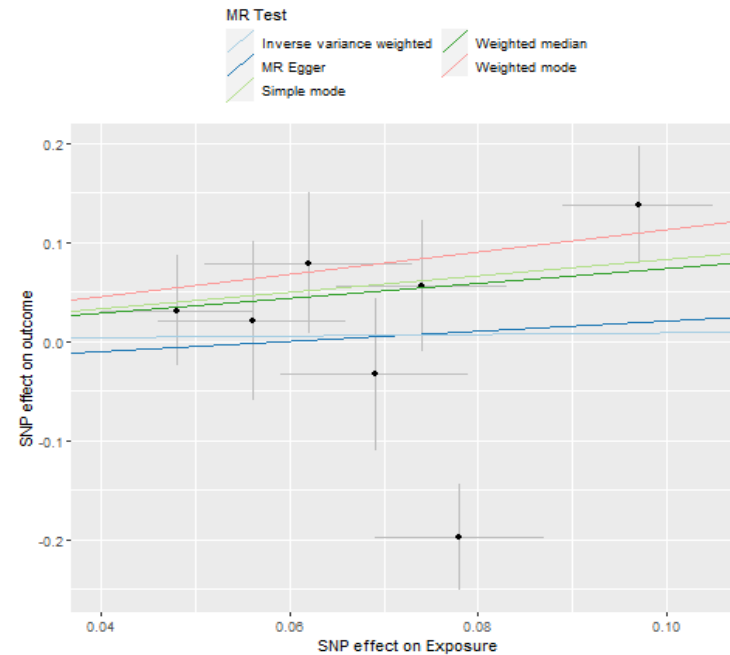
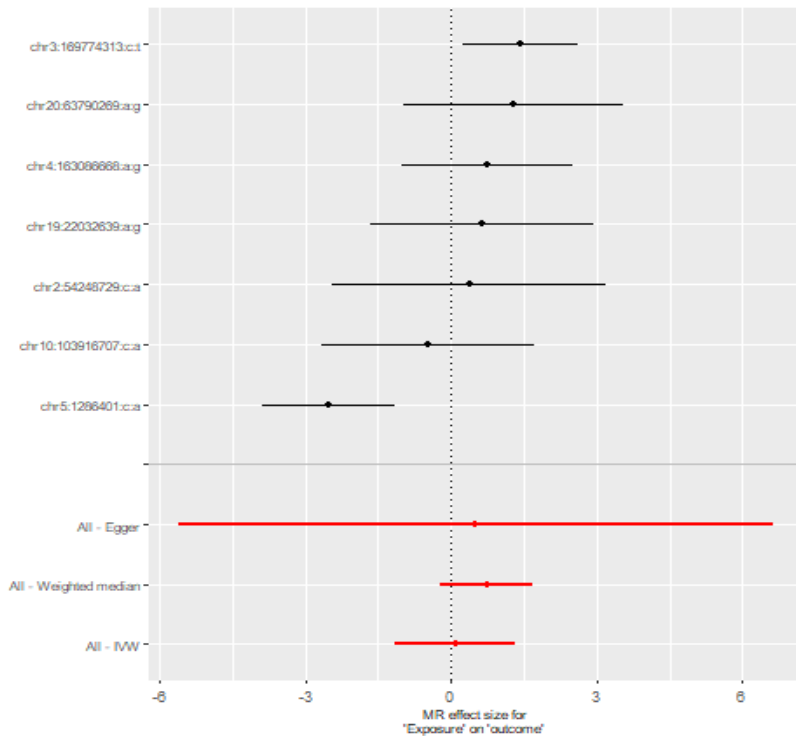


Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

a. Codd et al. 7 SNPs MR Analysis

SNP	Gene	rsID	beta (b)	standard error (se)	OR (95% CI)	pval
chr2:54248729:c:a	<i>TERT</i>	rs11125529	0.375	1.432	1.45 (0.09, 24.09)	0.793
chr3:169774313:c:t	<i>OBFC1</i>	rs10936599	1.423	0.602	4.15 (1.28, 13.50)	0.018
chr4:163086668:a:g	<i>ACYP2</i>	rs7675998	0.753	0.893	2.12 (0.37, 12.22)	0.399
chr5:1286401:c:a	<i>ZNF208</i>	rs2736100	-2.533	0.694	0.08 (0.02, 0.31)	0.0003
chr10:103916707:c:a	<i>NAF1</i>	rs9420907	-0.484	1.116	0.62 (0.07, 5.49)	0.664
chr19:22032639:a:g	<i>RTEL1</i>	rs8105767	0.648	1.171	1.91 (0.19, 18.98)	0.580
chr20:63790269:a:g	<i>TERC</i>	rs755017	1.274	1.156	3.58 (0.37, 34.46)	0.271
All - MR Egger			0.506	3.125	1.66 (0, 758.24)	0.878
All - Weighted median			0.732	0.499	2.08 (0.78, 5.53)	0.143
All - Inverse variance weighted (IVW)			0.093	0.634	1.10 (0.32, 3.80)	0.884



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Test for directional pleiotropy

	intercept	se	pval
MR Egger regression (test pleiotropy):	-0.031	0.226	0.897

*non-zero intercept suggests pleiotropy within this set of SNPs (although not significant)

Test heterogeneity using Cochran's Q-statistic

method	Q	Q_df	Q_pval
MR Egger	21.26	16	0.001
IVW	21.34	17	0.002

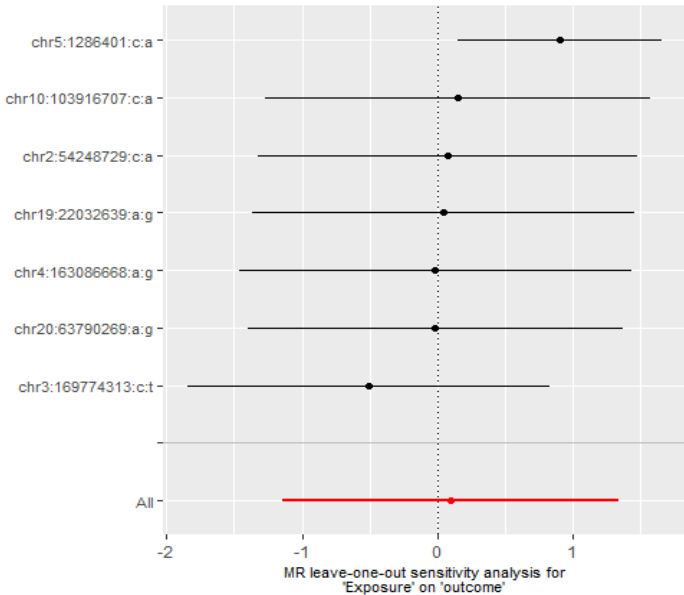
*significant p-value indicates heterogeneity and possible outliers (could also violate our MR assumption)

