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A mixed-methods, population-based study of a syndemic in Soweto, South Africa

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Abstract

A syndemic has been theorized as a cluster of epidemics driven by harmful social and structural conditions wherein the interaction between the constitutive epidemics drive excess morbidity and mortality. We conducted a mixed-methods study to investigate a syndemic in Soweto, South Africa, consisting of a population-based quantitative survey (N=783) and in-depth, qualitative interviews (N=88). We used ethnographic methods to design a locally relevant measure of stress. Here we show that multimorbidity and stress interacted with each other to reduce quality of life.

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Author Contributions Statement: EM conceived, designed, and supervised the project; led and oversaw the analysis; and wrote the paper. AWK organized the data collection and analysis of the data and commented on the manuscript. AP analyzed the survey data and commented on the manuscript. LC collected the data, analyzed the qualitative data, prepared some of the tables, and commented on the manuscript. FM validated the Soweto Syndemics Scale and commented on the manuscript. EB analyzed the qualitative data, helped prepare the tables, and commented on the manuscript. SAN conceived and designed the project and commented on the manuscript. ACT conceived and designed the project, led the conceptualization and execution of the quantitative data analysis, and significantly edited the manuscript.

Code Availability: The code that supports the findings of this study is available from the corresponding author upon request.

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The paired qualitative analysis further explored how the quality of life impacts of multimorbidity were conditioned by study participants' illness experiences. Together these findings underscore the importance of recognizing the social and structural drivers of stress and how they affect the experience of chronic illness and well-being.

Introduction

Syndemic theory integrates two concepts: disease concentration and disease interaction[1]. The concept of disease concentration emphasizes how and where multiple epidemics cluster together as a result of large-scale political, economic, ecological, and social forces, e.g., systemic racism, gender inequities, structural violence, drought and heat intensification[2]. The concept of disease interaction emphasizes the ways in which overlapping epidemics have mutually reinforcing effects on worsening health and disease via biological and social processes[3]. In this study, we evaluate which stressors interact, and how they interact, with convergent chronic conditions to influence quality of life in a population-based sample of adults living in a large, urban community in South Africa. We developed a locally-defined measure of stress based on two ethnographic studies investigating how people understand stress on their own terms amidst living with chronic illness. We argue that disentangling "what" drives disease concentrations and "how" they interact is crucial for the project of explaining how history and context shape the conditions of disease epidemics and when non-medical social interventions should be prioritized over, or augment, clinical interventions.

Anthropologists have long been concerned with the conventional practice of using standardized scales of stress and mental illness without taking into consideration local ways in which people experience stress and psychiatric disorder and communicate distress[4–7]. While the use of standardized instruments facilitates comparative studies of population mental health across contexts[8], building locally-relevant tools to evaluate social impact in large-scale studies has become increasingly relevant and critical for interrogating syndemics. Weaver and Kaiser argue that a "study designed to assess a presumptive syndemic" should "begin with freelists, ethnographic interviews, observation, and/or focus group discussions to identify common elements" that shape disease conditions across multiple valences of influence[9]. For example, Brewis and colleagues conducted a combined analysis of data from an epidemiological survey and qualitative interviews to study how the consequences of chronic social inequality (crime, hunger, and discrimination) drive health disparities across three low-resource but heterogeneous communities in Haiti. They analyzed epidemiological survey data to understand differences in exposures across communities and textual data from focus groups and one-on-one interviews to understand "the nuance, context, and local embeddedness of core themes as they emerged from respondents' own words"[10]. This work emphasizes the need to focus on what they call "syndemic localization," a process by which social, political, or ecological factors—defined and measured within and in relation to a local context—drives disease interactions differently within and between geographic areas.

Mixed-methods scholarship like this is increasingly needed to counter the idea of the "global syndemic"[11,12], a concept that threatens to erase local histories of inequity and oppression from contemporary accounts of disease morbidity and mortality. For instance,

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many researchers have demonstrated that the relationship between diabetes and depression is bidirectional[13] and is intensified by economic hardship around the globe[14] in wealthy and poor countries alike[15,16]. In contrast, clinical work tends to gloss over how local identities and power relations contribute to how people experience the chronicity of illness as well as recommended clinical care[17]. One reason why this disconnect may occur is because risk is conceived in individual terms (e.g., self-control) rather than social terms (e.g., what conditions and intersectional identities shape experience), which embodies a broader framing of what drives diabetes in the first place[18,19]. Sangaramoorthy warns, in the context of HIV, that clinicians and "counselors are trained to be experts in the mediation of disease-specific risk, transforming individual client's perceptions of external risk into internal risk and obscuring other non-HIV/AIDS threats to well-being" (p.303)[20]. For these reasons, a rigorous examination of how and why social dimensions of stress fuel diabetes and its comorbid companions (e.g., depression, hypertension, and HIV), particularly in settings of historically-engrained racism and inequality like South Africa, requires a mixed-methods (i.e., combined anthropological and epidemiological) approach.

