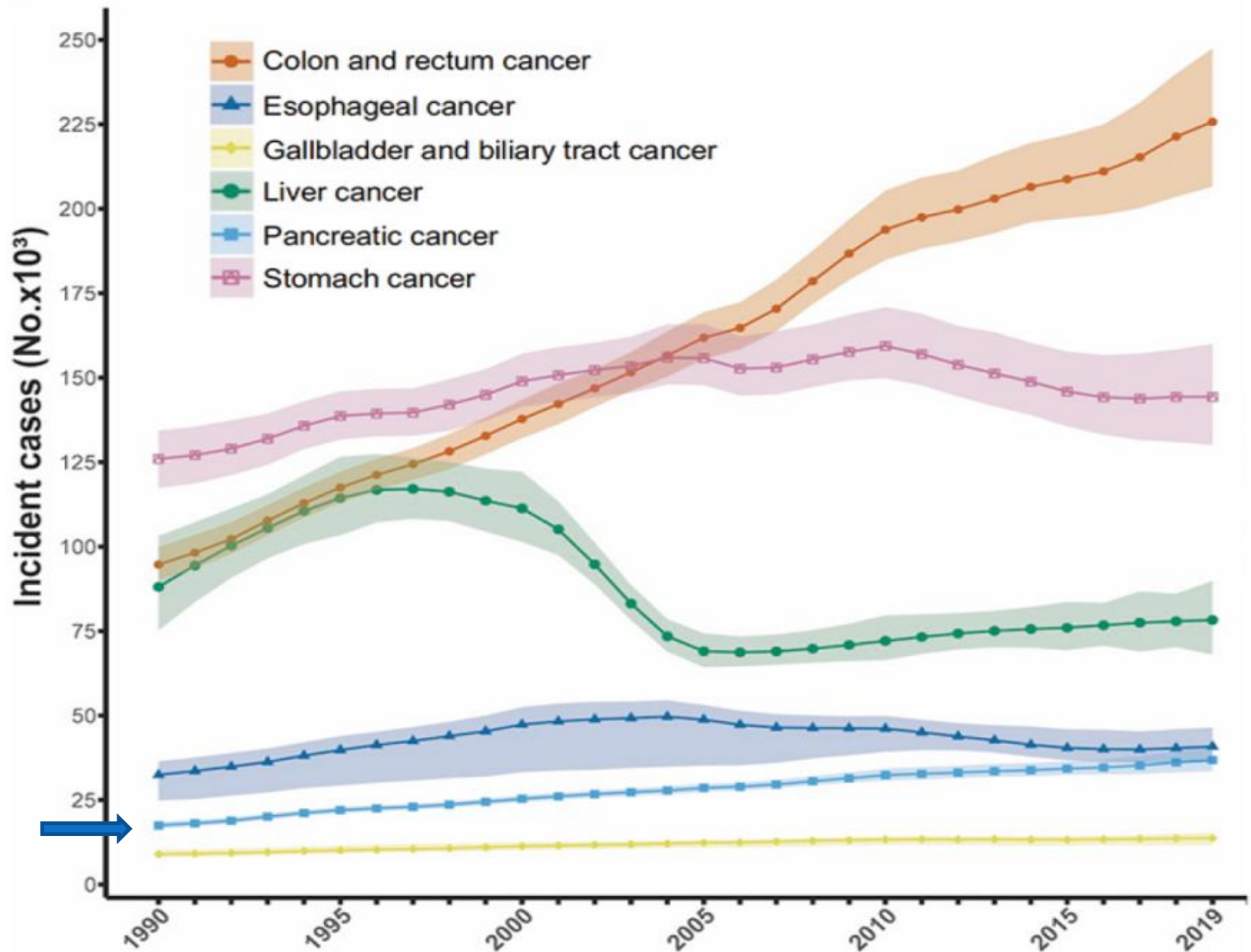
Definition

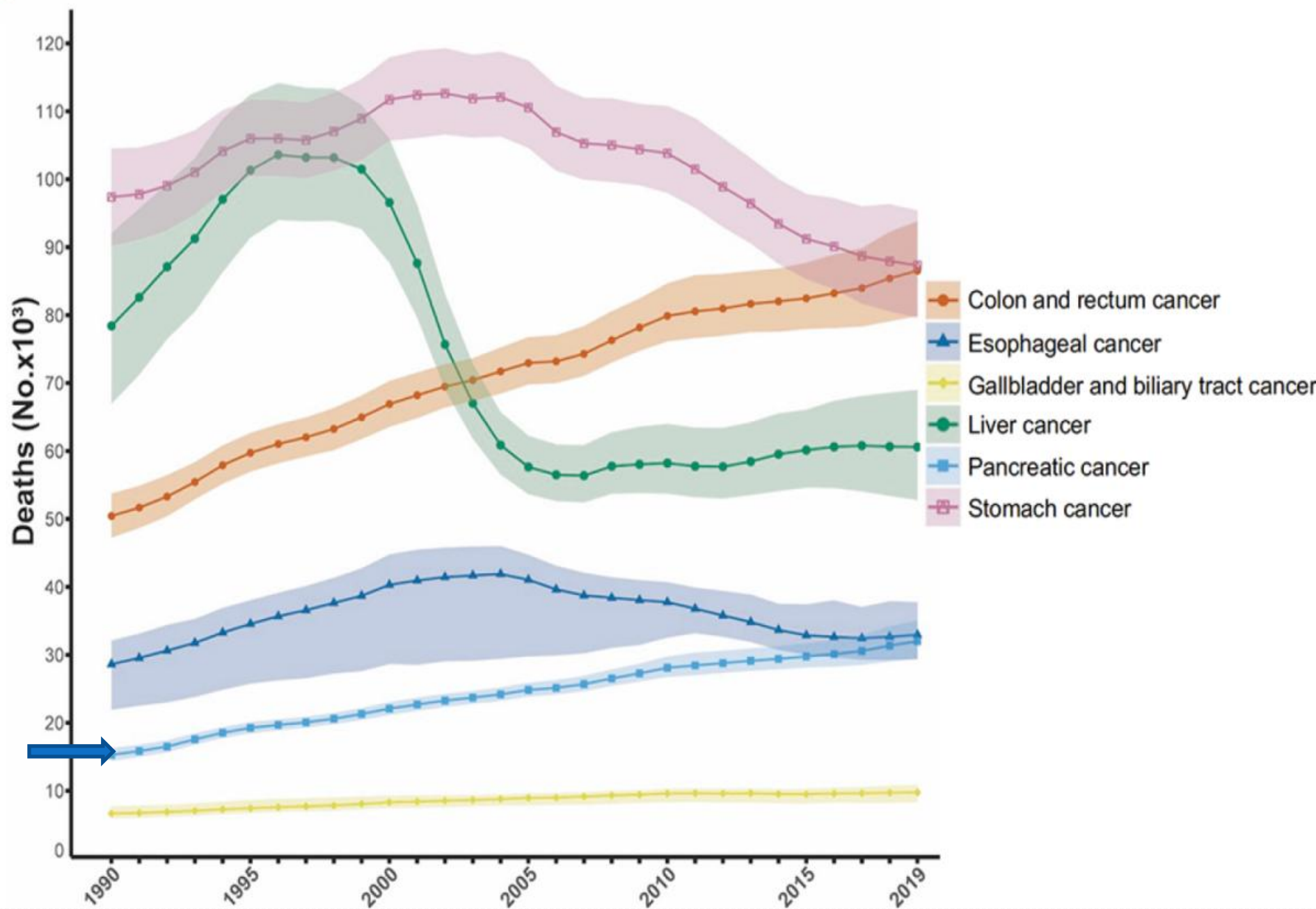
- Early-onset pancreatic cancer (**EOPC**) < 50 years
 - 45
 - 55
 - 60
 - 65
- 11.4 % of patients diagnosed with pancreatic cancer are under 55 years of age . (varies in different studies, from 4.4 % to 17 %)

Incidane & Death

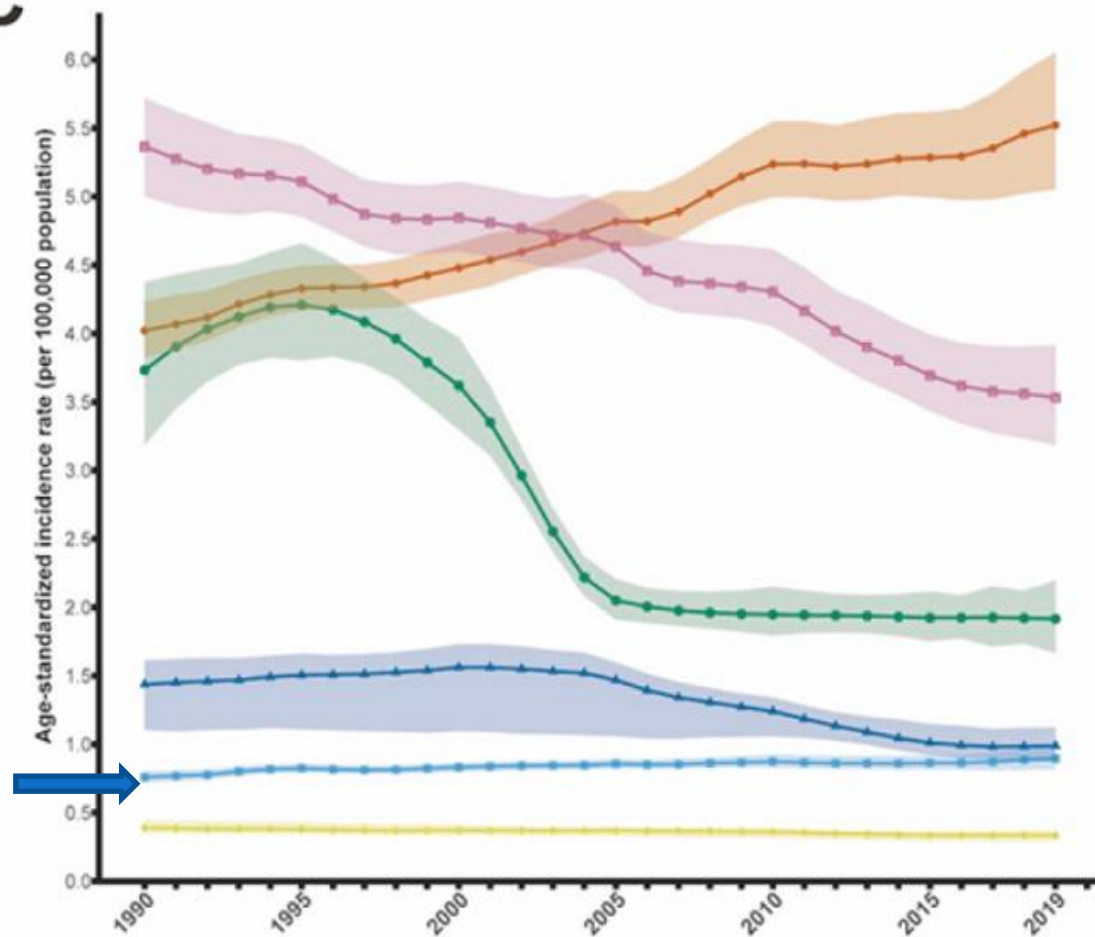
Estimated Annual Percentage Change

A



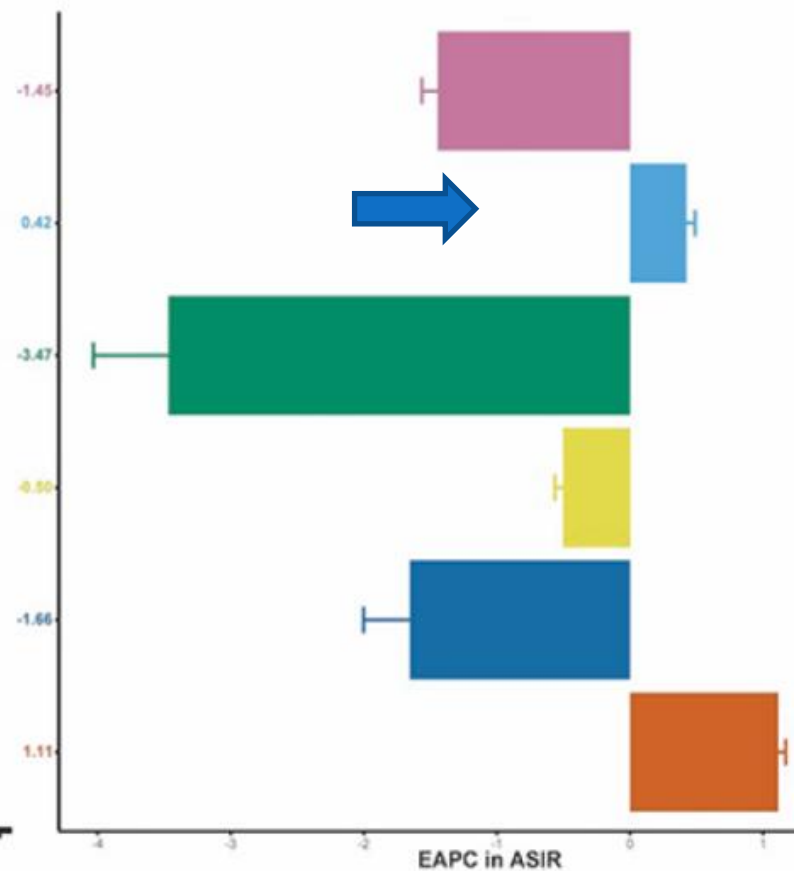
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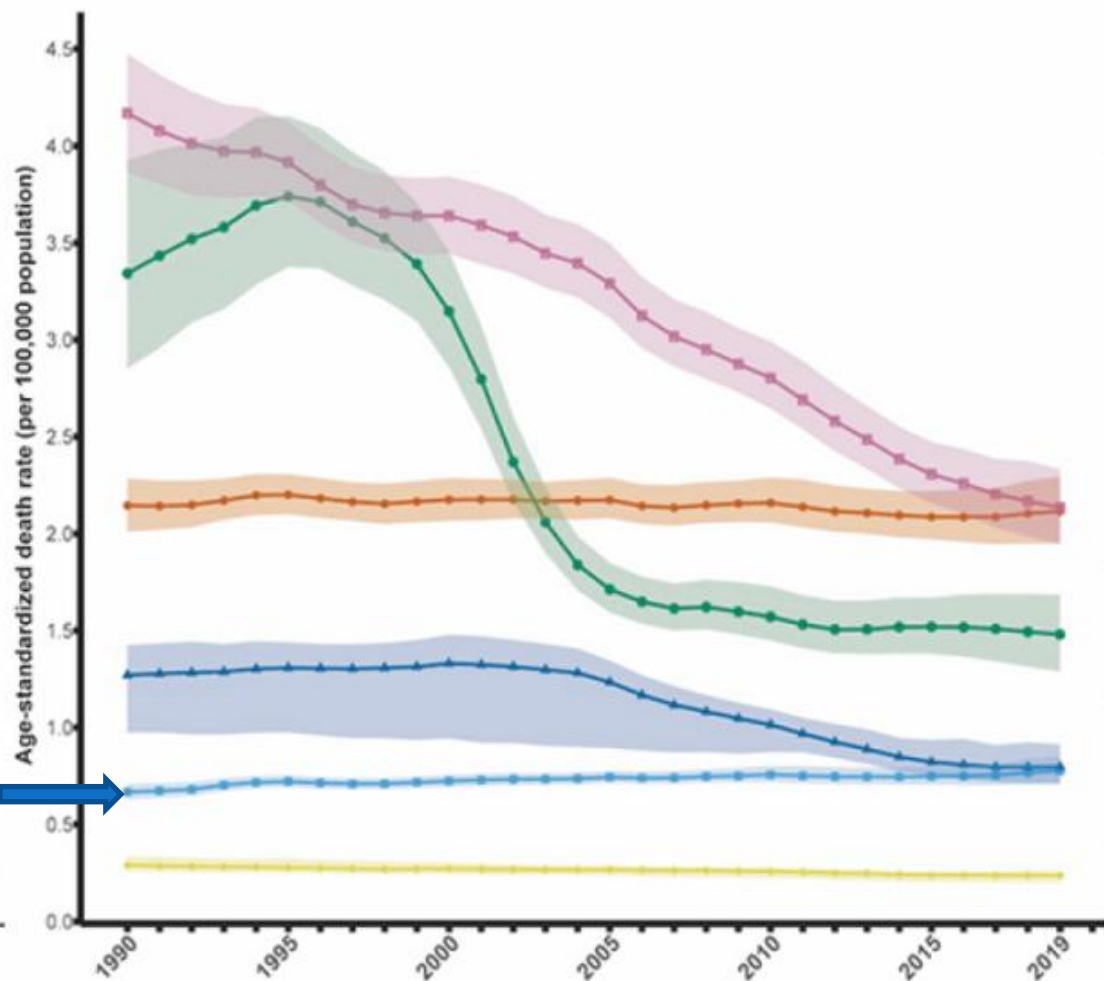
C



