Supplemental Methods.

The information of the data from the UK Biobank consortium are available online (URL: https://www.ukbiobank.ac.uk/data-showcase/), and the information is identified by field IDs.

The information of general happiness was collected from a touchscreen questionnaire (Field ID 20458) from a question “In general how happy are you?”. Belief that own life is meaningful (Field ID 20460) was collected from a question asking “To what extend do you feel your life to be meaningful?”. Broad depression was determined by presence of a history of seen doctor (Field ID 2090) or a psychiatrist (Field ID 2100) for nerves, anxiety, tension, or depression. The neuroticism score (Field ID 20127) was derived from the number of “yes” answers from the following 12 questions; "Does your mood often go up and down?"; "Do you ever feel 'just miserable' for no reason?"; "Are you an irritable person?”; "Are your feelings easily hurt?"; "Do you often feel 'fedup'?"; "Would you call yourself a nervous person?"; "Are you a worrier?";"Would you call yourself tense or 'highly strung'?"; "Do you worry too long after an embarrassing experience?"; "Do you suffer from 'nerves'?"; "Do you often feel lonely?"; "Are you often troubled by feelings of guilt?".

Baseline eGFR values were calculated from the information of serum creatinine levels (Field ID 30700), cystatin C levels (Field ID 10720), or both, along with information of ethnicity (Field ID 21000), calculated by the CKD-EPI equation. To determine prevalent history of end-stage kidney disease, we implemented the information for dates of end-stage kidney disease (Field ID 42026), algorithmically defined by the UK Biobank from self-reports and hospital admission records. The ICD-10 diagnostic codes to identify CKD stage 3-5 dialysis, or transplantation histories included N183 (chronic kidney disease, stage 3), N384 (chronic kidney disease, stage 4), N185 (chronic kidney disease, stage 5), N186 (end stage renal disease), Z94 (kidney transplant status), Z49 (encounter for care involving renal dialysis) and the subcodes of them. Presence of any eGFR < 60 mL/min/1.73 m^2, history of end-stage kidney disease, or ICD-10 diagnostic code indicating stage 3-5 CKD defined the CKD outcome in the UK Biobank data.

Other information was collected by as follows (the numbers of missing values in the clinical analysis dataset): age (Field ID 21003). sex (Field ID 31), smoking history (Field ID 20116,

missing N=1890), body mass index (Field ID 21001, missing N=1842), waist circumference (Field ID 48, missing N=977), total cholesterol (Field ID 30690, missing N=139), HDL cholesterol (Field ID 30760, missing N=39639), LDL cholesterol (Field ID 30780, missing N=922), and self-reported frequency of moderate physical activity per week (Field ID 884, missing N=24358). A history of cardiovascular disease was identified by angina, stroke or heart attack diagnosed by a doctor (Field ID 6150, missing N=1175). Hypertension was determined when people reported a history of treatment with hypertension medication (Field ID 6177 and 6153, missing N=3606). A history of diabetes mellitus was collected by self-report (Field ID 2443, missing N=1542). Glycated hemoglobin A1c levels were collected (Field ID 30750, missing N=24108). Systolic and diastolic BP was determined by the average of two automated measurements (Field ID 4080, missing N=40363, and Field ID 4079, missing N=40351), and those with a single missing measurement were considered to have missing information. Average total household income before tax (Field ID 738, missing N=67856) and number of household members (Field ID 709, missing N=3349) were collected by self-reports. The above missing numbers are presented based on the observational analysis dataset including 468,521 individuals in the UK Biobank.

R code to call the causal estimates through the TwoSampleMR package

Detailed methods to run and install TwoSampleMR package is available in the following URL.
URL: https://github.com/MRCIEU/TwoSampleMR

