Supplementary Online Content

Elmahdi R, Lemser CE, Thomsen SB, Allin KH, Agrawal M, Jess T. Development of cancer among patients with pediatric-onset inflammatory bowel disease: a meta-analysis of population-based studies. *JAMA Netw Open.* 2022;5(3):e220595. doi:10.1001/jamanetworkopen.2022.0595

- eTable 1. Embase Database Search Using Ovid
- eTable 2. MEDLINE (Pubmed With MeSH Headings) Search Terms
- **eFigure 1.** Newcastle-Ottawa Scale Tool Description for Assessment of Risk of Bias and Study Quality
- **eFigure 2.** Forest Plots of Meta-Analyses for Relative Cancer Risk for Individuals With Pediatric-Onset IBD Compared With Reference Populations by Gastrointestinal Cancer
- **eFigure 3.** Forest Plots of Meta-Analyses for Relative Cancer Risk for Individuals With Pediatric-Onset IBD Compared With Reference Populations by Extra-Intestinal Cancer
- **eFigure 4.** REM Meta-Analysis of Cancer Rates in Pediatric-Onset IBD Compared With Reference Populations Excluding Olen et al. and Penau et al.
- **eFigure 5.** REM Meta-Analysis of Cancer Rates in Paediatric-Onset IBD Compared With Reference Populations Including Deneau & Guthery, 2017
- eFigure 6. Funnel Plot for Assessment for Publication Bias of Included Studies

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Embase Database Search Using Ovid

Search Terms (Embase Ovid)								
	1	2	3	4				
Search Terms	Malignant neoplasm	Inflammatory Bowel Diseases	Pediatrics Juvenile Adolescent Child	Epidemiology Cohort analysis				
Free text	Cancer* Neoplasm* Neoplasia Adenocarcinoma Carcinoma Malignancy Tumour* / Tumor*	Inflammatory Bowel Disease* IBD* Crohn Crohn's Disease Morbus Crohn Colitis Ulcerosa Ulcerative colitis	Pediatric / Paediatric Early onset / Early-onset Children Child Adolescent Juvenile Infant	Cohort analysis Cohort study Population based				

eTable 2. MEDLINE (Pubmed With MeSH Headings) Search Terms

Subject headings (MEDLINE PubMed)								
	1	2	3	4				
Subject headings	Malignant neoplasm	Inflammatory Bowel Diseases	Pediatrics Juvenile Adolescent Child	Epidemiology Cohort analysis				
Free text	("Neoplasms" [MeSH] OR Cancer* OR Neoplasia OR Adenocarcinoma OR Carcinoma OR Malignancy OR Tumour* OR Tumor*)	("Inflammatory Bowel Diseases" [MeSH] OR "Inflammatory Bowel Disease*" OR IBD* OR Crohn OR "Crohn's Disease" OR "Morbus Crohn" OR "Colitis Ulcerosa" OR "Ulcerative colitis")	("Infant" [MeSH] OR "Child, Preschool" [MeSH] OR "Child" [MeSH] OR "Adolescent" [MeSH] OR Pediatric OR Paediatric OR Early onset OR Early onset OR Children OR Child OR Adolescent OR Juvenile OR Infant)	("Epidemiology"[MeSH] OR "Cohort analysis"[MeSH] OR Cohort analysis OR Cohort study OR Population based)				

RISK OF BIAS AND QUALITY ASSESSMENT:

eFigure 1. Newcastle-Ottawa Scale Tool Description for Assessment of Risk of Bias and Study Quality

Newcastle-Ottawa Quality Assessment Form for Cohort Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection

- 1) Representativeness of the exposed cohort
 - a) Truly representative (one star)
 - b) Somewhat representative (one star)
 - c) Selected group
 - d) No description of the derivation of the cohort
- 2) Selection of the non-exposed cohort
 - a) Drawn from the same community as the exposed cohort (one star)
 - b) Drawn from a different source
 - c) No description of the derivation of the non exposed cohort
- 3) Ascertainment of exposure
 - a) Secure record (e.g., surgical record) (one star)
 - b) Structured interview (one star)
 - c) Written self report
 - d) No description
 - e) Other
- 4) Demonstration that outcome of interest was not present at start of study
 - a) Yes (one star)
 - b) No

Comparability

- 1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
 - a) The study controls for age, sex and marital status (one star)
 - b) Study controls for other factors (list)
 - c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome

- 1) Assessment of outcome
 - a) Independent blind assessment (one star)
 - b) Record linkage (one star)
 - c) Self report
 - d) No description
 - e) Other
- 2) Was follow-up long enough for outcomes to occur
 - a) Yes (one star)
 - b) No

Indicate the median duration of follow-up and a brief rationale for the assessment above:

- 3) Adequacy of follow-up of cohorts
 - a) Complete follow up- all subject accounted for (one star)
 - Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. (one star)
 - c) Follow up rate less than 80% and no description of those lost
 - d) No statement

(one star)

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

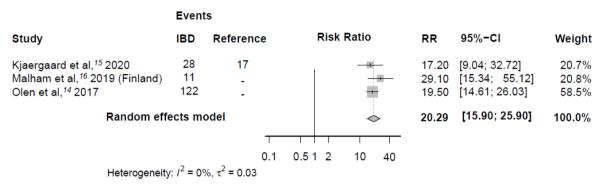
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

