UNIVERSITY OF THE WITWATERSRAND
SCHOOL OF PUBLIC HEALTH

# Urban Heat and Health in Johannesburg: A Multidimensional Analysis of Vulnerability, Explanatory Modelling, and Predictive Outcomes

# Multidimensional Analysis of Urban Heat, Vulnerability and Health in Johannesburg, South Africa

*PhD Protocol*

***MAJOR REVISION:*** *Title shortened and methodology removed as recommended by assessors. The new title focuses on content rather than methods and includes the geographical specification "South Africa" to better differentiate this PhD from the overall HE²AT project scope.*

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## Table of Contents

# ABSTRACT

***Revision:*** *Abstract maintained from original submission with minor adjustments to emphasise the multidimensional approach and sequential design whilst preserving the core research vision and personal voice.*

This research proposal investigates the complex relationship between urban heat and health in Johannesburg, South Africa. As climate change drives increasing temperatures globally, urban populations face heightened health risks, with vulnerable communities disproportionately affected. The study employs a **multidimensional approach** through three primary aims: (1) mapping intra-urban heat vulnerability by integrating environmental, socio-economic, and health data; (2) ~~delineating heat-health dynamics through a two-stage explanatory modeling approach that combines hypothesis generation with targeted testing to uncover physiological pathways and temporal effects~~ **identifying the specific physiological pathways through which heat exposure translates into health impacts using advanced explanatory modelling approaches that examine heat-health interactions across multiple biological systems**; and (3) developing ~~a stratified predictive model~~ **predictive models that integrate vulnerability patterns with environmental exposures** informing heat-related health outcomes.

Drawing on clinical trial data, satellite imagery, climate records, and socio-economic surveys, this research will apply advanced statistical and machine learning techniques to create vulnerability maps, explain complex relationships, and generate predictive models. **My approach recognises that heat vulnerability is not simply about temperature—it is fundamentally about power, access, and historical patterns of urban development that continue to shape who lives and who dies during extreme heat events.** The findings aim to inform targeted public health interventions, urban planning decisions, and climate adaptation strategies to protect vulnerable populations from increasing heat exposure in Johannesburg and potentially other African urban centres.

**Keywords:** urban heat, health outcomes, vulnerability mapping, machine learning, **spatial analysis**, climate change, Johannesburg

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# ABBREVIATIONS AND KEY TERMS

**MAJOR ADDITION: A Comprehensive abbreviations list has been added as specifically requested by assessors. This was identified as a missing component in the original protocol and is essential for clarity, given the technical nature of the research.**

| Term/Abbreviation | Definition | Reference |
|---|---|---|
| **DLNM** | Distributed Lag Non-linear Models | (Gasparrini et al., 2010) |
| **GW-PCA** | Geographically Weighted Principal Component Analysis | (C. Zhao et al., 2018) |
| **HVI** | Heat Vulnerability Index | (Reid et al., 2009) |
| **LST** | Land Surface Temperature | (Wan et al., 2001) |
| **NDVI** | Normalised Difference Vegetation Index | (Tucker, 1979) |
| **UHI** | Urban Heat Island | (Oke, 1981) |
| **SHAP** | SHapley Additive exPlanations | (Lundberg & Lee, 2017) |
| **Heat Vulnerability** | The degree to which individuals or communities are susceptible to heat-related health impacts, determined by exposure, sensitivity, and adaptive capacity. In this research, vulnerability is understood as a socially constructed condition rather than an inherent characteristic. | (IPCC, 2022; Cutter et al., 2003) |
| **Adaptive Capacity** | The ability of individuals, communities, or systems to adjust to heat exposure through behavioural, technological, or institutional responses. This includes both individual agency and structural enablers/constraints. | (Smit & Wandel, 2006) |
| **Heat-Health Interactions** | The complex relationships between thermal exposure and physiological responses across multiple biological systems, mediated by individual characteristics and environmental factors. | (Kovats & Hajat, 2008) |
| **Thermal Inequality** | The unequal distribution of heat exposure and adaptive capacity across urban populations, shaped by historical development patterns and ongoing socio-economic processes. This framework extends spatial justice and environmental inequality scholarship by operationalizing explicit connections between | (Mitchell & Chakraborty, 2018) |

| | | |
|---|---|---|
| | historical spatial development and contemporary heat vulnerability through three integrated analytical dimensions. | |

# 1. INTRODUCTION AND BACKGROUND

## 1.1 Problem Statement

**MAJOR ADDITION: Explicit problem statement section added as specifically requested by assessors. This was identified as missing from the original protocol and is essential for establishing the research rationale.**

Johannesburg faces an urgent and escalating threat from urban heat exposure that demands immediate scientific attention. Climate change is driving unprecedented temperature increases across South Africa, with projections indicating rapidly rising heat extremes that will disproportionately affect the country's urban populations (Engelbrecht et al., 2015; Romanello et al., 2023). Continental-scale analyses project that up to 2 billion urban Africans will be exposed to extreme heat events by 2100, with South African cities among the most vulnerable(Fotso-Nguemo et al., 2023). Yet our understanding of this threat remains fragmented and insufficient for effective intervention, particularly in African urban contexts where the intersection of climate change, historical spatial inequality, and complex disease burdens creates unique challenges for public health protection (Scovronick et al., 2018; Wright et al., 2021).

The problem is multifaceted and deeply rooted in the city's spatial legacy. First, we lack comprehensive knowledge of how heat vulnerability is distributed across Johannesburg's diverse socio-economic landscape. Existing studies provide city-wide averages that mask critical intra-urban variation, leaving policymakers blind to where interventions are most urgently needed (Souverijns et al., 2022; Parker et al., 2025). Recent high-resolution analysis has demonstrated that heat stress clusters in areas with high building density and low vegetation, often coinciding with lower socioeconomic areas; yet, spatially explicit vulnerability mapping remains limited (Souverijns et al., 2022). Second, whilst we know that heat exposure affects health through multiple pathways including cardiovascular strain, kidney dysfunction, and inflammatory responses (Liu et al., 2022; Zhang et al., 2024; Mohyuddin et al., 2021), the specific physiological pathways through which this occurs in African urban populations—particularly those with high burdens of HIV, tuberculosis, diabetes, and hypertension—remain poorly understood(Khine & Langkulsen, 2023; Manyuchi et al., 2022)

Third, current approaches to heat-health planning are reactive rather than predictive, responding to crises after they occur rather than anticipating and preventing them. Early warning systems remain underdeveloped for African contexts, with most applications focusing on temperate climates with different vulnerability profiles (Kapwata et al., 2022). The few existing heat-health studies in South Africa demonstrate significant mortality increases with temperature rises—with evidence of 1% mortality increase per 1°C temperature rise in South African cities, including Johannesburg—but lack the predictive capacity needed for effective early intervention (Scovronick et al., 2018; Wichmann, 2017).

