Body mass index at birth and early life and colorectal cancer: A two-sample Mendelian randomization analysis in populations of European and Asian ancestry

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Supplementary material

Table S1: SNPs of early life BMI												
SNP	Chr	Position (GRCh37)	EA	OA	EAF	beta	se	P-value	Cluster	N	R^2	F
rs2767486	1	65991203	G	A	0.16	0.143	0.012	6.40E-34	Transient	28,681	0.005497	159
rs10493544	1	74983835	T	C	0.43	0.054	0.009	1.40E-08	Early Rise	28,681	0.001429	41
rs545608	1	177899121	C	G	0.23	0.088	0.016	3.20E-08	Late Rise	28,681	0.002743	79
rs2816985	1	200072966	G	A	0.45	0.059	0.009	5.40E-11	Transient	28,681	0.001723	50
rs77165542	2	430975	C	T	0.98	0.187	0.032	3.50E-09	Early Rise	28,681	0.001371	39
rs11676272	2	25141538	G	A	0.49	0.089	0.009	2.80E-22	Early Rise	28,681	0.003959	114
rs1032296	4	145434688	T	C	0.38	0.052	0.009	1.10E-08	Transient	28,681	0.001274	37
rs6899303	5	95650975	C	A	0.63	0.057	0.009	5.30E-11	Transient	28,681	0.001515	44
rs263377	5	95884775	A	G	0.41	0.054	0.01	2.90E-08	Transient	28,681	0.001411	41
rs2268657	6	39020542	T	C	0.51	0.056	0.009	8.40E-10	Transient	28,681	0.001567	45
rs1820721	6	39110046	A	C	0.49	0.061	0.009	7.20E-12	Transient	28,681	0.00186	53
rs209421	6	83523684	G	T	0.26	0.073	0.01	5.40E-13	Transient	28,681	0.002051	59
rs1772945	6	154312285	A	G	0.56	0.056	0.009	3.20E-09	Transient	28,681	0.001545	44
rs17145750	7	73026378	C	T	0.84	0.07	0.012	6.80E-09	Transient	28,681	0.001317	38
rs10487505	7	127860163	C	G	0.49	0.056	0.009	3.20E-09	Early Rise	28,681	0.001567	45
rs287621	7	130435181	T	C	0.26	0.064	0.01	3.70E-10	Transient	28,681	0.001576	45
rs12672489	7	130483555	C	T	0.75	0.067	0.011	2.10E-09	Early Rise	28,681	0.001683	48
rs28457693	9	98217348	G	A	0.13	0.073	0.013	2.40E-08	Transient	28,681	0.001205	35
rs1830890	10	96019501	G	A	0.32	0.067	0.012	1.30E-08	Early Rise	28,681	0.001954	56
rs1985927	11	62193537	C	T	0.73	0.06	0.011	6.80E-09	Early Rise	28,681	0.001419	41
rs2298615	11	65352062	T	C	0.23	0.071	0.012	5.40E-09	Transient	28,681	0.001786	51
rs2728641	12	20111569	C	T	0.48	0.05	0.009	1.90E-08	Transient	28,681	0.001248	36
rs7132908	12	50263148	A	G	0.4	0.081	0.014	3.30E-09	Late Rise	28,681	0.003149	91
rs6538845	12	98544888	C	T	0.48	0.055	0.009	1.50E-09	Early Rise	28,681	0.00151	43

rs3741508	12	124812678	T	G	0.86	0.083	0.013	1.20E-09	Transient	28,681	0.001659	48
rs2585058	15	84284552	G	A	0.53	0.063	0.009	8.60E-12	Transient	28,681	0.001977	57
rs17817288	16	53807764	G	A	0.49	0.095	0.013	1.30E-12	Late Rise	28,681	0.004511	130
rs111810144	16	67216110	T	C	0.03	0.147	0.025	5.20E-09	Early Rise	28,681	0.001258	36
rs78263856	18	58042821	T	C	0.95	0.15	0.027	3.80E-08	Late Rise	28,681	0.002138	61
rs148252705	20	17851179	T	C	0.97	0.157	0.029	2.60E-08	Transient	28,681	0.001435	41
rs13038017	20	31467551	C	T	0.53	0.054	0.009	1.20E-08	Early Rise	28,681	0.001453	42
Abbreviations: BMI body mass index; chr chromosome; EA effect allele; EAF effect allele frequency; OA other allele; SNP single nucleotide polymorphism												

