**Covariate details for diabetic retinopathy (DR) analysis**

* Age at diagnosis
  + Self explanatory coding and units
  + According to research there’s an inherent susceptibility to diabetic retinopathy with earlier-onset T2 diabetes
    - <https://diabetesjournals.org/care/article/31/10/1985/25135/Timing-Is-Everything-Age-of-Onset-Influences-Long>
* Gender
  + 1 = male, 2 = female
  + Men with diabetes tend to be at a greater risk of complications (incl. retinopathy) irrespective of diabetes duration
    - <https://jech.bmj.com/content/78/8/479.abstract>
    - <https://onlinelibrary.wiley.com/doi/full/10.1155/2023/5919468>
* Ethnicity (5 category)
  + 0 = White, 1 = South Asian, 2 = Black, 3 = Other, 4 = Mixed
  + The prevalence of DR is higher in people of South Asian descent and often also other minority ethnic groups compared to White people, also possible disparities in screening uptake
    - <https://www.sciencedirect.com/science/article/pii/S0039625712000070>
    - <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0032182>
* IMD
  + Deciles
    - 1 = least deprived, 10 = most deprived
  + Quintiles
    - 1 = least deprived (deciles 1 and 2), 5 = most deprived (deciles 9 and 10)
  + Deprivation can be a risk factor for late presentation of proliferative diabetic retinopathy
    - Might be because T2 is also more prevalent overall in deprived populations
    - This paper also found that South Asian ethnicity was a risk factor for proliferative retinopathy, but wasn’t significant after controlling for HbA1c
    - <https://www.tandfonline.com/doi/full/10.2147/OPTH.S73272>
  + Again possibly caused by screening uptake disparities – higher deprivation is associated with poorer attendance at retinal screening
    - <https://diabetesjournals.org/care/article/31/11/2131/26810/Screening-Uptake-in-a-Well-Established-Diabetic>
* Baseline HbA1C
  + mmol/mol
  + average blood glucose over the past 90 days
  + HbA1c over 48mmol/mol is diagnostic of T2
  + Poorly controlled HbA1c is associated with DR – higher levels of HbA1c are linked to DR
    - <https://link.springer.com/article/10.1007/s40200-022-00986-5>
    - <https://d1wqtxts1xzle7.cloudfront.net/100096241/14149-libre.pdf?1679340900=&response-content-disposition=inline%3B+filename%3DAssociation_of_HbA1c_levels_with_diabeti.pdf&Expires=1756898097&Signature=d7Nnu0KdgfEKbfupTlAMzOUeWwd7Tyrzrx~ko7KVZh17h0nWw5kPb4wrz0hlek0nhGiv1VnwuVXeWeaFehG6mddBJsZ9ay01F-5Vejff3~S9~qSMwnrFx4qj0ZC23EHHdMWBkxOxSOJwGTI6B5xH3tjQ2hwxe4IWIq3BJ7-~xtoLcbgPvGR5ziabAMfWMrzlt5EWPCxOn8RSWv750WjDnkcGjGj1CsQx9cjZYtQM5g0AdfuP-q7Qml6P~VcmCy5BVUpO7Daf~ugA0Gvzmn~F1tvGVB-TAkQEQMPKPi8rTkbOeoBw8krmIascms0WeF7YoikXjMU9BDY5lF0oeKdbEg__&Key-Pair-Id=APKAJLOHF5GGSLRBV4ZA>
* Baseline BMI
  + kg/m2
  + A function of height and weight
  + Higher BMI is a strong risk factor for T2
  + Generally increased BMI/obesity is associated with increased prevalence of DR
    - <https://ec.bioscientifica.com/view/journals/ec/10/7/EC-21-0172.xml>
  + Although there is a slight debate over this, such as one paper finding an inverse relationship
    - <https://link.springer.com/article/10.1007/s40200-018-0339-5>
  + However Mendelian randomization has found genetically predicted BMI is associated with an increased risk of DR
    - <https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1108731/full>
* Baseline EGFR
  + ml/min/1.73m2
  + Estimated Glomerular Filtration Rate – kidney function
  + Higher than 90ml/min/1.73m2 is generally good
  + Lower numbers are bad, and are sometimes associated with diabetes
  + Systematic review and meta analysis found a significant association between reduced eGFR and DR
    - Seems to be a relatively robust finding
    - <https://link.springer.com/article/10.1007/s11255-025-04547-6>
* Baseline HDL
  + mmol/L
  + high density lipoproteins – “good” cholesterol
  + Low levels of HDL cholesterol are consistently associated with increased risk of T2
  + One novel study found a relationship between *high* HDL and DR, when previously most studies have shown a relationship between low HDL and DR
    - <https://www.sciencedirect.com/science/article/pii/S0168822719301482>
  + Also another study found an inverted U shape relationship
    - <https://link.springer.com/article/10.1186/s12902-024-01599-0>
  + And another found that HDL was not an independent risk factor for retinal microvascular disease
    - <https://diabetesjournals.org/care/article/35/11/2201/30665/Low-HDL-Cholesterol-and-the-Risk-of-Diabetic>
  + Basically the relationship is somewhat unclear
* Baseline ALT
  + U/L
  + Alanine aminotransferase – enzyme in the liver
  + Increased levels can indicate liver cell damage
  + Data indicates moderate associations between ALT and risk of T2 Has been found to not be an independent risk factor for DR
    - <https://www.tandfonline.com/doi/full/10.2147/DMSO.S502129>
  + Some studies have found an association between abnormal renal and liver function and diabetic retinopathy
    - <https://www.nature.com/articles/s41598-022-13164-7>
  + But non-alcoholic fatty liver disease was found to not have an association with DR by a meta-analysis
    - <https://onlinelibrary.wiley.com/doi/full/10.1111/jdi.13489>
  + Somewhat unclear relationship
* Baseline SBP
  + mmHg
  + Systolic blood pressure
  + Elevated SBP is associated with future onset of T2
  + Elevated SBP is pretty robustly associated with DR
    - <https://onlinelibrary.wiley.com/doi/full/10.1155/2022/7876786>