

Genetic variants related to longer telomere length are associated with increased risk of renal cell carcinoma

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Supplementary Tables

Supplementary Table 1. Minimac R² (IARC) or IMPUTE2 info scores (MDA, NCI1, NCI2, UK) for imputed variants.

| | rs11125529 | rs6772228 | rs10936599 | rs7675998 | rs2736100 | rs9420907 | rs3027234 | rs8105767 | rs755017 |
|------|------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|
| IARC | 1.00 | 0.70 | Genotyped | 0.99 | Genotyped | Genotyped | 0.99 | 0.95 | 1.00 |
| MDA | 1.00 | 0.84 | Genotyped | 1.00 | Genotyped | Genotyped | 1.00 | 1.00 | 1.00 |
| NCI1 | 1.00 | 0.83 | Genotyped | 1.00 | Genotyped | Genotyped | 1.00 | 1.00 | 1.00 |
| NCI2 | 1.00 | 0.81 | Genotyped | 1.00 | Genotyped | 1.00 | 1.00 | 1.00 | Genotyped |
| UK | 1.00 | 0.85 | Genotyped | 1.00 | Genotyped | 0.99 | 1.00 | 1.00 | Genotyped |

Variants that were directly genotyped are denoted as "Genotyped". Differences in which variants were imputed and genotyped across studies reflects differences in array coverage for commercially available Illumina genotyping platforms used by the studies.

| Variant | Alleles | | Clear Cell RCC | | Chromophobe RCC | | | Papillary RCC | | | RCC Overall | | | |
|------------|---------|------|----------------|-------|-----------------|-------|-------|---------------|-------|-------|-------------|-------|-------|-------|
| Variant | Short | Long | OR | LCL | UCL | OR | LCL | UCL | OR | LCL | UCL | OR | LCL | UCL |
| rs10936599 | Т | С | 1.126 | 1.063 | 1.192 | 1.055 | 0.830 | 1.341 | 1.015 | 0.878 | 1.172 | 1.105 | 1.059 | 1.154 |
| rs2736100 | А | С | 1.091 | 1.040 | 1.144 | 1.040 | 0.848 | 1.274 | 1.161 | 1.025 | 1.315 | 1.070 | 1.032 | 1.110 |
| rs7675998 | А | G | 0.976 | 0.921 | 1.033 | 1.163 | 0.908 | 1.489 | 0.976 | 0.843 | 1.131 | 1.013 | 0.969 | 1.059 |
| rs9420907 | А | С | 1.148 | 1.074 | 1.227 | 1.154 | 0.879 | 1.517 | 1.242 | 1.053 | 1.465 | 1.124 | 1.067 | 1.183 |
| rs8105767 | А | G | 1.002 | 0.951 | 1.057 | 0.982 | 0.785 | 1.228 | 1.013 | 0.884 | 1.160 | 1.049 | 1.007 | 1.092 |
| rs755017 | А | G | 1.030 | 0.956 | 1.109 | 1.290 | 0.967 | 1.720 | 1.080 | 0.898 | 1.298 | 1.012 | 0.956 | 1.071 |
| rs11125529 | С | А | 1.041 | 0.971 | 1.116 | 1.071 | 0.799 | 1.436 | 0.953 | 0.794 | 1.145 | 1.014 | 0.962 | 1.070 |
| rs6772228 | А | Т | 1.062 | 0.938 | 1.202 | 0.801 | 0.485 | 1.324 | 1.159 | 0.836 | 1.608 | 1.127 | 1.026 | 1.239 |
| rs3027234 | Т | С | 0.975 | 0.920 | 1.034 | 1.000 | 0.780 | 1.281 | 0.899 | 0.776 | 1.042 | 1.016 | 0.972 | 1.063 |