Table S2: SNPs of birth BMI											
SNP	Chr	Position (GRCh37)	EA	OA	EAF	Beta	SE	P-value	N	R^2	F
rs11708067	3	123065778	G	A	0.23	0.079	0.01	5.20E-16	28,681	0.002211	64
rs1482853	3	156798473	C	A	0.6	0.099	0.008	5.90E-32	28,681	0.004704	136
rs7772579	6	152042502	A	C	0.7	0.065	0.009	5.90E-13	28,681	0.001775	51
rs28642213	9	139248082	A	G	0.27	0.062	0.01	4.70E-11	28,681	0.001515	44
rs11187129	10	94429907	C	T	0.46	0.047	0.008	2.10E-08	28,681	0.001097	32
rs7310615	12	111865049	G	C	0.55	0.05	0.009	6.50E-09	28,681	0.001238	36
rs75806555	14	101189448	C	T	0.86	0.074	0.012	2.10E-09	28,681	0.001319	38
rs739669	17	7122377	A	G	0.62	0.072	0.009	4.70E-17	28,681	0.002443	70
Abbreviations: BMI body mass index; chr chromosome; EA effect allele; EAF effect allele frequency; OA other allele; SNP single nucleotide polymorphism											

Table S3: Cancer betas in the CRC consortium (overall cancer only) or CCFR/CORECT/GECCO (remaining outcomes) for SNPs of early life BMI										
A) men and women										
SNP	beta_ca	se_ca	beta_co	se_co	beta_prox	se_prox	beta_dist	se_dist	beta_re	se_re
rs2767486	0.0093	0.0092	0.0197	0.013	0.0119	0.0169	0.0273	0.0171	0.0187	0.0169
rs10493544	-0.0103	0.0075	0.0066	0.0108	0.0072	0.0139	0.013	0.0142	0.0021	0.014
rs545608	-0.0077	0.0093	0.0117	0.0135	0.0192	0.0174	0.0059	0.0178	0.0063	0.0175
rs2816985	0.0064	0.0074	0.0019	0.0107	-0.0136	0.0138	0.0084	0.014	0.012	0.0138
rs77165542	0.0401	0.0227	0.062	0.0321	0.0729	0.042	0.0471	0.0424	0.0342	0.0419
rs11676272	-0.0061	0.0073	0.0005	0.0106	0.0064	0.0137	-0.0012	0.014	0.0025	0.0137
rs1032296	0.0301	0.0075	0.0185	0.0108	0.0169	0.014	0.0168	0.0142	0.0314	0.014
rs6899303	-0.0037	0.0076	0.0121	0.0108	0.0065	0.014	0.0233	0.0143	-0.0028	0.0141
rs263377	-0.0068	0.0075	-0.0151	0.0108	-0.01	0.0139	-0.0234	0.0142	-0.003	0.0139
rs2268657	-0.0100	0.0075	-0.019	0.0108	-0.0042	0.014	-0.0303	0.0142	-0.0085	0.014
rs1820721	0.0058	0.0073	0.0046	0.0106	0.0132	0.0137	-0.005	0.0139	0.0045	0.0137
rs209421	0.0036	0.0083	-0.0086	0.012	-0.0124	0.0155	0.0008	0.0157	-0.022	0.0155
rs1772945	-0.0270	0.0074	-0.0242	0.0106	-0.0163	0.0137	-0.0302	0.0139	-0.0205	0.0137
rs17145750	-0.0172	0.0101	-0.0042	0.0147	0.0056	0.0191	-0.0075	0.0194	-0.0205	0.0189
rs10487505	0.0066	0.0074	0.0132	0.0106	0.0053	0.0137	0.021	0.014	-0.0116	0.0138
rs287621	0.0121	0.0082	0.008	0.0117	-0.0045	0.0152	0.0249	0.0154	0.0217	0.0152
rs12672489	-0.0051	0.0085	0.014	0.0123	0.0196	0.0159	0.0102	0.0161	-0.0135	0.0158
rs28457693	0.0081	0.0119	-0.0031	0.0173	-0.0173	0.0224	0.0203	0.0226	0.0185	0.0221
rs1830890	0.0121	0.0078	0.0001	0.0112	-0.0077	0.0145	0.007	0.0147	0.017	0.0145
rs1985927	0.0000	0.0083	-0.0014	0.0119	-0.005	0.0154	-0.0006	0.0157	-0.0113	0.0154
rs2298615	0.0062	0.0089	0.0121	0.0126	0.001	0.0163	0.0083	0.0167	-0.0166	0.0164
rs2728641	-0.0148	0.0074	-0.0098	0.0107	0.0008	0.0139	-0.0225	0.0141	-0.0161	0.0139
rs7132908	0.0027	0.0076	-0.0004	0.0109	-0.0029	0.0141	0.0005	0.0144	0.0001	0.0141
rs6538845	-0.0152	0.0074	-0.0265	0.0106	-0.0277	0.0137	-0.0178	0.014	0.003	0.0137
rs3741508	0.0262	0.0110	0.0068	0.0161	0.0129	0.0209	-0.0081	0.0212	0.0605	0.0211

