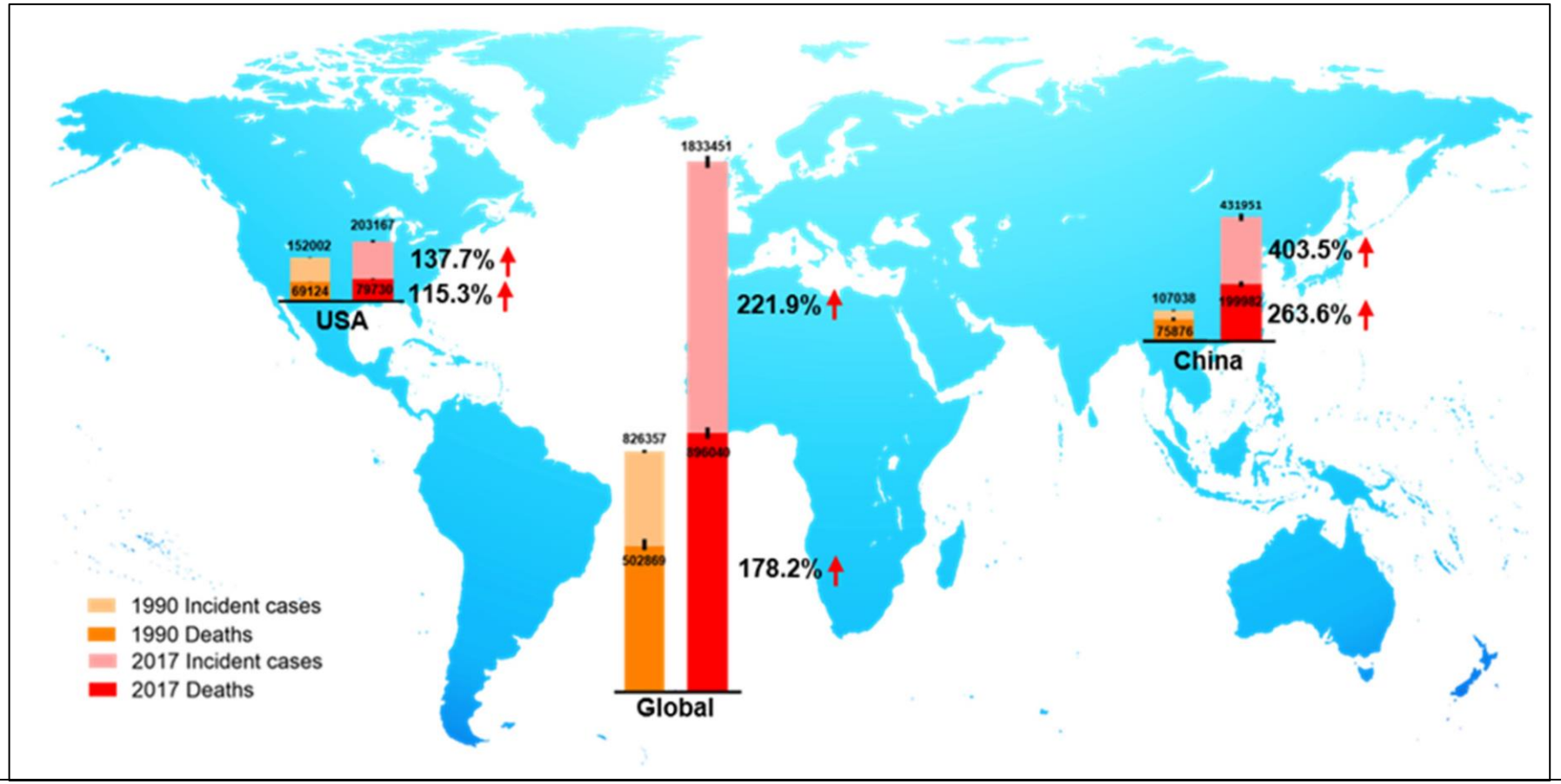
Severe Obesity (BMI > 35kg/m²) with Colorectal Cancer: How Should We Proceed?

Charles Peng Zhang
Capital Medical University Beijing Friendship Hospital
National Clinical Research Center for Digestive Diseases
National Key Laboratory for Digestive Health
Beijing, China

Prevalence of Colorectal Cancer is Escalating



Ye P, Xi Y, Huang Z, Xu P. Linking Obesity with Colorectal Cancer: Epidemiology and Mechanistic Insights. Cancers. 2020;12:1408.