This research problem is urgent because of Johannesburg's unique vulnerabilities. Its high altitude creates distinctive thermal dynamics that differ from coastal urban heat patterns (Naicker et al., 2017); its apartheid legacy has produced extreme spatial inequality in heat exposure and adaptive capacity, with informal settlements experiencing disproportionate heat impacts (Strauss, 2019; Ansah et al., 2024); and its rapidly changing urban form creates new thermal hot spots faster than our understanding can keep pace (Simwanda et al., 2019). The city's residents face a dual burden of infectious and non-communicable diseases, which may exacerbate heat vulnerability by compromising their adaptive capacity (Khine & Langkulsen, 2023; Wright et al., 2019). Without comprehensive, predictive knowledge of heat vulnerability patterns and health pathways, the city remains dangerously unprepared for the intensifying heat impacts that climate science tells us are inevitable (IPCC, 2022;Romanello et al., 2023).

### 1.2 Research Context and PhD Positioning

**MAJOR REVISION: Extensive rewrite to clearly distinguish PhD contributions from broader HE²AT project as specifically requested by assessors. This addresses their primary concern about delineating the PhD scope from the overall project work.**

This PhD research represents a distinct and independent scholarly contribution, situated within the broader HE²AT Centre initiative while maintaining complete methodological and intellectual autonomy. The HE²AT Center primarily examines maternal and child health outcomes during heat exposure, with a focus on the health impacts related to pregnancy and pediatric responses to heat. My PhD, by contrast, investigates adult populations (18 years and older) across multiple health conditions, examining heat vulnerability patterns and predictive modelling for general populations. This creates complementary rather than overlapping knowledge, using this PhD focus to fill critical gaps in understanding adult heat-health relationships that the broader project does not address.

My research makes several original methodological contributions that distinguish it from the broader HE²AT work. I am conducting the first application of geographically weighted vulnerability assessment methods in South African urban contexts, developing a novel integration of spatial analysis, heat health interaction analysis, and predictive modelling in a sequential framework explicitly designed for cities with extreme socio-spatial inequality. Additionally, I am working on extending theory through a 'spatial-temporal heat vulnerability' framework that advances environmental inequality scholarship as an analytical concept, explicitly linking heat vulnerability to historical development patterns. This theoretical contribution extends beyond the scope of the HE²AT Centre.

While I am not conducting primary data collection or basic harmonisation as part of this PhD, I am responsible for all analytical work, including statistical analysis decisions, method choice, model specifications, and validation approaches. All model development, validation, and methodological innovations represent original PhD work. My research focuses on adult populations with diverse health conditions, with a particular emphasis on multi-system health responses, including cardiovascular, renal, and inflammatory pathways. This creates comprehensive heat-health knowledge when combined with the HE²AT Centre's focus on maternal and child health.

My theoretical framework integrates three analytical lenses—infrastructural justice, climate resilience, and health equity—to examine heat vulnerability through both historical and contemporary perspectives. This **Spatial-Temporal Heat Vulnerability Framework** advances existing environmental inequality scholarship by operationalising the explicit connections between historical spatial development patterns and contemporary heat exposure through empiricallygrounded mediating pathways. This methodological contribution distinguishes this PhD from other work within the HE²AT Centre.

### 1.3 Climate Change and Heat-Health Impacts in the Johannesburg Context

***Minor revision:*** *Enhanced with more recent evidence and local context to strengthen the foundation for the research, whilst maintaining the original structure and flow.*

Climate change has intensified heat-related health risks in Johannesburg, where rising temperatures are associated with increased mortality and morbidity (Green et al., 2019; Romanello et al., 2023). With over 5.9 million inhabitants, the city faces substantial warming projections. By 2050, mean temperatures are projected to rise approximately 2°C, with hot nights expected to quadruple (Engelbrecht et al., 2015; World Bank Cities Support Program, 2024). Recent epidemiological evidence demonstrates the severity of this threat: above 18.7°C apparent temperature, all-cause mortality increases by 0.9% per 1°C rise, with seniors experiencing a 2.1% increase (Wichmann, 2017).

The last five years have seen a marked acceleration in heat-related mortality across global cities, with (Zhao et al., 2021) documenting a 68% increase in heat-attributable deaths in urban areas since 2018. For Sub-Saharan African cities specifically, Scovronick et al. found mortality impacts are found to be 2-3 times higher than global averages, due to the limited availability of adaptive infrastructure. The IPCC warns that beyond a 2 °C increase in global warming, heat-attributable health impacts in Africa are expected to rise, with urban populations facing disproportionate risks sharply (Intergovernmental Panel on Climate Change, 2024).

### 1.4 Socio-Spatial Inequity and Heat Vulnerability

Johannesburg's socio-spatial layout—largely a legacy of apartheid-era planning—significantly shapes contemporary heat vulnerability patterns (P. Chen, 2024; Nyangule, 2024). Historical policies created wealthy suburbs with green spaces alongside dense townships with minimal vegetation, resulting in temperature differentials of approximately 6°C between affluent neighbourhoods and informal settlements (World Bank Cities Support Program, 2024). Housing quality further exacerbates this disparity, with informal dwellings experiencing indoor temperatures up to 15°C higher than those in formal housing (Naicker et al., 2017). This embedded vulnerability continues to cluster heat-health risks in historically marginalised communities (Strauss, 2019).

The spatial patterns of vulnerability are not random but reflect deliberate planning decisions made during the apartheid era that continue to influence contemporary heat exposure(Knox et al., 2017; Nyangule, 2024). Wealthy Johannesburg areas, such as Sandton, benefit from mature tree canopies and green spaces established in the 1960s, alongside thermally efficient building designs, which reduce heat exposure (Li et al., 2022; Venter et al., 2020). Conversely, townships and informal settlements, like Soweto, face intensified urban heat islands due to dense construction, heat-retaining materials, and limited cooling infrastructure (Souverijns et al., 2022). Apartheid-era infrastructure and investment patterns perpetuate these spatial inequalities, shaping contemporary thermal environments and exacerbating heat vulnerability (Burbidge et al., 2022).