rs2585058	-0.0020	0.0073	-0.0109	0.0106	-0.0225	0.0137	0.0049	0.014	-0.0203	0.0137
rs17817288	-0.0056	0.0073	-0.0005	0.0106	0.0035	0.0137	-0.0071	0.014	-0.0097	0.0137
rs111810144	0.0055	0.0215	0.007	0.0306	0.0241	0.0395	0.0024	0.0402	0.0237	0.0393
rs78263856	0.0189	0.0192	0.0197	0.0274	0.0021	0.0354	0.0289	0.0362	0.0574	0.0359
rs148252705	-0.0120	0.0205	0.0025	0.0288	-0.0068	0.0371	-0.0092	0.0377	0.0215	0.0375
rs13038017	0.0085	0.0074	0.0145	0.0106	0.0149	0.0137	0.0159	0.014	-0.0162	0.0137
B) men										
SNP	beta_ca	se_ca								
rs2767486	0.0307	0.0153								
rs10493544	0.0045	0.0126								
rs545608	0.0108	0.0155								
rs2816985	0.0214	0.0124								
rs77165542	0.0531	0.038								
rs11676272	-0.0091	0.0122								
rs1032296	0.032	0.0125								
rs6899303	-0.0076	0.0126								
rs263377	0.0048	0.0126								
rs2268657	-0.014	0.0126								
rs1820721	-0.0033	0.0122								
rs209421	-0.0245	0.014								
rs1772945	-0.0269	0.0123								
rs17145750	-0.0059	0.0171								
rs10487505	-0.0041	0.0123								
rs287621	0.0002	0.0135								
rs12672489	-0.0067	0.0141								
rs28457693	0.0208	0.0196								
rs1830890	0.0204	0.0129								
rs1985927	-0.01	0.0137								
rs2298615	0.0207	0.0148								

rs2728641	-0.0177	0.0124								
rs7132908	-0.0045	0.0126								
rs6538845	-0.0211	0.0123								
rs3741508	0.0194	0.0183								
rs2585058	-0.0166	0.0123								
rs17817288	-0.0084	0.0122								
rs111810144	-0.0286	0.0356								
rs78263856	0.0714	0.0325								
rs148252705	0.002	0.0337								
rs13038017	0.0115	0.0124								
C) women										
SNP	beta_ca	se_ca								
rs2767486	-0.0034	0.0157								
rs10493544	-0.0109	0.0129								
rs545608	0.0188	0.0159								
rs2816985	-0.0113	0.0127								
rs77165542	0.0696	0.0393								
rs11676272	0.0012	0.0126								
rs1032296	0.008	0.0128								
rs6899303	0.023	0.0128								
rs263377	-0.0225	0.0129								
rs2268657	-0.0137	0.0129								
rs1820721	0.011	0.0126								
rs209421	0.0086	0.0144								
rs1772945	-0.0147	0.0126								
rs17145750	-0.0127	0.0174								
rs10487505	0.0147	0.0126								
rs287621	0.0203	0.0139								
rs12672489	0.0085	0.0145								

rs28457693	-0.0219	0.0201								
rs1830890	-0.0074	0.0132								
rs1985927	0.0137	0.0141								
rs2298615	-0.0066	0.0151								
rs2728641	-0.0051	0.0128								
rs7132908	0.011	0.013								
rs6538845	-0.0069	0.0126								
rs3741508	0.0023	0.0187								
rs2585058	-0.0043	0.0126								
rs17817288	-0.0024	0.0125								
rs111810144	0.0412	0.0376								
rs78263856	0.0127	0.033								
rs148252705	0.0192	0.035								
rs13038017	0.0022	0.0127								
Abbreviations: ca cancer; co colon; dist distal; prox proximal; re rectal; se standard error; SNP single nucleotide polymorphism										