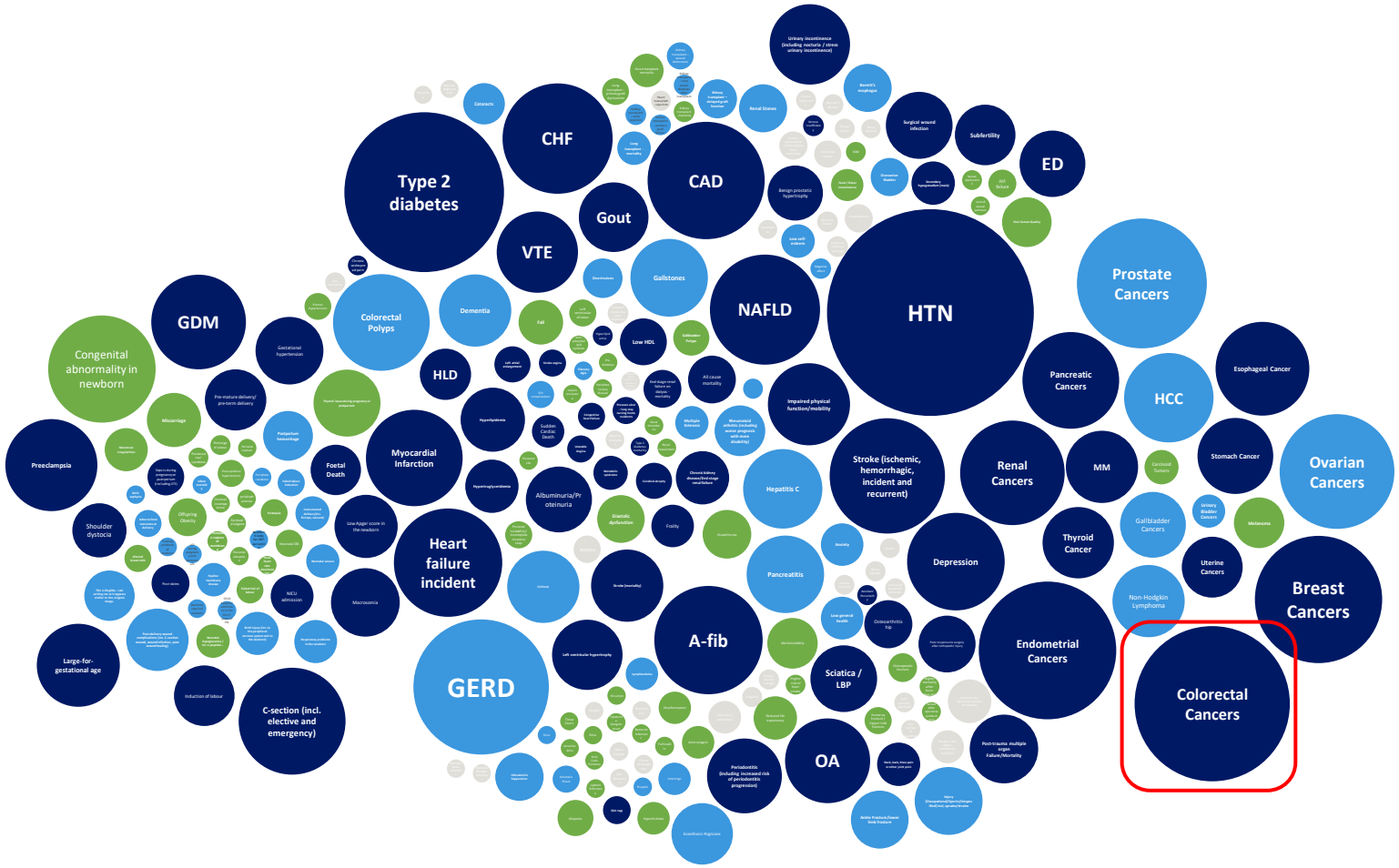
Obesity is strongly associated with CRC

	GRADE	Strength of evidence
	4	Very strong
	3	Strong
	2	Moderate
	1	Weak

Size of circle reflects number of articles

229+

complications affecting *EVERY* organ system and medical specialty



A-fib, atrial fibrillation; CAD, coronary artery disease; CHF, congestive heart failure; ED, erectile dysfunction; EOM, eosinophilic otitis media; GDM, gestational diabetes mellitus; GERD, gastroesophageal reflux disease; HCC, hepatocellular carcinoma; HTN, hypertension; HLD, hyperlipidemia; MM, multiple myeloma; NAFLD, non-alcoholic fatty liver disease; OA, osteoarthritis; VTE, venous thromboembolism.

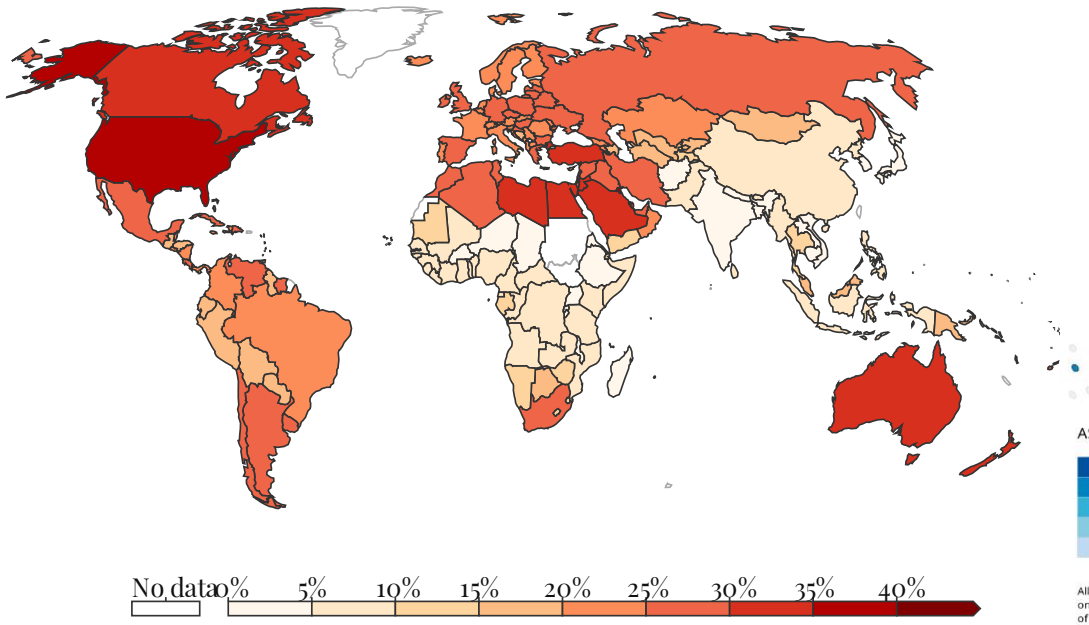
Horner et al. Postgrad Med J 2022;134:369–75.

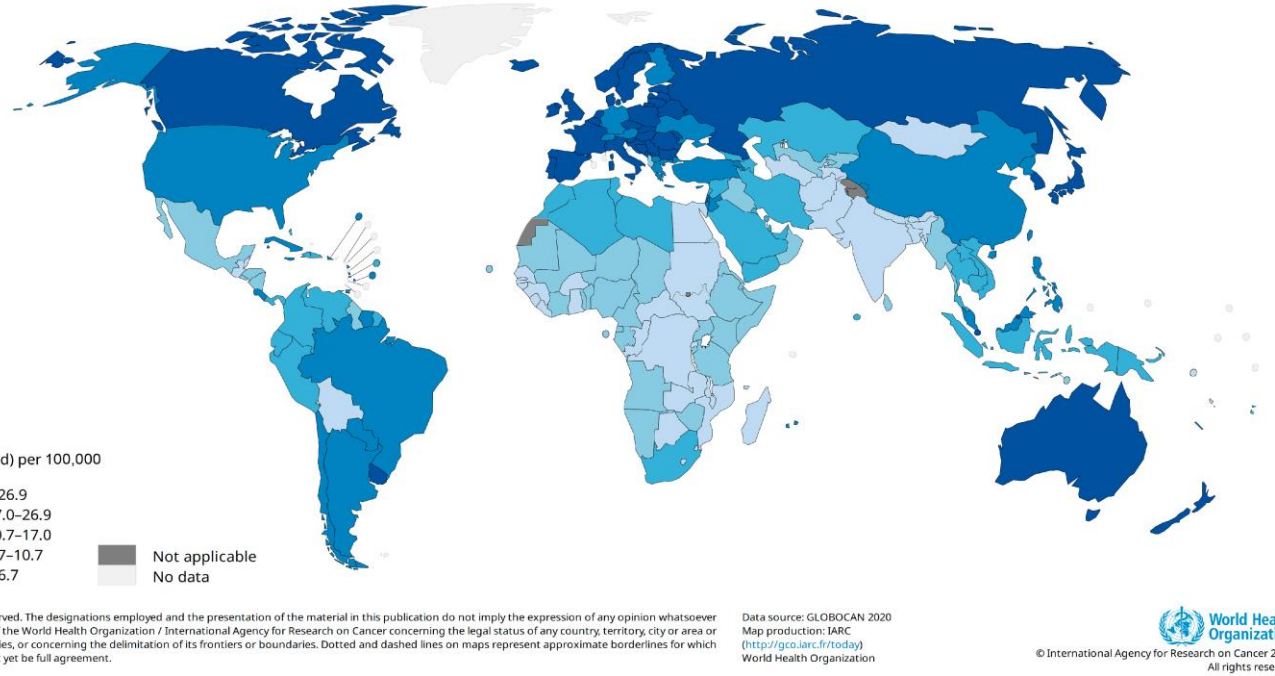
Incidences of Obesity and Colorectal Cancer are Parallel

