**Lipids**

This document describes steps for three traits and seven analyses:

* **High density lipoprotein (HDL-C)**
* **Triglycerides (TG)**:
  + Non-fasting
* **Low-density lipoprotein (LDL-C)**:
  + Unadjusted non-fasting
  + Adjusted non-fasting

**Overall procedure**

1. Extract trait measurements using measurement codes and calculations
2. Convert measurement units to expected units, if necessary
3. Apply measurement exclusion criteria
4. Prepare measurements for analysis
5. After preparing measurements for analysis, remove statistical outliers
6. Compute a single value per individual for inclusion in analysis
7. Calculate counts of flagged individuals

**Measurement codes and calculations**

The [primed\_consortia\_legacy\_project\_phenotypes GitHub repository](https://manning-lab.github.io/primed_consortia_legacy_project_phenotypes/) provides files containing codes for the following vocabularies. Files can be downloaded and used to identify measurements. These files are also present individually on the algorithm page for download.

**HDL-C**

* + HDL\_C\_Codes.csv
  + [HDL-C](https://athena.ohdsi.org/search-terms/terms/4101713)

**TG**

* + TG\_Codes.csv
  + [TG](https://athena.ohdsi.org/search-terms/terms/4032789)

**LDL-C**

* + LDL\_C\_Codes.csv
  + [LDL-C](https://athena.ohdsi.org/search-terms/terms/4012479)

If LDL-C levels are not directly measured, they can be estimated using the Friedewald equation or a similar formula, provided TG levels are less than 4.5 mmol/L (400 mg/dL):

|  |  |
| --- | --- |
| **Table 2.** Friedewald equation | |
| For values in (mg/dL) | LDL-C = Total Cholesterol - HDL-C - (TG/5) |
| For values in (mmol/L) | LDL-C = Total Cholesterol - HDL-C - (TG/2.2) |

**Medications**

Use available mapping to find all drugs/medication in the hierarchical [Anatomical Therapeutic Chemical (ATC) Classification](https://www.who.int/tools/atc-ddd-toolkit/atc-classification).

Lipid Lowering Medications

ATC 2nd level [C10: LIPID MODYFYING AGENTS](https://athena.ohdsi.org/search-terms/terms/21601853)

See this page for codes: [Lipid Lowering Medications](https://manning-lab.github.io/primed_consortia_legacy_project_phenotypes/Lipid-Lowering-Medications.html) and corresponding codes located in LipidLoweringMeds file attached in the algorithm page.

**Expected** **units**

Please convert values measured in other units of measurement to the following units:

* HDL-C: mmol/L
* TG: mmol/L
* LDL-C: mmol/L

**Unit conversion chart**

|  |  |
| --- | --- |
| **Table 1b.** Converting lipid values from mg/gl to mmol/L | |
| HDLC (mg/dL) \* 0.02586 | = HDLC (mmol/L) |
| LDLC (mg/dL) \* 0.02586 | = LDLC (mmol/L) |
| TG (mg/dL) \* 0.01129 | = TG (mmol/L) |

**Exclusion criteria**

**Individual exclusion criteria**

Not applicable for this analysis

* Optionally, you may exclude individuals without BMI measurements available. If they are not excluded at this stage, they will be dropped in the analysis (since BMI is a covariate).

**Measurement exclusion criteria**

The following measurements should be excluded from the analysis for all lipids traits. Other measurements from an individual may still be included in analysis.

* Age at measurement <18 years
* Exclude measurements taken at Inpatient or Emergency Department visits. Alternatively, keep only measurements taken at Outpatient visits. Take whichever approach is most appropriate for your EHR.

**Prepare measurements for analysis**

HDL

* Include both fasting and non-fasting measurements.
* No adjustment for medication

TG

* Include both fasting and non-fasting measurements.
* No adjustment for medication

LDL-C

* Include both fasting and non-fasting measurements.
* No adjustment for medication

Adjusted LDL-C

* Include both fasting and non-fasting measurements.
* If an individual is on lipid-lowering medication at the time of measurement, adjust their LDL-C value using the formula: LDLC\_adjusted = LDLC / 0.7.
  + Note that this analysis still includes LDL-C measurements without medication adjustment when the individual is not on lipid-lowering medication

**Remove statistical outliers**

This should be done after adjustment for medication (if applicable).

* Remove measurements that are outside +/- 6 SD from the overall mean lipid value in the total population, after applying all other exclusions

**Compute a single value per individual for inclusion in analysis**

After all exclusions are applied, the remaining measurements can be used to compute the final value for each individual for analysis.

HDL

* Select the HDL-C value at the earliest timepoint in the EHR.
* Use age at the same timepoint as HDL-C
* Use BMI at the same timepoint as HDL-C. If unavailable, use BMI at the closest timepoint to the HDL-C measurement.

TG

* Select the TG value at the earliest timepoint in the EHR.
* Use age at the same timepoint as TG
* Use BMI at the same timepoint as TG. If unavailable, use BMI at the closest timepoint to the TG measurement.

LDL-C

* Select the LDL-C value at the earliest timepoint in the EHR.
  1. If calculating LDL values, use the earliest timepoint that HDL-C and TG values are both available.
* Use age at the same timepoint as LDL-C
* Use BMI at the same timepoint as LDL-C. If unavailable, use BMI at the closest timepoint to the LDL-C measurement.

Adjusted LDL-C

* Select the LDL-C value at the earliest timepoint in the EHR.
  1. If calculating LDL values, use the earliest timepoint that HDL-C and TG values are both available.
* Use age at the same timepoint as LDL-C
* Use BMI at the same timepoint as LDL-C. If unavailable, use BMI at the closest timepoint to the LDL-C measurement.

**Flagged individuals**

Flagged individuals can still be included in analysis, but the number of participants with these conditions should be reported. Flags will be available for download on the algorithm page under the title Lipids\_flags.csv.

* Cushing's Syndrome
* Hypopituitarism
* Hypothyroidism
* Liver cirrhosis
* Nephrotic syndrome
* Polycystic Ovarian Syndrome (PCOS)
* Type 2 Diabetes