Leave one out analysis - removes one variant and re-estimate causal effect using inverse variance weighted (IVW) method

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr5:1286401:c:a	<i>ZNF208</i>	rs2736100	0.898	0.384	2.45 (1.16, 5.21)	0.019
chr10:103916707:c:a	<i>NAF1</i>	rs9420907	0.150	0.723	1.16 (0.28, 4.79)	0.835
chr2:54248729:c:a	<i>TERT</i>	rs11125529	0.076	0.713	1.08 (0.27, 4.36)	0.915
chr19:22032639:a:g	<i>RTEL1</i>	rs8105767	0.043	0.720	1.04 (0.25, 4.28)	0.952
chr4:163086668:a:g	<i>ACYP2</i>	rs7675998	-0.016	0.738	0.98 (0.23, 4.18)	0.983
chr20:63790269:a:g	<i>TERC</i>	rs755017	-0.016	0.706	0.98 (0.25, 3.93)	0.982
chr3:169774313:c:t	<i>OBFC1</i>	rs10936599	-0.509	0.684	0.60 (0.16, 2.30)	0.457
All - IVW			0.093	0.634	1.10 (0.32, 3.80)	0.884

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Leave one out analysis - Codd et al 7 SNPs



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Radial MR for Codd et al 7 SNPs

IVW model

	Estimate	Std.Error	Pr(> t)
Effect (Mod.2nd)	0.093	0.634	0.884
Iterative	0.093	0.634	0.884
Exact (FE)	0.099	0.336	0.769
Exact (RE)	0.094	0.728	0.901

Residual standard error: 1.886 on 6 degrees of freedom

F-statistic: 0.02 on 1 and 6 DF, p-value: 0.888

Q-Statistic for heterogeneity: 21.33078 on 6 DF , p-value: 0.001599665

Outliers detected

	rsID	Q-statistic	pval
chr5:1286401:c:a	rs2736100	14.333	0.0002

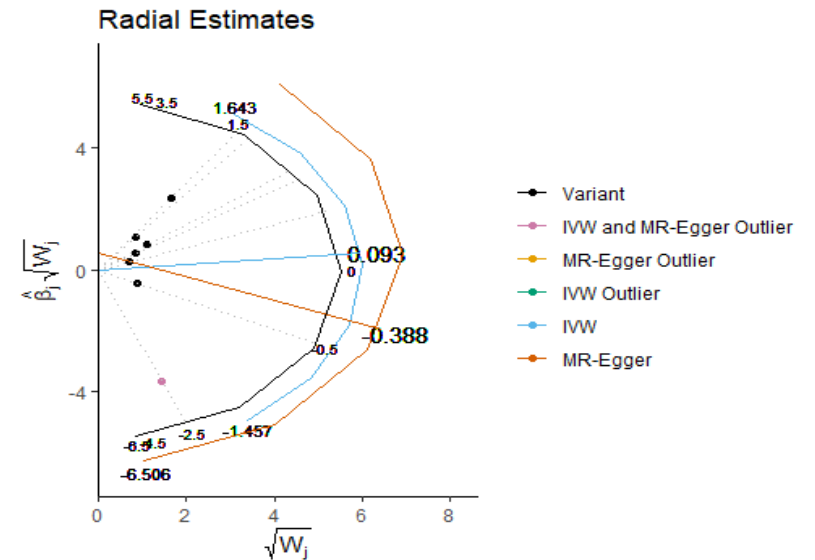
MR Egger model

	Estimate	Std. Error	Pr(> t)
(Intercept)	0.565	2.673	0.841
Wj	-0.388	2.380	0.877

Q-Statistic for heterogeneity: 21.06458 on 5 DF , p-value: 0.00178624

Outliers detected

SNP	rsID	Q-statistic	pval
chr5:1286401:c:a	rs2736100	13.334	0.0003



Pink dot indicates chr5:1286401:c:a (*TERT*/rs2736100) is the most influential variant in the IVW and MR Egger

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

****Remove TERT/rs2736100 SNP (chr5:1286401:c:a) from Codd et al predictor and re-test for heterogeneity using Cochran's Q-statistic***

***Codd et al 6 SNPs removing TERT**

Test for directional pleiotropy

	intercept	se	pval
MR Egger regression (test pleiotropy):	-0.090	0.110	0.458

Test heterogeneity using Cochran's Q-statistic

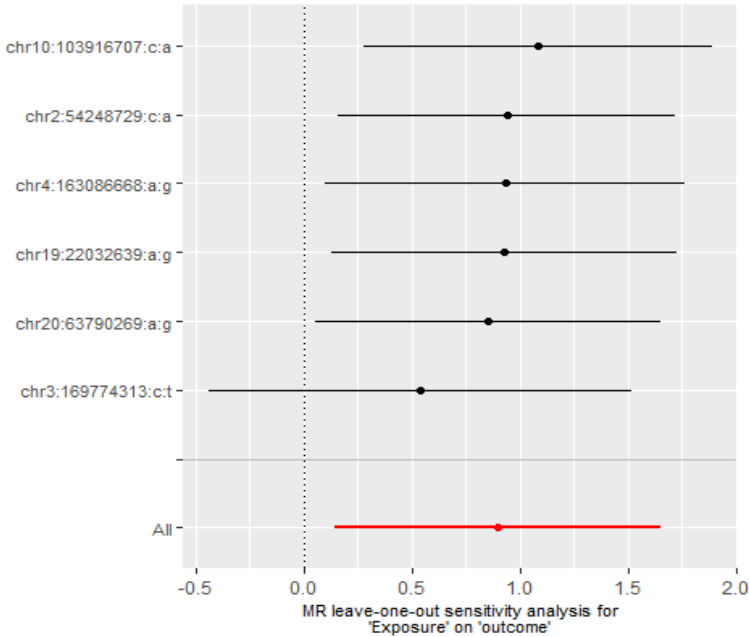
method	Q	Q_df	Q_pval
MR Egger	1.93	4	0.748
IVW	2.60	5	0.761

*non-significant p-value suggests no heterogeneity or outliers in the modified instrument

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Leave one out analysis - removes one variant and re-estimate causal effect using inverse variance weighted (IVW) method

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr10:103916707:c:a	<i>NAF1</i>	rs9420907	1.084	0.409	2.96 (1.33, 6.59)	0.008
chr2:54248729:c:a	<i>TERT</i>	rs11125529	0.938	0.399	2.56 (1.17, 5.58)	0.019
chr4:163086668:a:g	<i>ACYP2</i>	rs7675998	0.931	0.425	2.54 (1.10, 5.84)	0.029
chr19:22032639:a:g	<i>RTEL1</i>	rs8105767	0.928	0.407	2.53 (1.14, 5.61)	0.022
chr20:63790269:a:g	<i>TERC</i>	rs755017	0.851	0.407	2.34 (1.05, 5.20)	0.037
chr3:169774313:c:t	<i>OBFC1</i>	rs10936599	0.538	0.499	1.71 (0.64, 4.55)	0.281
All - IVW			0.898	0.384	2.45 (1.16, 5.21)	0.019