- Colon and rectum cancer
- Esophageal cancer
- Gallbladder and biliary tract cancer
- Liver cancer
- Pancreatic cancer
- Stomach cancer

D





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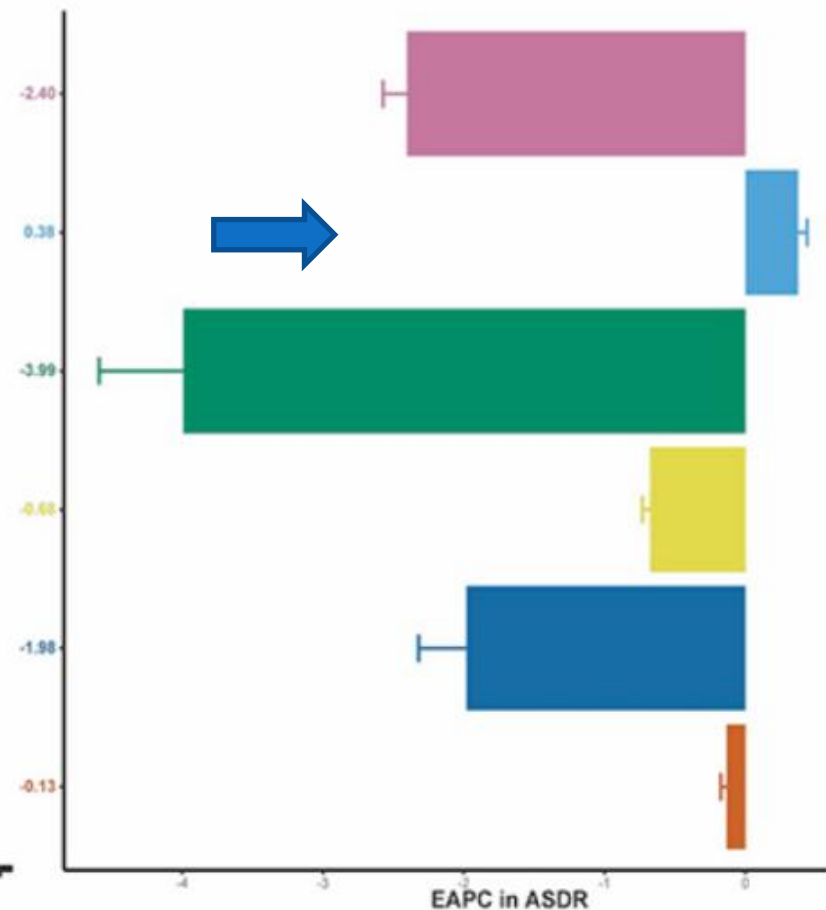
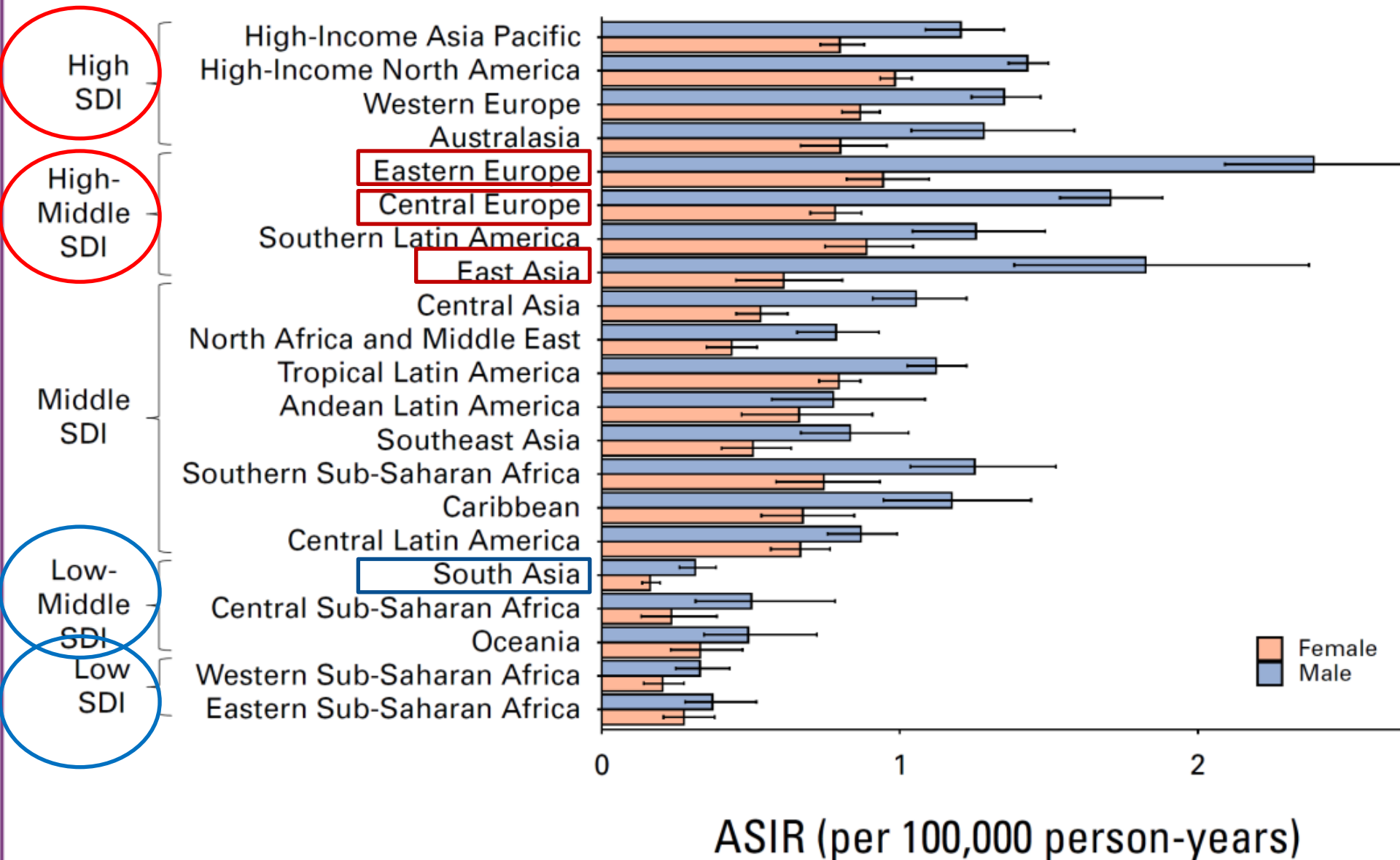


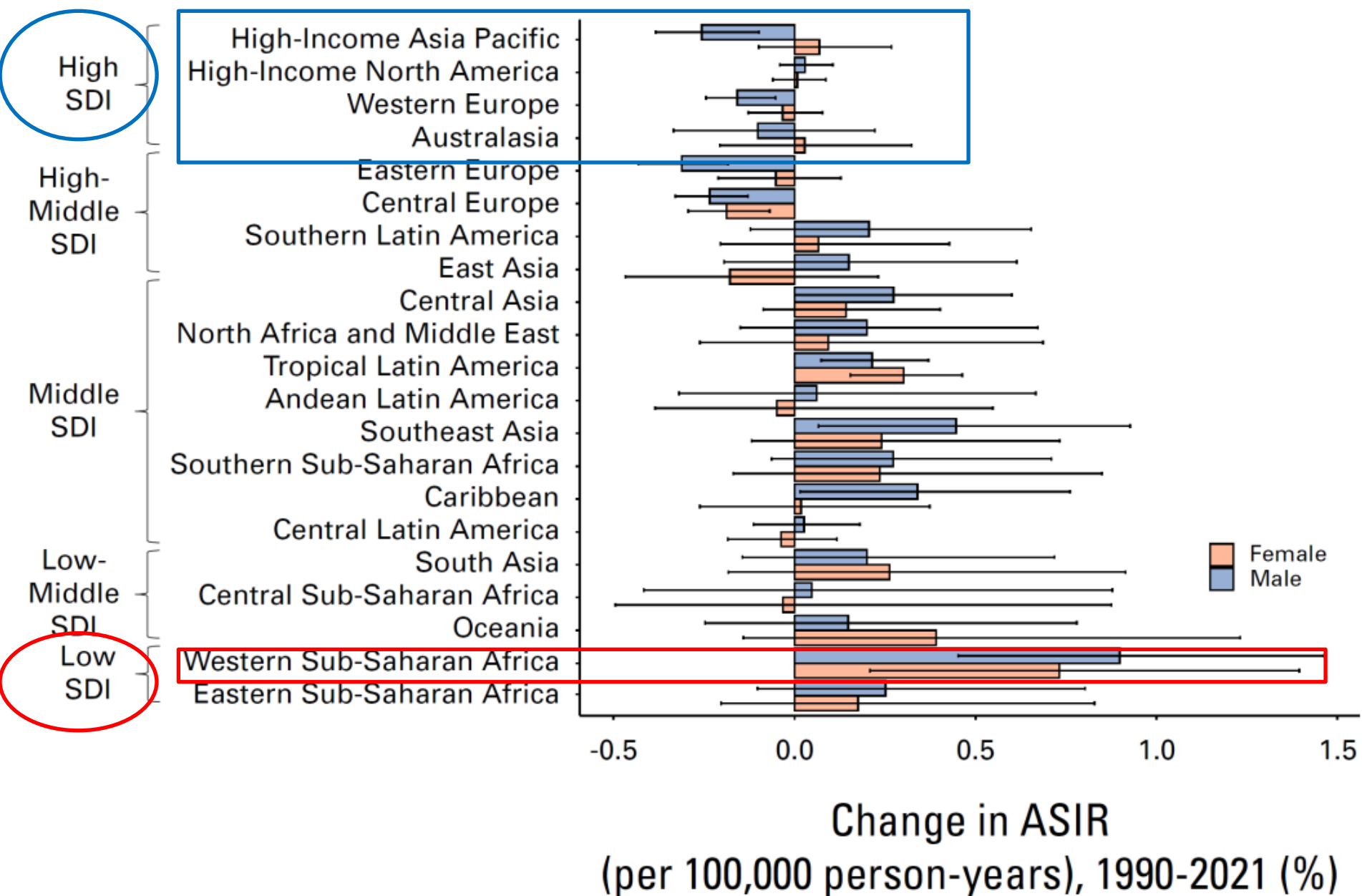
Table 1 The global incident cases, deaths, and their change trends of early-onset Gastrointestinal cancers from 1990 to 2019										
Type	Incidence (95% UI)				1990–2019	Deaths (95% UI)				1990–2019
	1990		2019			1990		2019		
	Incident cases, No. × 10 ³	ASR per 100,000	Incident cases, No. × 10 ³	ASR per 100,000		EAPC (95% CI)	Deaths, No. × 10 ³	ASR per 100,000	Deaths, No. × 10 ³	
Overall	367.74 (332.13 to 402.6)	15.7 (14.19 to 17.19)	539.75 (486.18 to 599.43)	13.19 (11.88 to 14.64)	-0.89 (-0.99 to -0.79)	276.82 (246.63 to 306.4)	11.89 (10.59 to 13.15)	309.2 (279.34 to 341.82)	7.54 (6.81 to 8.34)	-1.98 (-2.13 to -1.82)
EO-GI cancer										
Colon and rectum cancer	94.71 (89.99 to 99.86)	4.02 (3.83 to 4.23)	225.74 (206.57 to 247.43)	5.52 (5.05 to 6.05)	1.11 (1.05 to 1.17)	50.44 (47.25 to 53.75)	2.14 (2.01 to 2.28)	86.55 (79.85 to 93.81)	2.11 (1.95 to 2.29)	-0.13 (-0.17 to -0.09)
Esophageal cancer	32.45 (24.9 to 36.4)	1.44 (1.1 to 1.61)	40.82 (36.17 to 46.42)	0.99 (0.88 to 1.12)	-1.66 (-2 to -1.31)	28.63 (21.93 to 32.11)	1.27 (0.97 to 1.42)	32.96 (29.38 to 37.75)	0.8 (0.71 to 0.91)	-1.98 (-2.32 to -1.64)
Gallbladder and biliary tract cancer	9.01 (8.05 to 10.29)	0.39 (0.35 to 0.45)	13.72 (11.73 to 15.27)	0.33 (0.29 to 0.37)	-0.5 (-0.56 to -0.44)	6.66 (5.92 to 7.73)	0.29 (0.26 to 0.34)	9.76 (8.32 to 10.84)	0.24 (0.2 to 0.26)	-0.68 (-0.73 to -0.62)
Liver cancer	88.18 (75.28 to 103.24)	3.73 (3.19 to 4.37)	78.3 (68.04 to 89.88)	1.92 (1.67 to 2.2)	-3.47 (-4.03 to -2.9)	78.42 (66.96 to 92.05)	3.34 (2.85 to 3.93)	60.6 (52.79 to 68.99)	1.48 (1.29 to 1.68)	-3.99 (-4.59 to -3.39)
Pancreatic cancer	17.48 (16.51 to 18.52)	0.76 (0.72 to 0.8)	36.85 (33.5 to 40.44)	0.9 (0.82 to 0.98)	0.42 (0.36 to 0.49)	15.29 (14.39 to 16.25)	0.67 (0.63 to 0.71)	32 (29.39 to 35.03)	0.78 (0.71 to 0.85)	0.38 (0.31 to 0.44)
Stomach cancer	125.97 (117.39 to 134.29)	5.37 (5 to 5.72)	144.32 (130.1 to 159.99)	3.53 (3.19 to 3.91)	-1.45 (-1.56 to -1.33)	97.38 (90.17 to 104.522)	4.17 (3.86 to 4.47)	87.33 (79.61 to 95.4)	2.13 (1.95 to 2.33)	-2.4 (-2.57 to -2.23)