The underlined text requires customization for the data input.

```
##### Beginning of the code #####
require(TwoSampleMR)
require(data.table)

### Read in the genetic instrument data ###
instrument<-fread("file path for the genetic instrument")
instrument_dat<-format_data(instrument,type="exposure")

### Read in the outcome summary statistics ###
outcome_file<-read_outcome_data(
   snps=instrument_dat$SNP,
   filename="file path for the outcome summary statistics with predefined column names",
   sep=",",
   snp_col="SNP",
   beta_col="beta.outcome",
   se_col="se.outcome",
   effect_allele_col="effect_allele.outcome",
   other_allele_col="other_allele.outcome",
   eaf_col="eaf.outcome",
   pval_col="pval.outcome",
   samplesize_col="samplesize.outcome"
)

#### Harmonise data ###
dat <- harmonise_data(
   exposure_dat=instrument_dat,
   outcome_dat=outcome_file
)

### Perform Mendelian randomization analysis ###
res<-mr(dat,method_list=c("mr_ivw_mre","mr_egger_regression","mr_weighted_median","mr_simple_median"))
res

### Cochrane's Q statistics ###
mr_heterogeneity(dat)
```

MR-Egger intercept, pleiotropy test P value

```
mr_pleiotropy_test(dat)
```

MR-PRESSO, with significance threshold P < 0.05 by 5000 times of bootstrap replication

```
mrpresso<-run_mr_presso(dat, NbDistribution = 5000, SignifThreshold = 0.05)
mrpresso
```

Draw scatter plots for summary-level Mendelian randomization

```
mr_scatter_plot(res,dat)
```

Supplemental Table 1. The study population of the genome-wide association meta-analysis for well-being spectrum by Baselmans BML et al.

Phenotype	Included data	Number of observations	Brief description of the phenotyping methods
Positive affect	SSGAC meta-analysis [a]	180,281	Meta-analysis of cohorts with diverse methods to phenotype positive affect
	Understanding Society [b]	8741	Self-reported positive affect on a survey
	UK Biobank	221,575	Self-reported general happiness (Field ID 4526/20458), graded as extremely unhappy, very unhappy, moderately unhappy, moderately happy, very happy, and extremely happy.
Life satisfaction	SSGAC meta-analysis [a]	71,650	Meta-analysis of cohorts with diverse methods to phenotype life satisfaction [a]
	Understanding Society [b]	9202	Self-reported life satisfaction on a survey
Depressive symptoms	SSGAC meta-analysis [a]	161,460	Meta-analysis of cohorts with diverse methods to phenotype depressive symptoms [a]
	23andMe [c]	228,033	Self-reported online surveys, and the sources from survey answers collected for maximum 6 times were utilized to determine depression trait.
	CHARGE [d]	51,258	Depressive symptoms measured with the CES-D scale was used to determine ones' depressive symptoms.
	Understanding Society [b]	9203	Self-reported depression on a survey
	UK Biobank	422,483	Self-reported history of seen a doctor for nerves, anxiety, tension, or depression (Field ID 2090)
	UK Biobank	423,509	Self-reported history of seen a psychiatrist for nerves, anxiety, tension, or depression (Field ID 2100)
Neuroticism	SSGAC meta-analysis [a]	59,206	Meta-analysis of cohorts with diverse methods to phenotype neuroticism [a]
	23andMe [e]	170,911	Neuroticism score collected from online survey determined by the Big Five Personality trait.
	Understanding Society [b]	8198	Neuroticism score determined by the Big Five Personality trait
	UK Biobank	344,674	Neuroticism score (Field ID 20127), which was determined by the number of "yes" answers from the following 12 questions; "Does your mood often go up and down?"; "Do you ever feel 'just miserable' for no reason?"; "Are you an irritable person?"; "Are your feelings easily hurt?"; "Do you often feel 'fedup'?"; "Would you call yourself a nervous person?"; "Are you a worrier?";"Would you call yourself tense or 'highly strung'?"; "Do you worry too long after an embarrassing experience?"; "Do you suffer from 'nerves'?"; "Do you often feel lonely?"; "Are you often troubled by feelings of guilt?".

[a] Okbay A, Baselmans BM, De Neve JE, et al. Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. Nat Genet. 2016;48(6):624-33.

[b] Understanding society website (URL: https://www.understandingsociety.ac.uk/documentation, last accessed 2020-09-24).

[c] Hyde CL, Nagle MW, Tian C, et al. Nat Genet. 2016;48(9):1031-6.

[d] Hek K, Demirkan A, Lahti J, et al. A genome-wide association study of depressive symptoms. Biol Psychiatry. 2013;73(7):667-78.