Table S4: Cancer betas in the CRC consortium (overall cancer only) or CCFR/CORECT/GECCO (remaining outcomes) for SNPs of birth BMI										
A) men and women										
SNP	beta_ca	se_ca	beta_co	se_co	beta_prox	se_prox	beta_dist	se_dist	beta_re	se_re
rs11708067	0.0306	0.0089	0.0132	0.0128	0.0173	0.0166	0.007	0.0169	0.0089	0.0165
rs1482853	-0.0058	0.0075	0.008	0.0107	0.004	0.0139	0.011	0.0141	-0.0006	0.0139
rs7772579	0.0049	0.0082	-0.0073	0.0119	0.0045	0.0154	-0.0158	0.0157	-0.0119	0.0154
rs28642213	0.0058	0.0175	-0.0009	0.0127	0.0023	0.0164	-0.0089	0.0168	0.0219	0.0163
rs11187129	-0.0138	0.0075	0.0024	0.0107	0.0039	0.0139	0	0.0141	0.0021	0.0139
rs7310615	0.0755	0.0075	0.0914	0.0108	0.1002	0.0139	0.0831	0.0142	0.0565	0.0139
rs75806555	0.0057	0.0126	0.0057	0.0167	0.0297	0.0218	-0.0061	0.022	0.0261	0.0216
rs739669	-0.0230	0.0078	-0.014	0.0112	-0.0143	0.0145	-0.004	0.0147	-0.0233	0.0144
B) men										
SNP	beta_ca	se_ca								
rs11708067	0.0329	0.0151								
rs1482853	0.0017	0.0124								
rs7772579	0.0034	0.0137								
rs28642213	-0.0113	0.0148								
rs11187129	0.0002	0.0125								
rs7310615	0.0737	0.0127								
rs75806555	0.0179	0.0195								
rs739669	-0.012	0.013								
C) women										
SNP	beta_ca	se_ca								
rs11708067	-0.0005	0.0155								
rs1482853	0.004	0.0127								
rs7772579	-0.0072	0.0142								
rs28642213	0.0246	0.0152								
rs11187129	-0.0139	0.0128								

rs7310615	0.0727	0.013								
rs75806555	0.0045	0.02								
rs739669	-0.0224	0.0133								
Abbreviations: ca cancer; co colon; dist distal; prox proximal; re rectal; se standard error; SNP single nucleotide polymorphism										

Table S5: Cancer betas in Finngen for SNPs of early life BMI				
SNP	beta_co	se_co	beta_re	se_re
rs2767486	0.0074	0.0359	-0.0389	0.0461
rs10493544	0.0121	0.0225	0.0324	0.0289
rs545608	0.0279	0.0292	0.0153	0.0375
rs2816985	-0.0036	0.0229	-0.0216	0.0293
rs77165542	-0.0567	0.0876	-0.0845	0.1119
rs11676272	0.0083	0.0228	0.0176	0.0293
rs1032296	0.0272	0.0238	-0.0093	0.0305
rs6899303	-0.0089	0.0250	-0.0489	0.0322
rs263377	0.0160	0.0226	-0.0005	0.0290
rs2268657	0.0092	0.0226	0.0202	0.0290
rs1820721	-0.0192	0.0226	-0.0016	0.0290
rs209421	-0.0154	0.0250	-0.0021	0.0320
rs1772945	-0.0200	0.0226	-0.0293	0.0289
rs17145750	-0.0089	0.0315	-0.0120	0.0403
rs10487505	0.0176	0.0225	-0.0370	0.0289
rs287621	-0.0166	0.0249	0.0168	0.0319
rs12672489	-0.0147	0.0267	-0.0246	0.0341
rs28457693	-0.0358	0.0359	-0.0033	0.0460
rs1830890	-0.0065	0.0251	-0.0217	0.0322
rs1985927	-0.0346	0.0256	0.0151	0.0328
rs2298615	-0.0170	0.0315	0.0188	0.0404
rs2728641	-0.0198	0.0227	0.0580	0.0291
rs7132908	-0.0405	0.0232	0.0500	0.0297
rs6538845	0.0203	0.0226	-0.0557	0.0290
rs3741508	0.0352	0.0261	-0.0366	0.0335
rs2585058	-0.0187	0.0225	-0.0220	0.0289
rs17817288	-0.0189	0.0225	0.0242	0.0288
rs111810144	-0.0687	0.0888	-0.1273	0.1146
rs78263856	0.0406	0.0711	0.0611	0.0916
rs148252705	-0.0097	0.0806	-0.0830	0.1027
rs13038017	0.0296	0.0229	0.0010	0.0295
Abbreviations: co colon; re rectal; se standard error; SNP single nucleotide polymorphism				