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Radial MR for Codd et al SNPs removing *TERT*

Radial IVW

	Estimate	Std.Error	Pr(> t)
Effect (Mod.2nd)	0.897	0.277	0.001
Iterative	0.897	0.277	0.001
Exact (FE)	0.903	0.387	0.020
Exact (RE)	0.903	0.298	0.029

Residual standard error: 0.717 on 5 degrees of freedom

F-statistic: 10.47 on 1 and 5 DF, p-value: 0.023

Q-Statistic for heterogeneity: 2.567886 on 5 DF , p-value: 0.7662384

No significant outliers

Radial MR-Egger

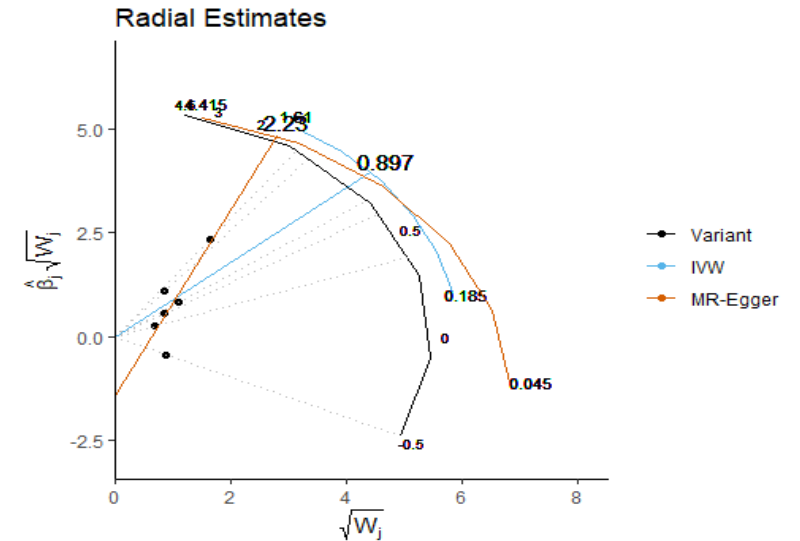
	Estimate	Std. Error	Pr(> t)
(Intercept)	-1.419	0.799	0.150
Wj	2.230	0.787	0.047

Residual standard error: 0.578 on 4 degrees of freedom

F-statistic: 8.03 on 1 and 4 DF, p-value: 0.0472

Q-Statistic for heterogeneity: 1.337641 on 4 DF , p-value: 0.9310112

No significant outliers



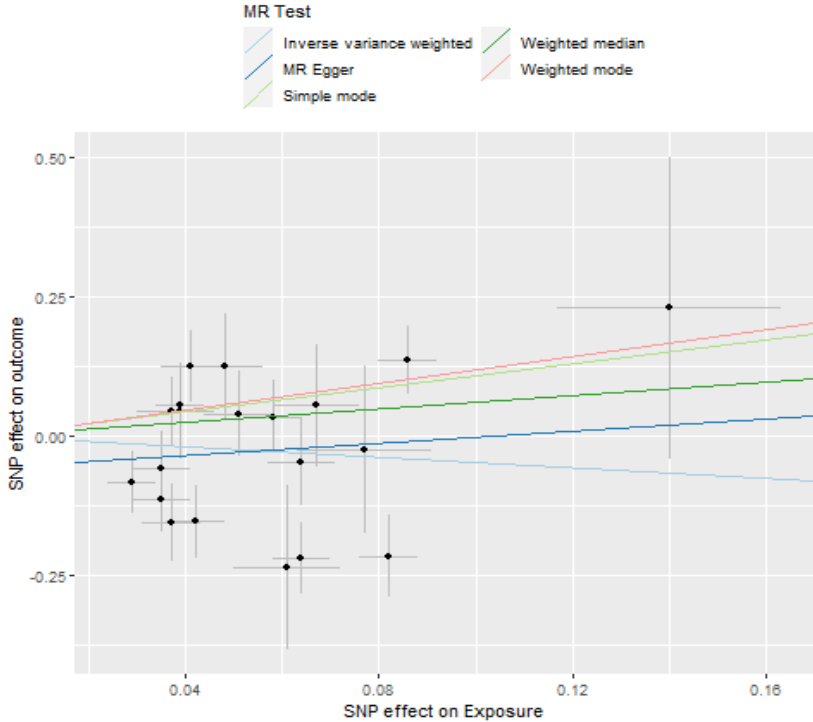
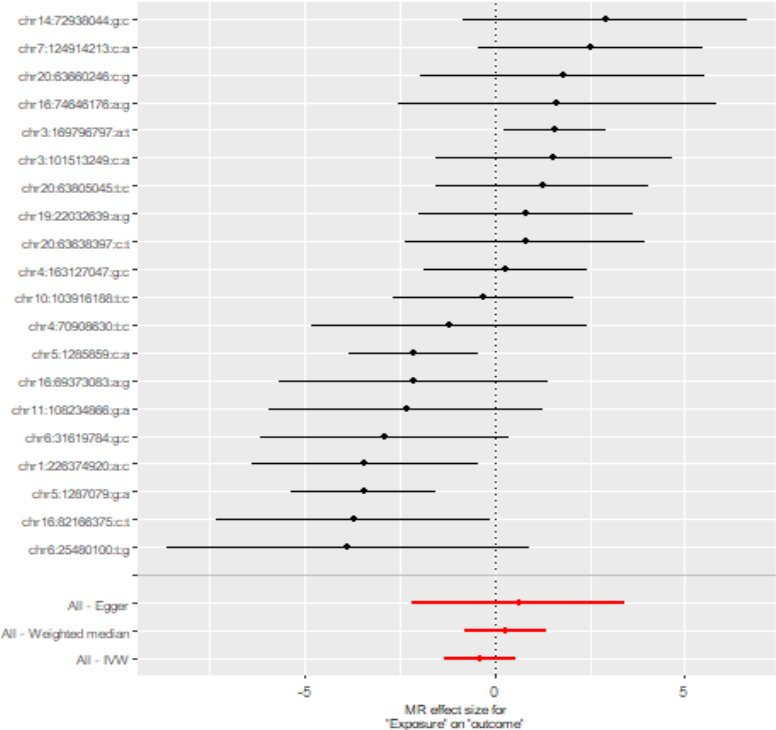
Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