[e] Lo MT, Hinds DA, Tung JY, et al. Genome-wide analyses for personality traits identify six genomic loci and show correlations with psychiatric disorders. Nat Genet. 2017;49(1):152-156.

Supplemental Table 2. Characteristics of the CKDGen genome-wide association meta-analysis dataset of the European ancestry.

	CKDGen of European ancestry
Number of studies meta-analyzed	85
Number of individuals with eGFR	567,460
Median age (years)	50.1
Median eGFR (mL/min/1.73 m^2)	91.4
Proportion of male sex (%)	48
Chronic kidney disease (%)	9 (total 460,698, cases 41,395)

The details of the dataset are available in Wuttke M, Li Y, Li M, Sieber KB, et al. A catalog of genetic loci associated with kidney function from analyses of a million individuals. Nat Genet. 2019;51(6):957-972.

Supplemental Table 3. Characteristics of the observational analysis dataset of the UK Biobank.

	Total (N=468,521)	Female (N=254,048)	Male (N=214,473)
General happiness			
Extremely happy	14,670 (10.0%)	7905 (9.6%)	6756 (10.6%)
Very happy	65,194 (44.4%)	36,638 (44.2%0	28,556 (44.6%)
Moderately happy	58,822 (40.1%)	33,751 (40.8%)	25,071 (39.1%)
Moderately unhappy	6512 (4.4%)	3540 (4.3%)	2972 (4.6%)
Very unhappy	1289 (0.9%)	756 (0.9%)	533 (0.8%)
Extremely unhappy	400 (0.3%)	224 (0.3%)	176 (0.3%)
Belief that own life is meaningful			
An extreme amount	18,676 (13.0%)	10,867 (13.3%)	7809 (12.5%)
Very much	76,136 (52.8%)	42,676 (52.2%)	33,460 (53.5%)
A moderate amount	38,386 (26.6%)	22,048 (27.0%)	16,338 (26.1%)
A little	8558 (5.9%)	4873 (6.0%)	3685 (5.9%)
Not at all	2430 (1.7%)	1221 (1.5%)	1209 (1.9%)
Broad depression (history of medical visit for depression-related psychiatric) symptom)	161349 (34.4%)	104692 (41.2%)	56,657 (26.4%)
Neuroticism score	4 [1;6]	4 [2;7]	3 [1;6]
Age (years)	58 [50;63]	57 [50;63]	58 [50;64]
Body mass index (kg/m^2)	26.7 [24.1;29.9]	26.1 [23.5;29.7]	27.3 [25.0;30.1]
Obesity (≥ 30 kg/m^2)	113,611 (24.3%)	59,414 (23.5%)	54,197 (25.4%)
Waist circumference (cm)	90 [80;99]	83 [75;92]	96 [89;103]
Central obesity (≥ 102 cm for male ≥ 86 cm for female)	156,991 (33.6%)	91,932 (36.3%)	65,059 (30.4%)
Smoking history			
Nonsmoker	255,391 (54.7%)	150,788 (59.6%)	104,603 (49.0%)
Ex-smoker	162,008 (34.7%)	79,697 (31.5%)	82,311 (38.5%)
Current smoker	49,232 (10.6%)	22,574 (8.9%)	26,658 (12.5%)
Frequency of moderate physical activity (days/week)	3 [2;5]	3 [2;5]	3 [2;5]
Household income before tax			
< 18000 £	91,106 (22.7%)	51,875 (24.7%)	39,231 (20.5%)
18000 to 30999 £	101,895 (25.4%)	55,176 (26.3%)	46,719 (24.5%)
31000 to 51999 £	104,435 (26.1%)	53,285 (25.4%)	51,150 (26.8%)
52000 to 100000 £	81,532 (20.4%)	39,237 (18.7%)	42,295 (22.1%)
> 100000 £	21,697 (5.4%)	10,100 (4.8%)	11,597 (6.1%)
Hypertension	97,723 (21.0%)	44,786 (17.7%)	52,937 (24.9%)
Systolic BP (mmHg)	136 [125;150]	133 [121;147]	139 [129;152]
Diastolic BP (mmHg)	82 [75;89]	80 [74;87]	84 [77;91]
Diabetes mellitus	24,468 (5.2%)	9533 (3.8%)	14,935 (7.0%)
Hemoglobin A1c (mmol/L)	35.2 [32.8;37.9]	35.2 [32.7;37.7]	35.3 [32.8;38.1]
Dyslipidemia medication	81,595 (17.6%)	32,304 (12.8%)	49,291 (23.2%)
Total cholesterol (mmol/L)	5.65 [4.91;6.42]	5.81 [5.09;6.59]	5.45 [4.71;6.21]
LDL cholesterol (mmol/L)	3.52 [2.94;4.12]	3.57 [3.01;4.18]	3.46 [2.87;4.05]
HDL cholesterol (mmol/L)	1.40 [1.17;1.67]	1.55 [1.32;1.82]	1.24 [1.06;1.45]
Hx of angina, heart attack, or stroke	27,061 (5.79%)	8672 (3.42%)	18,389 (8.60%)
CKD-EPI eGFR (mL/min/1.73 m^2) [a]	91.2 [81.4;100.4]	91.8 [81.6;101.1]	90.6 [81.2;99.6]
CKD stage 3-5	28,627 (6.1%)	15,465 (6.1%)	13,1623 (6.1%)
by creatinine-cystatin C eGFR < 60	11,608 (2.5%)	6040 (2.4%)	5568 (2.6%)
by cystatin C eGFR < 60	21,838 (4.7%)	11,588 (4.6%)	10,250 (4.8%)
by creatinine eGFR < 60	10,701 (2.3%)	5716 (2.3%)	5568 (2.6%)
by a history of end-stage kidney disease	986 (0.2%)	364 (0.1%)	622 (0.3%)
by ICD-10 diagnostic codes	5485 (1.2%)	2654 (1.0%)	2831 (1.3%)