ASR: age-standardized rate; CI: confidence interval; EAPC: estimated annual percentage change; UI: uncertainty interval

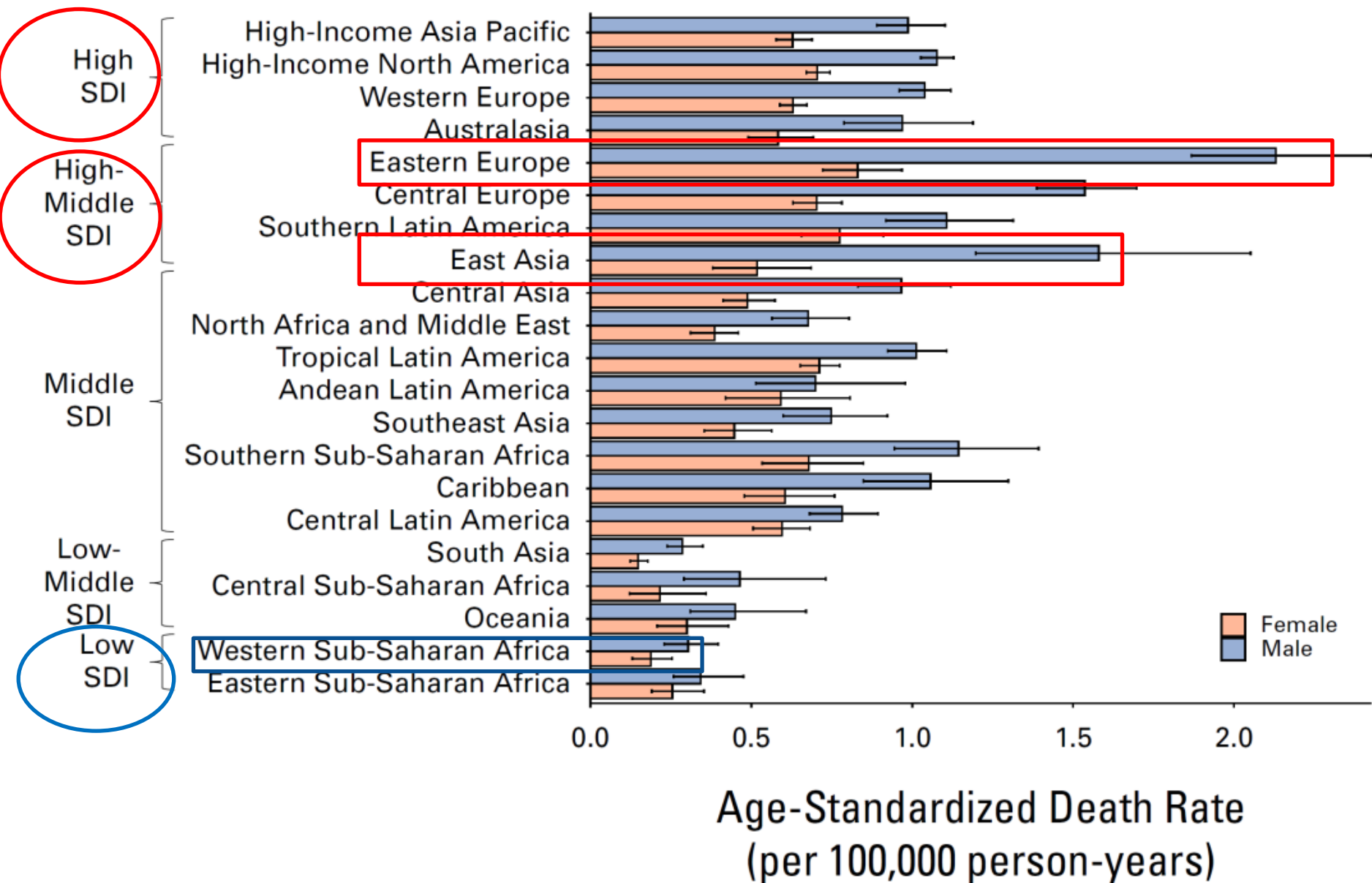
EOPC Burden by Regions

A

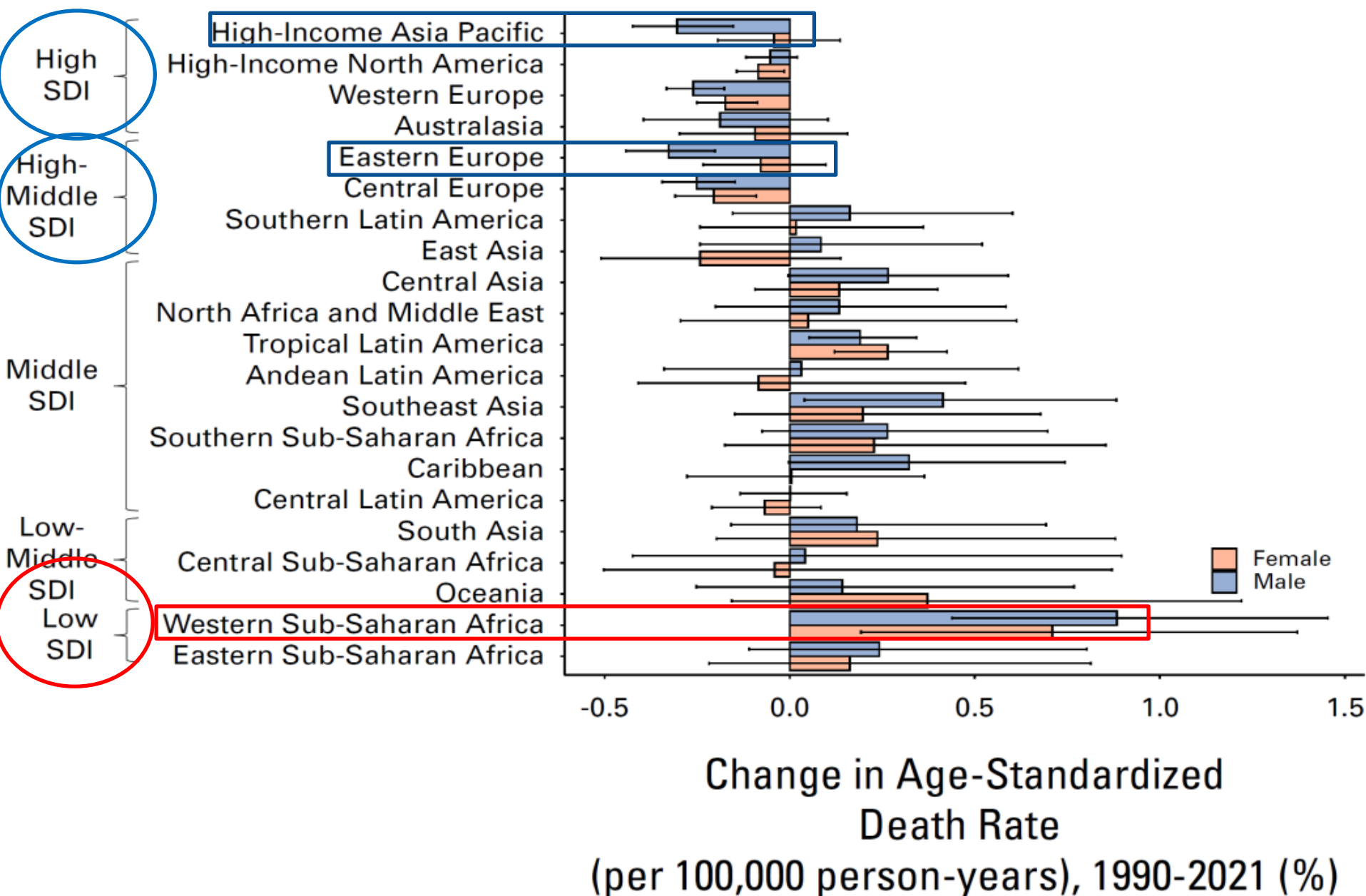


B

C



D



CLINICAL RISK FACTORS



Category	Risk	Type of study	Authors	Number of patients	Measure of Association	Comment
Hereditary factors						
Germline mutation	Pancreatic Cancer Genetic Epidemiology	Petersen et al.	379 familial PDAC	NA	7.4% of familial PDAC cases harbor pathogenic mutations in BRCA1, BRCA2, or CDKN2A	
	USA National Familial Pancreas Tumor Registry	Beeghly-Fadiel et al.	1407 PDAC	NA	31.9% of EOPC tested had pathogenic variants	
Environmental and lifestyle risk factors in PDAC						
Alcohol consumption	Retrospective Chinese cohort	Huang et al.	331 PDAC	P = 0.022	Younger age at diagnosis in case of Alcohol consumption (57.96 years vs 61.37 years)	
	Retrospective Romanian cohort	Bunduc et al.	148 PDAC	P = 0.01	Higher proportions of people consuming alcohol among younger PDAC (≤45 years VS ≥45 years)	
	United States case-control study	McWilliams et al.	1954 PDAC 3278 controls	≥26 g/day HR 2.18, 95% CI 1.17-4.09	No interaction between alcohol and age at PDAC onset (<45 years VS <60 years), P = 0.20	
	Retrospective Chinese cohort	Jiang et al.	1789 PDAC, 156 EOPC	P = 0.697	No significant differences in alcohol consumption were noted between patients diagnosed with PDAC at younger ages	
	Retrospective Japanese cohort	Eguchi et al.	36145 PDAC, 526 EOPC	P = 0.623 (frequency) P = 0.8530 (quantity)	No differences between EOPC and non-EOPC (≤40 years versus ≥40 years)	

Category Risk	Type of study	Authors	Number of patients	Measure of association	Comment
Environmental and lifestyle risk factors in PDAC					
Cigarette smoking	United States case-control study	Rulyak et al.	251 individuals of 28 families	HR 3.7, 95% CI 1.8-7.6	Smokers developed PDAC 10 years younger than nonsmokers
	Retrospective Chinese cohort	Huang et al.	331 PDAC	$P = 0.026$	<u>Mean PDAC diagnosis age of 59.0 years for smokers compared with 61.5 years for nonsmokers</u>
	Retrospective Chinese cohort	Jiang et al.	1789 PDAC, 156 EOPC	$P = 0.024$	Higher proportions of ever smokers among younger PDAC patients (≤ 45 years versus > 45 years)
	Retrospective US cohort	Salem et al.	1789 PDAC, 156 EOPC	$P = 0.03$	Higher proportions of ever smokers among younger PDAC patients (≤ 50 years versus ≥ 70 years)
	Retrospective Japanese cohort	Eguchi et al.	36145 PDAC, 526 EOPC	$P = 0.293$	No difference in smoking exposure between EOPC and non-EOPC
	Retrospective Romanian cohort	Bunduc et al.	148 PDAC	$P = 0.06$	No different proportion of ever smokers among younger PDAC patients (≤ 45 years versus ≥ 45 years)
	Retrospective Japanese cohort	Ohmoto et al.	908 PDAC, 17 > 40 years old	$P = 0.475$	No difference in smoking exposure between EOPC and non-EOPC
	United States case-control study	McWilliams et al.	1954 PDAC and 3278 control	$P = 0.20$	No interaction between smoking and age
The increasing burden of early-onset pancreatic and biliary tract cancers: a review of risk factors . A. Boilève et al. ESMO Gastrointestinal Oncology . 2025					

Category Risk	Type of study	Author s	Number of patients	Measure of Association	Comment
Pancreatitis	Retrospective United States cohort	Dzeleto vic et al.	2573 PDAC	$P = 0.005$	Patients with a pancreatitis history were <u>younger at diagnosis</u> than those without (<u>63 years vs 65 years</u>)
	Pooled analysis of 10 case-control studies	Duell et al.	4674 PDAC, 10 703 controls with history of pancreatitis	$P = 0.006$	Patients < 65 years were more likely to have a history of pancreatitis than older patients
	Cohort study	Augustine et al.	98 PDAC, 82 tropical pancreatitis	$P = 0.0035$	Patients with tropical pancreatitis were diagnosed at a significantly younger age (47.5 years) compared with those with PDAC alone
	Retrospective Romanian cohort	Bunduc et al.	148 PDAC	$P = 0.59$	No significant differences in chronic pancreatitis frequency between younger age (≤ 45 years) and older age (> 45 years) patients
	Retrospective Japanese cohort	Eguchi et al.	36145 PDAC, 526 EOPC	$P = 0.600$	No differences between those diagnosed before 40 years of age and those aged ≥ 40 years
	United States case-control study	McWilliams et al.	1954 PDAC and 3278 controls	HR 2.66, 95% CI 0.19-37.9	No significant correlation with diagnoses before age 45 years after adjustments
The increasing burden of early-onset pancreatic and biliary tract cancers: a review of risk factors . A. Boilève et al. ESMO Gastrointestinal Oncology . 2025					

Category Risk	Type of study	Authors	Number of patients	Measure of Association	Comment
Environmental and lifestyle risk factors in PDAC					
Diabetes	Retrospective United States cohort	Gupta et al.	149 PDAC and 36 482 controls with diabetes	$P = 0.07$	No trend in rate ratio between increasing age and rate of PDAC in case of diabetes
	Prospective Italian cohort	Dugnani et al.	296 PDAC	$P = 0.8$	No different mean age at diagnosis in case of diabetes
	United States case-control study	McWilliams et al.	1954 PDAC and 3278 control	HR 0.85, 95% CI 0.25-2.93	No interaction between diabetes and age at diagnosis
Obesity	United States case-control study	Li et al.	841 PDAC and 754 controls	$P < 0.001$	Younger age at diagnosis in case of obesity at age 20-49 years (56 years vs 63 years, $p = 0.003$)
	United States case-control study	McWilliams et al.	1954 PDAC and 3278 control	$P = 0.52$	No interaction of obesity with age at PDAC onset (<45 years VS<60 years
Physical activity	European case-control study	Noor et al.	88 PDAC and 3970 controls	HR 4.0, 95% CI 1.1-14.3	<u>Physical inactivity before the age of 60 years</u> was associated with a significantly <u>increased risk of PDAC</u> compared with active individuals
The increasing burden of early-onset pancreatic and biliary tract cancers: a review of risk factors . A. Boilève et al. ESMO Gastrointestinal Oncology . 2025					