b. Li et al. 20 SNPs MR Analysis

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr1:226374920:a:c	<i>PARP1</i>	rs3219104	-3.421	1.517	0.03 (0.00, 0.64)	0.024
chr3:101513249:c:a	<i>SENP7</i>	rs55749605	1.546	1.592	4.69 (0.21, 106.31)	0.331
chr3:169796797:a:t	<i>TERC</i>	rs10936600	1.585	0.685	4.88 (1.27, 18.68)	0.021
chr4:70908630:t:c	<i>MOB1B</i>	rs13137667	-1.209	1.855	0.30 (0.01, 11.32)	0.514
chr4:163127047:g:c	<i>NAF1</i>	rs4691895	0.272	1.103	1.31 (0.15, 11.40)	0.805
chr5:1285859:c:a	<i>TERT</i>	rs7705526	-2.128	0.874	0.12 (0.02, 0.66)	0.015
chr5:1287079:g:a	<i>TERT</i>	rs2853677	-3.45	0.978	0.03 (0.00, 0.22)	0.0004
chr6:25480100:t:g	<i>CARMIL1</i>	rs34991172	-3.879	2.433	0.02 (0.00, 2.43)	0.111
chr6:31619784:g:c	<i>PRRC2A</i>	rs2736176	-2.9	1.669	0.06 (0.00, 1.45)	0.082
chr7:124914213:c:a	<i>POT1</i>	rs59294613	2.527	1.517	12.52 (0.64, 244.77)	0.096
chr10:103916188:t:c	<i>STN1/OBFC1</i>	rs9419958	-0.292	1.206	0.75 (0.07, 7.94)	0.809
chr11:108234866:g:a	<i>ATM</i>	rs228595	-2.331	1.841	0.10 (0.00, 3.59)	0.206
chr14:72938044:g:c	<i>DCAF4</i>	rs2302588	2.906	1.906	18.28 (0.44, 766.44)	0.127
chr16:69373083:a:g	<i>TERF2</i>	rs3785074	-2.146	1.809	0.12 (0.00, 4.05)	0.235
chr16:74646176:a:g	<i>RFWD3</i>	rs62053580	1.644	2.138	5.18 (0.08, 341.89)	0.442
chr16:82166375:c:t	<i>MPHOSPH6</i>	rs7194734	-3.719	1.835	0.02 (0.00, 0.88)	0.043
chr19:22032639:a:g	<i>ZNF208</i>	rs8105767	0.838	1.441	2.31 (0.14, 38.95)	0.561
chr20:63638397:c:t	<i>RTEL1/STMN3</i>	rs75691080	0.809	1.612	2.25 (0.10, 52.91)	0.616
chr20:63660246:c:g	<i>RTEL1</i>	rs34978822	1.787	1.902	5.97 (0.14, 248.37)	0.347
chr20:63805045:t:c	<i>RTEL1/ZBTB46</i>	rs73624724	1.255	1.427	3.51 (0.21, 57.51)	0.379
All - MR Egger			0.631	1.425	1.88 (0.12, 30.69)	0.664
All - Weighted median			0.296	0.555	1.34 (0.45, 3.99)	0.594
All - Inverse variance weighted			-0.385	0.483	0.68 (0.26, 1.75)	0.425

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Li et al. 20 SNPs MR Analysis



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Test for directional pleiotropy - Li et al 20 SNPs

	intercept	se	pval
MR Egger regression (test pleiotropy):	-0.057	0.075	0.458

*The (small) MR Egger intercept close to zero/non-significant indicates no horizontal pleiotropy within set of SNPs

Test heterogeneity using Cochran's Q-statistic

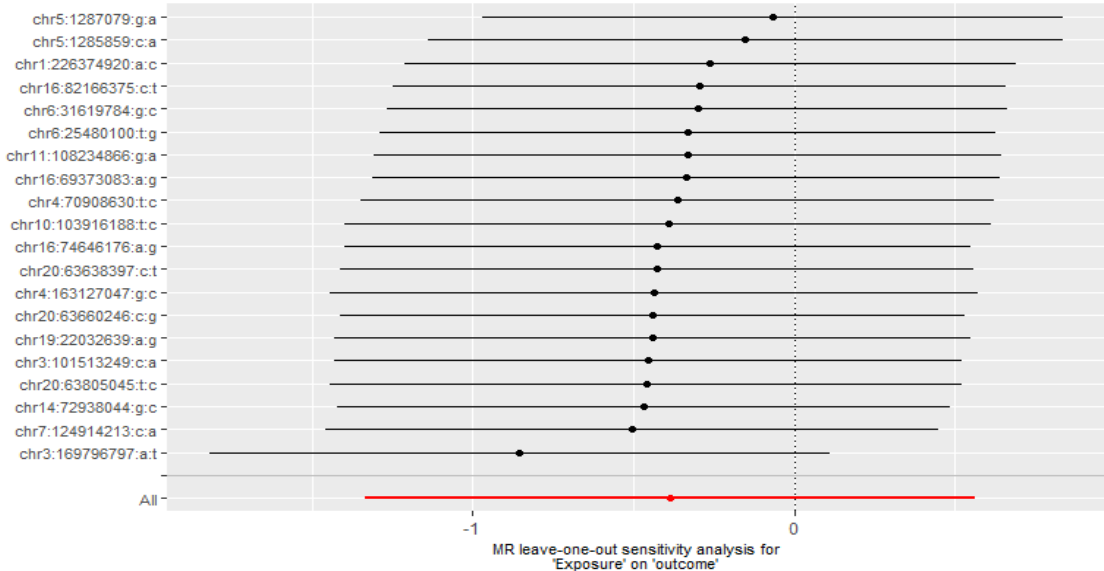
method	Q	Q_df	Q_pval
MR Egger	47.734	18	0.00016
IVW	49.261	19	0.00017

Leave one out analysis - removes one variant and re-estimate causal effect using inverse variance weighted (IVW) method