The research we present was originally based on two qualitative studies in Soweto, South Africa that illustrated how people perceived social and personal stress to be more challenging than disease diagnoses[21,22]. The preliminary anthropological work illustrated how structural and social factors may impede people's abilities to manage their own care for chronic illnesses, including diabetes, cancer, depression, physical pain, and infectious diseases. For example, women described how reconstructing their families and raising grandchildren after losing children to AIDS not only posed significant psychological burdens but also affected how they ate and how they accepted and managed their diabetes. Many related diabetes treatment to shared AIDS nosologies, referring to diabetes as "the same" or "worse"[21]. A further analysis of survey data from 1,000 middle-aged women in Soweto found a 40% prevalence of elevated psychological distress; women who reported two diseases had increased rates of psychological distress, and this upward trend continued with each additional physical disease reported[24]. Yet, in a study of breast cancer survivors in Soweto, we found that women relied on radical acceptance of their disease diagnoses and illness prognoses, as well as on family support and the public health system, to cope and foster their own well-being[25].

Acknowledgment of the manifold ways that social and biological stress interact is particularly important in Soweto as multiple comorbidity is an increasing public health concern. South Africa maintains 1) the highest number of people living with HIV globally, of which many also experience tuberculosis[26] and, increasingly, diabetes[27]; 2) elevated rates of automobile accidents, intimate partner violence, rape, and murder[28,29]; 3) elevated rates of infant and maternal mortality, despite a high level of wealth in the aggregate compared with other countries in the region[30]; and 4) a massive rise in non-communicable diseases (NCDs), including diabetes[31]. Thus, focusing on social and economic factors that affect diabetes alone and together with other medical conditions provides a more realistic understanding of people's experiences with sickness and health.

A clinical study in Khayelitsha, a peri-urban settlement near Cape Town, South Africa, found 45% of adults sought prescriptions for at least one of the following diseases: HIV,

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tuberculosis, diabetes, and hypertension[32]. The increases in longevity among those living with HIV which has, in turn, led to increased risks of developing type 2 diabetes[33]. Additionally, one in four patients had multiple comorbidities, a phenomenon that generally increased with age, while those receiving antiretroviral therapy (ART) were more likely to develop diabetes at a younger age[32]. Cohort studies in Uganda and South Africa were some of the first to document convergence of HIV with NCDs in Sub-Saharan Africa[34–39]. These cohort studies suggested that having multiple conditions increases the likelihood of depression and that NCDs are less common among those without HIV when compared with people who are living with HIV[40]. Studies also point to the increasing salience of diabetes and tuberculosis[41], which is of concern in South Africa given that the country has one of the largest concentrations of tuberculosis worldwide[26]. The demand for chronic care associated with any combination of diabetes, HIV, and tuberculosis poses extraordinary public health and health care challenges.

This article investigates how our locally-constructed measure of stress interacts with multiple medical conditions among people residing in six different neighborhoods in Soweto, an urban settlement in Johannesburg, South Africa. We first used ethnographic methods to shape the study questions and design locally valid measures, which we then applied to a large population-based study of Soweto residents. Finally, we tested the theory derived from our quantitative analysis by conducting a follow-up qualitative study of illness experiences among people with multiple comorbidities. In what follows, we describe the co-occurrence of these medical conditions and consider how these conditions interact with our locally designed measure of stress and other measures of psychological distress and well-being. In doing so, we discuss what interactions among medical and social conditions tell us about people's experiences in Soweto, and how it informs the study of syndemics more broadly~~.~~

Results

Epidemiological Findings

Among the study participants who completed surveys and had complete data available (n=783), there were 541 women and 242 men (Table 1). The mean age was 46.1 years (standard deviation, 12.7). Quality of life was slightly higher among men compared with women (60.1 vs. 57.6; t=1.67, p=0.10). Most reported no chronic medical comorbidities (428 [55%]), while 236 (30%) reported one comorbidity, 89 (11%) reported two comorbidities, and 30 (3.8%) reported three or more comorbidities. On the *emic* measure of stress, women reported considerably higher levels of stress compared with men (48.9 vs. 44.5; t=4.50, p<0.001), differing by more than 0.3 standard deviation units. On the *emic* measure of coping, no sex-based differences were observed.

Table 2 shows the results of the multivariable regression models. In the fully adjusted multivariable regression model, the multimorbidity sum score (b=−3.86; 95% CI, −5.39 to −2.33; p<0.001) and stress (b=−0.58; 95% CI, −0.67 to −0.48; p<0.001) both had statistically significant negative associations with quality of life. The disaggregated model in Supplementary Table 1 suggests that the multimorbidity estimates were primarily driven by diabetes (b=−9.06; 95% CI, −14.1 to −4.05; p<0.001) and cancer (b=−12.8; 95% CI,

−23.9 to −1.76; p=0.02). When the multimorbidity and stress product term was added to the model, the product term was statistically significant, suggestive of an interaction in which the negative association between multimorbidity and quality of life was amplified in the presence of high stress (b=−0.16; 95% CI, −0.27 to −0.05; p=0.005). Sensitivity analyses yielded estimates that were substantively similar to the primary analysis (Table 3): the binary measures of caseness had statistically significant associations with quality of life, although the interaction between caseness on the GHQ-28 and multimorbidity was not statistically significant; and the quintiles of the stress scale showed increasingly stronger associations, and stronger interactions with multimorbidity, with increasing levels of stress.