To analyse these complex relationships, this research employs an extended analytical framework termed 'spatial-temporal heat vulnerability,' which builds upon established environmental justice and spatial inequality theory (Figure 1). This framework operationalises these patterns through three analytical lenses, explicitly connecting contemporary vulnerability to historical spatial development decisions.

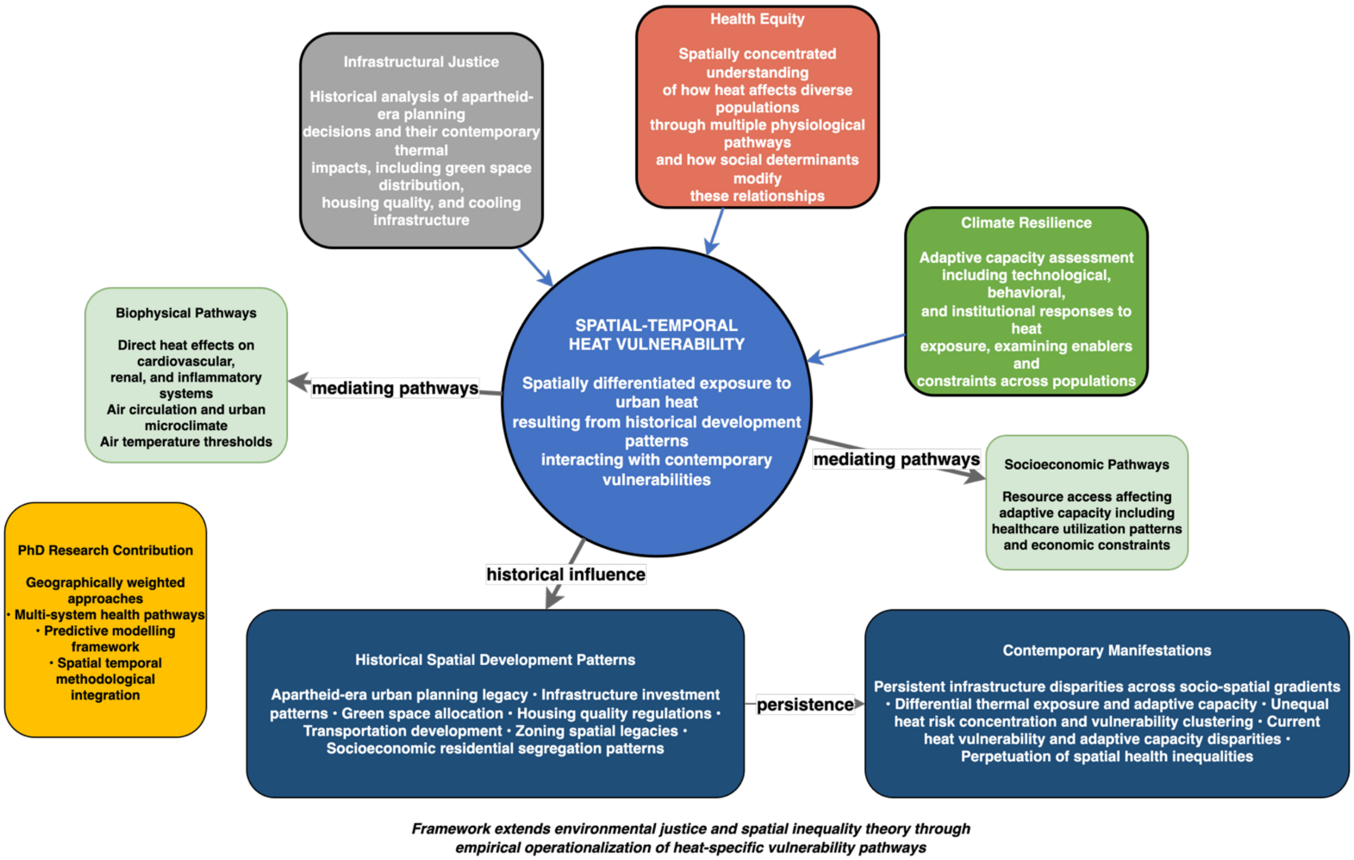


*Figure 1: Extended analytical framework operationalising urban heat vulnerability through three integrated lenses, advancing spatial justice theory through empirical application to heat-specific contexts.*

## 1.5 Literature Review

**MAJOR ADDITION: Complete literature review section added as explicitly requested by assessors. This section is organised by study objectives to provide a clear foundation for each research phase and addresses the assessor's concern about the absence of a distinct literature review.**

### Urban Heat Vulnerability and Mapping Methods (Objective 1 Foundation)

Urban heat vulnerability assessment has evolved dramatically over the past two decades, moving from simple temperature-based indices to sophisticated multi-dimensional frameworks that recognise vulnerability as a complex social-environmental phenomenon. Early vulnerability assessments primarily focused on exposure metrics, including land surface temperature, air temperature, and heat index calculations (Harris et al., 2011;Harlan et al., 2006; Cutter et al., 2003; Conlon et al., 2020). Whilst these provided essential baseline understanding, they suffered from what I term the "temperature fallacy"—the assumption that heat exposure alone determines vulnerability. This approach failed to capture the social dimensions that determine who suffers during heat events.

The recognition that vulnerability results from the interaction of exposure, sensitivity, and adaptive capacity marked a crucial theoretical advance (Reid et al., 2009; Wilhelmi & Hayden, 2010; Niu et al., 2021; Li et al., 2022). This framework, adapted from broader climate change vulnerability assessments, provides the conceptual foundation for contemporary approaches to assessing climate change vulnerability. However, most applications have relied on global statistical methods that assume spatial stationarity—a problematic assumption for cities like Johannesburg, which have extreme socio-spatial inequality.

Recent methodological advances include geographically weighted approaches that allow vulnerability relationships to vary spatially (Harris et al., 2011; Fotheringham et al., 2002; Fotheringham et al., 2017; Zhao et al., 2018; Oshan et al., 2019; Luo & Peng, 2016). These methods recognise that the same variables may have different importance in different locations, accounting for spatial heterogeneity in vulnerability patterns. However, applications in African urban contexts remain extremely limited, with Tsiko, 2016 representing one of the few studies to demonstrate the potential of locally weighted methods for capturing spatial variation in vulnerability relationships.

**Heat-Health Interactions and Pathways (Objective 2 Foundation)**

Understanding how heat exposure translates into health impacts requires examining physiological pathways across multiple biological systems. The evidence base has grown substantially but remains heavily biased toward populations in high-income countries, which have different baseline health profiles than those found in African urban contexts.