Obesity in adults, 2016

Estimated prevalence of obesity, based on general population surveys and statistical modeling. Obesity is factor for chronic complications, including cardiovascular disease, and premature death.

Our World in Data





Data source: World Health Organization – Global Health Observatory (2024)OurWorldInData.org/obesity

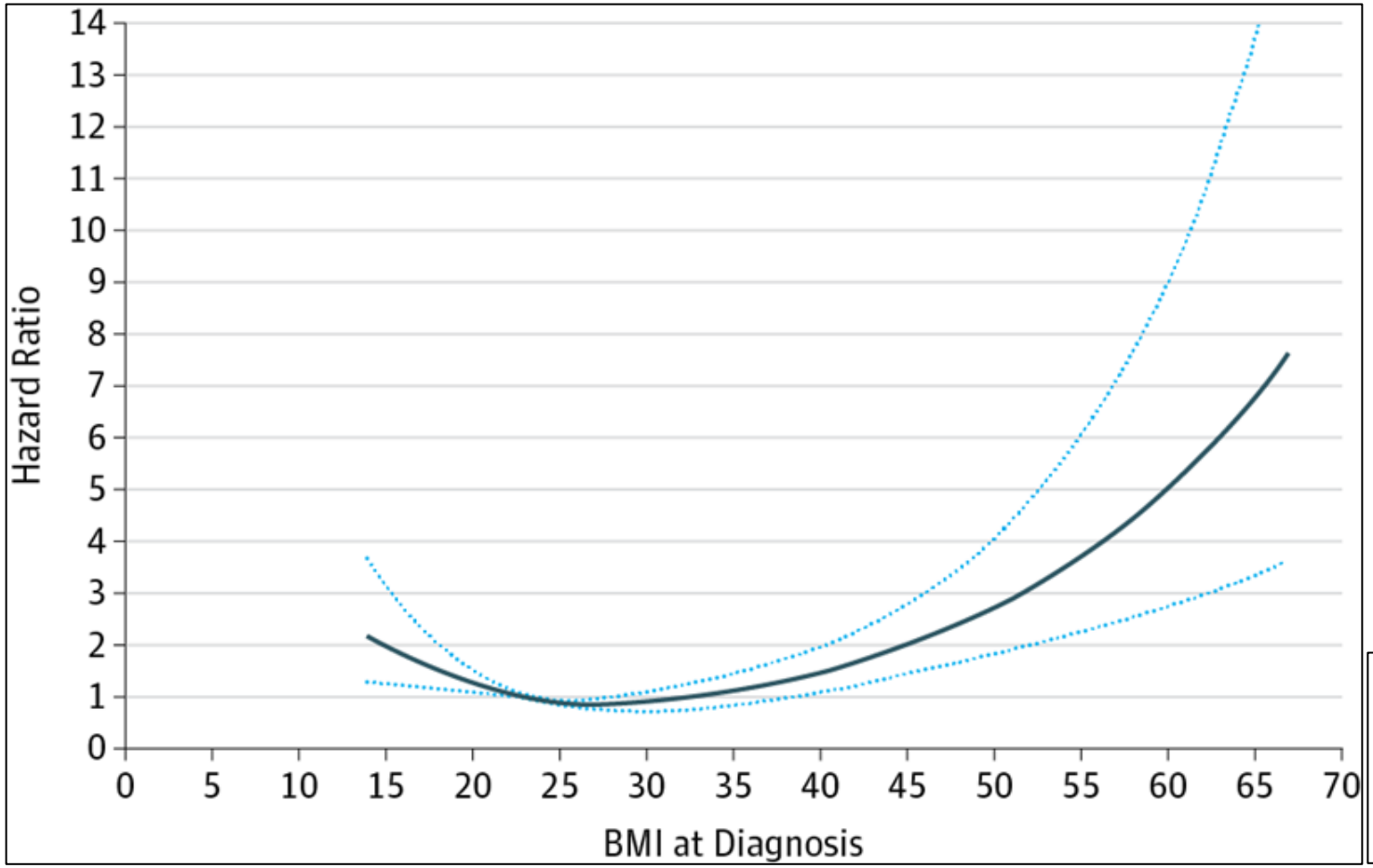
Data source: GLOBOCAN 2020
Map production: IARC
(http://gco.iarc.fr/today)
World Health Organization

World Health Organization

Obesity is a Risk Factor of CRC

- For every 2 kg/m² increase in BMI, the risk of CRC increases by 7% .
- Higher BMI patients have worse survival outcomes than lower BMIs .
- Hazard ratios indicate a significantly increased risk of death in severely obese CRC patients .

Moghaddam AA, Woodward M, Huxley R. Obesity and Risk of Colorectal Cancer: A Meta-analysis of 31 Studies with 70,000 Events. Cancer Epidemiology, Biomarkers & Prevention. 2007;16:2533–47.
Daniel CR, Shu X, Ye Y, Gu J, Raju GS, Kopetz S, et al. Severe obesity prior to diagnosis limits survival in colorectal cancer patients evaluated at a large cancer centre. Br J Cancer. 2016;114:103–9.



Original Investigation

FREE

September 2016

Analysis of Body Mass Index and Mortality in Patients With Colorectal Cancer Using Causal Diagrams

Candyce H. Kroenke, ScD[1]; Romain Neugebauer, PhD[1]; Jeffrey Meyerhardt, MD[2]; et al

» Author Affiliations | Article Information

JAMA Oncol. 2016;2(9):1137-1145. doi:10.1001/jamaoncol.2016.0732

Fig shows the BMI at Diagnosis and Overall Mortality
Adjusted for age, sex, race, stage, site, grade, chemotherapy, radiation, prediagnosis BMI, smoking, and physical activity; $P < .001$ (test for nonlinearity).