META-ANALYSES

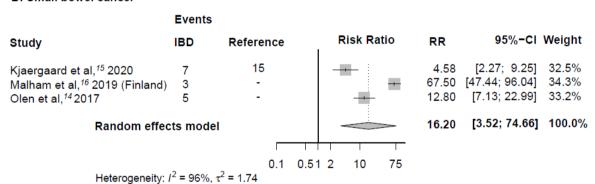
eFigure 2. Forest Plots of Meta-Analyses for Relative Cancer Risk for Individuals With Pediatric-Onset IBD Compared With Reference Populations* by Gastrointestinal Cancer

A. Colorectal cancer, B. Small bowel cancer, and C. Liver cancers

A: Colorectal cancer



B: Small bowel cancer



C: Liver cancers

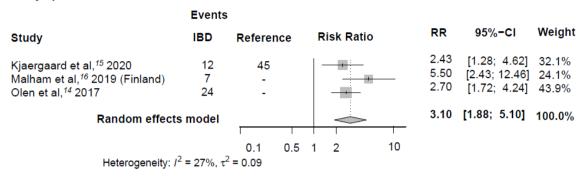
	Events					
Study	IBD	Reference	Risk Ratio	RR	95%-CI	Weight
Kjaergaard et al, ¹⁵ 2020 Malham et al, ¹⁶ 2019 (Finland) Olen et al, ¹⁴ 2017	14 3 66	5 - -		22.68 52.50 134.00	[8.15; 63.13] [13.80; 199.71] [52.93; 339.24]	01.070
Random effects model				55.45	[19.59; 156.99]	100.0%
Heterogeneity: /²	= 69%, τ ² =	0.01 0.1 0.54	1 10 100 350			

^{*}Including data from Kjaergaard et al., Malham et al. and Olen et al.

eFigure 3. Forest Plots of Meta-Analyses for Relative Cancer Risk for Individuals With Pediatric-Onset IBD Compared With Reference Populations* by Extra-Intestinal Cancer

A. Lymphoid cancers, B. Non-melanoma skin cancer and C. Melanoma skin cancer

A: Lymphoid cancers



B: Non-Melanoma skin cancer

Events IBD RR 95%-CI Weight Reference Study Risk Ratio 31 138 2.21 [1.49; 3.28] 42.7% Kjaergaard et al, 15 2020 Malham et al, 16 2019 (Finland) 4.10 [1.33; 12.61] 18.8% 5.90 25 [3.58; 9.72] Olen et al. 14 2017 38.5% [1.97; 6.66] 100.0% 3.62 Random effects model 0.1 0.5 1 10 2 Heterogeneity: $I^2 = 79\%$. $\tau^2 = 0.19$

C: Melanoma skin cancer

	Events					
Study	IBD	Refrence	Risk Ratio	RR	95%-CI	Weight
Kjaergaard et al, ¹⁵ 2020 Malham et al, ¹⁶ 2019 (Finland) Olen et al, ¹⁴ 2017	17 2 37	79 - -	*		[1.19; 3.41] [1.33; 12.61] [1.20; 2.40]	
Random effects model				2.05	[1.27; 3.29]	100.0%
Heterogeneity: I ²	= 11%, τ ²	0.1 0.5 = 0.09	1 2 10			

^{*}Including data from Kjaergaard et al., Malham et al. and Olen et al.

eFigure 4. REM Meta-Analysis of Cancer Rates in Pediatric-Onset IBD Compared With Reference Populations Excluding Olen et al. and Penau et al.

	Number		Even	ts				
Study	IBD	Reference	IBD	Reference	Risk Ratio	RR	95%-CI	Weight
El-Matary et al., 2020 Kjaergaard et al., 2020 Malham et al., 2019 (Finland)	947 5,380 3,345	9,272 53,800 2,899,565	17 158 34	75 701 8,160	-	2.16	[1.16; 3.44] [1.81; 2.57] [2.55; 5.09]	22.8% 43.8% 33.4%
	Randon	n effects mode	ı _	Т		2.52	[1.77; 3.59]	100.0%
			0.2	0.5	1 2	5		
	Heterogeneity: $I^2 = 72\%$, $\tau^2 = 0.07$							

eFigure 5. REM Meta-Analysis of Cancer Rates in Paediatric-Onset IBD Compared With Reference Populations Including Deneau & Guthery, 2017

	Number		Events				
Study	IBD	Reference	IBD	Refrence	Risk Ratio	RR	95%-CI Weight
El-Matary et al., 2020 Kjaergaard et al., 2020 Malham et al., 2019 (Finland) Olen et al., 2017 Peneau et al., 2013 Deneau M. & Guthery S., 2017		9,272 53,800 2,899,565 92,870 775 3880 om effects mod	17 158 34 497 9 9	75 701 8,160 2,256 3 7		2.16 [3.60 [2.20 [3.00 [12.90 [[1.16; 3.44] 16.6% [1.81; 2.57] 20.2% [2.55; 5.09] 18.8% [1.97; 2.46] 20.5% [1.41; 6.39] 14.0% 4.20; 39.64] 10.1%
				0.1 0.5	1 2 10		

Heterogeneity: $I^2 = 71\%$, $\tau^2 = 0.31$

eFigure 6. Funnel Plot for Assessment for Publication Bias of Included Studies