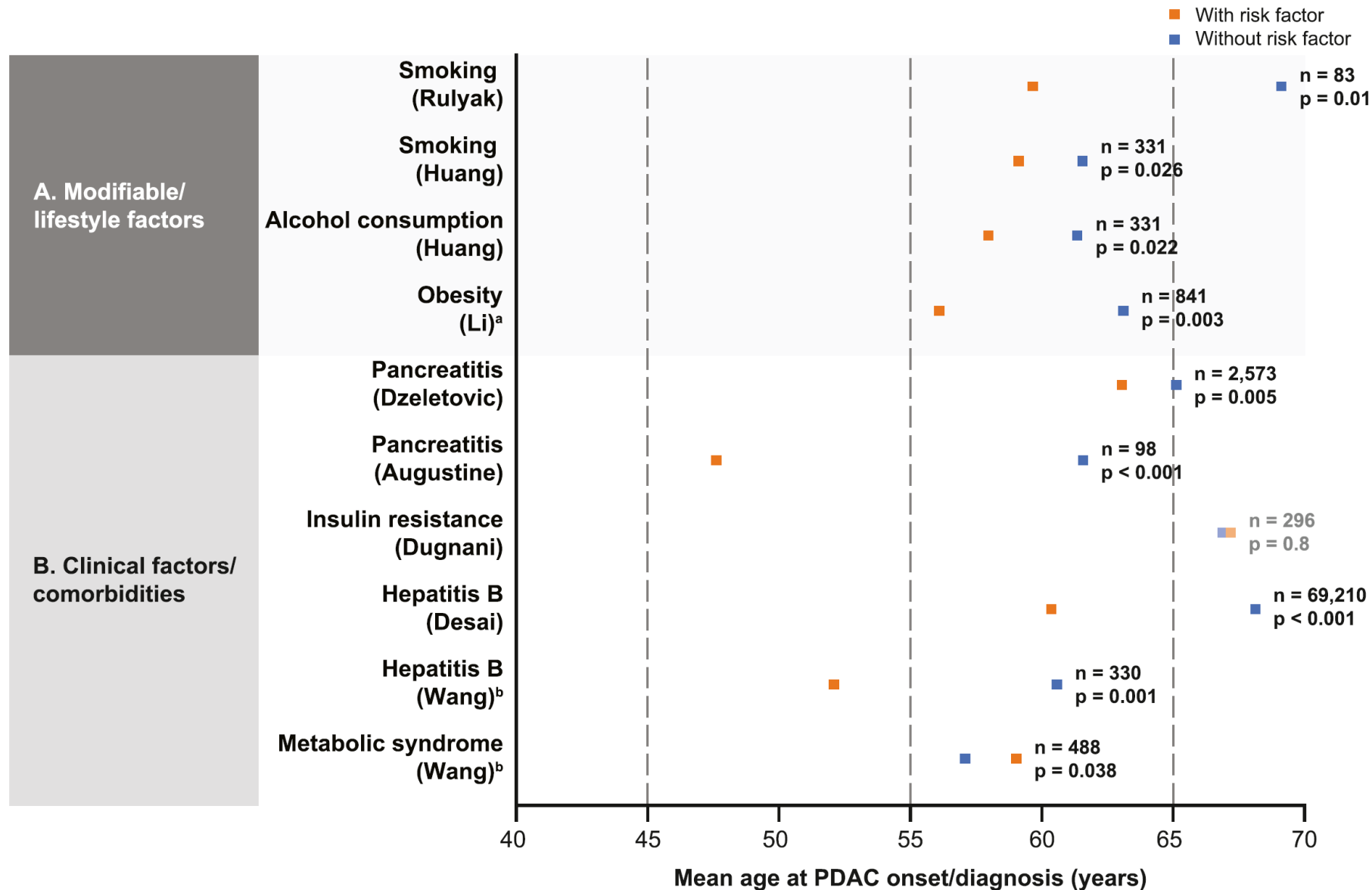
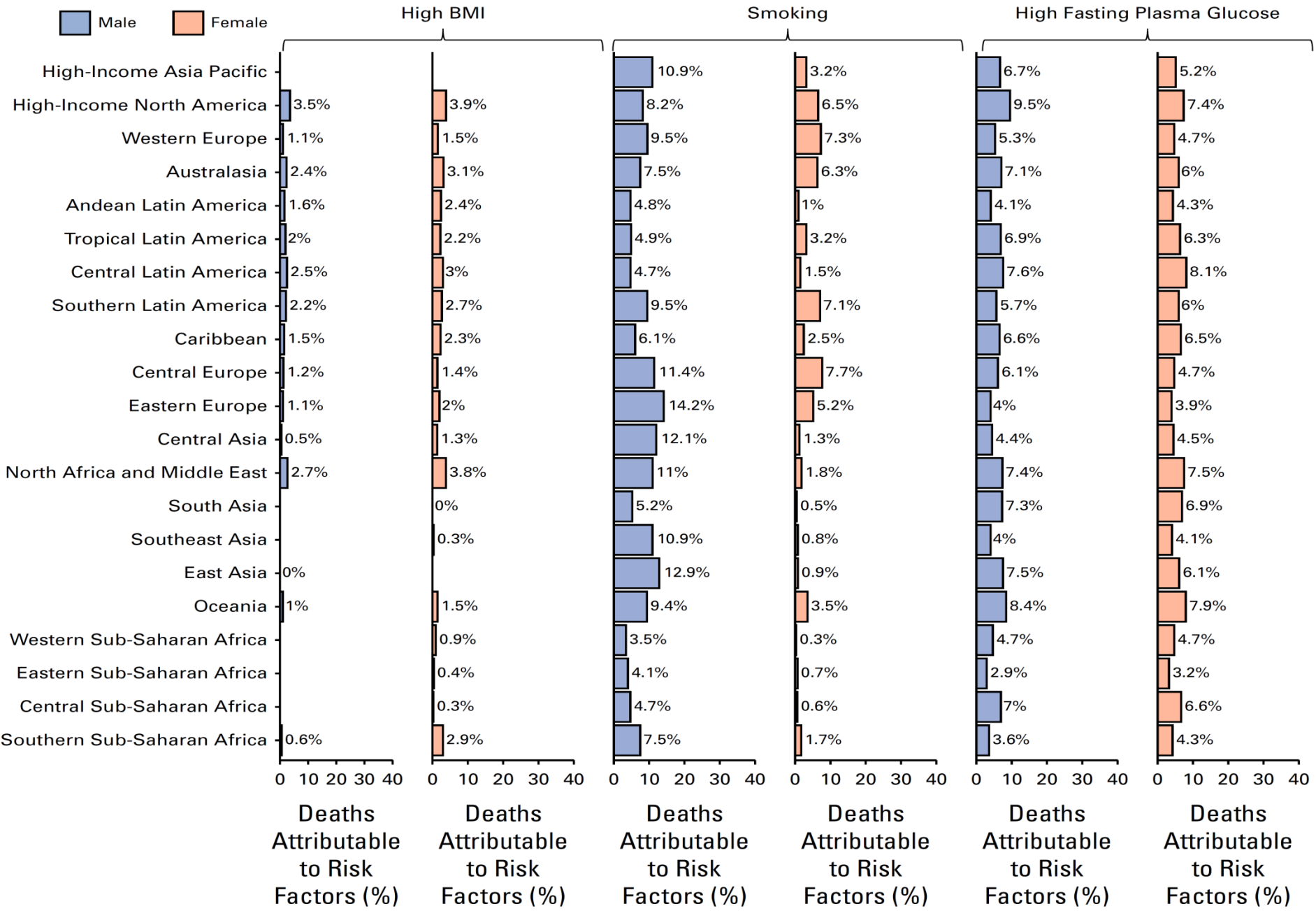


Fig. 2. Mean age at PDAC onset/diagnosis in patients with and without specific modifiable/lifestyle factors (A) and clinical factors/comorbidities (B). Statistically significant data in bold. ^aObesity at 20–29 years of age vs never overweight/obese. ^bMedian age. PDAC, pancreatic adenocarcinoma.



EOPAC comparison to AOPAC

Table 1 Patient demographics, risk factors and tumor characteristics for all study participants, EOPAC compared to average onset PAC

	EOPAC (n = 84)	Average onset PAC(n = 328)	P
Age (mean, SD)y.	43.6 ± 6.6	64.7 ± 8.2	
Sex			
Male	51 (60.7%)	204 (62.2%)	
Female	33 (39.3%)	124 (37.8%)	0.803
Performance status at presentation.			
ECOG PS ≤1	70 (83.3%)	202 (61.5%)	
ECOG PS >1	14 (16.7%)	126 (38.6%)	0.001
BMI mean ± SD	23.6 ± 5.1	23.2 ± 4.9	0.247
Comorbidity			
Yes	27 (32.1%)	168 (51.2%)	0.01
No	27 (32.1%)	62 (18.9%)	
Missing	30 (35.8%)	98 (29.8%)	
Type of comorbidity			
Diabetes.	20 (23.8%)	135 (41.1%)	0.83
Hypertension.	6 (7.1%)	29 (34.5%)	
Cardiac disease.	1 (1.1%)	4 (1.2%)	
Family history of malignancy.			
No family history of cancer.	64 (76.19%)	257 (78.3%)	0.81
1st degree relative with PAC.	1 (1.2%)	5 (1.5%)	
1st degree relative with any type of cancer.	9 (10.7%)	28 (8.5%)	
Missing.	10 (11.9%)	38 (11.5%).	
Weight and BMI			
Weight mean ± SD	66.2 ± 14.7	62.1 ± 14.1	0.021
Height mean ± SD	167.5 ± 8.7	163.8 ± 9.3	0.001
BMI mean ± SD	23.6 ± 5.1	23.2 ± 4.9	0.247
BMI classification			
Underweight	18 (21.4%)	80 (24.3%)	
Normal	39 (46.4%)	157 (47.8%)	
Overweight	27 (32.2%)	91 (27.7%)	0.821
Smoking			
Yes	27 (32.1%)	91 (27.7%)	
No	57 (67.9%)	237 (72.3%)	0.780
Alcohol intake			
No	24 (28.5%)	75 (22.8%)	
Missing	60 (71.5%)	253 (77.2%)	0.87
Duration of symptoms before diagnosis (months) Median (range)	2 (0.5–12)	1 (0.3–12)	0.030
Presenting symptoms.			
Jaundice	31 (36.9%)	110 (33.6%)	0.67
Weight loss	8 (9.5%)	17 (5.2%)	
Abdominal pain	39 (46.5%)	164 (50%)	
Missing	6 (7.1%)	37 (11.2%)	

Table 2 Tumor stage and pathological characteristics in EOPAC compared to AOPAC

	EOPAC (n = 84)	AOPAC (n = 328)	p
Stage at diagnosis.			0.003
Localized (resectable).	20 (23.8%)	47 (14.4%)	
Locally advanced/border-line resectable.	24 (28.6%)	58 (17.7%)	
Metastatic	38 (45.2%)	210 (64%)	
Missing.	2 (2.4%)	13 (3.9%)	
CA19-9 (Median-range)	135.5 (0.3-145851)	248 (0.4-600000)	0.120
Tumor site.			0.803
Head	53 (63%)	208 (63.4%)	
Body	12 (14.8%)	67 (20.4%)	
Tail	8 (9.3%)	35 (10.7%)	
Non specified.	11 (13%)	18 (5.4%)	
Tumour size (cm)			
Median (range)	4.2 (1.4–13)	4.2 (0.7–19)	0.699
Histopathological subtype.			
Adenocarcinoma	58 (69%)	280 (85.3%)	
Others (tubular, papillary and acinar).	19 (22.6%)	26 (7.9%)	0.001
unknown	7 (8.3%)	22 (6.7%)	
Grade.			0.233
Well differentiated	5 (5.9%)	18 (5.4%)	
Moderate differentiated	47 (55.9%)	188 (57.4%)	
Poorly differentiated	11 (13.1%)	57 (17.4%)	
Not reported	21 (25%)	65 (19.8%)	
Neuroendocrine differentiation.			0.269
Yes	4 (4.7%)	8 (2.4%)	
No	71 (84.6%)	292 (89%)	
Missing	9 (10.7%)	28 (8.5%)	

Early Onset Pancreatic Adenocarcinoma (EOPAC): presentation, clinical course and treatment outcomes in comparison to Average Onset Pancreatic Adenocarcinoma (AOPAC): a retrospective cohort study. Rashad *et al. BMC Cancer* (2024) 24:1289

Table 3 Therapeutic interventions for pancreatic cancer according to age group and stage at diagnosis