Table S6: Cancer betas in Finngen for SNPs of birth BMI				
SNP	beta_co	se_co	beta_re	se_re
rs11708067	-0.0122	0.0300	0.0974	0.0384
rs1482853	-0.0179	0.0243	0.0043	0.0312
rs7772579	-0.0515	0.0236	0.0007	0.0303
rs28642213	-0.0350	0.0244	-0.0094	0.0313
rs11187129	-0.0301	0.0226	-0.0213	0.0288
rs7310615	0.0430	0.0229	0.0600	0.0292
rs75806555	-0.0028	0.0318	0.0542	0.0406
rs739669	0.0215	0.0239	0.0634	0.0306
Abbreviations: co colon; re rectal; se standard error; SNP single nucleotide polymorphism				

Table S7: Cancer betas in ACCC for SNPs of early life BMI		
SNP	beta_ca	se_ca
rs2767486	-0.0185	0.0392
rs10493544	0.0366	0.0241
rs545608	0.0076	0.0148
rs2816985	-0.0219	0.014
rs11676272	-0.0291	0.0125
rs1032296	0.0005	0.0138
rs6899303	0.0018	0.0131
rs263377	0.0382	0.0212
rs2268657	-0.0186	0.014
rs1820721	-0.0262	0.014
rs1772945	0.0177	0.0147
rs17145750	0.0309	0.0206
rs10487505	-0.0035	0.0143
rs287621	0.0347	0.0131
rs12672489	0.0156	0.0167
rs28457693	0.0038	0.0168
rs1830890	0.0212	0.0142
rs1985927	-0.0166	0.0136
rs2298615	0.0017	0.0219
rs2728641	-0.0195	0.0141
rs7132908	-0.0005	0.0148
rs6538845	0.0141	0.014
rs3741508	-0.005	0.0136
rs2585058	-0.0049	0.0132
rs17817288	0.0132	0.0128
rs111810144	0.2045	0.1347
rs13038017	0.0367	0.0209
Abbreviations: ca cancer; se standard error; SNP single nucleotide polymorphism		

Table S8: Cancer betas in ACCC for SNPs of birth BMI		
SNP	beta_ca	se_ca
rs1482853	0.0134	0.0131
rs7772579	0.0251	0.0170
rs28642213	-0.0014	0.0255
rs11187129	-0.0041	0.0160
rs75806555	-0.0886	0.0641
rs739669	0.0211	0.0140
Abbreviations: ca cancer; se standard error; SNP single nucleotide polymorphism		

Table S9: Mendelian randomization results for overall early life BMI

	CRC consortium or CCFR/CORECT/GECCO				Finngen				ACCC			
	Estimates (OR)*	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**
MEN & WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.01	0.95, 1.07	0.80	8×10^{-5}					1.02	0.91, 1.14	0.73	0.01
MR-Egger	1.12	0.91, 1.36	0.27	0.02					0.94	0.55, 1.60	0.83	0.77
Weighted median	1.03	0.97, 1.11	0.28						1.01	0.89, 1.16	0.83	
MR-PRESSO (-rs1032296, rs1772945)	1.01	0.96, 1.06	0.73									
Colon cancer												
Inverse-variance weighted	1.03	0.96, 1.09	0.38	0.19	0.95	0.83, 1.11	0.53	0.78				
MR-Egger	1.25	1.02, 1.52	0.03	0.05	0.87	0.54, 1.40	0.57	0.70				
Weighted median	1.03	0.94, 1.13	0.48		0.90	0.75, 1.40	0.25					
Proximal colon cancer												
Inverse-variance weighted	1.02	0.94, 1.11	0.63	0.82								
MR-Egger	1.22	0.95, 1.55	0.12	0.14								
Weighted median	1.05	0.94, 1.16	0.39									
Distal colon cancer												
Inverse-variance weighted	1.04	0.96, 1.13	0.34	0.30								
MR-Egger	1.22	0.94, 1.60	0.13	0.20								
Weighted median	1.06	0.95, 1.19	0.28									
Rectal cancer												
Inverse-variance weighted	1.03	0.93, 1.11	0.67	0.16	0.95	0.80, 1.13	0.57	0.68				
MR-Egger	1.31	1.00, 1.70	0.05	0.05	0.93	0.51, 1.72	0.81	0.93				
Weighted median	1.03	0.92, 1.15	0.59		0.97	0.76, 1.26	0.82					
MEN												
Colorectal cancer												
Inverse-variance weighted	1.02	0.93, 1.12	0.64	0.03								
MR-Egger	1.28	0.98, 1.68	0.07	0.08								
Weighted median	0.95	0.85, 1.05	0.32									
WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.03	0.96, 1.11	0.44	0.69								
MR-Egger	1.19	0.94, 1.49	0.14	0.20								
Weighted median	1.01	0.91, 1.12	0.88									