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr5:1287079:g:a	<i>TERT</i>	rs2853677	-0.067	0.461	0.94 (0.38, 2.31)	0.884
chr5:1285859:c:a	<i>TERT</i>	rs7705526	-0.153	0.504	0.86 (0.32, 2.30)	0.762
chr1:226374920:a:c	<i>PARP1</i>	rs3219104	-0.262	0.485	0.77 (0.30, 1.99)	0.589
chr16:82166375:c:t	<i>MPHOSPH6</i>	rs7194734	-0.294	0.486	0.75 (0.29, 1.93)	0.545
chr6:31619784:g:c	<i>PRRC2A</i>	rs2736176	-0.301	0.493	0.74 (0.28, 1.94)	0.541
chr6:25480100:t:g	<i>CARMIL1</i>	rs34991172	-0.331	0.490	0.72 (0.27, 1.87)	0.498
chr11:108234866:g:a	<i>ATM</i>	rs228595	-0.332	0.497	0.72 (0.27, 1.90)	0.504
chr16:69373083:a:g	<i>TERF2</i>	rs3785074	-0.336	0.498	0.71 (0.27, 1.90)	0.501
chr4:70908630:t:c	<i>MOB1B</i>	rs13137667	-0.363	0.502	0.70 (0.26, 1.86)	0.469
chr10:103916188:t:c	<i>STN1/OBFC1</i>	rs9419958	-0.392	0.513	0.68 (0.25, 1.85)	0.445
chr16:74646176:a:g	<i>RFWD3</i>	rs62053580	-0.426	0.497	0.65 (0.25, 1.73)	0.391
chr20:63638397:c:t	<i>RTEL1/STMN3</i>	rs75691080	-0.428	0.502	0.65 (0.24, 1.74)	0.394
chr4:163127047:g:c	<i>NAF1</i>	rs4691895	-0.438	0.514	0.65 (0.24, 1.77)	0.394
chr20:63660246:c:g	<i>RTEL1</i>	rs34978822	-0.441	0.496	0.64 (0.24, 1.70)	0.374
chr19:22032639:a:g	<i>ZNF208</i>	rs8105767	-0.441	0.504	0.64 (0.24, 1.73)	0.381
chr3:101513249:c:a	<i>SENP7</i>	rs55749605	-0.457	0.498	0.63 (0.24, 1.68)	0.359
chr20:63805045:t:c	<i>RTEL1/ZBTB46</i>	rs73624724	-0.461	0.501	0.63 (0.24, 1.68)	0.357
chr14:72938044:g:c	<i>DCAF4</i>	rs2302588	-0.469	0.487	0.63 (0.24, 1.62)	0.335
chr7:124914213:c:a	<i>POT1</i>	rs59294613	-0.504	0.486	0.60 (0.23, 1.57)	0.300
chr3:169796797:a:t	<i>TERC</i>	rs10936600	-0.854	0.492	0.43 (0.16, 1.12)	0.082
All - IVW			-0.385	0.483	0.68 (0.26, 1.75)	0.425

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Leave one out analysis - Li et al 20 SNPs



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Radial MR for Li et al 20 SNPs

IVW model

	Estimate	Std.Error	Pr(> t)
Effect (Mod.2nd)	-0.386	0.483	0.425
Iterative	-0.386	0.483	0.425
Exact (FE)	-0.402	0.300	0.181
Exact (RE)	-0.392	0.571	0.501

Residual standard error: 1.609 on 19 degrees of freedom

F-statistic: 0.64 on 1 and 19 DF, p-value: 0.435

Q-Statistic for heterogeneity: 49.19581 on 19 DF , p-value: 0.000171947

Outliers detected

SNP	rsID	Q_statistic	p.value
chr5:1287079:g:a	rs2853677	9.802	0.002

Radial MR-Egger

	Estimate	Std. Error	Pr(> t)
(Intercept)	-0.494	1.093	0.656
Wj	0.239	1.467	0.872

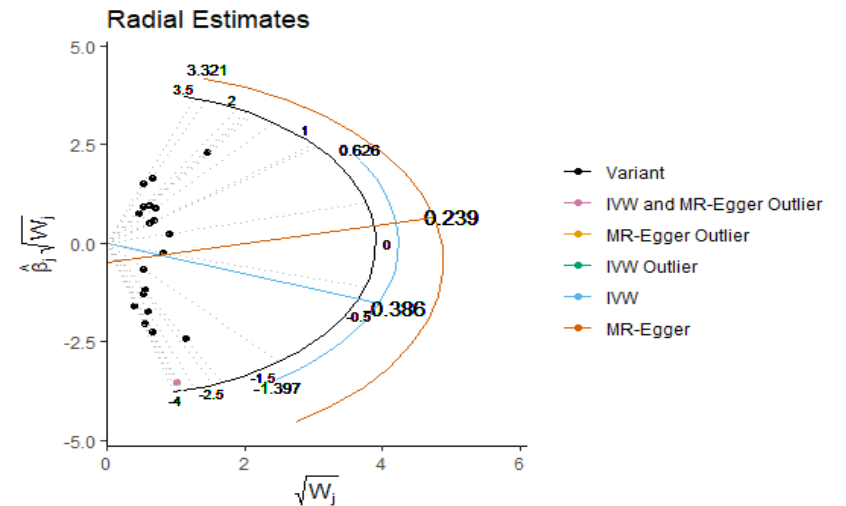
Residual standard error: 1.645 on 18 degrees of freedom

F-statistic: 0.03 on 1 and 18 DF, p-value: 0.872

Q-Statistic for heterogeneity: 48.68264 on 18 DF , p-value: 0.0002042631

Outliers detected

SNP	rsID	Q_statistic	p.value
chr5:1287079:g:a	rs2853677	10.736	0.001



Pink dot indicates chr5:1287079:g:a (*TERT*/rs2853677) is the most influential variant in the IVW and MR Egger

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

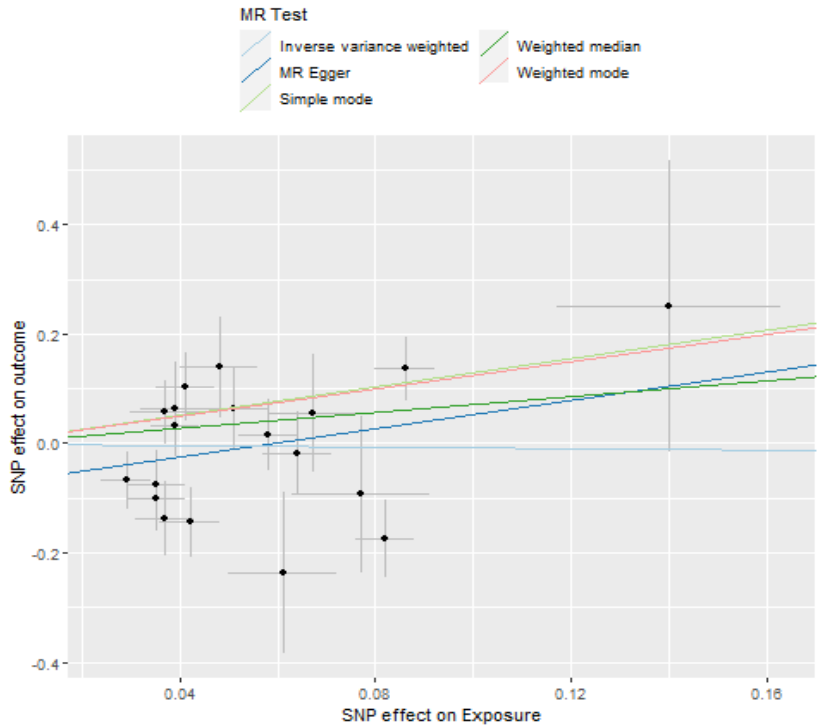
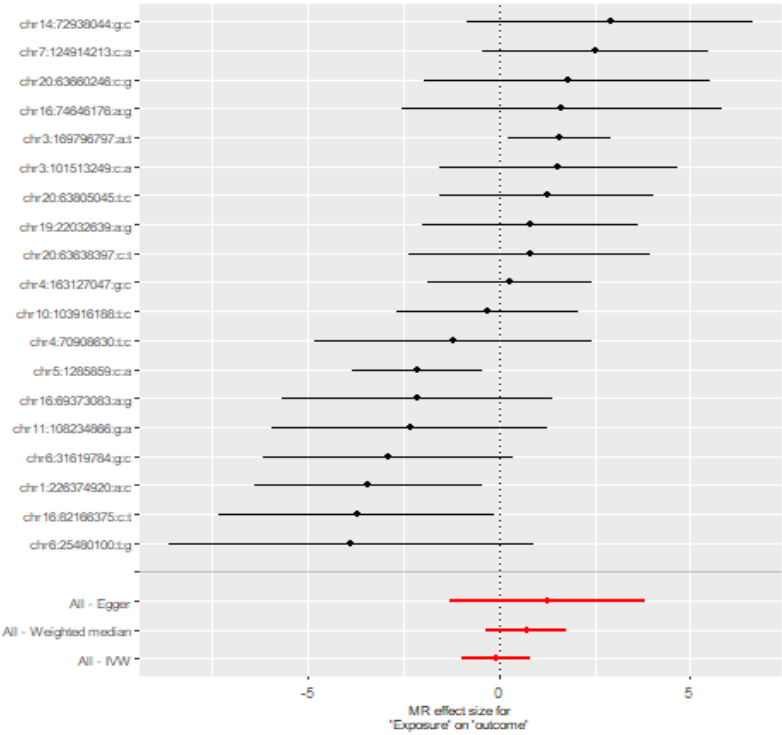
**Remove TERT/rs2853677 SNP (chr5: 1287079:g:a) due to outlier indication - 19 SNPs total*