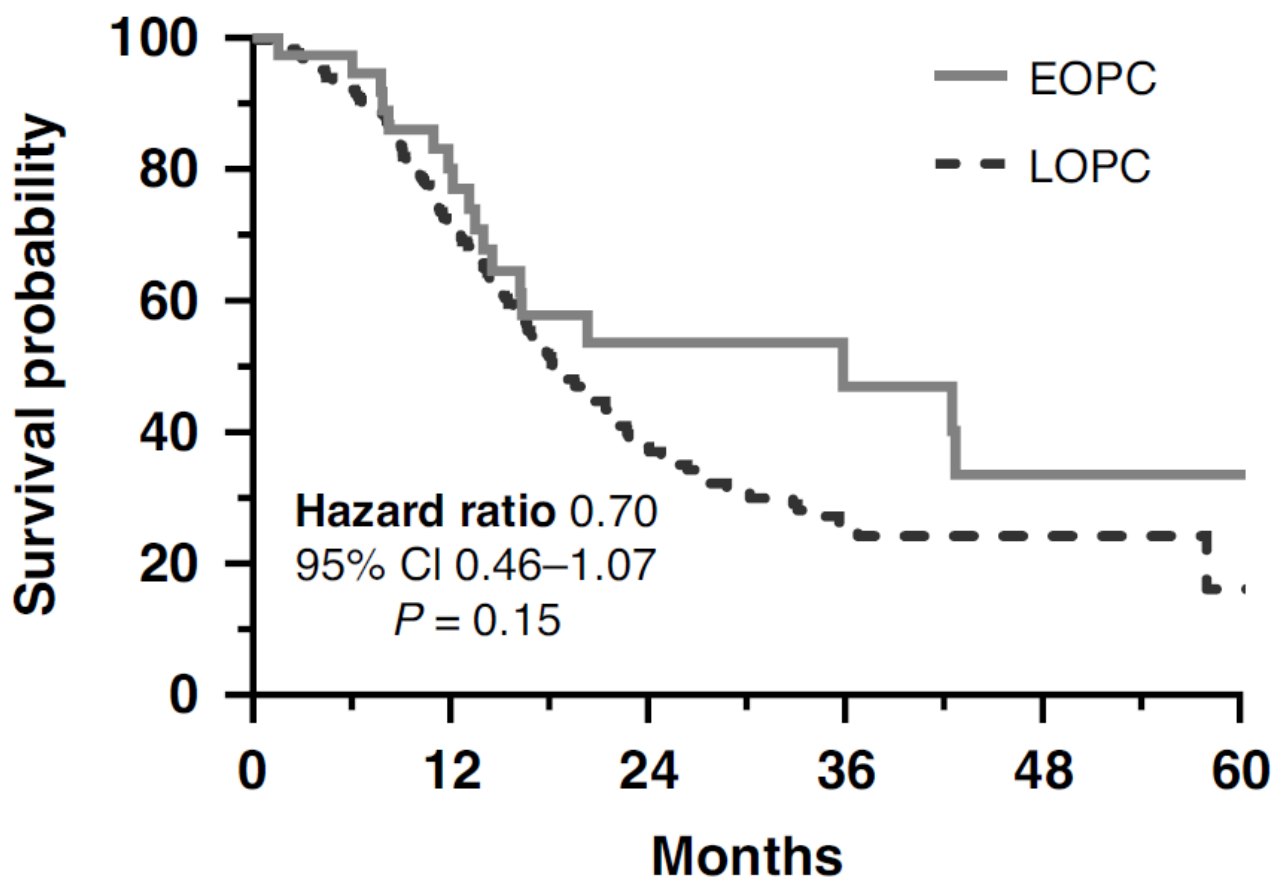
	EOPAC (n = 84)	AOPAC (n = 328)	p	
Treatment for patients presenting with localized resectable disease (n = 67).				
Upfront surgery				
Yes	19 (95%)	41(89.3%)	0.17	
No	0 -	6 (10.7%)		
unknown	1 (5%)	0		
Adjuvant chemotherapy.				
Yes.	11 (55%)	24 (51%)	0.573	
No.	4(20%)	7 (14.9%)		
Missing	5(25%)	16 (34.1%)		
Number of cycles				
Median (range)	6 (1–8)	6 (1–6)	0.9	
Treatment for patients with locally advanced and borderline resectable disease at diagnosis (n = 82).				
Preoperative treatment.				
Neoadjuvant chemotherapy.	24 (100%)	48 (82.7%)	0.257	
Pre-operative CCRT	0	4 (6.8%)		
BSC	0	6 (10.2%)		
Type of neoadjuvant chemotherapy				
Gemcitabine single agent.	11 (45.8%)	26 (54.1%)	0.57	
FOLFIRINOX	9 (37.5%)	12 (25%)		
Gemcitabine/cisplatin.	4(16.75)	7 (14.5%)		
unknown	-	3 (6.45%)		
Conversion to resectability.	4 (19%)	2 (5.3%)	0.112	
Treatment for patients with metastatic disease.				
First line systemic therapy for mets disease (n = 273).				
Chemotherapy.	43 (84.3%)	183 (82.4%)	0.001	
BSC	1 (2%)	13 (5.8%)		
Missing	7 (13.7%)	26 (11.7%)		
Median duration of treatment (in months).	3 (1–11)	3 (1–7)	0.278	
Types of chemotherapy used in first line treatment.				
Gemcitabine.	5 (11.6%)	122(62.2%)	<0.001	
Gem/cisplatin	11(25.6%)	18(9.25)		
Gem/cap	2 (4.7%)	7 (3.6%)		
FOLFIRINOX	15 (34.9%)	14(7.1%)		
GEMOX	2(4.7%)	4(2%)		
BSC	1(2.35)	13(6.6%)	-----	
Second line systemic therapy for mets disease (n = 99).				
Chemotherapy.	16 (66.6%)	55 (73.4%)		
BSC	1 (4.2%)	10 (13.3%)		
Missing	7 (29.2%)	10 (13.3%)		
Third line systemic therapy for mets disease (n = 32).				
Chemotherapy	3 (27.3%)	8 (38.1%)	----	
BSC	7 (63.6%)	6 (28.6%)		
Missing	1 (9.1%)	7 (33.3%)		
			Early Onset treatment a retrospective	

Early Onset Pancreatic Adenocarcinoma (EOPAC): presentation, clinical course and treatment outcomes in comparison to Average Onset Pancreatic Adenocarcinoma (AOPAC): a retrospective cohort study. Rashad et al. *BMC Cancer* (2024) 24:1289

EOPC & treatment Outcomes

a

Recurrence-free survival in resected patients

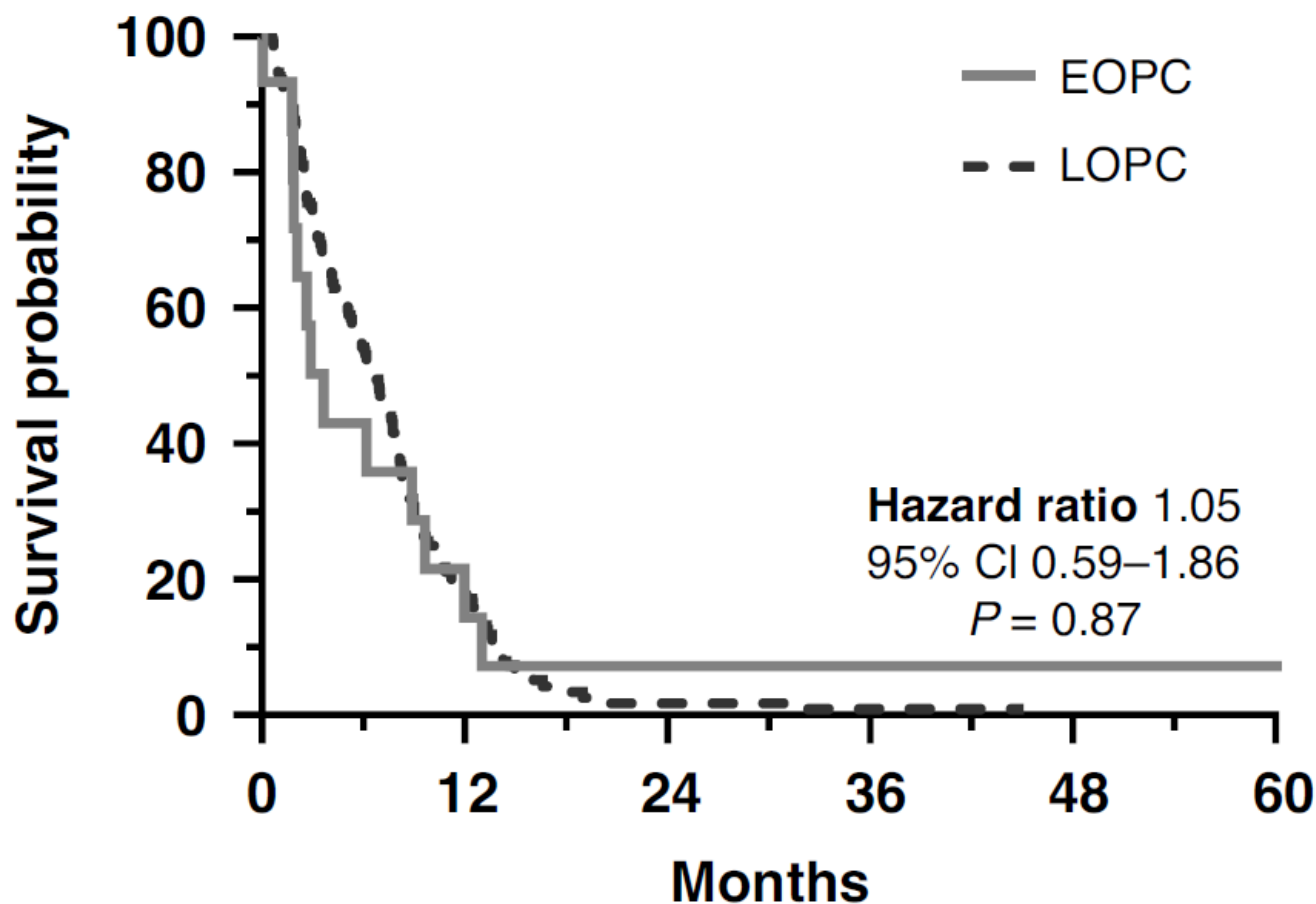


Number at risk

Months	0	12	24	36	48	60
EOPC	39	27	12	8	5	2
LOPC	364	206	56	26	12	3

b

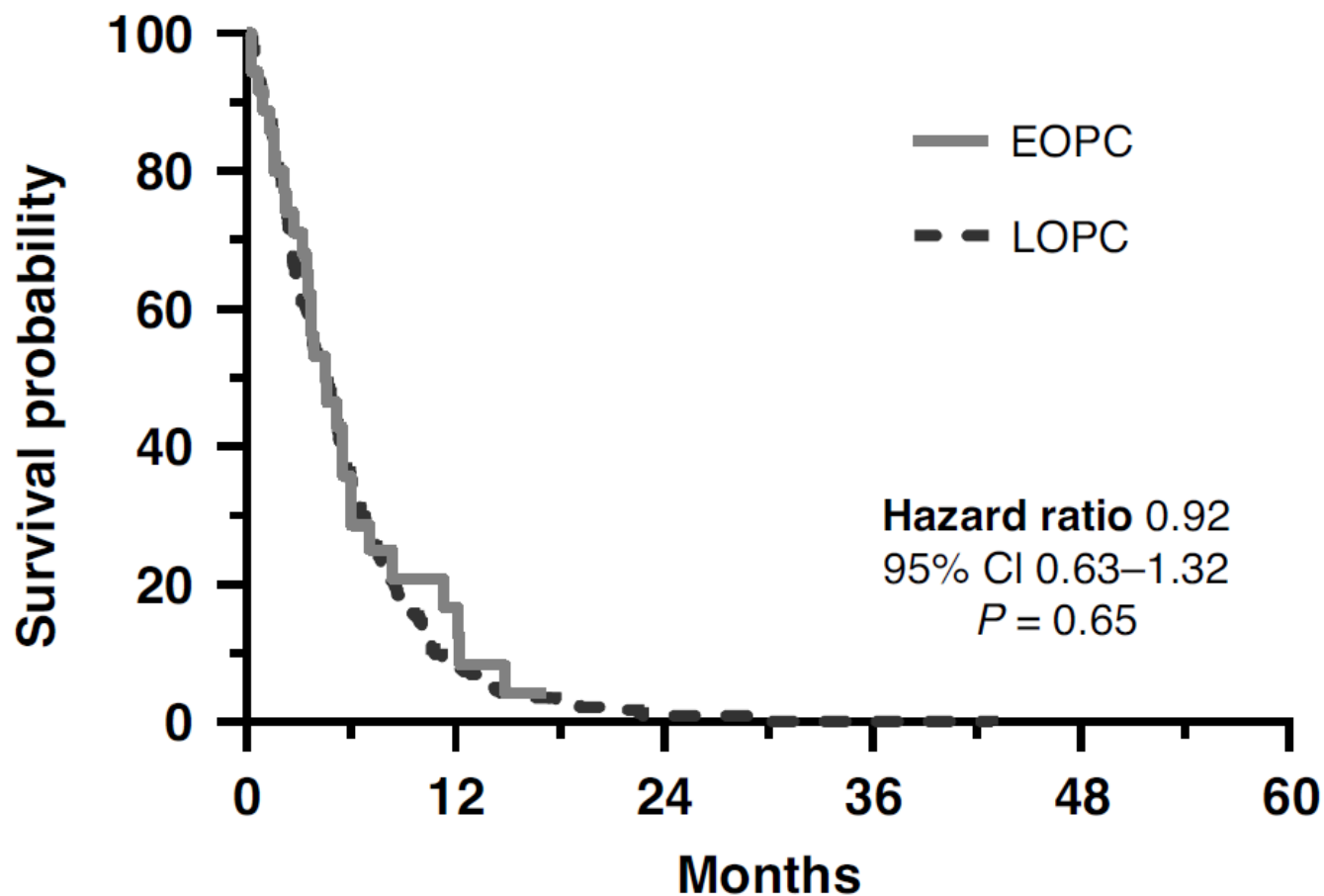
Progression-free survival in locally advanced patients



Number at risk						
Months	0	12	24	36	48	60
EOPC	15	3	2	2	2	2
LOPC	192	28	3	2	0	0

