Tutorial: a guide to performing polygenic risk score analyses

GRP1:
- Key elements
    - Why is the study conducted?
    - What is PRS about?
- Additional "highlights" (personal selection):
    - Score specific to an individual
    - Lack of guidelines
    - Link with SNP heritability
- "Digging in deep" opportunities include:
    - Liability
    - Summary statistics
    - Base and target data

GRP2:
- Key elements
    - How are PRS constructed?
        - QC
        - Technical formula
    - What is PRS about?
- Additional "highlights" (personal selection):
    - Two flavors of getting to a PRS score (shrinkage and classical → understanding == these are two approaches that include different ways to select your variants in the score)
    - LD: Can it be exploited when selecting the variants?
- "Digging in deep" opportunities include:
    - Leave-one-out (what? how is it used? Link with meta-analysis leave-one-out mentioned in the paper?)
    - Scale (transformations of the trait impact interpretation of PRS)

GRP3:
- Key elements
    - What are (additional attention points)?
        - Generalizability
        - Different traits
        - Multiple PRSs in a single analysis
    - Interpretation (graphical → direct visualization of numerics)
- Additional "highlights" (personal selection):
    - Goodness-of-fit
- "Digging in deep" opportunities include:
    - Generic sources of inflation/deflation of PRS-trait associations
    - Transferability (a term that is very popular in different contexts, is it linked to generalizability)

GRP4:
- Key elements
    - Interpretation – clinical perspective
        - Possibilities
        - Limitations
- Additional "highlights" (personal selection):
    - Interrelated biological and environmental network among human traits

- o Reasons for limitations
  - ▪ Overfitting associations
  - ▪ Sample sizes (base/target)
- "Digging in deep" opportunities include:
  - o Literature search on the use of PRS in "precision medicine" and link back to the paper (note: in the introduction it was mentioned that it was not an idea to give a review about potential applications)
  - o User-friendly code available ? (by following the URL and looking into annotation, documentation, toy examples