# ACTG DATA REQUEST (DR)

# INSTRUCTIONS AND Proposal format

Proposal Format

**STUDY TITLE:**

**Descriptive title of the proposed research project.**

The HE2AT Center Research Project 2: Advancing Understanding of Heat-Health Interactions in Large African Cities and Developing Locally Relevant and Risk-Stratified Early Warning Systems

**VERSION NUMBER:**

**Indicate whether this is the original submission (version 1) or a revision (version 2, etc.).**

Version 1

**SUMMARY OF MAJOR REVISIONS:**

**If the proposal is a revision (version 2 or higher), include a brief narrative of the major changes from the prior version (e.g., new relevant studies, new or modified objectives, resources, etc.). Any new language in the subsequent sections should be in bold text to facilitate review by the ACTG.**

NA

**PROPOSING STUDY CHAIR, VICE CHAIR(S), INVESTIGATOR(S) AND INSTITUTION(S):**

**Identify at least one investigator to serve as study chair. Indicate if the study chair is an ACTG investigator or a non-ACTG investigator. A vice chair(s) may also be identified, if desired. Provide the name, title, institution, address, telephone number, and e-mail address of the proposing investigator(s).**

Study Chair: Prof. MF Chersich (a non-ACTG Investigator). Wits RHI, University of the Witwatersrand, South Africa. Address: Esselen Street Hillbrow, Johannesburg, 2000, South Africa. Phone: +27727521123. Email: [mchersich@wrhi.ac.za](mailto:mchersich@wrhi.ac.za)

Vice Chair: Prof. Lee Fairlie (ACTG Investigator). Wits RHI, University of the Witwatersrand, South Africa. Address: Esselen Street Hillbrow, Johannesburg, 2000, South Africa. Phone: +27727521123. Email: LFairlie@wrhi.ac.za

Investigators:

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**SDUA RESPONSIBLE PARTIES:**

**Identify the investigator(s) and/or statistician(s) who will complete the ACTG Specimen and/or Data Usage Agreement and receive the data.**

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**Coordinating SDAC MEMBER (this may be blank at initial submission):**

**SDAC will provide the name, telephone number, and e-mail address of an SDAC member who will coordinate provision of data for the approved DR, if one is not among the proposing team members.**

**STUDY RATIONALE:**

**Complete, concise discussion of the proposed research project, including sufficient background information (e.g., data, references) to support the scientific merits of the project.**

Global temperatures have already risen about 1.2°C, and the world is on track for an increase of 1.5°C within the next decades. People living in large and rapidly growing African cities face significant health risks from observed past and projected future temperature increases. Many such cities constitute ‘Urban Heat Islands’, where concrete or asphalt surfaces, for example, absorb and retain heat, and ‘cooling’ areas, such as parks are limited. Data and understanding on heat-health outcomes, exposure, vulnerability, and potential solutions in African urban contexts are a major public health priority. In particular, additional research is necessary to provide a detailed understand of patterns of heat impacts in groups such as HIV-infected adults, and to define temperature sensitivity thresholds for Early Warning Systems, according to the specific vulnerabilities in different populations, settings, and microclimates across a city.

Understanding heat-health linkages allows one to identify high-risk groups and settings, as well as to document the burden of heat-related conditions. Quantifying current heat burdens and projecting future burdens can inform resource prioritisation and allocation. Additionally, understanding patterns of heat impacts will inform development of personalised Early Warning Systems. These Warning Systems aim to capture unique geospatial and individualized heat risk patterns in order to warn individuals at high risk during periods of high temperatures, but also to assist key stakeholders, including the public, government, workplaces, and sporting organizations, in preparing for heat waves or brief periods of extreme heat.

The study forms part of the HEat and HEalth in Africa Transdisciplinary Center (HEAT Center; <https://heatcenter.wrhi.ac.za/>). The HEAT Center is one of the Research Hubs in the NIH DS-I Africa initiative (<https://dsi-africa.org>), which is a major 5-10 year initiative across Africa, aiming to maximise use of existing health data on the continent and to find actionable solutions to the most pressing health issues facing people on the continent, especially vulnerable populations.