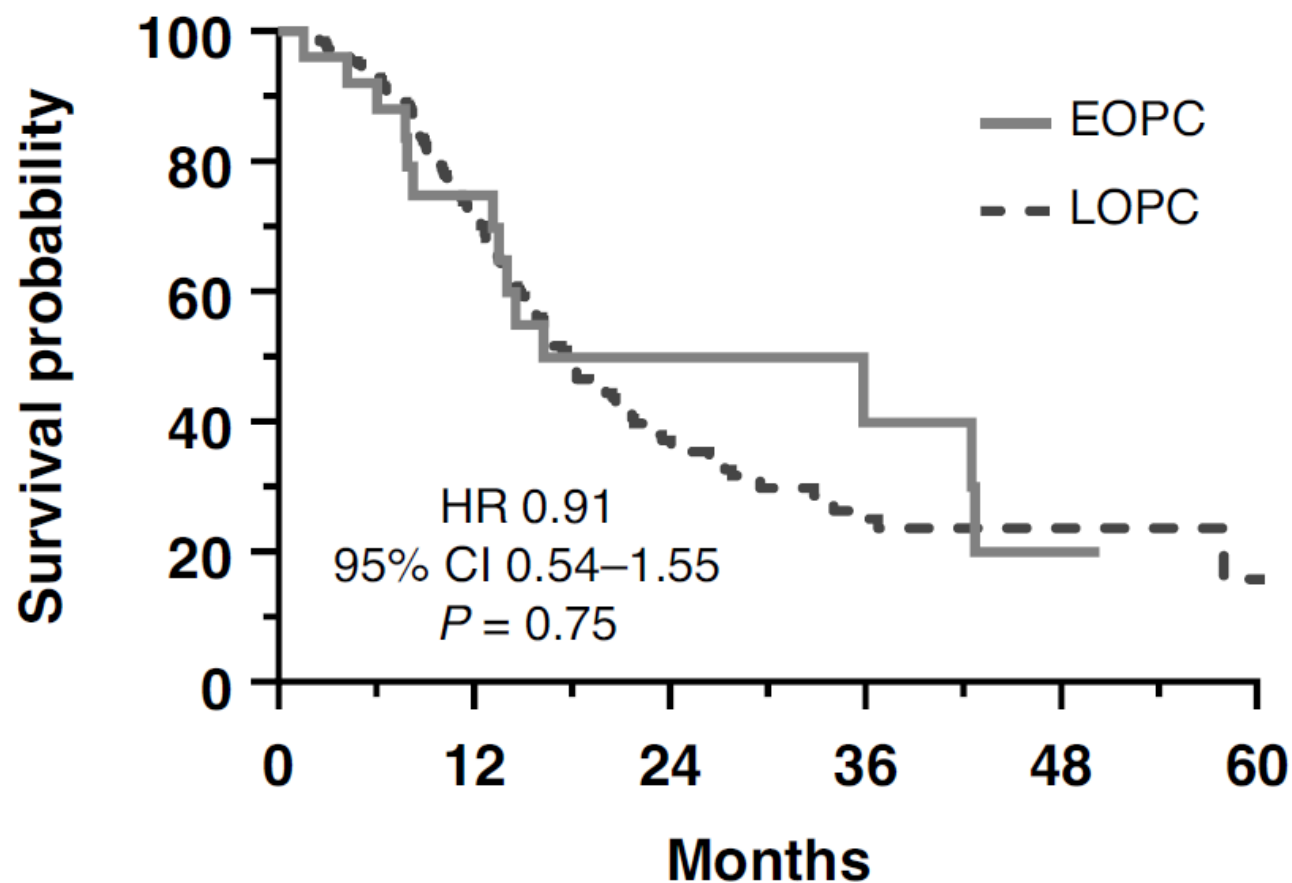
C

Progression-free survival in metastatic patients



a

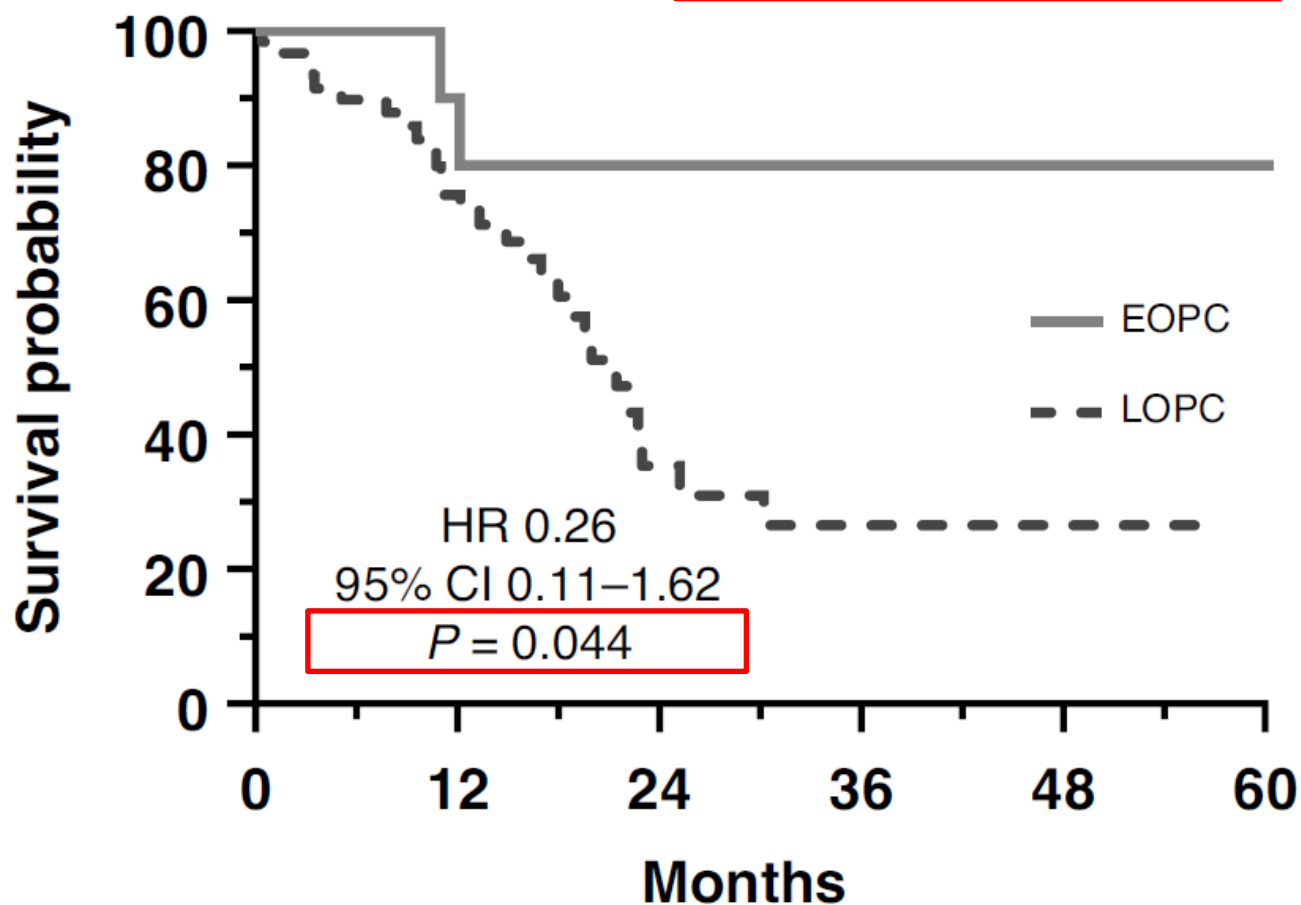
Recurrence-free survival in patients with head of pancreas tumours



Number at risk						
Months	0	12	24	36	48	60
EOPC	26	16	8	5	2	1
LOPC	275	154	43	20	8	3

b

Recurrence-free survival in patients with body and tail tumours

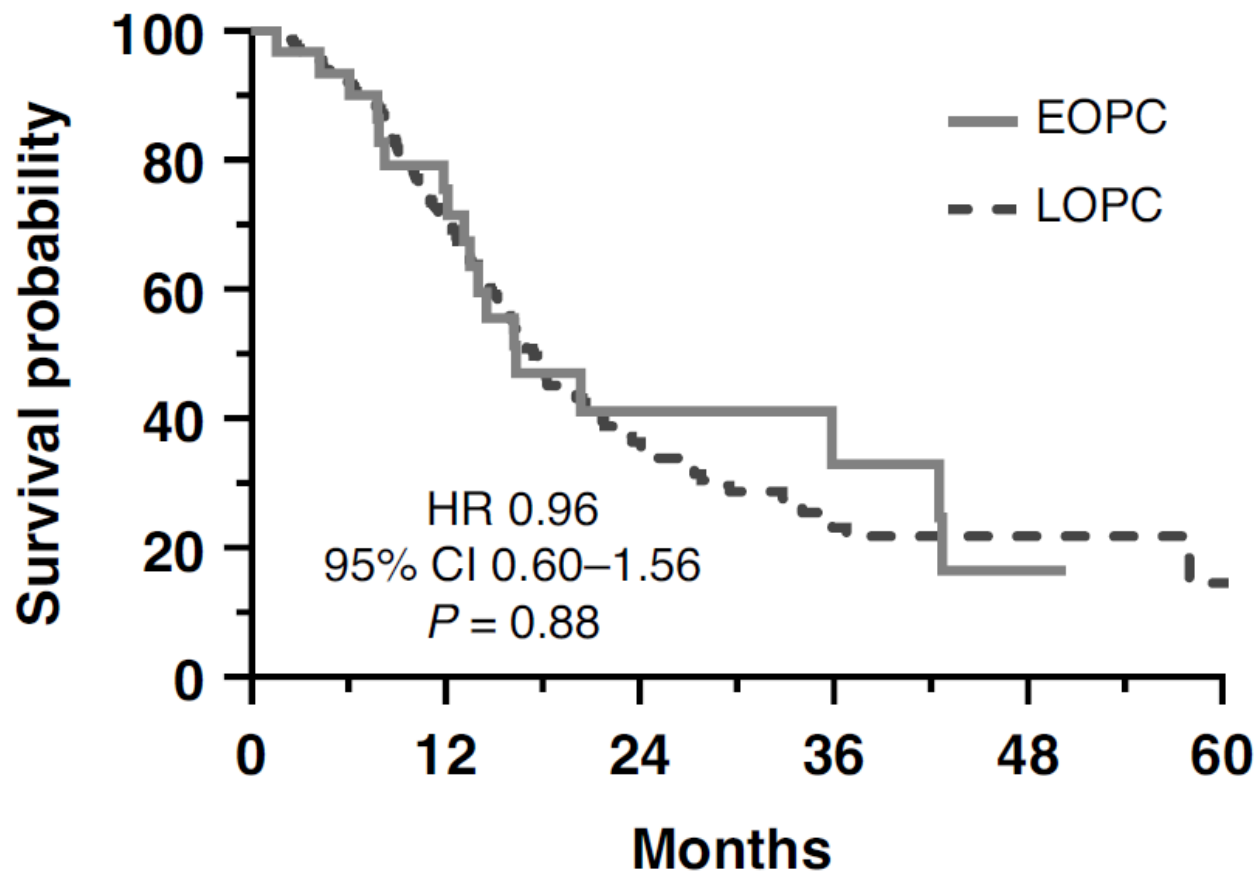


Number at risk

Months	0	12	24	36	48	60
EOPC	11	10	5	4	4	2
LOPC	60	36	9	5	4	1

C

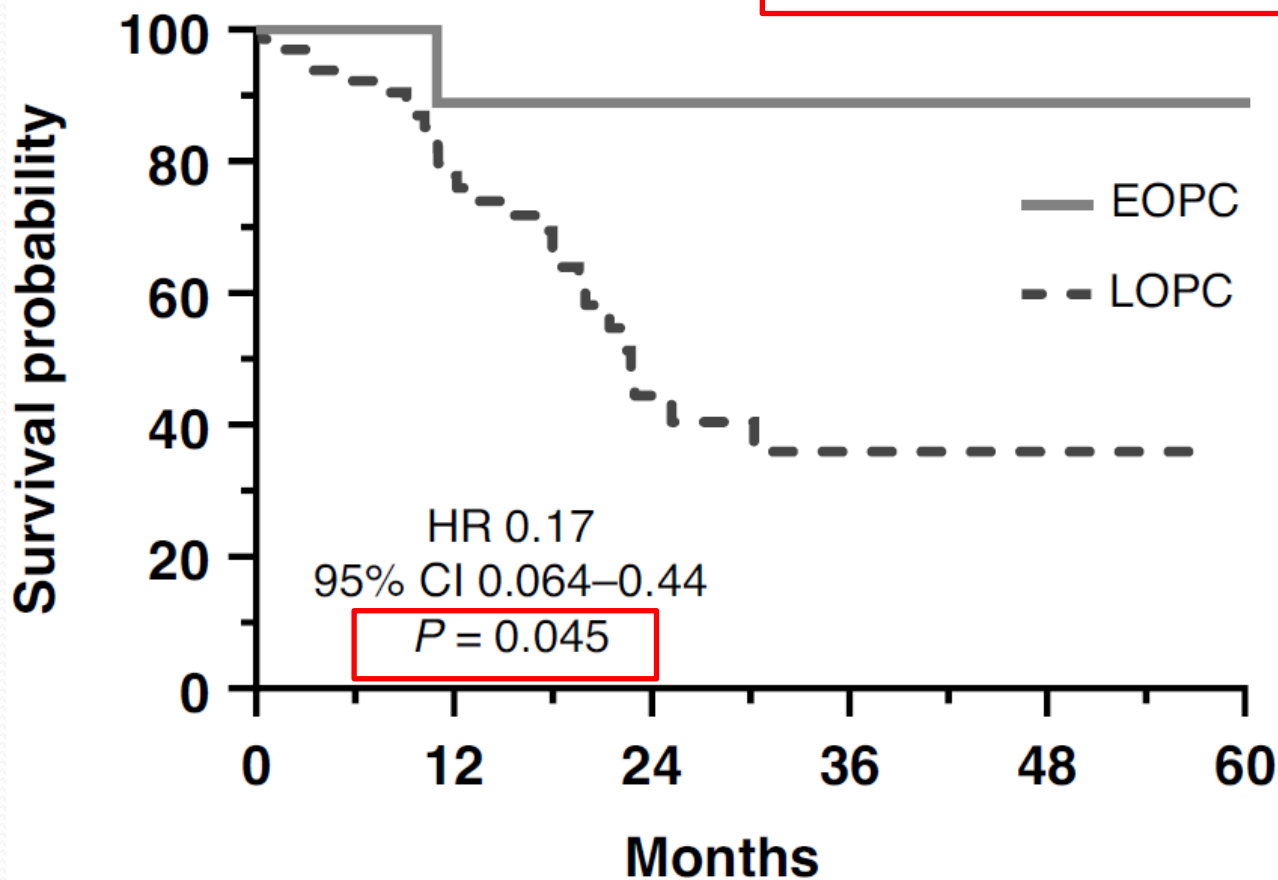
Recurrence-free survival in patients undergoing whipples