Kroenke CH, Neugebauer R, Meyerhardt J, Prado CM, Weltzien E, Kwan ML, et al. Analysis of Body Mass Index and Mortality in Patients With Colorectal Cancer Using Causal Diagrams. JAMA Oncology. 2016;2:1137–45.

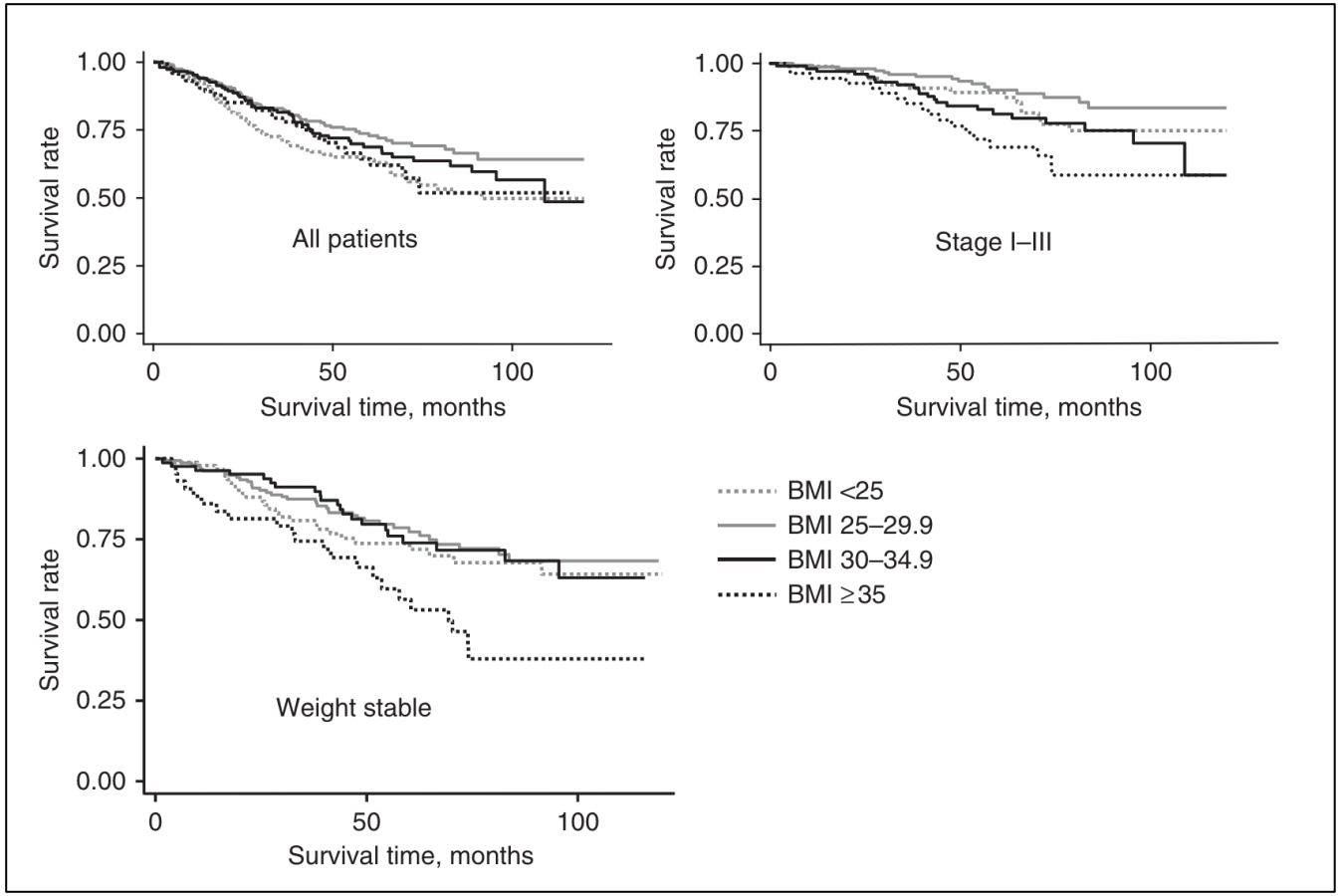
Obesity can affect long-term survival of CRC

Table 3. Association between prediagnostic BMI (kg m^{-2}) and 10-year mortality in colorectal cancer patients

	Univariate			Multivariate[a]		
Variables	**HR**	**95% CI**	P_{trend}	**HR**	**95% CI**	P_{trend}
All patients ($N = 634$)						
<25	1.60	1.13–2.26		1.04	0.71–1.52	
25–29.9	1.00	Ref		1.00	Ref	
30–34.9	1.22	0.84–1.77		1.13	0.76–1.68	
⩾35	1.45	0.93–2.25	0.54	1.55	0.97–2.48	0.14
Stage I–III patients ($N = 409$)						
<25	1.70	0.85–3.41		1.59	0.74–3.43	
25–29.9	1.00	Ref		1.00	Ref	
30–34.9	2.06	1.08–3.92		2.21	1.11–4.40	
⩾35	3.38	1.72–6.64	0.009	3.49	1.68–7.22	0.007
Stable-weight patients ($N = 379$)						
<25	1.25	0.76–2.07		1.17	0.66–2.09	
25–29.9	1.00	Ref		1.00	Ref	
30–34.9	1.05	0.61–1.79		1.36	0.75–2.46	
⩾35	2.35	1.38–3.98	0.07	2.60	1.42–4.76	0.01

