Supplemental Table 1 Comparison of cases and controls by selected descriptive characteristics, the Tennessee Colorectal Polyp Study [1]

Characteristic	Adenoma Cases (*N*=1336)	Controls (*N*=2891)	*P*-value
Age (years), Mean ± SD	59.5±7.2	57.6±7.6	<0.001
Sex, %			<0.001
Man	997 (74.7)	1619 (56.0)	
Race, %			0.27
Caucasian	1181 (88.5)	2590 (89.6)	
Recruitment sites, %			<0.001
Vanderbilt Medical Center	780 (58.4)	2159 (74.7)	
Education, %			<0.001
High school or below	426 (33.2)	620 (22.3)	
Some college	373 (29.0)	777 (27.9)	
College graduates	235 (18.3)	611 (22.0)	
Graduates	251 (19.5)	772 (27.8)	
Smoking status, %			<0.001
Never smoker	464 (36.0)	1517 (54.4)	
Former smoker	481 (37.3)	975 (34.9)	
Current smoker	343 (26.6)	298 (10.7)	
Alcohol consumption status, %			<0.001
Never drinker	633 (49.2)	1672 (60.0)	
Former drinker	370 (28.7)	568 (20.4)	
Current drinker	284 (22.1)	546 (19.6)	
Physically active past 10 years, %	624 (48.4)	1159 (41.5)	<0.001
BMI (kg/m2) , Mean ± SD	28.6±5.5	27.9±5.7	<0.001
Daily nutrients intake, Mean ± SD			
Total energy (kcal)[2]	1827±47	1791±44	0.15
Total calcium (mg)[3]	969±24	1054±26	<0.0001
Dietary calcium (mg) [3]	766±16	824±17	<0.0001
Supplement calcium (mg) [2]	262±24	268±23	0.59
Total magnesium (mg) [3]	341±6	363±7	<0.0001
Dietary magnesium (mg) [3]	301±5	318±5	<0.0001
Supplement magnesium(mg) [2]	75±5	79±5	0.09

[1] Phase I +Phase II

[2] Least square mean value ± SE, adjusting for age (year), site, sex, and race;

[3] Least square mean value ± SE, adjusting for age (year), site, sex, race and total energy

Supplemental table 2 The distribution of genotypes for 19 tagging SNPs in *KCNJ1* and *SLC12A1* in Phase I, the Tennessee Colorectal Polyp Study

SNP	Allele[1]	Chromosome	Gene	Location (bp)[2]	MAF[3]
rs11221484	C/G	11q24	*KCNJ1*	128244665	0.43/0.41
rs1148058	A/G	11q24	*KCNJ1*	128217991	0.17/0.17
rs17137982	G/C	11q24	*KCNJ1*	128227400	0.16/0.16
rs2855798	T/G	11q24	*KCNJ1*	128238171	0.19/0.19
rs3758766	G/A	11q24	*KCNJ1*	128221182	0.17/0.17
rs4529890	T/C	11q24	*KCNJ1*	128246290	0.15/0.15
rs4937378	T/C	11q24	*KCNJ1*	128248228	0.23/0.23
rs588472	A/G	11q24	*KCNJ1*	128206861	0.35/0.35
rs588957	T/C	11q24	*KCNJ1*	128206751	0.29/0.31
rs6590354	T/C	11q24	*KCNJ1*	128244573	0.03/0.04
rs675482	G/A	11q24	*KCNJ1*	128231804	0.31/0.31
rs675759	C/G	11q24	*KCNJ1*	128213185	0.16/0.16
rs7116606	T/C	11q24	*KCNJ1*	128246949	0.29/0.30
rs1531916	G/A	15q15	*SLC12A1*	46313563	0.17/0.18
rs2291340	C/T	15q15	*SLC12A1*	46335268	0.19/0.19
rs6493315	C/T	15q15	*SLC12A1*	46354306	0.19/0.19
rs8032420	A/C	15q15	*SLC12A1*	46332673	0.19/0.19
rs9635331	T/A	15q15	*SLC12A1*	46357429	0.16/0.16
rs964611	A/C	15q15	*SLC12A1*	46384806	0.16/0.17

[1] Minor/Major
[2] Location based on NCBI Human Genome Build 36.1
[3] Risk allele frequency in cases/controls

Supplemental table 3 Association of calcium supplement intake with colorectal adenoma risk stratified by the number of gene with variant alleles, the Tennessee Colorectal Polyp Study [1-2]