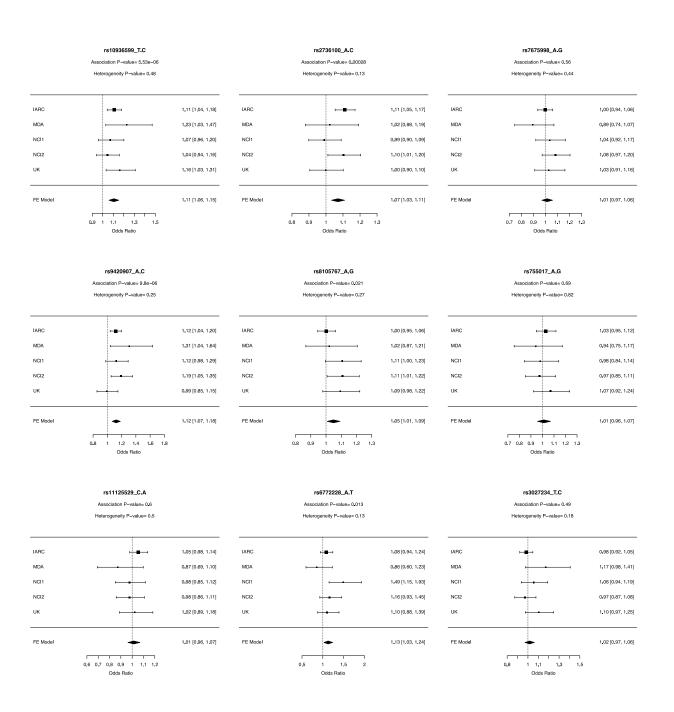
Supplementary Table 2. Telomere length associated variant associations with each major RCC subtype and RCC overall.

OR=odds ratio; LCL=lower 95% confidence interval; UCL=upper 95% confidence interval

Supplementary Figures

Supplementary Figure 1. Forest plots for associations of each telomere length associated

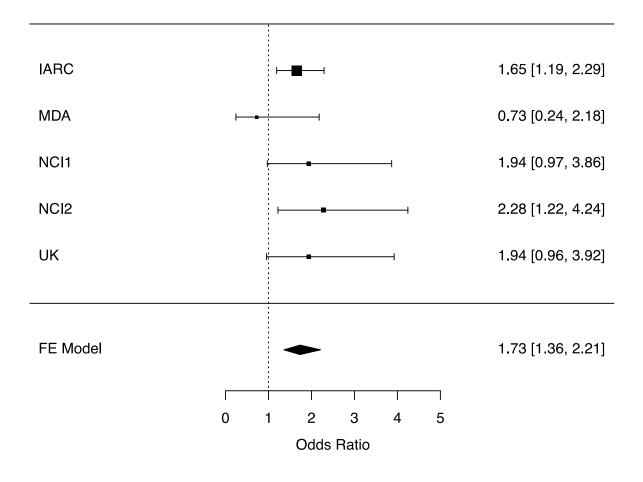
variant with RCC risk.



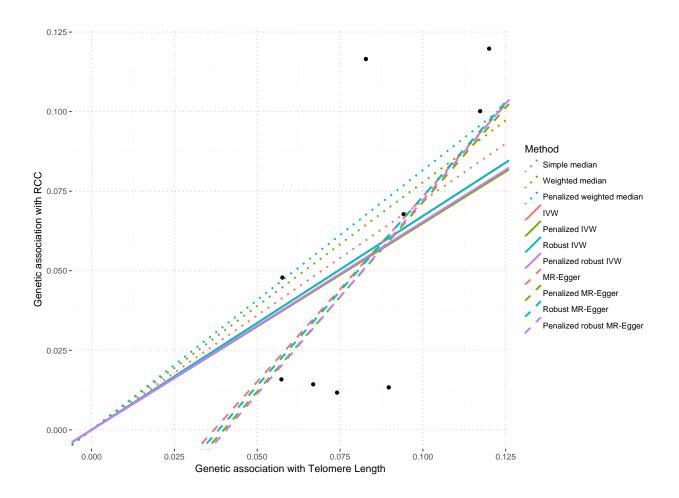
Supplementary Figure 2. Forest plot for RCC association of the telomere length associated GRS that removes rs10936599—TERC and rs9420907—OBFC1 GWAS variants.