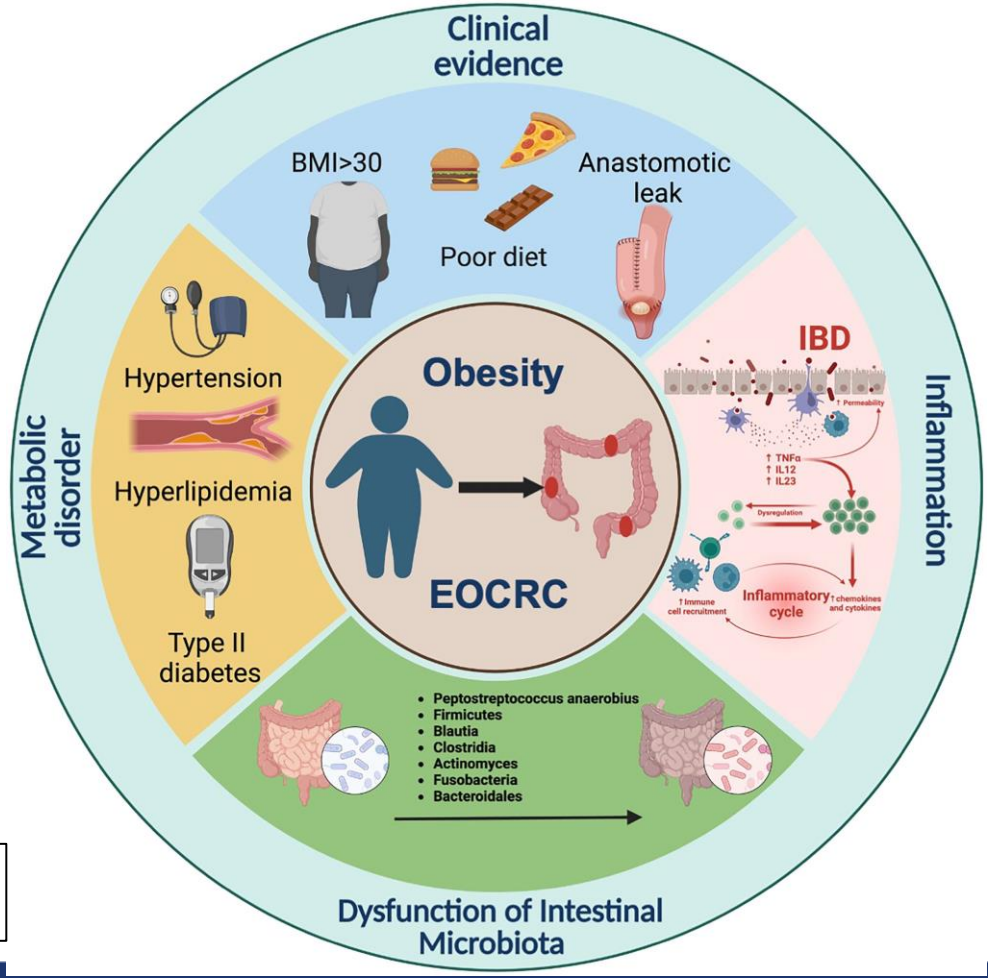
Abbreviations: CI = confidence interval; BMI = body mass index; HR = hazard ratio; Ref = reference.

[a]Model adjusted for age, sex, alcohol drinking status, weight change, clinical stage, grade, and treatment modality.



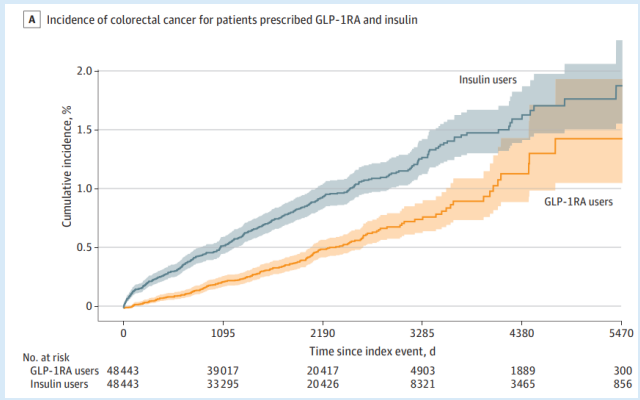
Mechanisms Linking Obesity and CRC

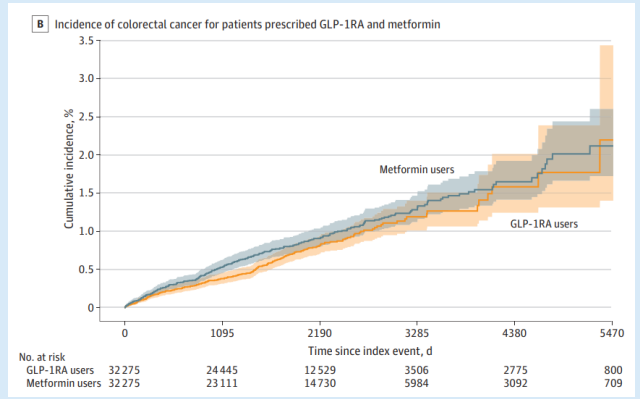
- Chronic inflammation
- Insulin resistance
- Altered adiponectin and hormonal levels
- Changes in gut microbiota
- Disorders of bile acid metabolism



Xu P, Tao Z, Yang H, Zhang C. Obesity and early-onset colorectal cancer risk: emerging clinical evidence and biological mechanisms. Front Oncol [Internet]. 2024 [cited 2024 Sep 1];14.

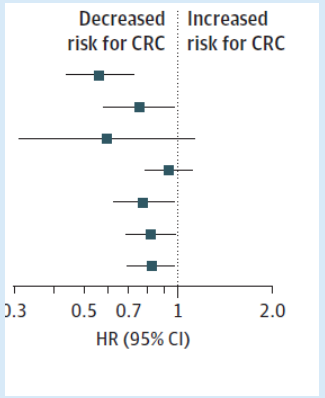
GLP-1RAs are associated with lower risks of CRC





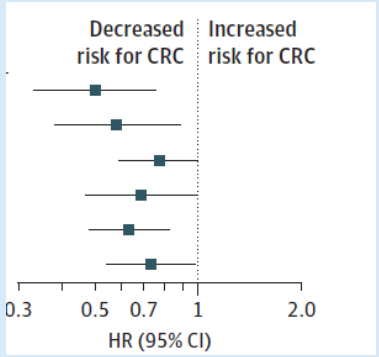
Overall study population

Exposure cohort (matched)
GLP-1RA(+)/insulin(-) (n = 22572)
GLP-1RA(+)/metformin(-) (n = 18518)
GLP-1RA(+)/AGI(-) (n = 2503)
GLP-1RA(+)/DDP-4(-) (n = 44146)
GLP-1RA(+)/SGLT2(-) (n = 25133)
GLP-1RA(+)/SU(-) (n = 36716)
GLP-1RA(+)/TZD(-) (n = 36481)



