**CORTIS-01 Public dataset**

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# Overview and abstract

The **CORTIS (Correlate of Risk Targeted Intervention Study)** was a randomized, partially-blinded clinical trial conducted to test for diagnostic and prognostic performance of the RISK11 biomarker for TB disease and evaluate the efficacy of Isoniazid and Rifapentine (3HP) therapy to prevent pulmonary tuberculosis in high-risk individuals identified based off the RISK11 biomarker status. The attached “ADSL.csv” is a public, subject-level dataset for the CORTIS-01 study containing key variables necessary to reconstruct the diagnostic, prognostic and treatment efficacy aims. A data dictionary is provided below.

“CORTIS-01 Protocol Version 3.0.pdf” and “CORTIS-01 SAP Version 3.0.pdf” are the protocol and the statistical analysis plan for the study respectively and have been included for reference.

The following is quoted from the abstract of the published manuscript:

**Biomarker-guided tuberculosis preventive therapy (CORTIS): a randomised controlled trial**

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**Abstract**

**Background**

Targeted preventive therapy for individuals at highest risk of incident tuberculosis might impact the epidemic by interrupting transmission. We tested performance of a transcriptomic signature of tuberculosis (RISK11) and efficacy of signature-guided preventive therapy, in parallel, using a hybrid three-group study design.

**Methods**

Adult volunteers were recruited at five communities in South Africa. Whole blood was sampled for RISK11 qRT-PCR assay from eligible volunteers without HIV, recent prior tuberculosis, or co-morbidities at screening. RISK11+ participants were block-randomised (1:2) to once-weekly, directly-observed, open-label isoniazid and rifapentine for 12 weeks (RISK11+/3HP+), or no treatment (RISK11+/3HP-). A subset of eligible RISK11- volunteers were randomised to no treatment (RISK11-/3HP-). Diagnostic discrimination of prevalent tuberculosis was tested in all participants at baseline. Thereafter, prognostic discrimination of incident tuberculosis was tested in the untreated RISK11+ versus RISK11- groups, and treatment efficacy in the 3HP treated versus untreated RISK11+ groups, during active surveillance through 15 months. The primary endpoint was microbiologically-confirmed pulmonary tuberculosis. The primary outcome measures were risk ratio for tuberculosis of RISK11+ to RISK11-; and treatment efficacy.

**Findings**

20,207 volunteers were screened to enrol 2,923 participants, including RISK11+ participants randomized to 3HP (n=375) or no 3HP (n=764); and 1,784 RISK11- participants. Cumulative probability of prevalent or incident tuberculosis disease was 0.066 (95% CI 0.049-0.084) in RISK11+ (3HP-) participants and 0.018 (95% CI 0.011-0.025) in RISK11- participants [Risk Ratio 3.69 (95% CI 2.25-6.05)] over 15 months. Tuberculosis prevalence was 4.1% (47/1139) vs 0.78% (14/1984) in RISK11+ compared to RISK11- participants [Diagnostic Risk Ratio 5.13 (95%CI 2.93-9.43)]. Tuberculosis incidence over 15 months was 2.09 (95% CI 0.97-3.19) vs 0.80 (95%CI 0.30-1.30) per 100 person years (py) in RISK11+ (3HP-) compared to RISK11- participants [Cumulative Incidence Ratio 2.6 (95%CI 1.2-5.9)]. Serious adverse events related to 3HP included one hospitalization for seizures (unintentional isoniazid overdose) and one death of unknown cause (possibly temporally related). Tuberculosis incidence over 15 months was 1.94 (95%CI 0.35-3.50) vs 2.09 per 100 py (95%CI 0.97-3.19) in 3HP-treated compared to untreated RISK11+ participants [efficacy 7.0% (95%CI -145 to 65)].

**Interpretation**

The RISK11 signature discriminated between individuals with prevalent tuberculosis, or progression to incident tuberculosis, and those who remained healthy, but provision of 3HP to signature-positive individuals after exclusion of baseline disease did not reduce progression to tuberculosis over 15 months (*Clinicaltrials.gov ID: NCT02735590).*

**Funding**

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# Privacy of Information disclosed

While the Fred Hutchinson Cancer Research Center and by extension the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) is not a covered entity regarding HIPAA requirements, SCHARP uses the 'limited dataset' model as described in HIPAA when publishing public use datasets. This limited Dataset is used for public health and research purposes only. No personal identifying information is used in the Datasets, such as names or social security numbers. The Dataset uses its own unique identifiers that cannot identify the research participants (i.e., the Dataset identifiers are not participant IDs used in the research). SCHARP staff is trained on and sign an agreement to follow SCHARP's privacy and confidentiality policy.

