Supplemental Material

Bone Lead Levels and Risk of Incident Primary Open-Angle Glaucoma: The VA Normative Aging Study

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Figure S1. Causal diagram representing the impact of two types of selection bias at the baseline of KXRF measurement and during follow-ups in the unweighted (A) and IPW-weighted (B) models. SKXRF is the selection bias caused by participation of KXRF sub-study from the NAS inception; SCohort is the selection bias due to survivorship from either POAG diagnosis or loss to follow-up during current study. U and C refer to unmeasured and measured covariates at the baseline. Health Status0 and Health Status1 are severe health conditions which may affect the attendance of study at baseline and during the follow-ups. Bone Pb refer to the bone lead concentration at baseline, which reflects past cumulative lead exposure (by tibia lead) and baseline endogenous source of stored lead (by patella lead). The rectangular blue shade illustrates the main association we investigated in this study. The inverse probability weighting (IPW) applied in the current study has already accounted for the effect of SKXRF; this IPW removed the dash red lines in A. Standard solution for the 2nd selection bias occurred during the follow-up time (SCohort) was still the application of another IPW (which can remove the bold red lines). However, since it was challenging to combine two IPWs into one model, SCohort was hard to be avoided.
**Figure S2.** Schoenfeld residual for bone lead levels vs. time plots for all follow-ups and follow-ups cut at 15 years in the fully adjusted models (Above: patella lead; below: tibia lead). We used non-parametric smoothing strategy by SAS to provide Loess of Schoenfeld residuals (solid line) together with 95%CI (dark part), to better illustrate the trend of Schoenfeld residuals for risk of incident POAG against the follow-up time.

**Figure S3.** Splines Illustrating non-linear association between bone lead levels and log of Hazard Ratio (logHR) for incident POAG adjusted for baseline age, BMI, educational levels, job types, smoking, systemic hypertension, diabetes mellitus, and ocular hypertension. IPW was applied. Dark black line illustrated the Natural Splines with knots at 25th, 50th, and 75th percentiles, together with the 95% CI (red dash lines). X-axis is log(bone lead). Histogram illustrates the distribution of log(bone lead) of all participants by count (right y-axis). The left y-axis is logHR, with the reference horizontal blue dash line illustrating logHR=0 at the mean of log(bone lead) (21.8 μg/g for tibia lead and 31.0 μg/g for patella lead). A. Spline for tibia lead; B. Spline for patella lead.