MR Analysis - Li et al 19 SNPs (removing TERT/rs2853677 SNP [chr5: 1287079:g:a])

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr1:226374920:a:c	<i>PARP1</i>	rs3219104	-3.42	1.52	0.03 (0, 0.64)	0.024
chr10:103916188:t:c	<i>STN1/OBFC1</i>	rs9419958	-0.29	1.21	0.75 (0.07, 7.94)	0.809
chr11:108234866:g:a	<i>ATM</i>	rs228595	-2.33	1.84	0.10 (0, 3.59)	0.206
chr14:72938044:g:c	<i>DCAF4</i>	rs2302588	2.91	1.91	18.29 (0.44, 767.01)	0.127
chr16:69373083:a:g	<i>TERF2</i>	rs3785074	-2.15	1.81	0.12 (0, 4.05)	0.235
chr16:74646176:a:g	<i>RFWD3</i>	rs62053580	1.64	2.14	5.17 (0.08, 342.06)	0.442
chr16:82166375:c:t	<i>MPHOSPH6</i>	rs7194734	-3.72	1.84	0.02 (0, 0.89)	0.043
chr19:22032639:a:g	<i>ZNF208</i>	rs8105767	0.84	1.44	2.31 (0.14, 38.97)	0.561
chr20:63638397:c:t	<i>RTEL1/STMN3</i>	rs75691080	0.81	1.61	2.25 (0.1, 52.90)	0.616
chr20:63660246:c:g	<i>RTEL1</i>	rs34978822	1.79	1.90	5.97 (0.14, 248.48)	0.347
chr20:63805045:t:c	<i>RTEL1/ZBTB46</i>	rs73624724	1.25	1.43	3.51 (0.21, 57.55)	0.379
chr3:101513249:c:a	<i>SENP7</i>	rs55749605	1.55	1.59	4.69 (0.21, 106.28)	0.331
chr3:169796797:a:t	<i>TERC</i>	rs10936600	1.58	0.68	4.88 (1.27, 18.68)	0.021
chr4:163127047:g:c	<i>NAF1</i>	rs4691895	0.27	1.10	1.31 (0.15, 11.42)	0.805
chr4:70908630:t:c	<i>MOB1B</i>	rs13137667	-1.21	1.85	0.30 (0.01, 11.31)	0.514
chr5:1285859:c:a	<i>TERT</i>	rs7705526	-2.13	0.87	0.12 (0.02, 0.66)	0.015
chr6:25480100:t:g	<i>CARMIL1</i>	rs34991172	-3.88	2.43	0.02 (0, 2.43)	0.111
chr6:31619784:g:c	<i>PRRC2A</i>	rs2736176	-2.90	1.67	0.06 (0, 1.45)	0.082
chr7:124914213:c:a	<i>POT1</i>	rs59294613	2.53	1.52	12.51 (0.64, 244.76)	0.096
All - Inverse variance weighted			-0.07	0.46	0.94 (0.38, 2.31)	0.884
All - MR Egger			1.28	1.30	3.61 (0.28, 46.1)	0.338
All - Weighted median			0.72	0.53	2.05 (0.73, 5.76)	0.176

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

MR Analysis - Li et al 19 SNPs (removing TERT/rs2853677 SNP [chr5: 1287079:g:a])



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Test for directional pleiotropy - Li et al. 19 SNPs (removing TERT/rs2853677 SNP [chr5: 1287079:g:a])

	intercept	se	pval
MR Egger regression (test pleiotropy):	-0.075	0.067	0.283

Test heterogeneity using Cochran's Q-statistic

method	Q	Q_df	Q_pval
MR Egger	35.831	17	0.0048
IVW	38.425	18	0.0034

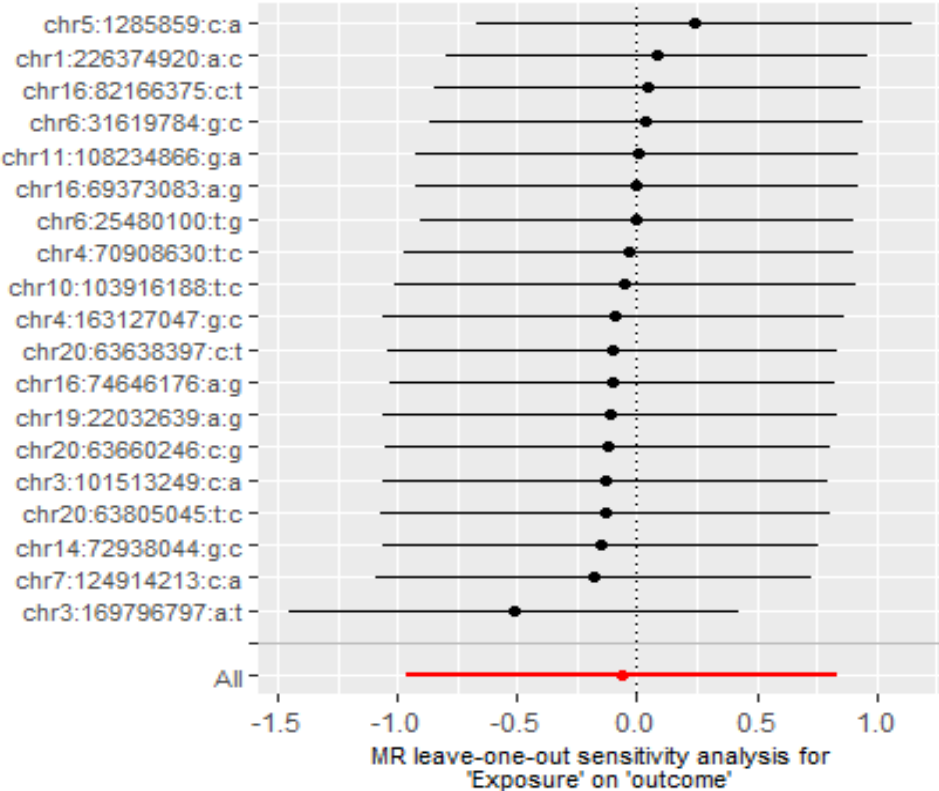
*Significance suggests heterogeneity across SNPs