BP = blood pressure, LDL = low-density lipoprotein, HDL = high-density lipoprotein, CKD = chronic kidney disease

Descriptive statistics are presented as numbers (%) for categorical variables and medians [interquartile ranges] for continuous variables. The numbers of individuals with missing information are presented in Supplemental Method.

[a] eGFR values by creatinine-cystatin C CKD-EPI equation.

Supplemental Table 4. Association between psychological well-being and age or sex.

Outcome	Exposure	adjusted OR (95% CI) [a]	P
General happiness (Moderately, very, or extremely happy)	Age (years)	1.05 (1.05-1.05)	< 0.001
	Male sex (ref. female)	0.90 (0.86-0.94)	< 0.001
Belief that own life is meaningful (very or an extreme amount)	Age (years)	1.02 (1.02-1.02)	< 0.001
	Male sex (ref. female)	1.00 (0.98-1.03)	0.80
Broad depression	Age (years)	0.99 (0.99-0.99)	< 0.001
	Male sex (ref. female)	0.51 (0.51-0.52)	< 0.001
Neuroticism (score ≥ 5)	Age (years)	0.98 (0.98-0.98)	< 0.001
	Male sex (ref. female)	0.61 (0.60-0.62)	< 0.001

Multivariable logistic regression model including age and sex was constructed to investigate the associations.

Supplemental Table 7. Summary-level MR results for the causal estimates from psychological well-being on risk of CKD from the genetic instrument with stronger association ($P<1\times10^{-10}$) with the well-being exposures.

Genetically predicted exposure	N of SNPs of the genetic instrument	Cochran's Q statistics P value	MR-Egger pleiotropy test P value	MR method	OR (CKD) (95% confidence interval) [a]	P
Positive affect	43	0.003	0.79	Multiplicative random-effect IVW	0.58 (0.38; 0.89)	0.01
				MR-Egger	0.46 (0.08; 2.75)	0.40
				Weighted median	0.60 (0.37; 0.98)	0.04
				Simple median	0.46 (0.28; 0.75)	0.002
				MR-PRESSO (identified 2 outlier SNPs)	0.59 (0.40; 0.85)	0.008
Life satisfaction	27	0.02	0.34	Multiplicative random-effect IVW	0.65 (0.39; 1.07)	0.09
				MR-Egger	0.17 (0.01; 2.61)	0.22
				Weighted median	0.74 (0.43; 1.27)	0.27
				Simple median	0.74 (0.42; 1.30)	0.29
				MR-PRESSO (identified 2 outlier SNPs)	0.66 (0.45; 0.97)	0.047
Depressive symptom	60	< 0.001	0.72	Multiplicative random-effect IVW	1.59 (1.04; 2.43)	0.03
				MR-Egger	2.45 (0.23; 26.11)	0.46
				Weighted median	2.01 (1.24; 3.25)	0.004
				Simple median	2.22 (1.36; 3.61)	0.001
				MR-PRESSO (identified 1 outlier SNPs)	1.47 (0.98; 2.21)	0.07
Neuroticism	57	< 0.001	0.79	Multiplicative random-effect IVW	1.30 (0.97; 1.74)	0.08
				MR-Egger	1.65 (0.28; 9.65)	0.58
				Weighted median	1.74 (1.23; 2.46)	0.002
				Simple median	1.75 (1.23; 2.50)	0.002
				MR-PRESSO (identified 1 outlier SNP)	1.23 (0.94; 1.63)	0.14

