Ancestry-specific effects of lipid-lowering medications on atopic dermatitis: Evidence from Mendelian Randomisation and a Nested Case-Control Study

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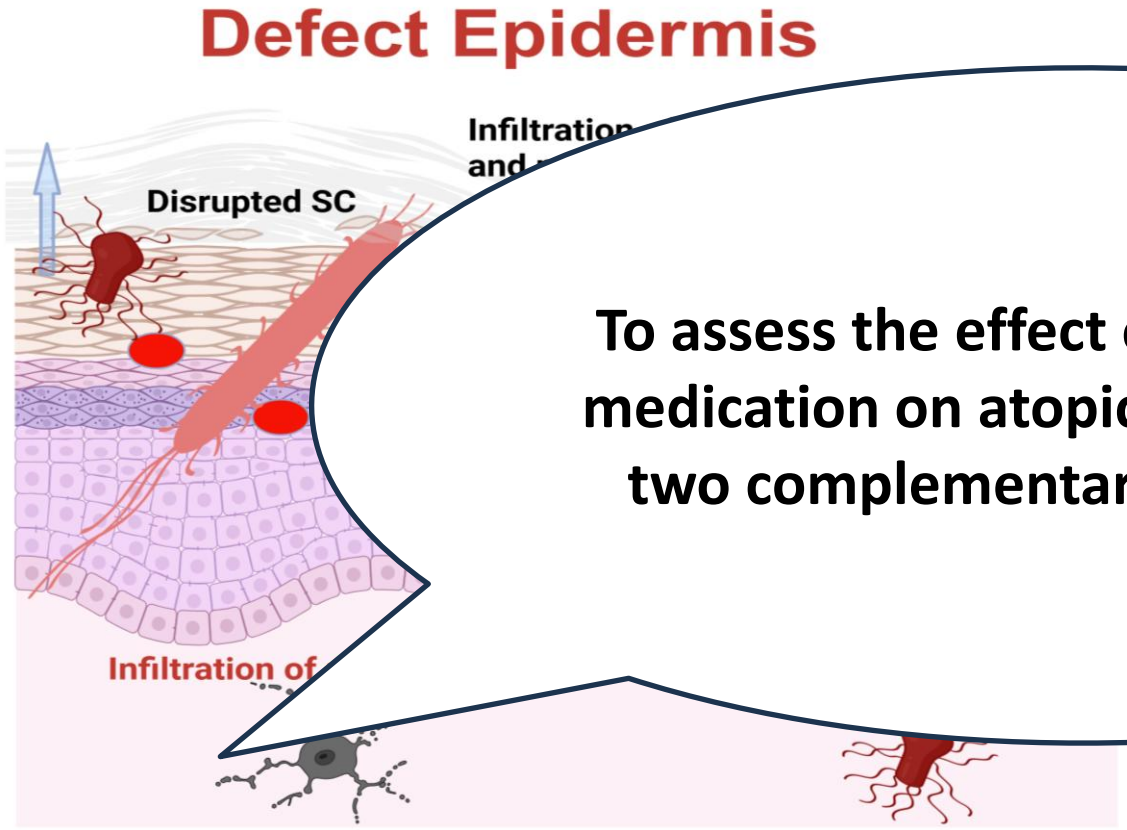
INTRODUCTION



To assess the effect of Lipid-lowering medication on atopic dermatitis using two complementary study designs