Patients with overweight/obesity

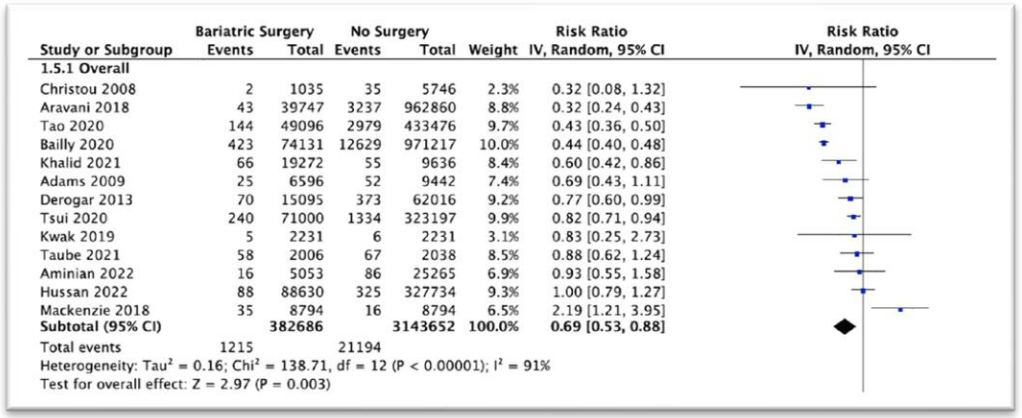
Exposure cohort (matched)
GLP-1RA(+)/insulin(-) (n = 9398)
GLP-1RA(+)/metformin(-) (n = 8057)
GLP-1RA(+)/DDP-4(-) (n = 16699)
GLP-1RA(+)/SGLT2(-) (n = 8148)
GLP-1RA(+)/SU(-) (n = 15551)
GLP-1RA(+)/TZD(-) (n = 11099)



Lindsey Wang , Rong Xu, JAMA Netw Open,2024 Jul 1;7(7):e2421305.

Bariatric surgery can reduce the incidence of colorectal cancer in obese patients

regardless of gender



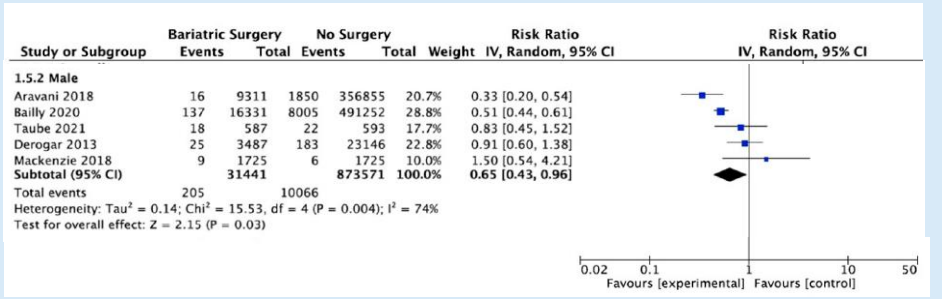
Study or Subgroup	Bariatric Surgery Events	Total	No Surgery Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.5.1 Overall						
Christou 2008	2	1035	35	5746	2.3%	0.32 [0.08, 1.32]
Aravani 2018	43	39747	3237	962860	8.8%	0.32 [0.24, 0.43]
Tao 2020	144	49096	2979	433476	9.7%	0.43 [0.36, 0.50]
Bailly 2020	423	74131	12629	971217	10.0%	0.44 [0.40, 0.48]
Khalid 2021	66	19272	55	9636	8.4%	0.60 [0.42, 0.86]
Adams 2009	25	6596	52	9442	7.4%	0.69 [0.43, 1.11]
Derogar 2013	70	15095	373	62016	9.2%	0.77 [0.60, 0.99]
Tsui 2020	240	71000	1334	323197	9.9%	0.82 [0.71, 0.94]
Kwak 2019	5	2231	6	2231	3.1%	0.83 [0.25, 2.73]
Taube 2021	58	2006	67	2038	8.5%	0.88 [0.62, 1.24]
Aminian 2022	16	5053	86	25265	6.9%	0.93 [0.55, 1.58]
Hussan 2022	88	88630	325	327734	9.3%	1.00 [0.79, 1.27]
Mackenzie 2018	35	8794	16	8794	6.5%	2.19 [1.21, 3.95]
Subtotal (95% CI)		**382686**		**3143652**	**100.0%**	**0.69 [0.53, 0.88]**
Total events	1215		21194			

Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 138.71$, df = 12 ($P < 0.00001$); $I^2 = 91\%$

Test for overall effect: $Z = 2.97$ ($P = 0.003$)

Risk Ratio IV, Random, 95% CI

Male



Study or Subgroup	Bariatric Surgery Events	Total	No Surgery Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.5.2 Male						
Aravani 2018	16	9311	1850	356855	20.7%	0.33 [0.20, 0.54]
Bailly 2020	137	16331	8005	491252	28.8%	0.51 [0.44, 0.61]
Taube 2021	18	587	22	593	17.7%	0.83 [0.45, 1.52]
Derogar 2013	25	3487	183	23146	22.8%	0.91 [0.60, 1.38]
Mackenzie 2018	9	1725	6	1725	10.0%	1.50 [0.54, 4.21]
Subtotal (95% CI)		**31441**		**873571**	**100.0%**	**0.65 [0.43, 0.96]**
Total events	205		10066			

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 15.53$, df = 4 ($P = 0.004$); $I^2 = 74\%$

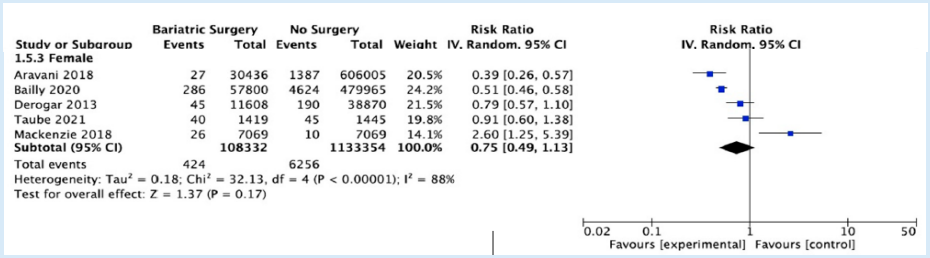
Test for overall effect: $Z = 2.15$ ($P = 0.03$)

Risk Ratio IV, Random, 95% CI

0.02 0.1 1 10 50

Favours [experimental] Favours [control]

Female



Study or Subgroup	Bariatric Surgery Events	Total	No Surgery Events	Total	Weight	Risk Ratio IV, Random, 95% CI
1.5.3 Female						
Aravani 2018	27	30436	1387	606005	20.5%	0.39 [0.26, 0.57]
Bailly 2020	286	57800	4624	479965	24.2%	0.51 [0.46, 0.58]
Derogar 2013	45	11608	190	38870	21.5%	0.79 [0.57, 1.10]
Taube 2021	40	1419	45	1445	19.8%	0.91 [0.60, 1.38]
Mackenzie 2018	26	7069	10	7069	14.1%	2.60 [1.25, 5.39]
Subtotal (95% CI)		**108332**		**1133354**	**100.0%**	**0.75 [0.49, 1.13]**
Total events	424		6256			