Telomere Length GRS without TERC and OBFC1

Association P-value= 1.01e-05



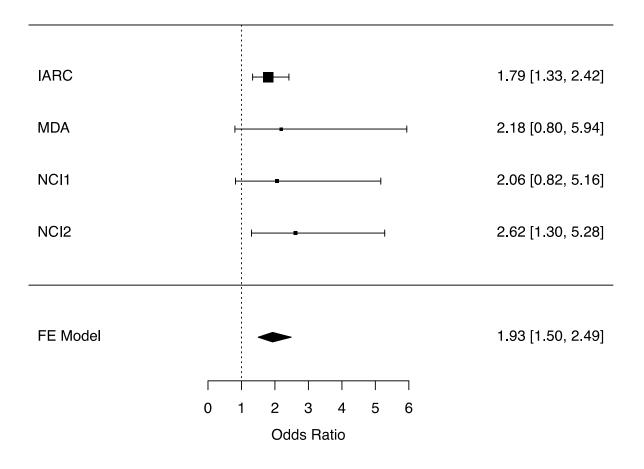
Supplementary Figure 3. Comparison of Egger regression effect estimates (dashed lines) to standard (dotted lines) and IVW based estimation approaches. Egger regression estimated an intercept of -0.043 (95% CI=-0.133-0.047, P-value=0.352) and an estimated odds ratio of 3.20 (95% CI=1.10-9.27, P-value=0.03).



Supplementary Figure 4. Forest plot for associations of the telomere length associated GRS with clear cell RCC risk.

Clear Cell Telomere Length GRS

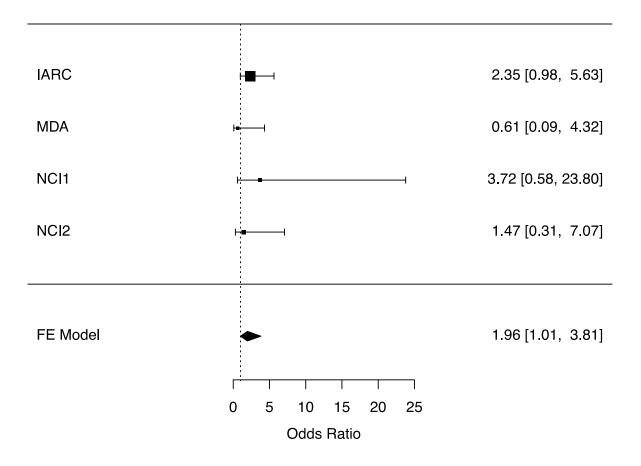
Association P-value= 3.86e-07



Supplementary Figure 5. Forest plot for associations of the telomere length associated GRS with papillary RCC risk.

Papillary Telomere Length GRS

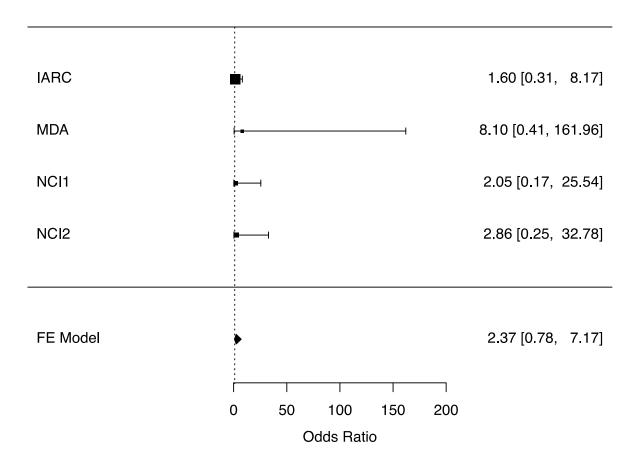
Association P-value= 0.046



Supplementary Figure 6. Forest plot for associations of the telomere length associated GRS with chromophobe RCC risk.