Abbreviations: CI, confidence intervals; MR: Mendelian Randomization; OR: odds ratio; MR-PRESSO: MR pleiotropy residual sum and outlier test

* The estimates correspond to a standard deviation increase in duration of sedentary activity

† P-value or pleiotropy based on MR-Egger intercept

‡ P-value for heterogeneity based on Q statistic

Table S10: Mendelian randomization results for transient BMI

	CRC consortium or CCFR/CORECT/GECCO				Finngen				ACCC			
	Estimates (OR)*	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**
MEN & WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.02	0.92, 1.13	0.74	2×10^{-5}					0.99	0.84, 1.16	0.94	0.04
MR-Egger	1.14	0.93, 1.62	0.46	0.51					1.06	0.44, 2.53	0.89	0.88
Weighted median	1.06	0.97, 1.16	0.17						0.96	0.80, 1.15	0.69	
MR-PRESSO (-rs1032296, rs1772945)	1.02	0.96, 1.08	0.53									
Colon cancer												
Inverse-variance weighted	1.00	0.91, 1.11	0.97	0.18	0.94	0.78, 1.13	0.50	0.92				
MR-Egger	1.26	0.95, 1.68	0.11	0.10	1.11	0.55, 2.18	0.78	0.63				
Weighted median	1.07	0.95, 1.20	0.27		0.87	0.68, 1.12	0.28					
Proximal colon cancer												
Inverse-variance weighted	0.97	0.88, 1.08	0.65	0.84								
MR-Egger	1.11	0.79, 1.55	0.55	0.44								
Weighted median	1.01	0.88, 1.17	0.84									
Distal colon cancer												
Inverse-variance weighted	1.02	0.91, 1.13	0.75	0.06								
MR-Egger	1.38	0.90, 2.10	0.14	0.14								
Weighted median	1.11	0.94, 1.28	0.23									
Rectal cancer												
Inverse-variance weighted	1.03	0.89, 1.19	0.71	0.03	0.88	0.69, 1.11	0.27	0.81				
MR-Egger	1.30	0.82, 2.03	0.27	0.30	0.55	0.23, 1.31	0.18	0.28				
Weighted median	1.08	0.92, 1.27	0.32		0.83	0.61, 1.13	0.24					
MEN												
Colorectal cancer												
Inverse-variance weighted	1.03	0.90, 1.17	0.65	0.01								
MR-Egger	1.36	0.90, 2.05	0.15	0.18								
Weighted median	1.03	0.89, 1.20	0.71									
WOMEN												
Colorectal cancer												
Inverse-variance weighted	0.98	0.89, 1.08	0.69	0.48								
MR-Egger	1.05	0.76, 1.45	0.75	0.65								
Weighted median	0.97	0.84, 1.12	0.65									

Abbreviations: CI, confidence intervals; MR: Mendelian Randomization; OR: odds ratio; MR-PRESSO: MR pleiotropy residual sum and outlier test

* The estimates correspond to a standard deviation increase in duration of sedentary activity