SNP = single nucleotide polymorphism, MR = Mendelian randomization, eGFR = estimated glomerular filtration rate, CKD = chronic kidney disease, IVW = inverse variance weighted

[a] The effect sizes were from the genetic predisposition scaled to a z score in the previous model-averaging genome-wide association meta-analysis setting phenotype variance to 1.

Supplemental Table 8. Summary-level MR results for the causal estimates from psychological well-being on eGFR change (%) from the genetic instrument with stronger association ($P<1\times10^{-10}$) with the well-being exposures.

Genetically predicted exposure	N of SNPs of the genetic instrument	Cochran's Q statistics P value	MR-Egger pleiotropy test P value	MR method	beta (eGFR change, %) (95% confidence interval) a	P
Positive affect	43	< 0.001	0.96	Multiplicative random-effect IVW	1.58 (-0.62; 3.83)	0.16
				MR-Egger	1.35 (-7.70; 11.27)	0.78
				Weighted median	-0.05 (-2.12; 2.08)	0.97
				Simple median	0.41 (-1.71; 2.57)	0.71
				MR-PRESSO (identified 3 outlier SNPs)	1.34 (-0.69; 3.41)	0.20
Life satisfaction	27	< 0.001	0.02	Multiplicative random-effect IVW	1.90 (-0.57; 4.43)	0.09
				MR-Egger	17.89 (4.45; 33.06)	0.01
				Weighted median	1.27 (-1.10; 3.69)	0.30
				Simple median	0.90 (-1.40; 3.26)	0.45
				MR-PRESSO (identified 1 outlier SNPs)	-1.14 (-3.21; 0.98)	0.30
Depressive symptom	60	< 0.001	0.30	Multiplicative random-effect IVW	-3.20 (-5.16; -1.20))	0.002
				MR-Egger	-8.75 (-18.41; 2.04)	0.11
				Weighted median	-1.90 (-3.74; -0.02)	0.048
				Simple median	-2.11 (-4.05; -0.12)	0.04
				MR-PRESSO (identified 2 outlier SNPs)	-2.53 (-4.32; -0.70)	0.009
Neuroticism	57	< 0.001	0.60	Multiplicative random-effect IVW	-1.57 (-3.20; 0.09)	0.06
				MR-Egger	-4.13 (-13.32; 6.02)	0.41
				Weighted median	-0.97 (-2.37; 0.44)	0.18
				Simple median	-0.93 (-2.30; 0.47)	0.19
				MR-PRESSO (identified 4 outlier SNP)	-1.54 (-2.88; -0.19)	0.03

SNP = single nucleotide polymorphism, MR = Mendelian randomization, eGFR = estimated glomerular filtration rate, IVW = inverse variance weighted

[a] The effect sizes were from the genetic predisposition scaled to a z score in the previous model-averaging genome-wide association meta-analysis setting phenotype variance to 1