**STUDY OBJECTIVE(S):**

**A clear and thorough description of all study objectives of the research project that will involve the use of existing data from one or more ACTG protocols, DACS, or NWCS.**

Overall, the study aims to analyze heat-health vulnerability and exposure in Johannesburg, South Africa. The objectives are as follows:

1. Map heat vulnerability and exposure across urban areas in African cities using a combination of health, socioeconomic, geospatial climate, and satellite imagery data.
2. Develop a heat-health outcome forecast model using statistical, machine learning, and deep learning techniques to predict the probability of adverse health outcomes at different temperature thresholds, stratified by geography and demographics.
3. Investigate the impact of socio-economics and demographics such as housing types and density, commuting distances, and working conditions on heat exposure and heat-health vulnerability.
4. Determine the most dangerous types of heat exposure for people living in different conditions in African cities, including night-time temperatures, daily maximums, extremes, or long-term accumulated heat burden.
5. Create an app-based Heat-Health Early Warning System to provide timely warnings to city planners, public health officials, and community leaders. The system will reflect the unique risk patterns identified through mapping and forecasting.

**STUDY DESIGN:**

**A clear and thorough explanation of study design and analysis methods such that the appropriateness of use of data from the ACTG protocol, DACS, or NWCS can be evaluated.**

In summary, the study involves applying data science techniques to document the impacts of heat exposure on health outcomes using geospatially and temporally linked data. We apply data science analyses to document the impact of heat-related health hazards in Johannesburg, South Africa. Identical research activities are taking place in Abidjan, Côte d'Ivoire, but are not part of this data request. The study has received approval from the Human Research Ethics Committee of the Faculty of Health Sciences, University of the Witwatersrand HREC approval reference number 220606: HEAT002).

We will draw on satellite image analysis, socio-economic data, and open mapping data. These geospatial data will be brought together with geo-located health data to identify the size and patterns of temperature impacts on health. Dates of health events are linked temporally with the prevailing weather and other environmental exposure on that date. Information of the geolocation of participants will be obtained directly from the site investigators. Depending on what information is available on geolocation, we will use the location of the research site where activities took place, or household addresses, if available, such as from patient tracking log books. We have several means of safeguarding and anonymizing household addresses and other potentially identifiable data, as detailed in our ethics application. These methods include jittering and aggregation to local level areas, such as wards.

The study analysis involves deploying a range of machine learning methods to construct an index of intra-urban socio-economic and environmental vulnerability factors (e.g. housing types, formal versus informal areas, green compared to built-up areas, population mobility, commuting conditions, and distance from health services).

In this paragraph we describe the analysis methods in more detail. Data analysis methods include natural language processing, geospatial analysis, and predictive analytics to identify individuals at high risk for heat-related conditions. The statistical components of the analysis include applying existing image processing techniques to satellite images, combining data from high-resolution climate models and meteorological station observations, superimposing health outcomes on vulnerability-hazard maps, and using traditional statistical and machine learning methods, including deep learning techniques, to develop heat-health outcome forecast models. The study will also evaluate the efficacy and accuracy of different machine learning techniques, such as recurrent neural networks (RNNs), long short-term memories (LSTMs), gated recurrent units (GRUs), Multi-Layer Perceptron (MLP), Bayesian Neural Networks (BNN), Radial Basis Functions (RBF), K-Nearest Neighbor regression (KNN), and Gaussian Processes (GRU), to build the best possible model for predicting the health effects of extreme heat.

The HE2AT Center will then utilize a vulnerability-heat-hazard model to provide operational heat health risk forecasts for daily and seasonal time frames, differentiated by susceptible populations as determined through demographics and specific geographic locations. The forecasts will trigger early warnings when certain risk thresholds are reached. The thresholds for when warnings are sent will be selected based on an analysis of heat health outcomes in this study, inputs from experts in the consortium, and external specialists in physiology and clinical medicine.

**RELEVANT ACTG PROTOCOL(S), DACS OR NWCS:**

**List of all ACTG protocols, DACS, and NWCS from which existing data are being requested, and a detailed description of the data required from each.**

Please note that we only require data from the Johannesburg study sites of the below listed studies. All study activities described above take place in Johannesburg only.