Heat exposure triggers well-documented cardiovascular responses, including increased heart rate, altered blood pressure regulation, and changes in blood viscosity (Bouchama & Knochel, 2002; Kovats & Hajat, 2008; Liu et al., 2022; Meade et al., 2024; Barry et al., 2024). During heat exposure, the cardiovascular system faces the challenge of balancing competing demands for blood flow to the skin for cooling and to vital organs for function. In individuals with pre-existing cardiovascular conditions—highly prevalent in Johannesburg due to the dual burden of infectious and non-communicable diseases—this balance becomes precarious (Kazi et al., 2024; Zhu et al., 2024).

Heat stress affects kidney function through multiple mechanisms, including increased risk of dehydration, electrolyte imbalances, and direct thermal stress on renal tissues (Roncal-Jimenez et al., 2015; 2025; Zhang et al., 2024). Emerging evidence suggests that chronic heat exposure may contribute to chronic kidney disease progression, particularly relevant for populations with existing renal impairment from conditions like diabetes and hypertension, both highly prevalent in Johannesburg.

Recent research has identified inflammatory pathways as key mediators of the relationship between heat and health. Heat exposure increases the production of pro-inflammatory cytokines and oxidative stress markers (Lim et al., 2015; Mohyuddin et al., 2021; Lim, 2018). This is particularly concerning for populations with chronic inflammatory conditions, which are prevalent in Johannesburg due to high rates of HIV, tuberculosis, and metabolic diseases.

**Predictive Modelling for Heat-Health Outcomes (Objective 3 Foundation)**

Predictive modelling for heat-health outcomes has evolved from simple statistical relationships to sophisticated machine learning applications. However, most existing models focus on mortality prediction in temperate climates, with limited applications in African urban contexts where data availability and quality present unique challenges.

Early heat-health warning systems relied on simple temperature thresholds based on historical temperature-mortality relationships (Hajat et al., 2010; Kapwata et al., 2022; Lowe et al., 2016). Whilst these provided basic early warning capabilities, they suffered from several limitations: a focus on mortality rather than morbidity, the use of city-wide thresholds that ignore spatial variation, and limited consideration of vulnerability factors that modify heat-health relationships (Wu et al., 2020).

Recent advances have incorporated machine learning methods to capture complex non-linear relationships between environmental exposures and health outcomes (Basu et al., 2018; Shafiq et al., 2025; Hirano et al., 2021; Wang et al., 2019). Ensemble methods show particular promise for balancing predictive accuracy with uncertainty quantification (Li et al., 2023; Jacques-Dumas et al., 2022). However, most applications focus on well-resourced health systems with comprehensive health surveillance, conditions that do not exist in most African urban contexts.

Operational early warning systems have demonstrated the potential for transforming weather forecasts into health forecasts (Issa et al., 2021), with evolving threshold methodologies showing promise for seasonal adaptation and extended warning periods in diverse climatic contexts.

**Research Gaps and Study Justification**

This literature review reveals three critical research gaps that my PhD directly addresses. First, no previous research has applied geographically weighted vulnerability assessment methods to South African urban contexts, despite the extreme spatial inequality that makes such methods essential. Second, there is a limited understanding of physiological pathways in African urban populations, which have distinctive disease burdens and environmental exposures. Third, there is a lack of spatially explicit predictive models that integrate vulnerability factors with ecological exposures in African urban contexts. Addressing these gaps is essential for protecting vulnerable populations in rapidly warming African cities.

## 1.6 Recent Evidence and Research Gaps

Recent studies have strengthened our understanding of the relationships between heat and mortality in African urban contexts. Parker et al. (2025) demonstrated that in Johannesburg, heat vulnerability clusters in historically disadvantaged areas, with environmental exposure accounting for 31.5% of the variance. The Lancet Countdown (Romanello et al., 2023) reports escalating impacts, with an estimated 5 million people globally dying annually from suboptimal temperatures. Studies across African cities demonstrate significant spatial inequalities in heat exposure, with informal settlements experiencing disproportionate impacts (Simwanda et al., 2019; Li et al., 2021; Pasquini et al., 2020; Garuma, 2023).

Continental-scale projections estimate that up to 2 billion urban Africans will be exposed to extreme heat events by 2100 (Marcotullio et al., 2021; Fotso-Nguemo et al., 2023), with Johannesburg-specific research documenting meter-scale heat vulnerability patterns that are strongly correlated with socioeconomic factors. Despite this growing evidence, significant research gaps persist in African urban contexts, including: (1) scarcity of region-specific studies; (2) siloed disciplinary approaches failing to capture multifaceted heat-health relationships; and (3) limited recognition of unique urban challenges stemming from historical development patterns and disease profiles (Ansah et al., 2024; Buyana, 2020; Kareem et al., 2020; Khine & Langkulsen, 2023). Johannesburg exemplifies these challenges through its urban disparities and accelerated warming projections (Engelbrecht et al., 2015; Scovronick et al., 2018; Vogel et al., 2021).

The evidence base indicates that heat vulnerability is not uniformly distributed across urban populations, but rather clusters in predictable patterns that mirror broader social and economic inequalities. This clustering effect means that interventions designed for average populations may miss the most vulnerable groups. At the same time, universal approaches may be inefficient in addressing the specific needs of high-risk areas. Understanding these patterns requires sophisticated analytical techniques that can capture spatial heterogeneity whilst accounting for the complex interactions between environmental exposures, social conditions, and health outcomes.

## 2. AIMS AND OBJECTIVES

**MAJOR REVISION: Complete restructuring of aims and objectives as specifically requested by assessors. The primary aim has been expanded to cover all objectives, including vulnerability assessment. All objectives have been reframed as clear purpose statements, rather than method-focused descriptions, with each including a setting, timeframes, and specific outcomes.**

### 2.1 Primary Aim

To comprehensively analyse spatial patterns of heat vulnerability, physiological pathways of heat-health interactions, and predictive relationships between environmental exposures and health outcomes in Johannesburg (2000-2022), providing evidence-based insights for targeted public health interventions and climate adaptation strategies that address spatial-temporal heat vulnerability in the city.

### 2.2 Three Interconnected Objectives

**Objective 1:** To map and analyse spatial patterns of heat vulnerability across Johannesburg (2000–2022), integrating environmental exposure, socio-economic sensitivity, and adaptive capacity indicators using geographically weighted methods to identify priority areas for targeted interventions and characterise intra-urban inequality in heat vulnerability.

