

eTable 1 Conditional logistic regression odds ratios with 95 % confidence intervals for colorectal cancer risk for tertiles of plasma concentrations of one-carbon metabolites over subclasses of tumors.

	Tumor site						Tumor stage				
	Right colon			Left colon		Rectum		Stage I & II		Stage III & IV	
	Tertiles ^a	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b
Choline	1 (<8.0)	73/127	ref	70/131	ref	70/139	ref	103/196	ref	98/181	ref
	2 (8.0-9.3)	55/125	0.77 (0.49-1.2)	73/143	0.93 (0.60-1.4)	67/127	1.0 (0.67-1.6)	101/181	1.1 (0.74-1.5)	86/196	0.79 (0.55-1.2)
	3 (≥9.3)	53/105	0.86 (0.54-1.4)	70/145	0.88 (0.56-1.4)	74/145	0.97 (0.63-1.5)	102/222	0.83 (0.57-1.2)	88/156	1.0 (0.71-1.5)
	P _{trend} ^c		0.80		0.71		0.91		0.27		0.39
Betaine	1 (<27.7)	68/129	ref	92/153	ref	61/115	ref	107/198	ref	100/177	ref
	2 (27.7-33.8)	68/117	1.2 (0.74-1.8)	68/130	0.83 (0.55-1.2)	79/155	0.98 (0.64-1.5)	120/203	1.1 (0.78-1.5)	91/180	0.89 (0.61-1.3)
	3 (≥33.8)	45/111	0.76 (0.47-1.2)	53/136	0.59 (0.38-0.93)	71/141	0.97 (0.62-1.5)	79/198	0.69 (0.47-1.0)	81/176	0.81 (0.56-1.2)
	P _{trend} ^c		0.19		0.08		0.72		0.09		0.30
DMG	1 (<3.2)	66/120	ref	80/154	ref	68/123	ref	102/195	ref	105/181	ref
	2 (3.2-4.1)	49/133	0.68 (0.43-1.1)	55/131	0.82 (0.54-1.3)	64/123	0.87 (0.57-1.3)	89/203	0.83 (0.58-1.2)	71/176	0.69 (0.47-1.0)
	3 (≥4.1)	66/104	1.2 (0.76-1.9)	78/134	1.1 (0.75-1.7)	69/166	0.77 (0.50-1.2)	115/201	1.1 (0.77-1.5)	96/176	0.94 (0.65-1.4)
	P _{trend} ^c		0.49		0.89		0.32		0.93		0.99
Sarcosine	1 (<1.3)	78/133	ref	73/143	ref	71/120	ref	108/195	ref	110/186	ref
	2 (1.3-1.8)	58/119	0.83 (0.54-1.3)	67/151	0.88 (0.59-1.3)	69/133	0.81 (0.53-1.3)	102/201	0.91 (0.65-1.3)	73/177	0.70 (0.48-1.0)
	3 (≥1.8)	47/105	0.68 (0.40-1.2)	75/125	1.3 (0.80-2.2)	74/159	0.76 (0.48-1.2)	98/204	0.80 (0.53-1.2)	93/170	0.96 (0.63-1.5)
	P _{trend} ^c		0.36		0.39		0.34		0.31		0.80
Methionine	1 (<24.4)	64/130	ref	83/145	ref	71/120	ref	115/191	ref	89/182	ref
	2 (24.4-28.5)	80/116	1.4 (0.90-2.1)	74/147	0.87 (0.58-1.3)	69/133	0.84 (0.55-1.3)	111/208	0.85 (0.61-1.2)	102/169	1.2 (0.86-1.7)
	3 (≥28.5)	39/111	0.63 (0.38-1.1)	58/127	0.76 (0.49-1.2)	74/159	0.71 (0.46-1.1)	82/201	0.59 (0.40-0.87)	85/182	0.92 (0.63-1.4)
	P _{trend} ^c		0.42		0.27		0.26		0.01		0.86

OR: odds ratio- CI: confidence interval-DMG: Dimethylglycine

^a The cut-offs for tertiles of plasma concentrations were based on the distribution of the controls (concentrations in μmol/l).^b Unadjusted ORs calculated by conditional logistic regression. Adjusting for potential confounders had essentially no effect on parameter estimates.^c P-values were calculated by modeling plasma concentration variables divided into quintiles with cut-offs based on the distribution of the controls as continuous variables (labeled 1-5).

eTable 2 Conditional logistic regression odds ratios with 95 % confidence intervals for colorectal cancer risk for tertiles of plasma concentrations of one-carbon metabolites after stratification by baseline characteristics.