1. ACTG A5349 (NCT00864383/TBTC Study 31): Controlled Comparison of Two Moxifloxacin Containing Treatment Shortening Regimens in Pulmonary Tuberculosis and Rifapentine With and Without Moxifloxacin for Pulmonary Tuberculosis in People With Human Immunodeficiency Virus. We will request data on treatment outcomes, safety profiles, adherence rates, and interactions between antiretroviral therapy and tuberculosis treatment for the study participants.

2. ACTG A5271: International neurocognitive normative study: neurocognitive comparison data in diverse resource-limited settings. We will request data on neurocognitive performance across different antiretroviral regimens and diverse settings.

3. ACTG A5175 (PEARLS Trial): Psychosocial Predictors of Non-Adherence and Treatment Failure. We will request data on psychosocial factors that influence adherence to antiretroviral therapy and treatment outcomes in a multinational context.

4. ACTG A5221 (STRIDE Study): Relationship between weight, efavirenz exposure, and virologic suppression in HIV-infected patients on rifampin-based tuberculosis treatment. We will request data on the impact of weight and efavirenz exposure on virologic suppression rates in patients co-infected with HIV and tuberculosis.

5. ACTG A5199: Improved neuropsychological and neurological functioning across three antiretroviral regimens in diverse resource-limited settings. We will request data on the effects of different antiretroviral regimens on neuropsychological and neurological functioning in resource-limited settings.

6. ACTG A5208 (OCTANE Study): Nevirapine- versus lopinavir/ritonavir-based initial therapy for HIV-1 infection among women in Africa. We will request data on the comparative efficacy, safety, and tolerability of nevirapine and lopinavir/ritonavir-based initial therapy in African women with HIV-1 infection.

7. ACTG A5221 (NCT00108862): Timing of antiretroviral therapy for HIV-1 infection and tuberculosis. We will request data on the optimal timing of antiretroviral therapy initiation in the context of HIV-1 and tuberculosis co-infection.

8. ACTG A5073: Comparison of once-daily versus twice-daily combination antiretroviral therapy in treatment-naive patients and Modified directly observed antiretroviral therapy compared with self-administered therapy in treatment-naive HIV-1-infected patients. We will request data on the comparative efficacy, safety, and adherence rates of once-daily and twice-daily antiretroviral therapy, as well as modified directly observed antiretroviral therapy versus self-administered therapy in treatment-naive patients.

**POSTING OF GWAS DATA TO THE NIH DATABASE OF GENOTYPES AND PHENOTYPES, OR dbGaP:**

**Any DR involving ACTG genome-wide association studies (GWAS) data must contain a section addressing NIH Policy NOT-OD-07-088 and related policies, including a statement in the DR that ACTG GWAS will not be posted to dbGaP or a similar repository by the DR investigator. Posting will have been done by the ACTG or the investigator who generated the GWAS data with non-ACTG funding, if required and consistent with the signed informed consent forms under which the specimens were obtained.**

NA

**DATA FORMAT:**

**If the data are required in a specific format, then this should be described. The cost of providing data in formats other than already existing formats will need to be covered by the proposing investigator(s).**

For this study, we will accept the data formats already being used by the ACTG Network and pre-process the data ourselves. We understand that the standard data format used by the ACTG Network is the CDISC format, specifically the Study Data Tabulation Model (SDTM) and Analysis Data Model (ADaM), but we will work with the available data in their existing format. We have the necessary expertise and resources to preprocess the data to the format required for our analysis.

We have allocated funds to cover any costs incurred in data preparation or transfer.

**EXTERNAL SUPPORT/COLLABORATION/FUNDING:**

**Provide the source of funding for the Proposing Investigator and/or additional team members, as relevant, including any anticipated collaboration with and/or funding support from industry or other programs or institutes within the NIH. If required, send a request for a letter of support as per SOP ACTG-152, ACTG-Related Grant Applications and Letters of Support.**

This research was made possible by support from the Fogarty International Center, the National Institute of Environmental Health Sciences (NIEHS), and OD/Office of Strategic Coordination (OSC) of the National Institutes of Health, under Award Number U54TW012083. Although this study was supported by the NIH, the content and responsibility of the authors are not necessarily representative of the official views of the National Institutes of Health.

SIGNATURES:



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Proposing Investigator DATE

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ACTG CRS Leader DATE

(required only if the Proposing Investigator is

receiving funding from an ACTG CTU/CRS)