Heterogeneity: $Tau^2 = 0.18$; $Chi^2 = 32.13$, df = 4 ($P < 0.00001$); $I^2 = 88\%$

Test for overall effect: $Z = 1.37$ ($P = 0.17$)

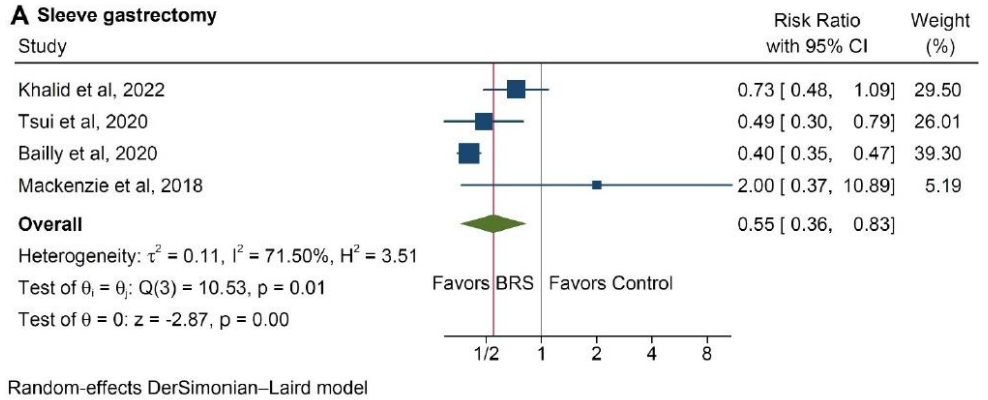
Risk Ratio IV, Random, 95% CI

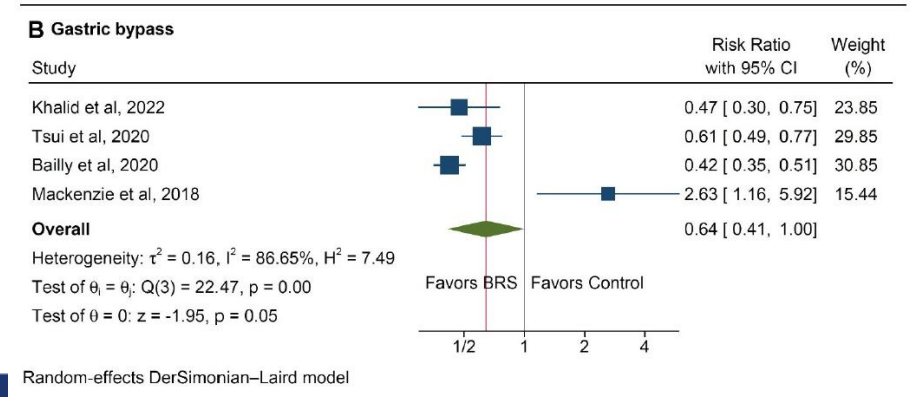
0.02 0.1 1 10 50

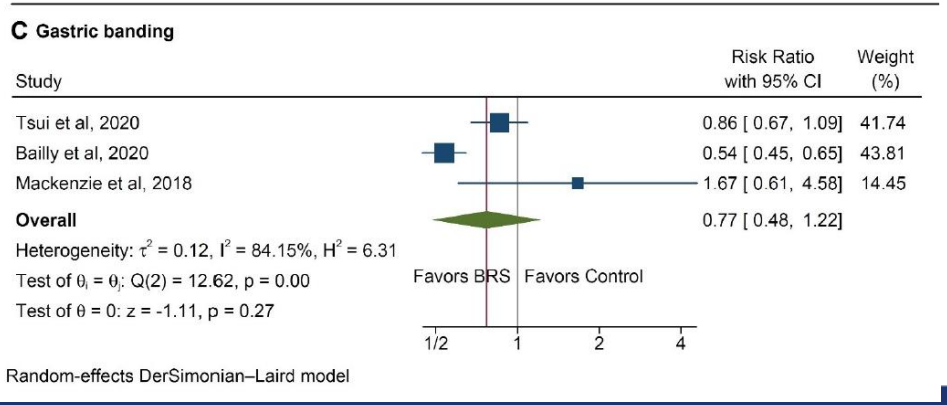
Favours [experimental] Favours [control]

Bariatric surgery can reduce the incidence of colorectal cancer in obese patients