Number at risk						
Months	0	12	24	36	48	60
EOPC	31	20	8	5	2	1
LOPC	297	165	45	20	8	3

d

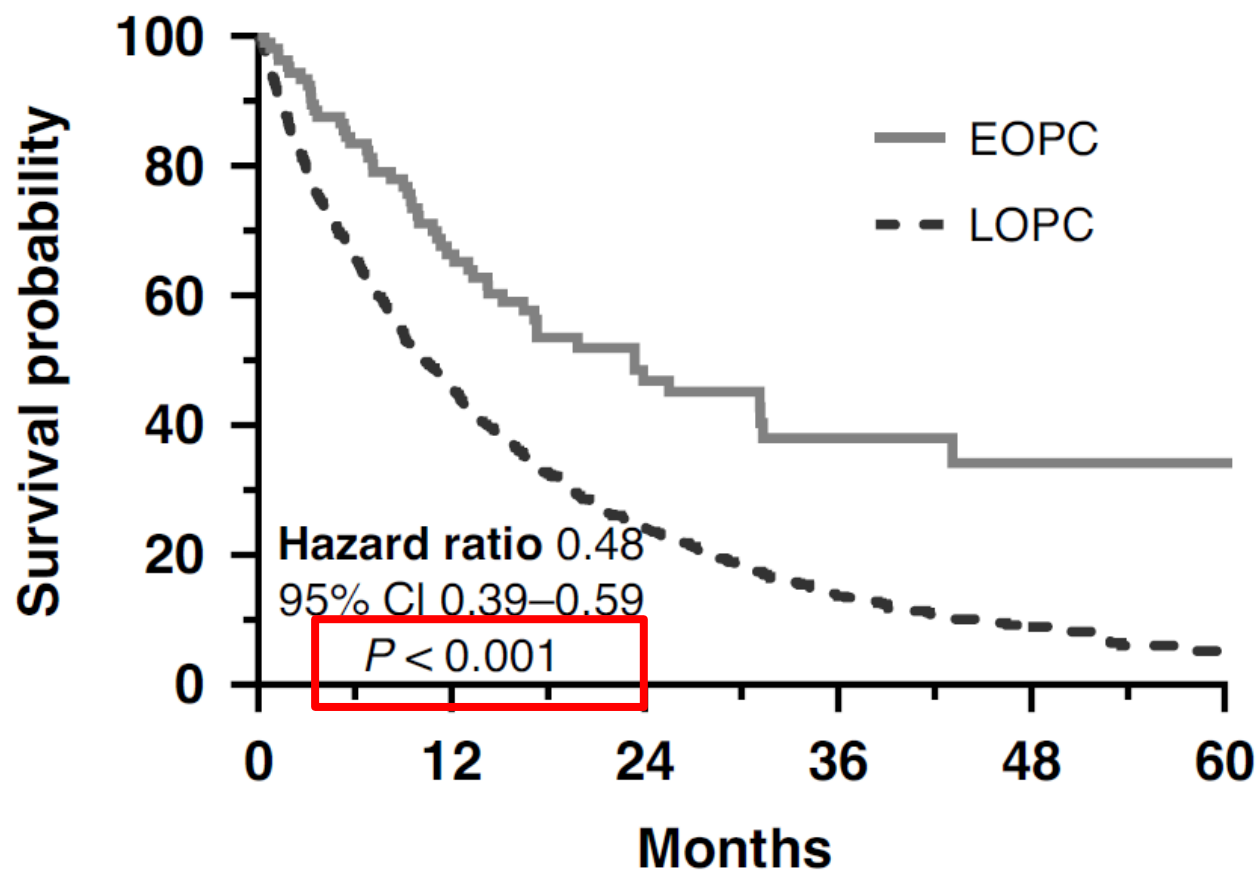
Recurrence-free survival in patients undergoing distal pancreatectomy



Number at risk						
Months	0	12	24	36	48	60
EOPC	10	9	5	4	4	2
LOPC	67	42	12	7	5	1

a

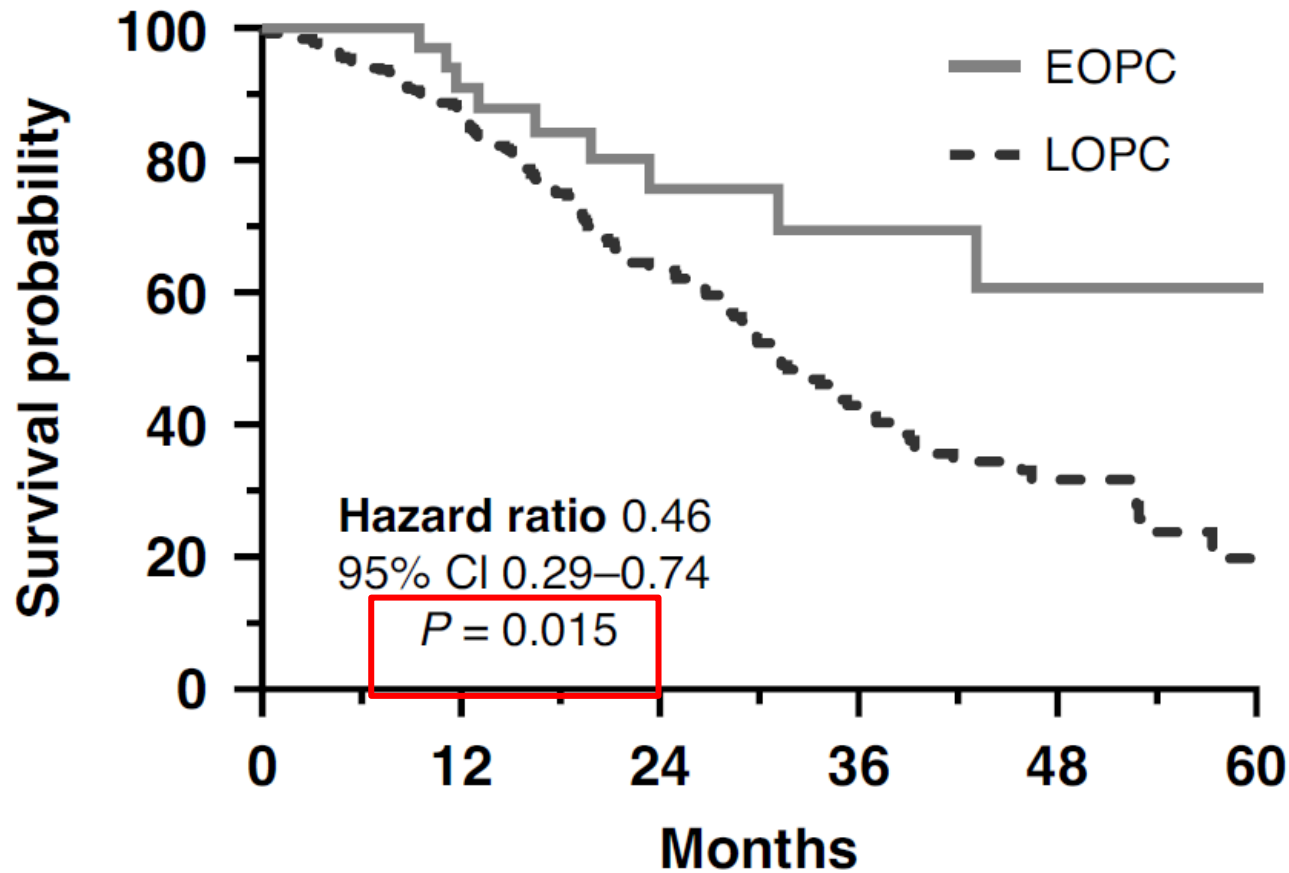
Overall survival in all patients



Number at risk						
Months	0	12	24	36	48	60
EOPC	110	55	27	14	8	4
LOPC	1563	547	183	72	28	6

b

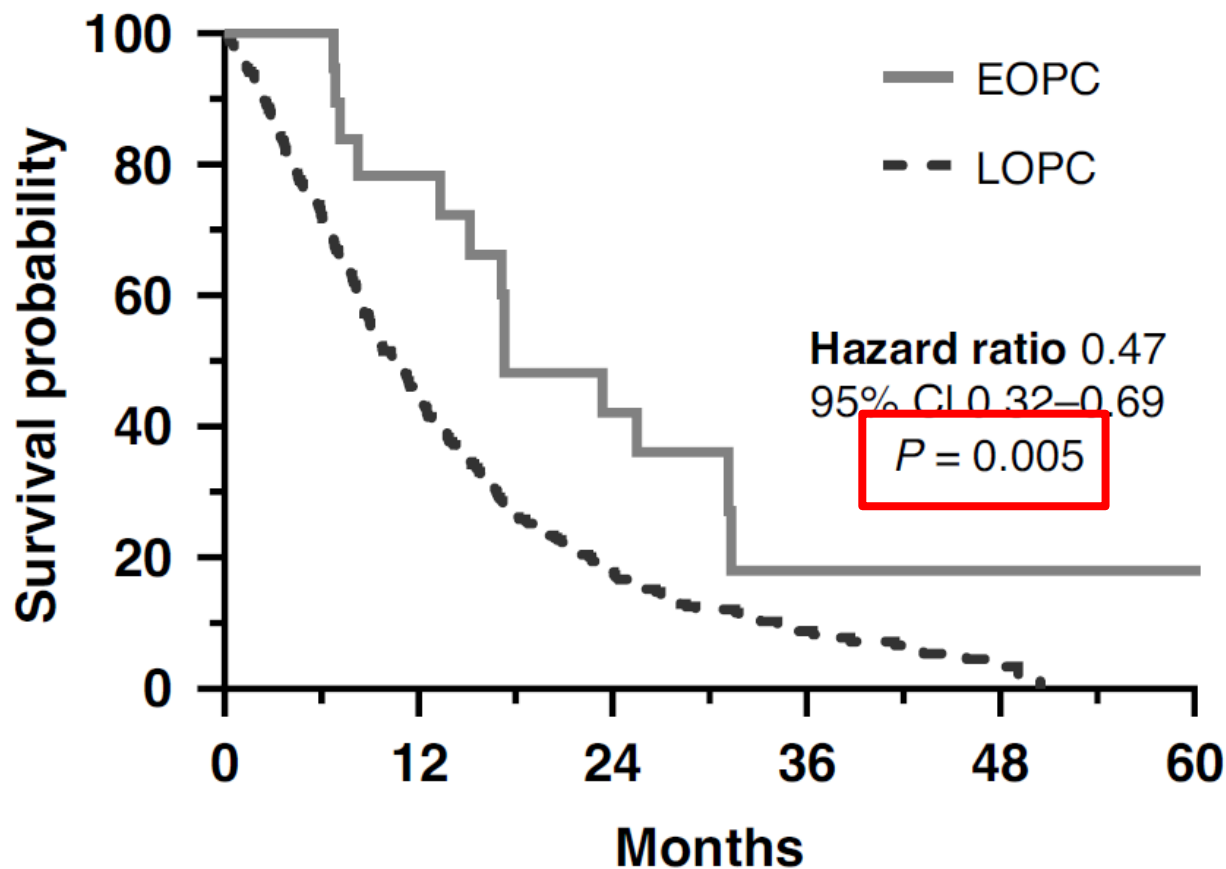
Overall survival in resected patients



Number at risk						
Months	0	12	24	36	48	60
EOPC	39	30	17	9	7	4
LOPC	364	260	108	51	23	6

C

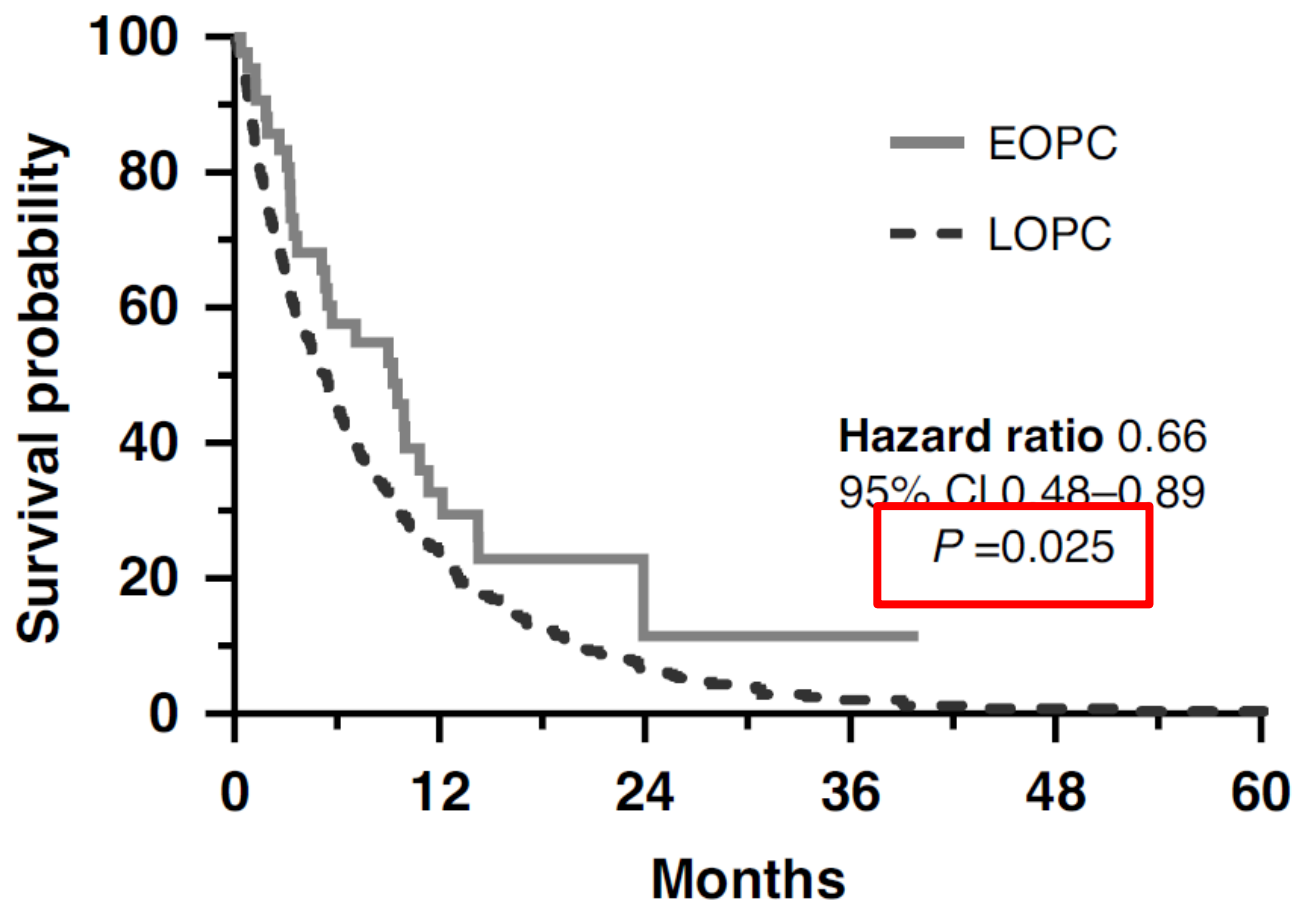
Overall survival in locally advanced patients