† P-value or pleiotropy based on MR-Egger intercept

‡ P-value for heterogeneity based on Q statistic

Table S11: Mendelian randomization results for early rise BMI

	CRC consortium or CCFR/CORECT/GECCO				Finngen				ACCC			
	Estimates (OR)*	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**
MEN & WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.01	0.91, 1.12	0.89	0.09					1.01	0.79, 1.28	0.94	0.02
MR-Egger	1.17	0.85, 1.62	0.32	0.32					0.41	0.13, 1.34	0.14	0.13
Weighted median	0.99	0.89, 1.12	0.91						0.92	0.71, 1.20	0.53	
MR-PRESSO (- rs11676272)									1.20	0.94, 1.51	0.14	
Colon cancer												
Inverse-variance weighted	1.07	0.93, 1.22	0.32	0.13	1.03	0.81, 1.31	0.80	0.67				
MR-Egger	1.27	0.82, 1.97	0.29	0.42	0.58	0.24, 1.43	0.24	0.19				
Weighted median	1.04	0.90, 1.21	0.60		1.07	0.77, 1.49	0.68					
Proximal colon cancer												
Inverse-variance weighted	1.07	0.92, 1.25	0.33	0.33								
MR-Egger	1.49	0.93, 2.36	0.09	0.15								
Weighted median	1.09	0.90, 1.32	0.36									
Distal colon cancer												
Inverse-variance weighted	1.11	0.95, 1.27	0.18	0.72								
MR-Egger	1.08	0.68, 1.73	0.73	0.95								
Weighted median	1.11	0.91, 1.34	0.31									
Rectal cancer												
Inverse-variance weighted	1.00	0.87, 1.15	0.97	0.75	0.84	0.62, 1.15	0.28	0.46				
MR-Egger	1.35	0.86, 2.14	0.19	0.17	0.78	0.23, 2.61	0.69	0.90				
Weighted median	1.03	0.85, 1.25	0.74		0.85	0.56, 1.31	0.48					
MEN												
Colorectal cancer												
Inverse-variance weighted	0.99	0.87, 1.13	0.86	0.32								
MR-Egger	1.11	0.69, 1.75	0.68	0.63								
Weighted median	0.90	0.76, 1.08	0.28									
WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.08	0.95, 1.23	0.25	0.63								
MR-Egger	1.45	0.94, 2.25	0.09	0.15								
Weighted median	1.04	0.87, 1.23	0.70									

Abbreviations: CI, confidence intervals; MR: Mendelian Randomization; OR: odds ratio; MR-PRESSO: MR pleiotropy residual sum and outlier test

* The estimates correspond to a standard deviation increase in duration of sedentary activity

† P-value or pleiotropy based on MR-Egger intercept

‡ P-value for heterogeneity based on Q statistic

Table S12: Mendelian randomization results for late rise BMI

	CRC consortium or CCFR/CORECT/GECCO				Finngen				ACCC			
	Estimates (OR)*	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**
MEN & WOMEN												
Colorectal cancer												
Inverse-variance weighted	0.98	0.90, 1.08	0.76	0.52					1.09	0.91, 1.31	0.34	0.81
MR-Egger	1.23	0.70, 2.20	0.47	0.43					2.64	0.17, 40.4	0.49	0.53
Weighted median	0.97	0.86, 1.09	0.60						1.11	0.90, 1.36	0.33	
Colon cancer												
Inverse-variance weighted	1.04	0.91, 1.20	0.54	0.83	0.88	0.62, 1.26	0.48	0.23				
MR-Egger	1.26	0.55, 2.89	0.58	0.64	2.80	0.23, 34.8	0.42	0.36				
Weighted median	1.00	0.84, 1.17	0.95		0.84	0.57, 1.25	0.39					
Proximal colon cancer												
Inverse-variance weighted	1.05	0.89, 1.26	0.56	0.80								
MR-Egger	1.03	0.35, 2.97	0.96	0.96								
Weighted median	1.03	0.84, 1.27	0.79									
Distal colon cancer												
Inverse-variance weighted	1.01	0.85, 1.21	0.88	0.80								
MR-Egger	1.39	0.47, 4.14	0.55	0.56								
Weighted median	1.00	0.80, 1.25	0.99									
Rectal cancer												
Inverse-variance weighted	1.03	0.86, 1.22	0.74	0.38	1.43	0.97, 2.10	0.07	0.85				
MR-Egger	2.03	0.69, 5.93	0.20	0.21	1.00	0.07, 14.01	0.99	0.79				
Weighted median	0.99	0.79, 1.25	0.96		1.36	0.85, 2.16	0.20					
MEN												
Colorectal cancer												
Inverse-variance weighted	1.04	0.84, 1.30	0.71	0.61								
MR-Egger	2.61	0.96, 7.10	0.06	0.07								
Weighted median	0.94	0.77, 1.16	0.58									
WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.08	0.92, 1.27	0.32	0.73								
MR-Egger	0.92	0.34, 2.48	0.87	0.74								
Weighted median	1.09	0.90, 1.34	0.35									