Leave one out analysis - removes one variant and re-estimate causal effect using inverse variance weighted (IVW) method

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr5:1285859:c:a	<i>TERT</i>	rs7705526	0.241	0.464	1.27 (0.51, 3.16)	0.603
chr1:226374920:a:c	<i>PARP1</i>	rs3219104	0.085	0.451	1.09 (0.45, 2.64)	0.851
chr16:82166375:c:t	<i>MPHOSPH6</i>	rs7194734	0.044	0.455	1.05 (0.43, 2.55)	0.923
chr6:31619784:g:c	<i>PRRC2A</i>	rs2736176	0.038	0.464	1.04 (0.42, 2.58)	0.935
chr6:25480100:t:g	<i>CARMIL1</i>	rs34991172	-0.002	0.462	1.00 (0.40, 2.47)	0.997
chr11:108234866:g:a	<i>ATM</i>	rs228595	0.001	0.471	1.00 (0.40, 2.52)	0.998
chr16:69373083:a:g	<i>TERF2</i>	rs3785074	-0.002	0.473	1.00 (0.40, 2.52)	0.997
chr4:70908630:t:c	<i>MOB1B</i>	rs13137667	-0.033	0.479	0.97 (0.38, 2.47)	0.945
chr10:103916188:t:c	<i>STN1/OBFC1</i>	rs9419958	-0.050	0.491	0.95 (0.36, 2.49)	0.918
chr16:74646176:a:g	<i>RFWD3</i>	rs62053580	-0.105	0.475	0.90 (0.35, 2.29)	0.825
chr20:63638397:c:t	<i>RTEL1/STMN3</i>	rs75691080	-0.102	0.481	0.90 (0.35, 2.32)	0.833
chr4:163127047:g:c	<i>NAF1</i>	rs4691895	-0.097	0.494	0.91 (0.34, 2.39)	0.844
chr20:63660246:c:g	<i>RTEL1</i>	rs34978822	-0.119	0.475	0.89 (0.35, 2.25)	0.801
chr19:22032639:a:g	<i>ZNF208</i>	rs8105767	-0.112	0.483	0.89 (0.35, 2.30)	0.816
chr3:101513249:c:a	<i>SENP7</i>	rs55749605	-0.133	0.477	0.88 (0.34, 2.23)	0.781
chr20:63805045:t:c	<i>RTEL1/ZBTB46</i>	rs73624724	-0.135	0.480	0.87 (0.34, 2.24)	0.779
chr14:72938044:g:c	<i>DCAF4</i>	rs2302588	-0.151	0.465	0.86 (0.35, 2.14)	0.746
chr7:124914213:c:a	<i>POT1</i>	rs59294613	-0.184	0.465	0.83 (0.33, 2.07)	0.692
chr3:169796797:a:t	<i>TERC</i>	rs10936600	-0.511	0.480	0.60 (0.23, 1.54)	0.287
All - IVW			-0.067	0.461	0.94 (0.38, 2.31)	0.884

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Leave one out analysis - Li et al 19 SNPs (removing TERT/rs2853677 SNP [chr5: 1287079:g:a])



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Radial MR for Li et al 19 SNPs (removing *TERT*/rs2853677 SNP [chr5: 1287079:g:a])

IVW method

	Estimate	Std.Error	Pr(> t)
Effect (Mod.2nd)	-0.067	0.461	0.884
Iterative	-0.067	0.461	0.884
Exact (FE)	-0.069	0.315	0.826
Exact (RE)	-0.068	0.531	0.900

Residual standard error: 1.461 on 18 degrees of freedom

F-statistic: 0.02 on 1 and 18 DF, p-value: 0.886

Q-Statistic for heterogeneity: 38.42319 on 18 DF , p-value: 0.003403432

No significant outliers

Radial MR-Egger

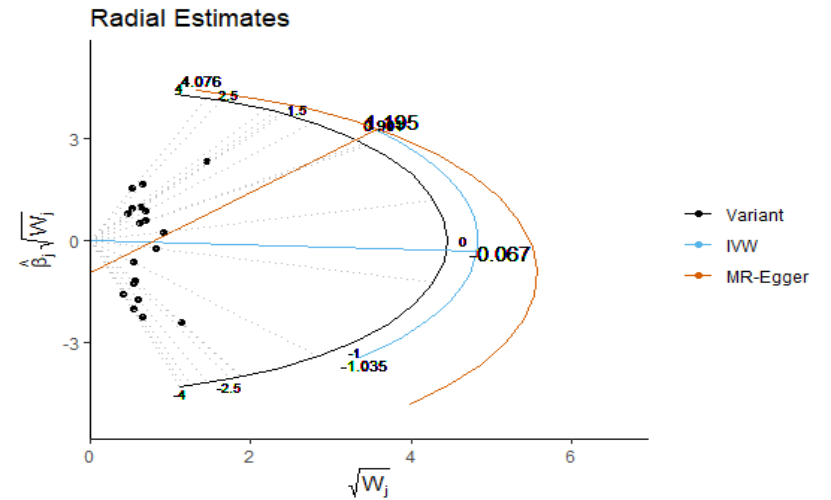
	Estimate	Std. Error	Pr(> t)
(Intercept)	-0.970	0.987	0.339
Wj	1.195	1.366	0.394

Residual standard error: 1.453 on 17 degrees of freedom

F-statistic: 0.77 on 1 and 17 DF, p-value: 0.394

Q-Statistic for heterogeneity: 35.90944 on 17 DF , p-value: 0.007246888

No significant outliers



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

**Remove TERT/rs7705526 SNP (chr5:1285859:c:a) due to evidence of heterogeneity in both Radial IVW and Egger models and could suggest possible outlier - 18 SNPs total*