These procedures comply with relevant models required in FDA regulations such as Title 21 CFR Parts 20, 21, 803, Title 45 CFR Part 164.514(e)(3)(i), and as recommended in Good Clinical Data Management Practices (GCDMP) defined by the Society of Data Quality Management.

# Subject-Level Dataset Data Dictionary with Example Values

| **Variable Name** | **Variable Description** | **Format** | **Example Values** |
| --- | --- | --- | --- |
| 1) pubid | Unique identification number for each subject in trial | char | 1. 100001, 2. 356282 … |
| 2) group | Indicator for Treatment/Observation group | char | 1. “RISK11+/3HP+”, 2. “RISK11+/3HP-”, 3. “RISK11-/3HP-”   4. NA |
| 3) itt | Binary indicator for ITT cohort | int | 1. 0, 2. 1 |
| 4) mitt\_osts | Binary Indicator for mITT.OSTS cohort (subjects in ITT cohort that were not Prevalent TB cases by the one or two-sample definition and had a follow-up time of >0) | int | 1. 0, 2. 1 |
| 5) mitt\_ts | Binary Indicator for mITT.TS cohort (subjects in ITT cohort that were not Prevalent TB cases by the two-sample definition and had a follow-up time of >0) | int | 1. 0, 2. 1 |
| 7) risk11\_score | RISK11 score | num | 1. 19.895, 2. 60.234, … |
| 6) risk11\_status | RISK11\_status is positive if RISK11 score is >60 | char | 1. “RISK11+”, 2. “RISK11-”, 3. “INDETERMINATE” |
| 8) xpert | Indicator for sample being positive via Xpert assay | int | 1. 0, 2. 2, 3. 5, … |
| 9) mgit | Indicator for sample being positive via MGIT assay | int | 1. 0, 2. 1, 3. 2, … |
| 10) endpoint\_definition | Indicator for endpoint being considered in two sample or one+two sample definition. | char | 1. “one+two sample”, 2. “two sample” |
| 11) tevent\_osts | Follow-up time (FUtime) for OSTS analysis (months) | num | 1. 12.72, 2. 14.13, … |
| 12) tevent\_ts | FUtime for TS analysis (months) | num | 1. 12.72, 2. 14.13, … |
| 14) endpoint\_osts | Binary Indicator for Endpoint for OSTS analysis | int | 1. 0, 2. 1 |
| 15) endpoint\_ts | Binary Indicator for Endpoint for TS analysis | int | 1. 0, 2. 1 |
| 16) prevalent\_endpoint\_osts | Binary Indicator for Prevalent TB case including one or two sample positive cases | int | 1. 0, 2. 1 |
| 17) prevalent\_endpoint\_ts | Binary Indicator for Prevalent TB case including only two sample positive cases | int | 1. 0, 2. 1 |
| 18) 3hp\_per\_protocol | Binary Indicator for subjects in RISK11+/3HP+ group that had treatment as per protocol | int | 1. 0, 2. 1 |
| 19) risk11\_weights | Weights based on RISK11 status (weights for RISK11+ and RISK11- subjects) to correct for RISK11+ enrichment in trial | num | 1. 0, 2. 1.2634, 3. 7.9198 |
| 20) group\_weights | Weights based on group assignment to correct for RISK11+ enrichment in trial | num | 1. 0, 2. 1.8835, 3. 3.8373 |
| 21) IGRAscore | IGRA score | num | 1. 0.02,  2. 4.62,  3. 9.41 |
| 22) IGRAstatus | IGRA status is positive if the max of IGRA score for tb1 and tb2 antigens is ≥ 0.35. | char | 1. IGRA+  2. IGRA- |
| 23) gender | Participant gender | char | 1. MALE  2. FEMALE |
| 24) age | Participant age | num | 1. 18,  2. 30.26,  3. 55 |
| 25) race | Participant race | char | 1. ASIAN,  2. BLACK,  3. CAUCASIAN,  4. MIXED RACE,  5. OTHER |
| 26) bmi | Body-mass index of participant | num | 1. 14.2,  2. 21.01,  3. 24.76 |
| 27) tb\_history | History of TB disease in participant | char | 1. YES  2. NO |
| 28) tb\_family\_history | Family history of TB disease | char | 1. YES  2. NO |
| 29) smoking\_history | History of smoking by participant | char | 1. YES  2. NO |
| 30) tbsymptoms\_at\_baseline | Any TB symptoms at baseline (at enrollment visit) | char | 1. POSITIVE  2. NEGATIVE |