		Sex				Age at screening			
		Male		Female		≤59 y		>59 y	
		Tertiles ^a	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)	OR (95%CI) ^b	Cases/ controls (n)
Choline	1 (<8.0)	90/164	ref	118/235	ref	107/200	ref	106/197	ref
	2 (8.0-9.3)	76/162	1.0 (0.65-1.5)	116/234	0.86 (0.63-1.2)	89/171	0.97 (0.67-1.4)	107/225	0.85 (0.60-1.2)
	3 (≥9.3)	84/160	0.92 (0.61-1.4)	122/234	0.90 (0.64-1.3)	64/149	0.79 (0.54-1.2)	133/247	0.99 (0.7-1.4)
	P _{trend} ^c		0.88		0.67		0.35		0.83
Betaine	1 (<27.7)	97/167	ref	131/229	ref	104/175	ref	117/222	ref
	2 (27.7-33.8)	82/159	0.92 (0.59-1.4)	122/235	0.95 (0.71-1.3)	85/179	0.78 (0.53-1.1)	131/225	1.1 (0.81-1.5)
	3 (≥33.8)	71/160	0.70 (0.45-1.1)	103/229	0.80 (0.57-1.1)	71/166	0.65 (0.43-0.98)	98/222	0.83 (0.59-1.2)
	P _{trend} ^c		0.17		0.15		0.11		0.15
DMG	1 (<3.2)	75/164	ref	139/235	ref	110/200	ref	106/197	ref
	2 (3.2-4.1)	84/160	0.96 (0.63-1.5)	103/236	0.73 (0.53-1.0)	76/175	0.79 (0.54-1.2)	96/221	0.81 (0.57-1.1)
	3 (≥4.1)	91/162	1.3 (0.87-1.9)	114/232	0.85 (0.61-1.2)	74/145	0.91 (0.62-1.3)	144/251	1.1 (0.76-1.5)
	P _{trend} ^c		0.27		0.32		0.68		0.97
Sarcosine	1 (<1.3)	90/163	ref	129/240	ref	107/188	ref	118/212	ref
	2 (1.3-1.8)	81/162	0.77 (0.53-1.1)	111/229	0.89 (0.65-1.2)	86/174	0.84 (0.58-1.2)	100/220	0.83 (0.60-1.2)
	3 (≥1.8)	82/162	0.81 (0.52-1.3)	120/234	0.93 (0.64-1.4)	71/159	0.67 (0.42-1.1)	131/237	1.0 (0.72-1.5)
	P _{trend} ^c		0.92		0.52		0.19		0.84
Methionine	1 (<24.4)	90/163	ref	132/235	ref	107/186	ref	135/211	ref
	2 (24.4-28.5)	76/162	1.1 (0.73-1.7)	123/234	0.95 (0.71-1.3)	86/163	1.3 (0.91-1.9)	1125/233	0.79 (0.58-1.1)
	3 (≥28.5)	84/162	0.79 (0.52-1.2)	105/234	0.69 (0.48-0.99)	71/172	0.99 (0.67-1.5)	89/225	0.54 (0.38-0.78)
	P _{trend} ^c		0.36		0.12		0.82		0.007

OR: odds ratio- CI: confidence interval- DMG: Dimethylglycine

^a The cut-offs for plasma concentrations were based on the distribution of the controls (concentrations in μmol/l).

^b Unadjusted ORs calculated by conditional logistic regression. Adjusting for potential confounders had essentially no effect on parameter estimates.

^c P-values were calculated by modeling plasma concentration variables divided into quintiles with cut-offs based on the distribution of the controls as continuous variables (labeled 1-5).