**Objective 2:** Quantify the cardiovascular, renal, and inflammatory pathways mediating urban heat exposure's impact on health outcomes in Johannesburg's adult population (2000–2022), focusing on heat-sensitive biomarkers and effect modification by socio-economic factors across demographic groups.

**Objective 3:** Develop and validate neighbourhood-level predictive models for heat-related health risks in Johannesburg, using data from 2000 to 2022 for training and 2023 to 2024 for testing, to enable 1–to 3–day risk forecasts for public health early warning systems.

### 2.3 Integration Across Objectives

***Addition:*** *Explicit description of how objectives relate to each other, as requested by assessors, to clarify the sequential nature of the research design.*

The three objectives form an integrated framework addressing the spatial, physiological, temporal, and policy dimensions of heat vulnerability in Johannesburg. The sequential design builds knowledge progressively: Objective 1's vulnerability patterns guide population and area selection for Objective 2's pathway analysis, which informs feature selection and model architecture for Objective 3's predictive modelling. Spatial methods from Objective 1 are incorporated into Objectives 2 and 3, while iterative refinement allows later findings to enhance earlier analyses, creating a cohesive framework for evidence-based interventions (Trisos et al., 2022).

## 3. STUDY DESIGN

**MAJOR REVISION: Complete rewrite of study design section as specifically requested by assessors. Changed from listing "Quantitative" as design to specifying multi-method sequential design with clear description of phase relationships. This addresses the assessor concern that "Quantitative is a methodology, not a design."**

### 3.1 Overall Study Design

~~This study employs a quantitative research design focusing on computational and statistical approaches across three primary phases.~~

This research employs a multi-method sequential design combining spatial analysis, heat-health interaction inference, and predictive modelling across three phases. This approach addresses the multidimensional nature of urban heat vulnerability, advancing knowledge from vulnerability mapping to physiological explanations and predictive solutions.

### 3.2 Design Rationale and Phase Structure

***Addition:*** *Detailed description of how the three phases relate to each other as requested by assessors to clarify the sequential nature and internal design logic.*

**Phase 1: Descriptive Spatial Analysis (Months 1-9):** This phase employs cross-sectional spatial analysis using geographically weighted methods to establish a comprehensive baseline understanding of vulnerability patterns across Johannesburg. The design approach recognises that vulnerability relationships are not spatially stationary, requiring locally weighted statistical methods to capture spatial heterogeneity. Key methods include Geographically Weighted

Principal Component Analysis, spatial autocorrelation analysis, and vulnerability index construction, with outputs including spatial vulnerability maps, identification of priority areas, and quantification of inequality.

**Phase 2: Explanatory Heat Health Interaction Analysis (Months 10-18):** This phase uses longitudinal analysis with heat health interaction analysis methods to understand physiological pathways and mechanisms underlying observed vulnerability patterns. The design approach combines hypothesis generation through machine learning with targeted hypothesis testing using heat health interaction analysis methods. Key methods include distributed lag non-linear models, machine learning, and mediation analysis, with outputs including pathway diagrams, effect quantification, and mechanism identification.

**Phase 3: Predictive Model Development (Months 19-30):** This phase employs prospective validation using ensemble machine learning to create operational tools for heat-health risk prediction. The design approach integrates insights from previous phases into predictive frameworks that can forecast health risks under varying environmental conditions. Key methods include ensemble modelling, temporal cross-validation, and uncertainty quantification, with outputs including validated prediction models, risk thresholds, and early warning capabilities.

### 3.3 Design Strengths and Limitations

**Strengths:** The sequential design enables progressive knowledge building from description to prediction, integrates spatial, temporal, and heat health interaction perspectives in a coherent framework, and maintains practical relevance through focus on actionable outputs at each stage. The multi-method approach allows each phase to use the most appropriate methods for its specific research questions, whilst maintaining overall coherence.

**Limitations:** Sequential dependencies mean that delays in early phases affect later phases, requiring careful project management and built-in flexibility. Reliance on observational data limits causal inference, even with the use of advanced analytical methods, and necessitates cautious interpretation of the results. Spatial aggregation may mask critical micro-scale processes, necessitating the use of sensitivity analyses at multiple spatial scales.

## 4. METHODOLOGY

### 4.1 Multi-Cohort Data Harmonisation

***Enhanced description:*** *More detailed explanation of data sources and harmonisation process to address assessor questions about data adequacy for answering research questions.*

The research will integrate and harmonise datasets from ten previously conducted studies in Johannesburg as part of the HE²AT Centre initiative. This harmonisation process involves standardising variable definitions across cohorts, aligning outcome measures for metabolic, renal, and inflammatory physiological systems, cross-validating measurement techniques, assessing data quality, and developing a unified database structure that preserves spatial and temporal dimensions. This approach enables the investigation of heat-health relationships across multiple physiological systems while maximising statistical power and demographic representation.

**Primary Health Data Source:** Harmonised clinical data from 10 prospective cohort studies conducted in Johannesburg health facilities (2000-2022), comprising approximately 12,000 adult participants (age 18+ years) with 22-year temporal coverage, allowing examination of both long-term trends and acute responses to heat exposure.

**Key Health Variables:** Cardiovascular parameters include systolic and diastolic blood pressure, heart rate, heart rate variability, and electrocardiogram abnormalities. Renal function measures include serum creatinine, estimated glomerular filtration rate, electrolyte balance (sodium, potassium), and urinalysis results. Inflammatory markers include C-reactive protein, erythrocyte sedimentation rate, white blood cell count, and available cytokine measurements. Metabolic indicators include blood glucose, lipid profiles, body mass index, and waist circumference. Clinical outcomes include hospitalisation episodes, emergency department visits, medication changes, and documented heat-related symptoms.

**Population Characteristics:** The cohort represents demographic diversity representative of Johannesburg's racial, ethnic, and age distribution. The socio-economic range spans the income spectrum, with an overrepresentation of middle- and lower-income groups, typical of users of the public health system. Disease burden reflects high prevalence of HIV, tuberculosis, diabetes, and hypertension characteristic of South African urban disease patterns. Geographic distribution includes participants from across the Johannesburg metropolitan area(MacLeod et al., 2022).

### 4.2 Environmental and Climate Data

**Satellite-Derived Environmental Data**: Landsat 8 thermal infrared data (2013–2022) provide land surface temperature measurements for day and night at 30-meter spatial resolution with a 16-day repeat cycle, enabling seasonal analysis (USGS and NASA, 2025). Sentinel-2 multispectral data (2015–2022) offer vegetation indices (NDVI, EVI) and built-up area identification at 10-meter resolution for detailed urban analysis (Drusch et al., 2012).