Chromophobe Telomere Length GRS

Association P-value= 0.13



Supplementary Figure 7. Forest plot for associations of telomere length associated GRS with RCC by strata of sex.

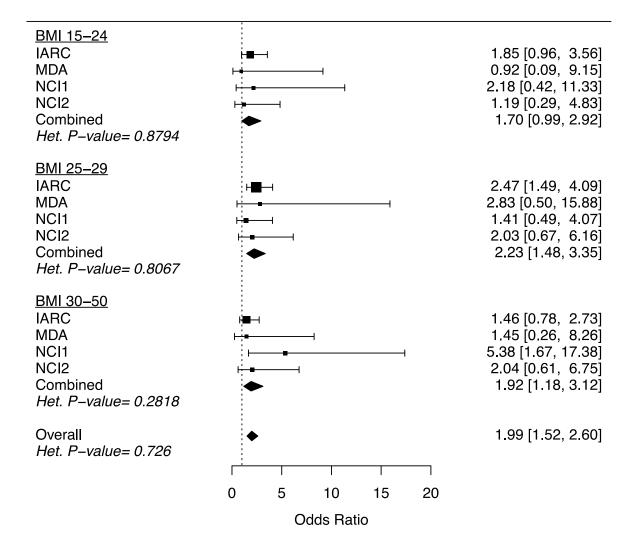
<u>Male</u> 1.96 [1.40, 2.77] IARC H MDA 1.78 [0.62, 5.11] NCI1 2.01 [0.94, 4.30] NCI2 3.23 [1.66, 6.29] Combined 2.13 [1.62, 2.79] Het. P-value= 0.6059 <u>Female</u> IARC 2.03 [1.32, 3.12] MDA 1.83 [0.33, 10.08] 2.45 [0.79, 7.65] NCI1 NCI2 1.54 [0.68, 3.52] 1.96 [1.38, 2.79] Combined *Het. P*-*value*= 0.9184 Overall 2.06 [1.66, 2.56] *Het. P–value=* 0.7165 ٦ Г Т Т T 0 2 4 6 8 10 12 Odds Ratio

GRS by Sex

Supplementary Figure 8. Forest plot for associations of telomere length associated GRS with

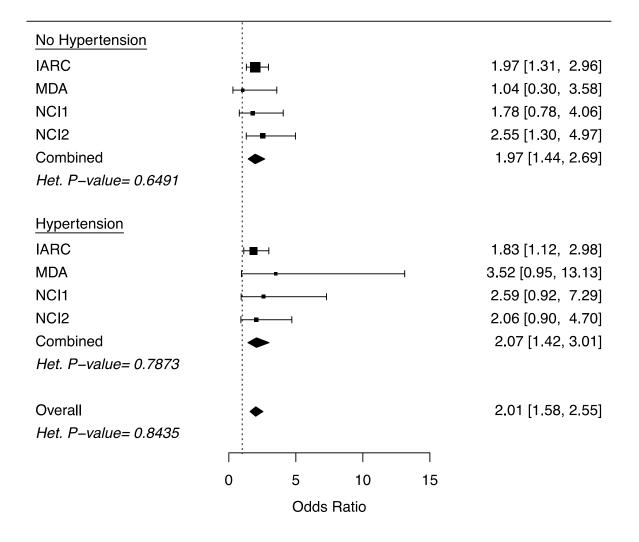
RCC by strata of BMI.

GRS by Body Mass Index



Supplementary Figure 9. Forest plot for associations of telomere length associated GRS with RCC by strata of hypertension.

GRS by Hypertension



Supplementary Figure 10. Forest plot for associations of telomere length associated GRS with

RCC by strata of smoking.

GRS by Smoking