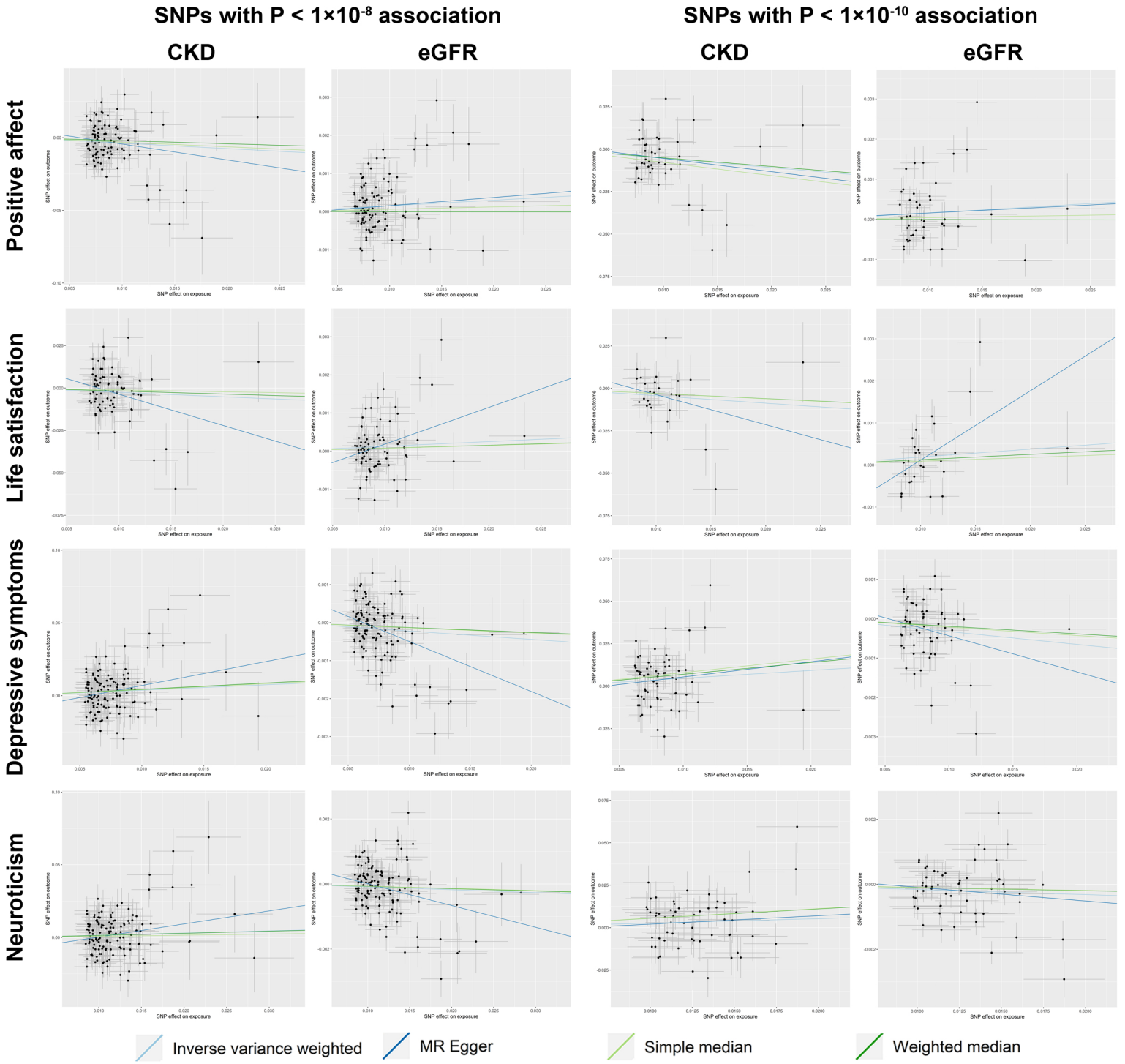
Supplemental Table 9. Sensitivity analysis results by including SNPs ranges of association strengths for psychologic well-being as the genetic instruments for summary-level MR.