Abbreviations: CI, confidence intervals; MR: Mendelian Randomization; OR: odds ratio; MR-PRESSO: MR pleiotropy residual sum and outlier test

* The estimates correspond to a standard deviation increase in duration of sedentary activity

† P-value or pleiotropy based on MR-Egger intercept

‡ P-value for heterogeneity based on Q statistic

Table S13: Mendelian randomization results for birth BMI

	CRC consortium or CCFR/CORECT/GECCO				Finngen				ACCC			
	Estimates (OR)*	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**	**Estimates (OR)***	**95% CI**	**P-value**	**P-value for pleiotropy† or heterogeneity‡**
MEN & WOMEN												
Colorectal cancer												
Inverse-variance weighted	1.12	0.79, 1.58	0.55	4×10^{-23}					1.17	0.98, 1.42	0.08	0.48
MR-Egger	0.54	0.14, 2.25	0.40	0.31					1.27	0.58, 2.75	0.55	0.85
Weighted median	1.00	0.88, 1.14	0.97						1.20	0.97, 1.49	0.10	
MR-PRESSO (-rs11708067, rs1482853, rs11187129, rs7310615, rs739669)	1.08	0.90, 1.30	0.41	0.95								
Colon cancer												
Inverse-variance weighted	1.16	0.81, 1.68	0.41	3×10^{-12}	0.85	0.61, 1.19	0.33	0.10				
MR-Egger	0.49	0.11, 2.16	0.35	0.24	0.81	0.18, 3.67	0.78	0.94				
Weighted median	1.08	0.92, 1.27	0.34		0.84	0.59, 1.20	0.34					
MR-PRESSO (-rs7310615)	1.02	0.90, 1.15	0.80	0.72								
Proximal colon cancer												
Inverse-variance weighted	1.23	0.83, 1.84	0.30	3×10^{-8}								
MR-Egger	0.44	0.11, 1.84	0.26	0.14								
Weighted median	1.06	0.86, 1.30	0.59									
MR-PRESSO (-rs7310615)	1.06	0.90, 1.15	0.80	0.72								
Distal colon cancer												
Inverse-variance weighted	1.13	0.80, 1.58	0.48	2×10^{-5}								
MR-Egger	1.73	0.14, 2.39	0.45	0.34								
Weighted median	1.05	0.85, 1.28	0.65									
MR-PRESSO (-rs7310615)	0.99	0.84, 1.16	0.94	0.90								
Rectal cancer												
Inverse-variance weighted	1.09	0.84, 1.43	0.50	0.003	1.49	0.98, 2.25	0.06	0.12				
MR-Egger	0.56	0.19, 1.62	0.28	0.20	1.52	0.23, 10.28	0.66	0.98				
Weighted median	1.02	0.83, 1.26	0.86		1.34	0.84, 2.14	0.22					
MR-PRESSO (-rs7310615)	1.00	0.85, 1.19	0.96									
MEN												
Colorectal cancer												
Inverse-variance weighted	1.16	0.85, 1.58	0.33	8×10^{-6}								
MR-Egger	0.60	0.17, 2.16	0.44	0.30								
Weighted median	1.02	0.85, 1.23	0.80									
MR-PRESSO (-rs7310615)	1.05	0.90, 1.21	0.52	0.35								
WOMEN												
Colorectal cancer												

Inverse-variance weighted	1.08	0.79, 1.49	0.62	5×10^{-6}
MR-Egger	0.58	0.15, 2.25	0.43	0.35
Weighted median	1.02	0.84, 1.23	0.87	
MR-PRESSO (rs7310615)	0.97	0.83, 1.13	0.69	0.33

Abbreviations: CI, confidence intervals; MR: Mendelian Randomization; OR: odds ratio; MR-PRESSO: MR pleiotropy residual sum and outlier test

* The estimates correspond to a standard deviation increase in duration of sedentary activity

† P-value or pleiotropy based on MR-Egger intercept

‡ P-value for heterogeneity based on Q statistic