Systemic inhibition of LLMs

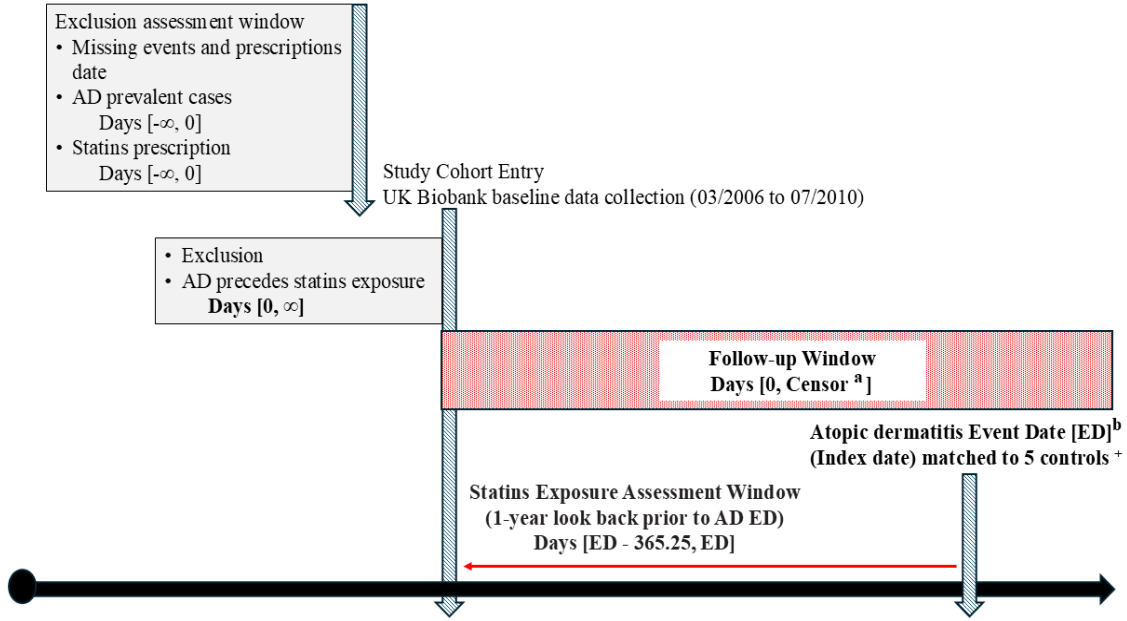
Reduce pro-inflammatory cytokines like IL-4 and IL-13

METHOD – 2SMR

- Mendelian Randomisation (2SMR) design
- MR uses genetic variants as instrumental variables to proxy causal effects of exposures on outcome
- Drug target
  - *HMGCR*, *NPC1L1*, *PCSK9*, and *CETP* genes
- Genome-wide association studies (Cholesterol traits)
  - Low-density lipoprotein (LDL)
  - Total cholesterol
  - High-density lipoprotein (HDL)
  - Non-HDL cholesterol
  - Triglycerides
- GWAS Atopic Dermatitis
  - 60,653 AD cases and 804,329 controls of European
  - 31,245 AD cases and 432,874 controls from FinnGen
  - 2,385 AD cases and 209,651 controls from East Asian
  - 7,063 AD cases and 15,879 controls from Africa
- Fixed-effect inverse-variance weighted analysis and derived pooled estimates through meta-analysis
- Pleiotropy and Colocalisation analyses were performed