By surgical type

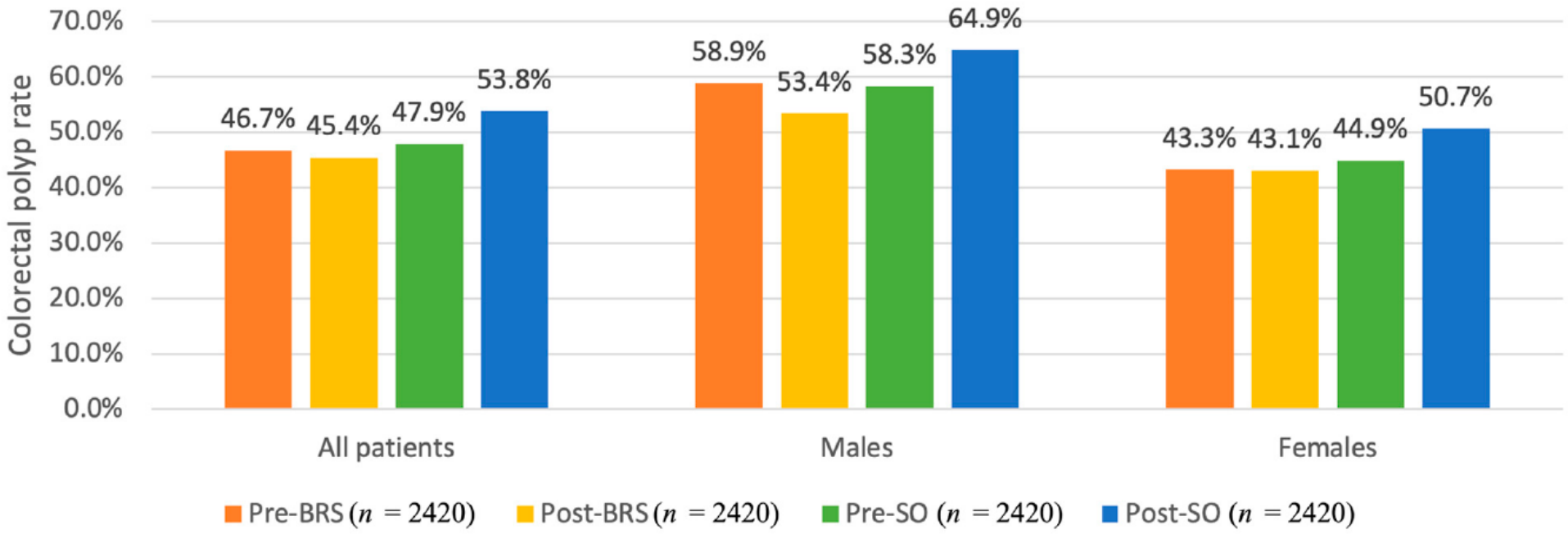






Int. J. Environ. Res. Public Health 2023, 20, 3934

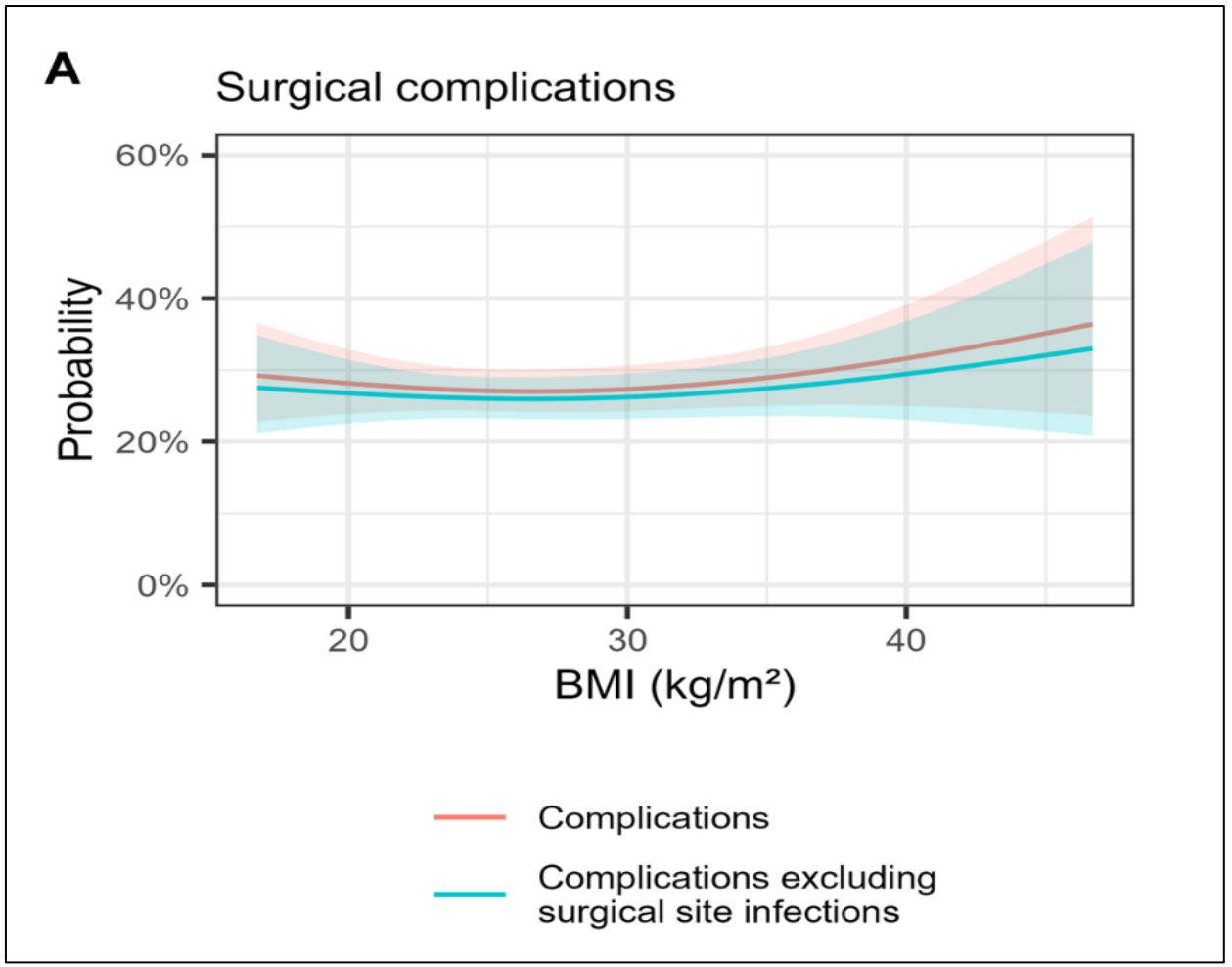
Obesity is associated with an increased risk of colorectal polyps, an effect that is ameliorated after bariatric surgery



The propensity-matched analysis. Colorectal polyp rates by group and sex.
BRS: Bariatric Surgery; SO: Severe Obesity

- Cancers 2023, 15, 4820.

Obesity Increases Risks of Colorectal Cancer Surgery



International Journal of Colorectal Disease (2023) 38:163
https://doi.org/10.1007/s00384-023-04447-0

RESEARCH

Check for updates

Impact of obesity on patients undergoing surgery for rectal cancer in Australia and New Zealand

Phillip F Yang[1] · Zhen Hao Ang[1,2] · Sarit Badiani[1] · Christophe R Berney[1,2] · Matthew J Morgan[1,2]

Accepted: 24 May 2023 / Published online: 8 June 2023

Clinical Implications: Management Strategies

1. Multidisciplinary Approach:

- **Team Composition:** surgeons, oncologists, gastroenterologists, nutritionists, and bariatric specialists.
- **Comprehensive Preoperative Evaluation:** Includes assessment of obesity-related comorbidities and nutritional status.
- **Individualized Treatment Plans:** Tailored to patient's BMI, cancer stage, and overall health status.

2. Preoperative Weight Management:

- **Lifestyle Modifications:** Dietary interventions, exercise programs, and behavioral therapy to reduce surgical risks.
- **Pharmacotherapy:** Use of weight-loss medications in selected patients to achieve modest weight reduction preoperatively.
- **Bariatric Surgery:** Considered in select cases to improve outcomes, especially in those with BMI > 40 kg/m^2.

3. Postoperative Follow-Up:

- **Close Monitoring:** Regular follow-ups to manage obesity-related complications and monitor for cancer recurrence.
- **Nutritional Support:** Continuous support to prevent malnutrition and promote weight maintenance or further weight loss.

Conclusions

- Obesity is a risk factor of CRC
- Weight loss can reduce the risk of CRC
- GLP-1 RA has weight independent benefit to CRC ?
- Obesity increase the risk of CRC surgery
- Weight management in CRC patient is beneficial

Thank you for your attention!