**Climate Reanalysis Data**: ERA5 reanalysis data (2000–2022) provide hourly air temperature at 2 meters, relative humidity, wind speed, solar radiation, and precipitation at 0.25° resolution (~25 km) (Hersbach et al., 2020). South African Weather Service (SAWS) stations provide quality-controlled daily and hourly ground-based temperature and humidity measurements from multiple Johannesburg stations for spatial validation (South African Weather Service, 2023).

**Socioeconomic and Demographic Data**: Gauteng City-Region Observatory (GCRO) Quality of Life Surveys (2011, 2013, 2015/16, 2017/18, 2020/21) offer ward-level data on housing quality (structure type, overcrowding, amenities), infrastructure access (electricity, water, sanitation), healthcare utilization, income, employment, and social cohesion (Gauteng City-Region Observatory, 2021). South African Census data (2001, 2011, 2022) provide population density, demographic composition, educational attainment, employment, housing characteristics, tenure, and migration patterns (Statistics South Africa, 2022).

### 4.3 Data Adequacy Assessment

**MAJOR ADDITION: Comprehensive data adequacy assessment added as specifically requested by assessors to address concerns about whether available data can answer the research questions. This section includes detailed mitigation strategies for identified limitations.**

**Data Strengths Supporting Research Objectives:** The 22-year data span allows examination of both long-term trends and acute responses to heat exposure, providing sufficient temporal depth for robust analysis. The large sample size of approximately 12,000 participants with diverse socio-economic and health characteristics provides adequate statistical power for subgroup analyses. Complete spatial coverage across the entire Johannesburg metropolitan area ensures representativeness and enables comprehensive vulnerability assessment. The combination of health, environmental, and social data from multiple domains enables the integrated analysis required for this research.

**Potential Data Limitations and Mitigation Strategies:** Several potential limitations have been identified with corresponding mitigation strategies to ensure research objectives can be achieved.

**Temporal Coverage Gaps:** Some datasets have limited temporal overlap, particularly in earlier years when some data collection systems were not yet established. This limitation is mitigated through multiple imputation methods for missing data, sensitivity analyses comparing different periods, and a focus on periods with complete data coverage. If temporal gaps prove problematic for achieving research objectives, the study will focus on the 2015-2022 period, which has the most complete data coverage across all domains.

**Spatial Resolution Mismatches:** Socio-economic data available at the ward level may mask important intra-ward variation, particularly in areas with mixed income levels. This limitation is addressed through sub-ward analysis using satellite-derived proxies where possible, heterogeneity assessment within administrative units, and mixed-effects models that account for within-ward variation. If spatial resolution proves inadequate for detailed analysis, the research will be supplemented with targeted analysis of high-contrast areas where vulnerability patterns are most pronounced.

**Health Outcome Specificity:** The limited availability of data on explicitly heat-related health outcomes necessitates a focus on heat-sensitive biomarkers and conditions. This limitation is addressed by focusing on heat-sensitive biomarkers and conditions with established heat relationships documented in the literature, utilising validated heat-health indicators from international research, and examining physiological pathways known to be affected by heat exposure. If heat-specific outcomes prove insufficient for robust analysis, the research will be expanded to include heat-sensitive chronic conditions, such as cardiovascular and renal diseases.

**COVID-19 Impact on 2020-2022 Data:** The pandemic may have altered healthcare utilisation patterns and health outcomes, potentially confounding heat-health relationships. This limitation is addressed through stratified analysis by pandemic periods, adjustment for healthcare disruptions using available health system data, and incorporation of COVID-19 case data as a confounding variable in models. If pandemic effects prove too disruptive for reliable analysis, the primary analysis will focus on 2000-2019 data with the pandemic period treated as a sensitivity analysis.

### 4.4 Research Methods by Objective

***Enhanced methodology:*** *More detailed descriptions of analytical approaches for each objective as requested by assessors, with emphasis on novel methodological contributions.*

**Methods for Objective 1: To comprehensively analyse spatial heat vulnerability patterns, physiological pathways of heat-health interactions, and predictive relationships between environmental exposures and health outcomes in Johannesburg (2000–2022), providing evidence-based insights for targeted public health interventions and climate adaptation strategies addressing spatial-temporal vulnerability.**

Geospatial data will undergo preprocessing, including normalisation, completeness assessments, and spatial harmonisation. A key innovation is the application of Geographically Weighted Principal Component Analysis (GWPCA) to account for spatially heterogeneous relationships between vulnerability indicators, particularly relevant to Johannesburg's socio-spatial fragmentation (Harris et al., 2011). This involves selecting indicators across exposure, sensitivity, and adaptive capacity domains, optimising spatial bandwidth via cross-validation, extracting local components that vary spatially, constructing location-specific vulnerability indices, and comparing global versus local statistical approaches. Implementation utilises the GWmodel package in R (Gollini et al., 2015), resulting in a Heat Vulnerability Index that captures spatial non-stationarity in urban contexts—a novel extension to African cities characterised by extreme inequality.

**Methods for Objective 2: Quantify the cardiovascular, renal, and inflammatory pathways mediating urban heat exposure's impact on health outcomes in Johannesburg's adult population (2000–2022), focusing on heat-sensitive biomarkers and effect modification by socio-economic factors across demographic groups.**

Using harmonised multi-cohort data, a two-stage framework explores heat-health pathways. Stage 1 generates hypotheses through exploratory machine learning using Random Forest (Breiman, 2001) and XGBoost (T. Chen & Guestrin, 2016) to identify patterns. It employs SHAP (Lundberg & Lee, 2017) and LIME (Ribeiro et al., 2016) to enhance the interpretability of variables, interactions, and temporal lags. Stage 2 tests hypotheses through double machine learning (Chernozhukov et al., 2018) and causal forests (Wager & Athey, 2018) to quantify impacts, mediation analysis to dissect direct/indirect pathways, and effect modification to assess socio-economic influences. In collaboration with clinical experts, validated physiological pathway diagrams will represent mechanisms, a novel integration of computational and domain expertise for African heat-health contexts.

