Abstract

Aim: To estimate the lifetime causal association of systolic blood pressure (SBP) with quality-adjusted life years (QALYs).

Methods: Mendelian randomisation (MR) was used to estimate the lifetime causal effect of SBP on QALYs. Genetic variants associated with SBP (181 single nucleotide polymorphisms (SNPs)) were used as instrumental variables. SBP was used as the exposure variable and QALYs as the outcome variable.

Statistical analysis: Two-stage least square regression (2SLS) was performed to estimate the effect of SBP on QALYs. Several sensitivity analyses were run to test the robustness of the main estimate and MR assumptions including Inverse-variance weighting, MR Egger, MR Median, MR Mode, MR-Pleiotropy Residual Sum and Outlier (MR-PRESSO), and MR-Robust Adjusted Profile Score (MR-RAPS). The primary outcome was reported as the percentage change in QALYs per 10 mmHg increase in SBP over an average year of follow-up. Multivariable MR was used to account the mediating effect of diastolic blood pressure on the association of SBP and QALYs.

Data source: Individuals' sociodemographic, clinical- and genetic data sourced from the UK Biobank. Allele dosages of the relevant genetic variants were derived from the third version of imputed BGEN v1.2.

Result: The 2SLS analysis demonstrated that for every 10 mmHg increase in SBP, the annual QALYs declined by 1.17% (95% CI -1.46% to -0.88%). Sensitivity analyses showed a consistent direction of effect. However, there was high heterogeneity (Cochran's Q = 409.4, p value <0.00001) in the association of genetic variants with QALYs, with evidence of directional pleiotropy (MR Egger intercept -0.36%, 95%CI -0.66 to -0.05%). Further analysis using MR-PRESSO global test revealed directional pleiotropy due to outlier SNPs; however, the distortion test showed that the detected outlier SNPs did not significantly affect the observed SNP-QALY association. The MR-RAPS estimate with Tukey loss function showed a 1.92% (95%CI: -2.30% to -1.54%) decline in the annual QALYs per 10 mm Hg increase in SBP over the average year of follow-up. The model showed little evidence of residual pleiotropic variance. From multivariable MR, the direct effect of SBP on QALYs, conditional on diastolic blood pressure, was -0.78% (95% CI -1.49% to -0.06%) reduction in QALYs for every 10 mmHg increase in SBP.

Conclusion: MR provides consistent estimates in the presence of unmeasured confounding, and we showed the effect of SBP on QALYs. Increased SBP was observed to be associated with reduced QALYs. However, the heterogeneity of SNPs affecting QALYs indicates that other traits could influence the observed association through alternative pathways.