Number at risk						
Months	0	12	24	36	48	60
EOPC	23	14	8	3	2	1
LOPC	478	163	52	18	4	0

d

Overall survival in metastatic patients



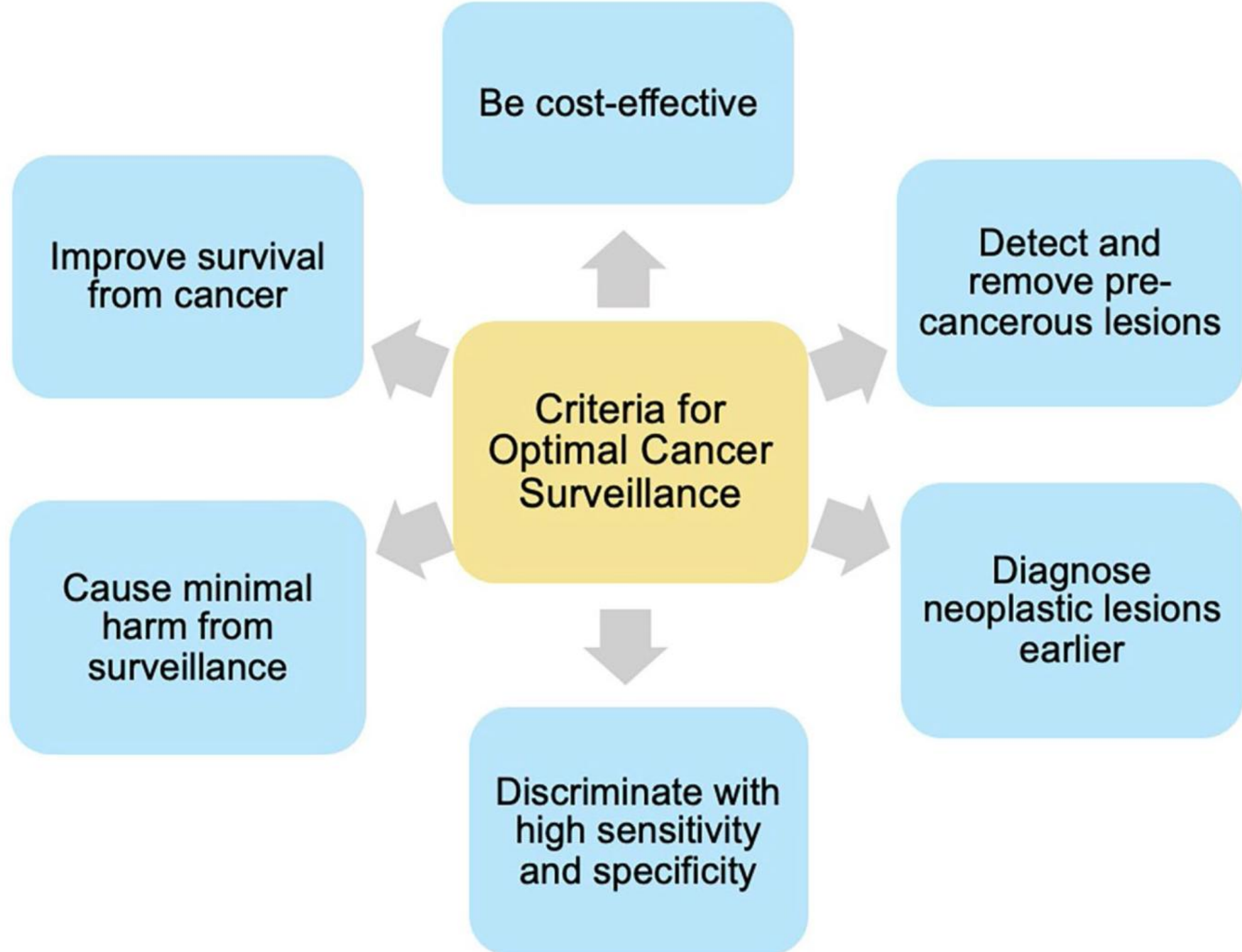
Number at risk						
Months	0	12	24	36	48	60
EOPC	45	11	2	2	0	0
LOPC	696	121	25	5	2	1

Source	Country (study design)	stage	Study population		Survival outcome, early-onset vs later-onset GI cancer
			EOPC	LOPC	
Mendis et al, 2024	Australia, New Zealand, and Singapore (prospective database analysis)	ALL	112	1571	<ul style="list-style-type: none"> Overall survival: median, 23.4 mo vs 10.3 mo Resected cancer group: median, 65.6 mo vs 31.3 mo Locally advanced unresectable group: median, 17.3 mo vs 10.6 mo Metastatic disease group: median, 9.3 mo vs 5.4 mo
Whitley et al, 2023	Czech Republic (national registry analysis)	All	1324	17 564	Overall survival: median, 5.9 mo vs 4.5 mo (<i>P</i> < .01)
Castet et al, 2023	Spain (retrospective cohort study)	All	Aged ≤50 y: 139	Aged ≥70 y: 197	Overall survival: median, 18.7 mo vs 17.6 mo
Takeda et al, 2022	Japan (single-institution retrospective analysis)	All	127	1519	Progression-free survival: median, 4.4 mo vs 5.3 mo (<i>P</i> = .65) Overall survival: median, 11.5 mo vs 9.5 mo (<i>P</i> = .18)
Saadat et al, 2021	US (National Cancer Database analysis)	All	15710	232924	1-Year overall survival: stage 0/I/II, 72% vs 53%; stage III, 48% vs 38%; stage IV, 25% vs 15%
Early-Onset Gastrointestinal Cancers: A Review. JAMA.2025					

Oncologic outcomes in EOPC patients are satisfactory even in locally advanced cancers, justifying aggressive surgical approaches

**Prevention is Better than
Treat**

Screening



Surveillance : EUS vs MRI

Review of the cost-effectiveness of surveillance for hereditary pancreatic cancer

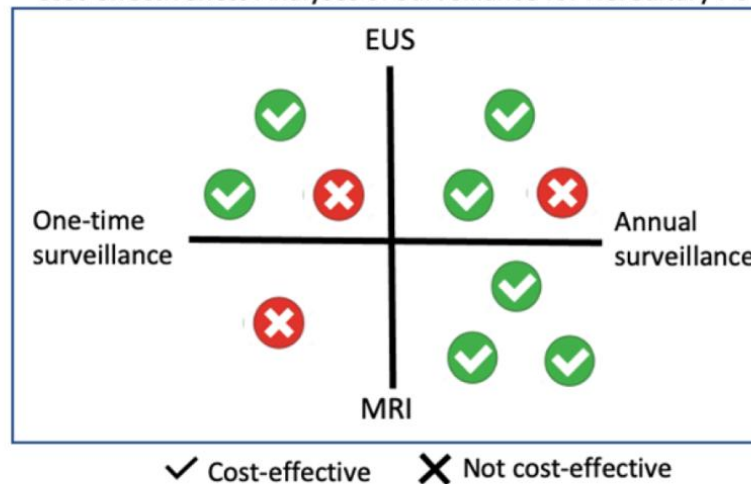
Question



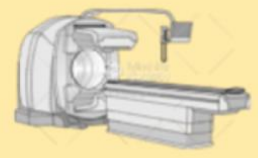
What surveillance intervals, age range, and surveillance modalities are cost-effective for pancreatic cancer (PC) surveillance?

Review

Cost-effectiveness Analyses of Surveillance for Hereditary PC



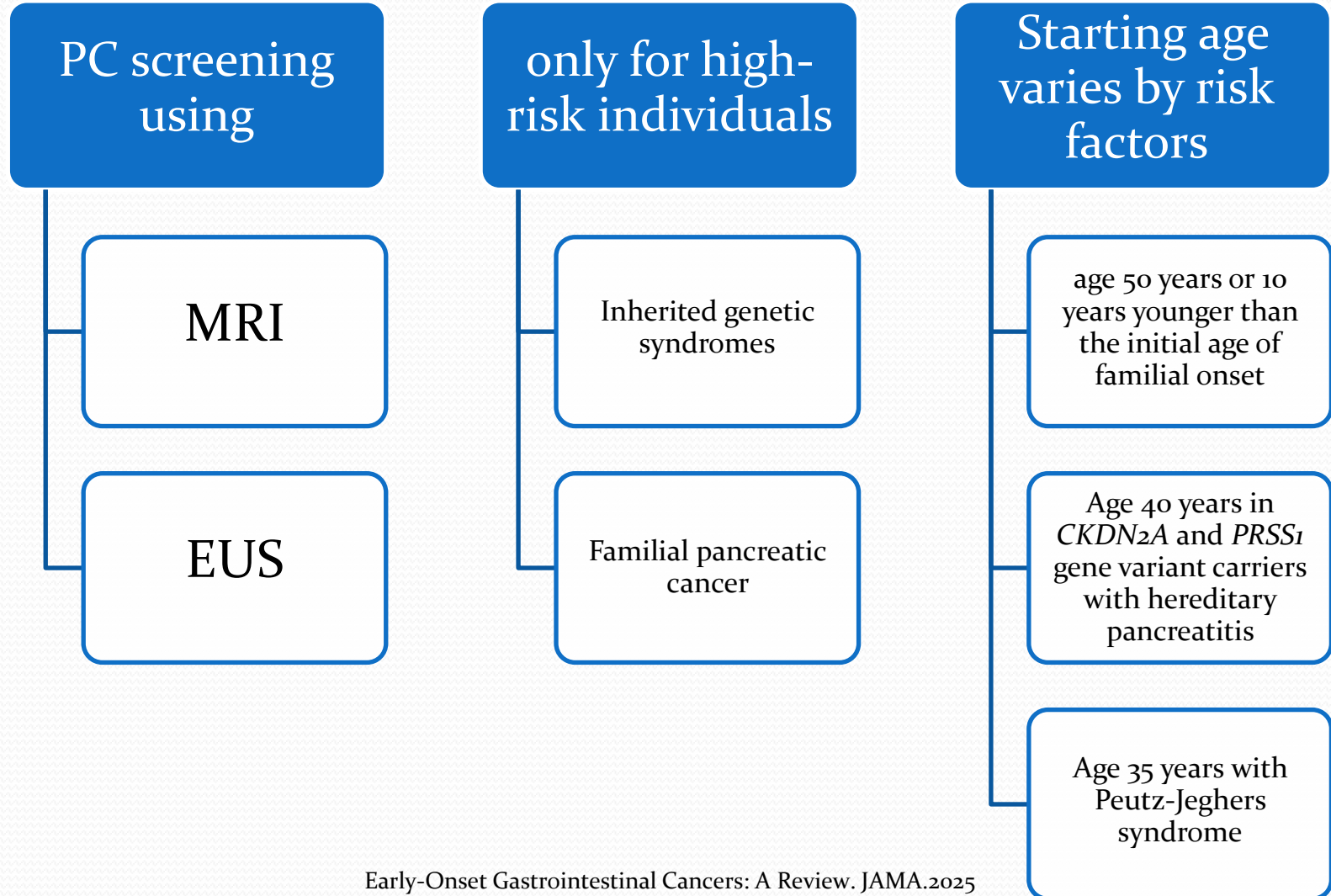
Future Directions

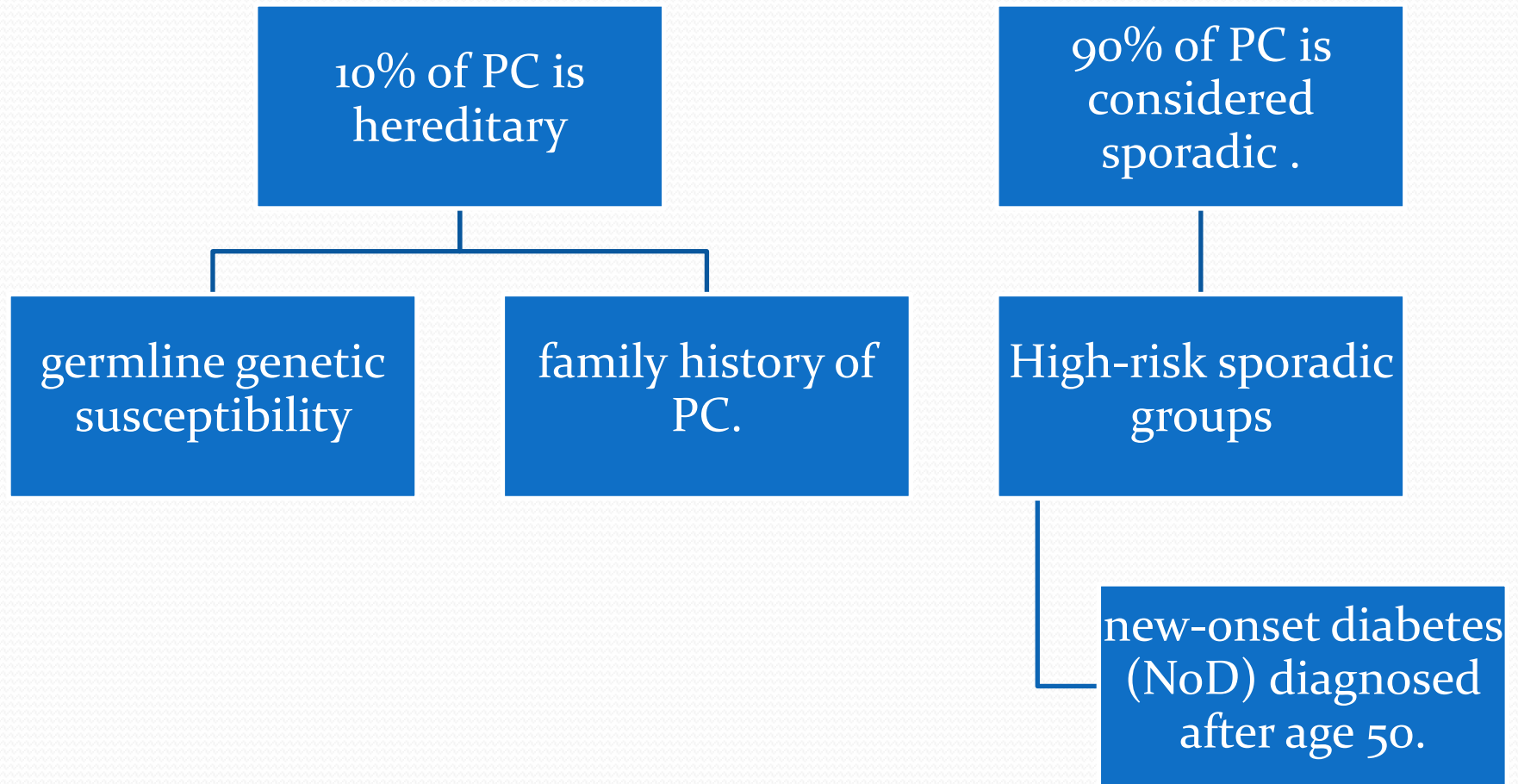


Evaluate cost-effectiveness of varying the surveillance interval and modality based on PC risk. Directly compare cost-effectiveness of EUS vs. MRI.

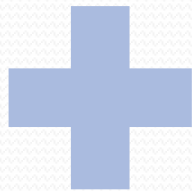
Research highlight: Most studies found that MRI and EUS could be cost-effective for both index and annual surveillance between ages 40-75, though the risk thresholds for cost-effectiveness were often higher than the risk reported for moderate PC risk groups (e.g. *BRCA1*, *BRCA2*, *ATM*, *PALB2*, Lynch syndrome). Surveillance costs and PC risk influenced the level of cost-effectiveness.

Recommendations





Non
familiar



Non
hereditary

Non
HRI

???

Take home messages

EOPC < 50 years

↑EAPC, ASIRs , ASDRs, per 100 000 population.

↑ASIR+ASDR in high & high middle SDI

↑Change in ASIR+ASDR per 100 000 person-years (1990-2021) % in low SDI

Risk Factors : smoking , alcohol, pancreatitis

EOPC more aggressive but better outcomes than LOPC (better PS & lower comorbidity & more aggressive treatment)

Screening only in HRI using MRI or EUS

شكراً لا صغائكم