**Methods for Objective 3: Develop and validate neighbourhood-level predictive models for heat-related health risks in Johannesburg, using data from 2000 to 2022 for training and 2023 to 2024 for testing, to enable 1–to 3–day risk forecasts for public health early warning systems.**

An ensemble approach integrates the findings of prior objectives, featuring gradient boosting via XGBoost (T. Chen & Guestrin, 2016) for non-linear relationships, random forest (Breiman, 2001) for robustness, neural networks for pattern recognition, and linear models with spatial terms for interpretability. Stacking with a meta-learner (Wolpert, 1992) combines predictions, incorporating spatial weighting based on local performance. Uncertainty is quantified using quantile regression (Koenker & Bassett, 1978) and conformal prediction (Vovk et al., 2005)for intervals. Validation employs forward-chaining cross-validation with 5-year rolling windows, 1–3 day forecasts, walk-forward simulation, and recalibration—innovatively tailoring these to Johannesburg's data constraints for real-time public health forecasting.

### 4.5 Sample Size and Statistical Power

***Enhanced justification:*** *More detailed sample size justification addressing assessor questions about data adequacy for achieving research objectives.*

**Objective 1 (Vulnerability Mapping):** Complete coverage of 135 wards provides sufficient spatial resolution for vulnerability assessment whilst maintaining adequate population sizes for stable estimates (Statistics South Africa, 2022). Ward-level analysis supports the use of geographically weighted methods (e.g., GWPCA) to detect spatial patterns with high statistical reliability (Harris et al., 2011).

**Objective 2 (Pathway Analysis):** Approximately 12,000 participants substantially exceeds requirements for detecting clinically meaningful effects in heat-health relationships. Power calculations indicate greater than 90% power to detect effect sizes of 0.3 standard deviations, well within the range of clinically significant heat-health relationships reported in the literature (Cohen, 1988). The sample size also enables robust subgroup analyses across different demographic and socio-economic categories.

**Objective 3 (Predictive Modelling):** The sample size exceeds the recommended 10-20 observations per predictor variable by a substantial margin, enabling the development of complex models with adequate validation samples. The temporal depth of the data enables robust cross-validation procedures that simulate real-world prediction scenarios (Riley et al., 2019).

## 5. LIMITATIONS

**MAJOR ADDITION: A Comprehensive limitations section has been added as specifically requested by assessors. This was identified as missing from the original protocol and is essential for demonstrating methodological awareness and scientific rigour.**

### 5.1 Methodological Limitations

**Causal Inference Constraints**: Observational data limit definitive causal claims, despite the use of advanced methods such as double machine learning and causal forests (Chernozhukov et al., 2018; Wager & Athey, 2018). Mitigation includes applying multiple causal inference techniques, conducting sensitivity analyses to assess robustness, and framing results as associations with appropriate caveats. Findings will emphasise heat-health interaction relationships rather than causal assertions, acknowledging the strength of the evidence.

**Temporal Resolution**: Daily temperature data may overlook diurnal variations, which are critical for populations with limited cooling access and facing prolonged heat exposure. Maximum, minimum, and mean daily temperatures, alongside humidity and heat index measures, capture physiological stress (Wan et al., 2001). Temperature persistence analysis addresses the effects of prolonged exposure. However, nighttime and diurnal pattern impacts may be underestimated.

**Spatial Aggregation**: Ward-level analysis may mask micro-scale variations in vulnerability, especially in mixed-income areas. Sub-ward analysis (where data allow), within-ward heterogeneity assessments, and mixed-effects modelling account for variation (Harris et al., 2011). Vulnerability estimates reflect ward averages, potentially missing individual-level risk differences.

### 5.2 Data Limitations

**Population Representativeness**: Clinical cohorts may over-represent healthcare-engaged individuals, under-representing marginalised groups at high risk. Weighting for demographic differences and population-level data comparisons enhances generalizability, but findings may primarily apply to less vulnerable populations.

**Health Outcome Specificity**: Limited heat-specific outcomes necessitate reliance on heat-sensitive biomarkers, potentially missing novel pathways. Multi-system analyses capture diverse impacts, but undiscovered heat-health effects may be overlooked.

**Socioeconomic Dynamics**: Periodic surveys may miss rapid urban change or mobility, thereby risking misclassification of vulnerability. Satellite-derived proxies and multi-source validation mitigate this, though assessments may lag behind dynamic urban changes.

### 5.3 Contextual Limitations

**Geographic Generalizability**: Johannesburg's unique socio-spatial context may limit the applicability of this study to other African cities. Contextual documentation and transferable methods mitigate this, but specific patterns remain context-dependent.

**Intervention Focus**: The study informs intervention design but does not evaluate effectiveness. Policymaker engagement ensures practical relevance; however, implementation research is necessary to assess the impact.

**Temporal Transferability**: Historical data (2000–2022) may not reflect future heat-health dynamics. Climate projections and sensitivity analyses address this, but models require periodic recalibration.

## 6. ETHICAL CONSIDERATIONS

***Enhanced ethical section:*** *Expanded discussion of ethical considerations, including community engagement and potential risks, as requested by assessors.*

This study operates under comprehensive ethical oversight and protection frameworks designed to safeguard participant privacy whilst enabling research that benefits vulnerable communities. The research has received ethical approval from the Wits Human Research Ethics Committee (reference 220606) and complies with South African and international ethical standards, including the South African Protection of Personal Information Act (POPIA, 2013) and U.S. Department of Health and Human Services regulations (45 CFR 46).

### 6.1 Privacy Protection Measures

Privacy protection encompasses comprehensive data minimisation, ensuring only essential variables are retained for analysis. This is achieved through secure storage on encrypted servers with restricted access protocols, as well as geographical jittering and aggregation to prevent location identification while maintaining analytical utility. For the use of secondary data, contractual guarantees from data providers confirm the appropriate consent practices and ethical approval for secondary analysis.

### 6.2 Risk Mitigation

Ethical risks, including potential re-identification of participants, secondary consent issues, and community stigmatisation, are mitigated through multiple layers of protection. Data aggregation at the ward level prevents individual identification while maintaining spatial analytical capabilities. Secure storage protocols ensure data access is limited to authorised research personnel. Broad consent waivers obtained by original studies cover secondary analysis for public health research purposes. Community engagement strategies ensure that research findings are communicated in ways that support rather than stigmatise vulnerable populations.

### 6.3 Community Engagement and Benefit

The research includes explicit community engagement components to ensure that findings benefit the populations studied. Results will be disseminated to communities through accessible presentations and materials that avoid technical jargon whilst maintaining scientific accuracy. Policy engagement includes direct briefings with municipal and provincial health authorities to ensure research findings inform decision-making.

### 6.4 Detailed POPIA Compliance

Detailed POPIA compliance framework and data protection procedures ensure full compliance with South African privacy legislation. This includes explicit consent documentation for all data use, regular audit procedures to ensure ongoing compliance, and clear protocols for data retention and disposal. The research adheres to principles of lawfulness, fairness, and transparency in all data processing activities (Parliament of South Africa, 2013).