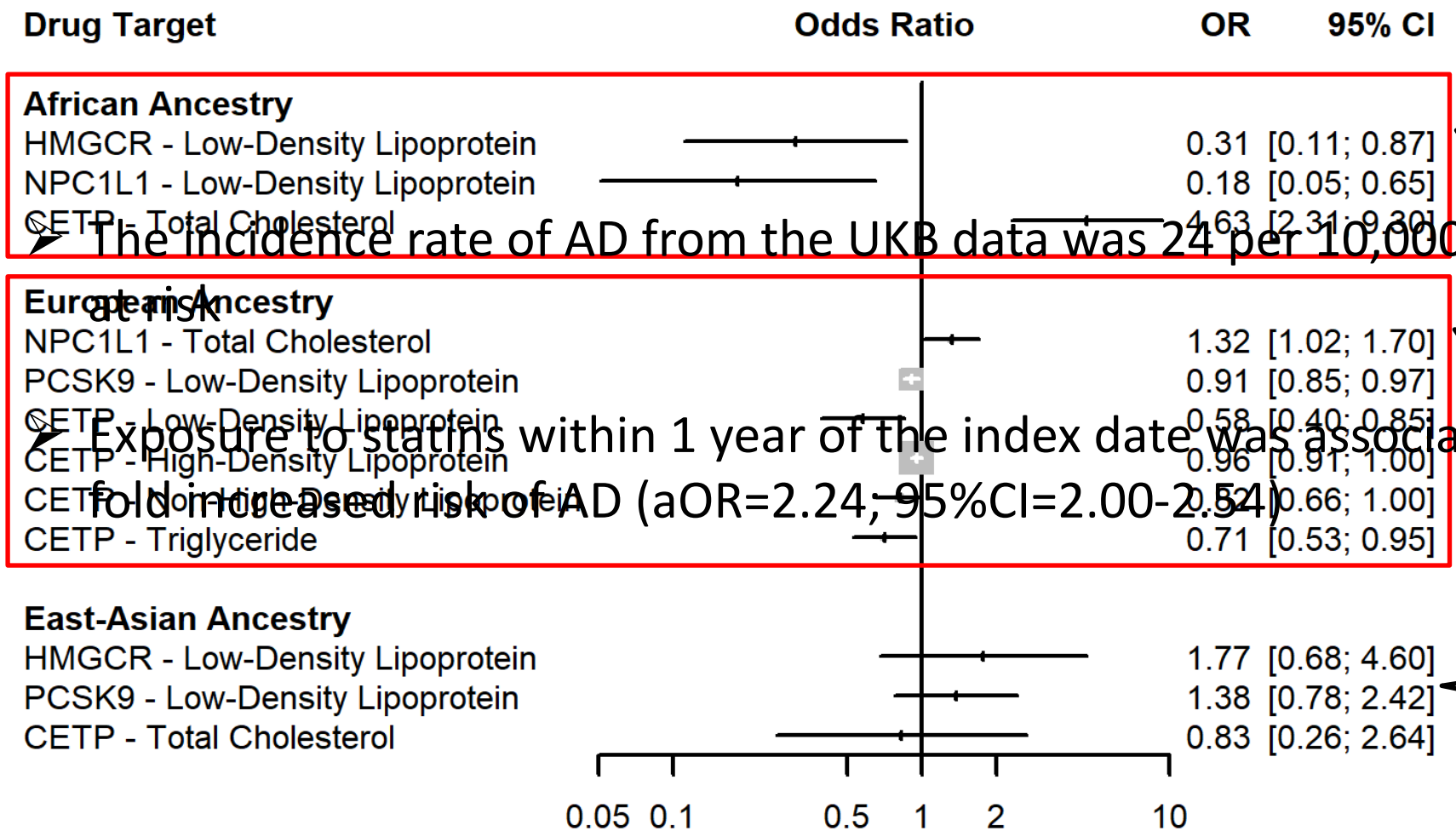
METHOD – NCCS

- Nested case-control study using UK Biobank (UKB) data
- Predominantly European ancestry (≈ 96% of UKB)
- Statins exposure



- Incident AD cases were matched to 5 controls on;
  - ✓ date of cohort entry (±6 months),
  - ✓ age (±2 years),
  - ✓ sex, and
  - ✓ centre
- Odds ratio was estimated using conditional logistic regression
- Adjusting for potential confounders using sIPTW

RESULTS



- The incidence rate of AD from the UKB data was 24 per 10,000 patients-years at risk
- Exposure to statins within 1 year of the index date was associated with over 2-fold increased risk of AD (aOR=2.24; 95%CI=2.00-2.54)

Statins and Ezetimibe drug targets suggest a protective effect

CETPi suggest Ezetimibe drug target harmful effect increased risk

PSCK9i and CETPi suggest a protective effect

Imprecise estimates

CONCLUSION

- Indicate that lipid-lowering medications may have ancestry-specific effects on AD risk
- Short-term initiation of statins increased the risk of AD in real-world data from the UKB, predominantly made up of individuals of European ancestry
- Highlight statins initiation as a potential reason for onset of AD in European ancestry

Protecting the heart must not come at the expense of the skin barrier

ACKNOWLEDGEMENT

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