Number of gene with variant alleles		calcium supplement intake level (mg/d)			
		T1 (low) 0	T2 0-324	T3 >324	*P*_trend
		all adenomas vs controls			
Total	Cases/Controls	566/936	378/911	302/890	
	OR (95% CI)	1.00	0.73(0.54-0.99)	0.78(0.58-1.06)	0.38
0	Cases/Controls	219/363	157/412	152/356	
	OR (95% CI)	1.00	0.56(0.35-0.90)	0.79(0.49-1.28)	0.76
≥1	Cases/Controls	347/573	221/499	150/534	
	OR (95% CI)	1.00	0.92(0.60-1.41)	0.80(0.52-1.22)	0.22
		multiple/advanced adenomas vs controls			
Total	Cases/Controls	256/936	166/911	116/890	
	OR (95% CI)	1.00	0.57(0.37-0.89)	0.53(0.34-0.84)	0.02
0	Cases/Controls	92/363	69/412	54/356	
	OR (95% CI)	1.00	0.52(0.26-1.07)	0.63(0.31-1.28)	0.54
≥1	Cases/Controls	164/573	97/499	62/534	
	OR (95% CI)	1.00	0.59(0.30-1.13)	0.46(0.24-0.89)	0.02

[1] Phase I +Phase II

[2] Unconditional logistic regression models adjusting for age (continuous), sex, race (Caucasian, others), education (categorical), recruitment sites, body mass index (categorical), smoking status (never, former, current), alcohol drinking status (never, former, current), physical activity (yes, no), and daily total energy, daily diet intakes of calcium, magnesium and magnesium supplement intake (continuous)

Supplemental table 4 Association of calcium intake with colorectal adenoma risk stratified by the number of gene with variant alleles among those screening participants, the Tennessee Colorectal Polyp Study [1-2]

Number of genes with variant alleles		calcium intake level (mg/d)			
		<1000	1000-1300	≥1300	*P*_trend
		all adenomas vs controls			
Total	Cases/Controls	313/598	131/328	289/660	
	OR (95% CI)	1.00	0.82(0.62-1.08)	0.94(0.71-1.25)	0.71
0	Cases/Controls	114/259	60/126	143/256	
	OR (95% CI)	1.00	1.18(0.76-1.81)	1.28(0.83-1.96)	0.26
≥1	Cases/Controls	199/339	71/202	146/404	
	OR (95% CI)	1.00	0.62(0.43-0.90)	0.71(0.48-1.03)	0.08
1	Cases/Controls	154/275	65/161	126/319	
	OR (95% CI)	1.00	0.75(0.50-1.12)	0.81(0.53-1.22)	0.33
2	Cases/Controls	45/64	6/41	20/85	
	OR (95% CI)	1.00	0.20(0.07-0.61)	0.41(0.16-1.09)	0.06
		Multiple/advanced adenomas vs controls			
Total	Cases/Controls	136/598	62/328	116/660	
	OR (95% CI)	1.00	0.88(0.61-1.29)	0.83(0.57-1.23)	0.36
0	Cases/Controls	44/259	29/126	58/256	
	OR (95% CI)	1.00	1.58(0.87-2.89)	1.46(0.78-2.71)	0.25
≥1	Cases/Controls	92/339	33/202	58/404	
	OR (95% CI)	1.00	0.57(0.35-0.95)	0.52(0.31-0.87)	0.01
1	Cases/Controls	69/275	31/161	51/319	
	OR (95% CI)	1.00	0.77(0.45-1.32)	0.66(0.38-1.16)	0.15
2	Cases/Controls	23/64	2/41	7/85	
	OR (95% CI)	1.00	0.08(0.01-0.51)	0.13(0.03-0.60)	0.006

[1]Phase I +Phase II

[2]Unconditional logistic regression models adjusting for age (continuous), sex, race (Caucasian, others), education (categorical), recruitment sites, body mass index (categorical), smoking status (never, former, current), alcohol drinking status (never, former, current), physical activity (yes, no), and daily intakes of total energy, magnesium (continuous)

[3]The *P* for interactions between calcium intake (continuous) and combined SNPs polymorphism (rs2855798 in *KCNJ1* and rs1531916 in *SLC12A1*) were 6.6×10^{-7} for adenomas and 5.7×10^{-5} for multiple /advanced adenomas.