## 7. EXPECTED OUTCOMES AND IMPACT

***Enhanced outcomes section:*** *Strengthened discussion of original PhD contributions and expected impact as requested by assessors.*

This research will deliver: (1) a comprehensive heat vulnerability index for Johannesburg, (2) characterisation of heat-health pathways in African urban populations, and (3) validated predictive models for proactive health protection. The novel methodological approaches and "spatial-temporal heat vulnerability" framework will enhance the understanding of urban heat vulnerability, providing practical tools for evidence-based interventions and early warning systems. Outputs include peer-reviewed publications, policy briefs, and conference presentations targeting academic, policy, and practitioner audiences.

### 7.1 Research Outputs

This doctoral research will generate several significant outputs, including a spatially explicit heat vulnerability index for Johannesburg that provides actionable intelligence for intervention planning, a comprehensive explanatory model of urban heat-health relationships that advances understanding of physiological pathways in African urban populations, and a validated predictive framework for heat-health outcomes under varied climate scenarios that enables proactive public health responses. These outputs will provide a foundation for future policy development and intervention design, though the actual implementation of specific interventions falls outside the scope of this PhD.

### 7.2 Anticipated Impact

This research will advance understanding of urban heat vulnerability in African contexts through methodological innovations applicable to other rapidly warming cities. The findings will provide an evidence base for targeted heat-health interventions, enabling public health authorities to shift from reactive to proactive approaches and more effectively protect vulnerable populations. By identifying high-risk communities and elucidating heat-health pathways, this work contributes to climate justice efforts while providing insights relevant to broader discussions of urban equity and environmental justice.

### 7.3 Incorporation of Published Work and PhD by Publication Approach

This PhD adopts a hybrid thesis format per Wits Faculty of Health Sciences guidelines (2024) and Senate Standing Orders (2015), incorporating post-registration publications as core chapters with integrative linking text for coherence. This allows 2-4 papers to be produced during candidacy, ensuring originality and thematic unity.

#### Policy Alignment

The format supports compilation of theses with at least three peer-reviewed papers (one as lead author), plus approximately 20,000 words of linking chapters. Pre-registration work provides continuity but does not count as core output. This complies with requirements for work "undertaken during registration" and encourages dissemination.

#### Case for Including Vulnerability Analysis Paper

The 2025 paper (Parker et al., *International Journal of Biometeorology*) forms a core chapter for Objective 1. Published post-registration (accepted June 2025), it represents original PhD work under supervision, aligning with the protocol's vulnerability framework. Linking text (2-3 pages) will connect it to other objectives; no reanalysis needed unless updated data arises.

#### New Publications for Objectives 2 and 3

- **Paper 2 (Objective 2):** Pathway analysis via mediation models; target: *Environmental Health Perspectives*; submit Month 25.
- **Paper 3 (Objective 3):** Predictive ensemble models; target: *Science of the Total Environment*; submit Month 31.

Both will be lead-authored, original analyses forming Chapters 5-6.

**Role of Published Protocol**

The protocol (pre-2025 publication) is referenced in the introduction/methods for continuity but does not count as a publication, per policies on pre-PhD work.

## 8. PROJECT TIMELINE

***Enhanced timeline:*** *Updated timeline with clearer milestone definitions and risk considerations as requested by assessors.*

### 8.1 36-Month PhD Timeline

**Phase 1: Foundation and Vulnerability Mapping (Months 1-9):** The initial phase focuses on data acquisition, processing, and quality assessment (months 1-3), followed by geographically weighted vulnerability analysis (months 4-6), and vulnerability mapping completion and validation (months 7-9). The key milestone (M1) is a validated heat vulnerability index for Johannesburg, providing actionable intelligence for policy and intervention planning.

**Phase 2: Pathway Analysis (Months 10-18):** The second phase involves exploratory analysis and hypothesis generation (months 10-12), heat health interaction analysis and pathway quantification (months 13-15), and pathway validation and sensitivity analysis (months 16-18). The key milestone (M2) involves comprehensive characterisation of the heat-health pathway, identifying the most essential physiological mechanisms and vulnerable populations.

**Phase 3: Predictive Modelling (Months 19-30):** The third phase includes model development and feature engineering (months 19-21), model training and validation (months 22-24), ensemble integration and uncertainty quantification (months 25-27), and real-world validation and performance assessment (months 28-30). The key milestone (M3) is a validated predictive modelling framework that can forecast heat-health risks with sufficient accuracy for operational use.

**Phase 4: Synthesis and Completion (Months 31-36):** The final phase involves thesis writing and integration of findings across all objectives (months 31-33), followed by final revisions and examination preparation (months 34-36). The key milestone (M4) is the submission of the thesis and its successful examination.

### 8.2 Risk Mitigation

Several risk mitigation strategies are in place to ensure project completion within the timeline. Data access delays are addressed through early engagement with data providers and identification of alternative data sources where necessary. Methodological challenges are mitigated through pilot analyses to test feasibility and availability of expert consultation for complex analytical problems.

## 9. SUPERVISION AND SUPPORT

***Enhanced supervision section:*** *Expanded description of supervision structure and support systems as requested by assessors.*

### 9.1 Supervisory Team

The research is conducted under a multidisciplinary supervisory team that provides expertise across all aspects of the research. Dr. Admire Chikandiwa (Wits University) serves as Primary Supervisor, bringing expertise in clinical epidemiology, African health systems, and statistical analysis. Professor Matthew Chersich (Wits University/Trinity College) serves as Co-Supervisor, providing expertise in public health, climate-health interactions, and policy translation. Professor Akbar Waljee (University of Michigan) serves as Co-Supervisor, contributing expertise in machine learning, predictive modelling, and clinical applications of advanced analytics.

### 9.2 Advisory Support

Additional support is provided through the HE²AT Centre Research Team, which provides access to multidisciplinary expertise and regular scientific discussions with researchers working on related topics. Statistical consulting is available through the Wits School of Public Health's statistical support services for complex methodological questions.

**AI Assistance Acknowledgement:** This protocol development received assistance from Claude AI (Anthropic) for document structure optimisation, formatting, and revision tracking. All analytical decisions, methodological choices, and intellectual content remain the original work of the author.

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**Correction: As requested by assessors, all references were verified. The erroneous Armstrong et al. (2021) citation was corrected to Zhao et al. (2021), which includes Armstrong as a co-author and aligns with the study's focus on temperature-related mortality.**

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