Outcome	Genetically predicted exposure	P threshold for filtering SNPs	Remining N of SNPs in the genetic instrument	Beta (eGFR, % change) or OR (CKD) (95% confidence interval) [a]	P by mulplicative random-effect IVW	MR-Egger pleiotropy test P value
CKD	Positive affect	$< 5\times10^{-8}$	139	0.77 (0.60; 0.99)	0.04	0.06
		$< 1\times10^{-8}$	102	0.69 (0.52; 0.91)	0.008	0.23
		$< 1\times10^{-9}$	66	0.68 (0.49; 0.94)	0.02	0.56
		$< 1\times10^{-10}$	43	0.58 (0.38; 0.89)	0.01	0.79
	Life satisfaction	$< 5\times10^{-8}$	103	0.90 (0.69; 1.18)	0.45	0.01
		$< 1\times10^{-8}$	76	0.77 (0.57; 1.04)	0.09	0.05
		$< 1\times10^{-9}$	50	0.69 (0.48; 1.00)	0.05	0.19
		$< 1\times10^{-10}$	27	0.65 (0.39; 1.07)	0.09	0.34
	Depressive symptom	$< 5\times10^{-8}$	176	1.34 (1.03; 1.73)	0.03	0.14
		$< 1\times10^{-8}$	125	1.45 (1.07; 1.96)	0.02	0.07
		$< 1\times10^{-9}$	83	1.43 (1.00; 2.04)	0.049	0.13
		$< 1\times10^{-10}$	60	1.59 (1.04; 2.43)	0.034	0.72
	Neuroticism	$< 5\times10^{-8}$	187	1.13 (0.95; 1.34)	0.18	0.43
		$< 1\times10^{-8}$	133	1.16 (0.96; 1.41)	0.12	0.11
		$< 1\times10^{-9}$	88	1.24 (0.98; 1.55)	0.07	0.12
		$< 1\times10^{-10}$	57	1.30 (0.97; 1.74)	0.07	0.79
eGFR (% change)	Positive affect	$< 5\times10^{-8}$	139	1.34 (0.09; 2.6)	0.04	0.67
		$< 1\times10^{-8}$	102	1.50 (0.09; 2.93)	0.04	0.83
		$< 1\times10^{-9}$	66	1.09 (-0.73; 2.95)	0.24	0.87
		$< 1\times10^{-10}$	43	1.58 (-0.62; 3.83)	0.16	0.96
	Life satisfaction	$< 5\times10^{-8}$	103	0.81 (-0.48; 2.12)	0.22	0.17
		$< 1\times10^{-8}$	76	1.25 (-0.30; 2.83)	0.11	0.04
		$< 1\times10^{-9}$	50	0.99 (-0.92; 2.94)	0.31	0.04
		$< 1\times10^{-10}$	27	1.90 (-0.57; 4.43)	0.13	0.02
	Depressive symptom	$< 5\times10^{-8}$	176	-2.00 (-3.24; -0.75)	0.002	0.002
		$< 1\times10^{-8}$	125	-2.18 (-3.61; -0.72)	0.003	0.001
		$< 1\times10^{-9}$	83	-2.58 (-4.34; -0.78)	0.005	0.02
		$< 1\times10^{-10}$	60	-3.20 (-5.16; -1.20)	0.002	0.30
	Neuroticism	$< 5\times10^{-8}$	187	-0.91 (-1.76; -0.05)	0.04	0.06
		$< 1\times10^{-8}$	133	-0.88 (-1.87;0.13)	0.09	0.02
		$< 1\times10^{-9}$	88	-1.09 (-2.34;0.18)	0.09	0.07
		$< 1\times10^{-10}$	57	-1.57 (-3.20;0.09)	0.06	0.06

SNP = single nucleotide polymorphism, MR = Mendelian randomization, eGFR = estimated glomerular filtration rate, CKD = chronic kidney disease, IVW = inverse variance weighted

[a] The effect sizes were from the genetical predisposition scaled to a z-score in the previous N-weighted multivariate genome-wide association meta-analysis setting phenotype variance to 1.

Supplemental Figure 1. Scatter plots visualizing the summary-level Mendelian randomization results.



Of the scatter plots, the x-axes indicate the SNP effect on exposure (positive affect, life satisfaction, depressive symptoms, or neuroticism), and the y-axes indicate the SNP effect on outcome (eGFR or chronic kidney disease). The left eight graphs show the results when all Bonferroni-adjusted significant SNPs ($P < 1\times10^{-8}$) were utilized as the genetic instrument. The right eight graphs show the results when SNPs with stronger ($P < 1\times10^{-10}$) associations with each psychologic well-being phenotype were utilized. The four lines indicate the results from the inverse variance weighted (purple), MR-Egger (blue), simple median (light green), and weighted-median (green) methods.