Test for directional pleiotropy - Li et al. 18 SNPs (removing TERT/rs7705526 SNP (chr5:1285859:c:a))

	intercept	se	pval
MR Egger regression (test pleiotropy):	-0.128	0.062	0.054

Test heterogeneity using Cochran's Q-statistic

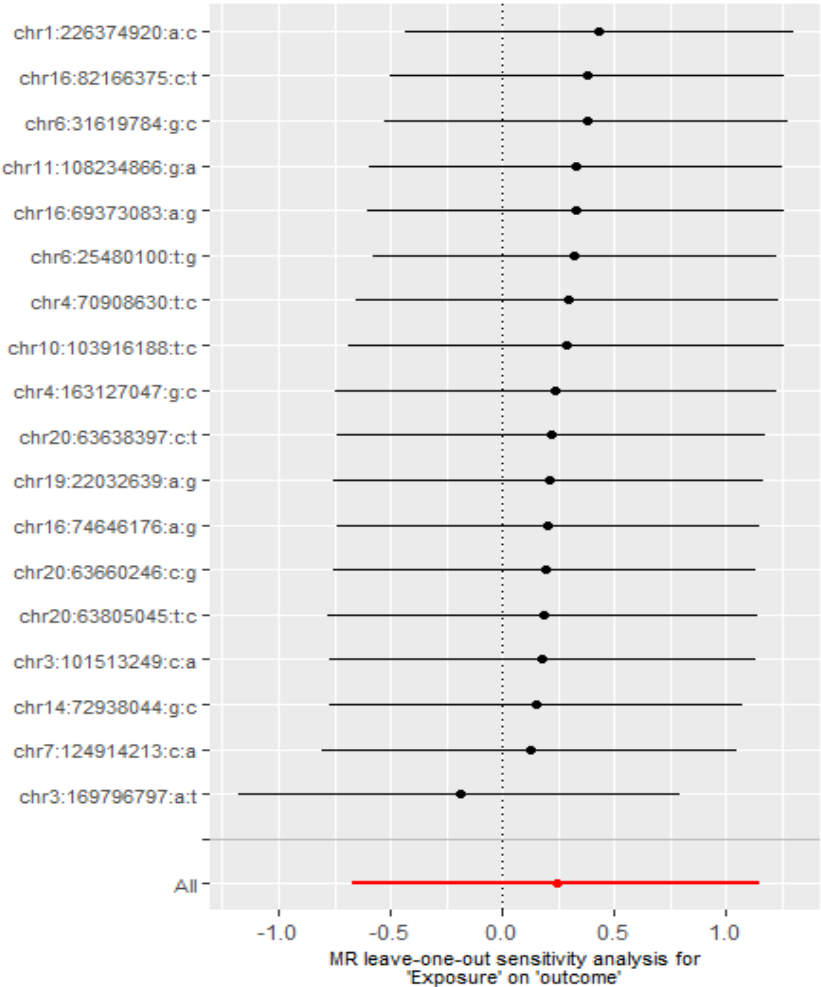
method	Q	Q_df	Q_pval
MR Egger	25.232	16	0.066
IVW	32.038	17	0.015

Leave one out analysis - removes one variant and re-estimate causal effect using inverse variance weighted (IVW) method

SNP	Gene	rsID	b	se	OR (95% CI)	pval
chr1:226374920:a:c	<i>PARP1</i>	rs3219104	0.433	0.441	1.54 (0.65, 3.66)	0.327
chr16:82166375:c:t	<i>MPHOSPH6</i>	rs7194734	0.380	0.449	1.46 (0.61, 3.53)	0.397
chr6:31619784:g:c	<i>PRRC2A</i>	rs2736176	0.376	0.460	1.46 (0.59, 3.59)	0.414
chr6:25480100:t:g	<i>CARMIL1</i>	rs34991172	0.322	0.461	1.38 (0.56, 3.41)	0.484
chr11:108234866:g:a	<i>ATM</i>	rs228595	0.331	0.471	1.39 (0.55, 3.50)	0.482
chr16:69373083:a:g	<i>TERF2</i>	rs3785074	0.328	0.473	1.39 (0.55, 3.51)	0.489
chr4:70908630:t:c	<i>MOB1B</i>	rs13137667	0.291	0.482	1.34 (0.52, 3.44)	0.546
chr10:103916188:t:c	<i>STN1/OBFC1</i>	rs9419958	0.287	0.497	1.33 (0.50, 3.53)	0.564
chr16:74646176:a:g	<i>RFWD3</i>	rs62053580	0.205	0.481	1.23 (0.48, 3.15)	0.67
chr20:63638397:c:t	<i>RTEL1/STMN3</i>	rs75691080	0.215	0.488	1.24 (0.48, 3.23)	0.66
chr4:163127047:g:c	<i>NAF1</i>	rs4691895	0.238	0.503	1.27 (0.47, 3.40)	0.636
chr20:63660246:c:g	<i>RTEL1</i>	rs34978822	0.191	0.481	1.21 (0.47, 3.11)	0.692
chr19:22032639:a:g	<i>ZNF208</i>	rs8105767	0.206	0.491	1.23 (0.47, 3.22)	0.674
chr3:101513249:c:a	<i>SENP7</i>	rs55749605	0.180	0.484	1.20 (0.46, 3.09)	0.711
chr20:63805045:t:c	<i>RTEL1/ZBTB46</i>	rs73624724	0.181	0.488	1.20 (0.46, 3.12)	0.711
chr14:72938044:g:c	<i>DCAF4</i>	rs2302588	0.155	0.471	1.17 (0.46, 2.94)	0.742
chr7:124914213:c:a	<i>POT1</i>	rs59294613	0.122	0.472	1.13 (0.45, 2.85)	0.796
chr3:169796797:a:t	<i>TERC</i>	rs10936600	-0.192	0.505	0.83 (0.31, 2.22)	0.704

Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Leave one out analysis - Li et al 18 SNPs (removing TERT/rs7705526 SNP [chr5:1285859:c:a])



Supplemental Table S2. Sensitivity analysis for the MR analyses of genetically predicted telomere length on pediatric germ cell tumor

Radial MR for Li et al 18 SNPs (removing TERT/rs7705526 SNP [chr5:1285859:c:a])

IVW method

	Estimate	Std.Error	Pr(> t)
Effect (Mod.2nd)	0.241	0.464	0.603
Iterative	0.241	0.464	0.603
Exact (FE)	0.249	0.338	0.461
Exact (RE)	0.245	0.512	0.638

Residual standard error: 1.373 on 17 degrees of freedom

F-statistic: 0.27 on 1 and 17 DF, p-value: 0.61

Q-Statistic for heterogeneity: 32.03764 on 17 DF , p-value: 0.01488674

No significant outliers

Radial MR-Egger

	Estimate	Std. Error	Pr(> t)
(Intercept)	-1.752	0.900	0.069
Wj	2.691	1.333	0.061

Residual standard error: 1.453 on 17 degrees of freedom

F-statistic: 4.08 on 1 and 16 DF, p-value: 0.0606

Q-Statistic for heterogeneity: 24.36702 on 16 DF , p-value: 0.1098009

No significant outliers