Qualitative Findings

Table 4 describes key themes and sub-themes that emerged from the interviews, along with exemplar quotations, for each sub-group. Study participants with diabetes, hypertension, and high levels of stress (Group 2) often described a constant fear of having a debilitating medical complication (e.g., amputation). They also described financial burdens associated with paying for medications and food, and social burdens such as those due to family conflict. Study participants with diabetes and HIV/tuberculosis (Group 3) reported similar concerns over access to care, the importance of self-care, and financial stressors.

In contrast, study participants with diabetes and hypertension but low levels of stress (Group 1) commonly described more social support, less trouble accessing or managing medication and care-seeking, acceptance of their illness, and a more positive outlook on their illness and future. This perspective was more aligned with that most commonly described among study participants who reported no medical comorbidities, who rarely sought care or focused on their health (Group 4).

Nearly everyone reported feelings of stress about financial difficulties. Most described finding comfort in being able to access health care through the public system (even when voicing concerns about stockouts or long waits). Although few relied on traditional herbal remedies to care for physical illness, most people described how they coped with psychological distress through individual religious practices (e.g., prayer, reading the Bible) and group/social religious practices (e.g., small group Bible study, attending services, church-based counseling).

Discussion

Developing methods to evaluate syndemic theory poses challenges and opportunities as more scholars adopt a syndemic orientation for understanding and developing interventions for communities facing multiple clustered social and health conditions. Syndemic theory is predicated on the idea that social and structural factors precipitate disease concentration and disease interaction, and that local phenomena may differentially affect disease interactions and disease experiences across contexts. In previous work anthropological work, we have argued that structural violence, social trauma, and chronic distress all have important roles to play in shaping syndemic experiences. In this article we evaluated *how* such experiences cluster with multiple convergent conditions and therefore become syndemic through an epidemiological lens.

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First, we argue that our theoretical postulates hold up for stress and multimorbidity. Our strongest finding in this study reveals a robust interaction between a locally designed stress scale and multimorbidity. This finding was consistent with our ethnographic findings, which showed that stress was associated with medical complications, financial difficulties, family discord, and an unsettled future, while those doing well were more likely to describe social and emotional wellbeing—even when financial difficulties were common. Taken together, these mixed-methods findings support the important interplay between stress and living with multiple chronic illnesses. The high burden of physical and mental illness in this population substantiates this point.

Second, the study reveals the importance of grounding epidemiological work in detailed ethnographic study[42]. Constructing a locally relevant scale revealed the complex roles of various stressors such as financial stress, which is embedded in the local political economy, as defined by participants, in conditioning the associations between multimorbidity and quality of life. Similarly, the coping scale emphasizes the fundamental importance of religious practices, social cohesion, and caring for others in this community -- thereby underscoring how *ubuntu*, or thinking about the self in relation to others, may play a role in reducing stress and fostering quality of life[43]. Using a generic life events scale, however useful, may have missed what people in this context themselves define as most critical for determining quality of life. The priority that our interlocutors put on these life stressors would likely have been less fully understood in a “rapid” or strictly quantitative study.

Third, the qualitative data enriched our understanding of the epidemiological data by explaining what types of social stresses emerged within each group and how those social stressors clustered together and in relation to multiple morbidities. The qualitative data show how interlocking stresses produced undue burden on our study participants and affected their quality of life in more severe or enduring ways, or, in some cases, in ways that were mutually reinforcing with their co-occurring health conditions. People faced different challenges depending upon their previous diagnoses, their outlook on those illnesses, the level of social support available to them, and their financial security. In other words, the effects of multimorbidity on quality of life differed for people who had the same co-occurring diagnoses in part because of non-medical social and structural factors like family stress and fear. We emphasize that, while the negative association between multimorbidity and quality of life is amplified by high levels of stress, it is not wholly explained by or cannot be reduced to that variable. People with diabetes and hypertension may perceive their illnesses differently if they report more or less psychological morbidity. Recognizing how people live well with multiple illnesses, therefore, requires critical attention to the non-medical factors that shape living with chronic illnesses, especially when they overlap and cause multiple burdens of medication, care-seeking, and living well. Individual and group religious practices like prayer, small group gathering, and attending services featured in many people’s narratives of what non-medical factors are crucial to good health[43,44]. Moreover, many people without previous medical diagnoses tended to avoid clinics and hospitals, even for preventive care, which substantiates the point that people with multiple conditions are often diagnosed only when severe symptoms force them to seek urgent or acute care[45]. Thus, these qualitative data demonstrate how social and medical conditions are not isolated experiences but instead are interactive and contingent with social experiences.

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Interpretation of our findings is subject to several important limitations. First, we had planned on surveying a much larger sample of study participants, but data collection was stopped prematurely due to the first surge of the COVID-19 pandemic. Second, very few people in our sample reported diabetes and an infectious disease (either HIV or tuberculosis). This finding may have resulted from our study design: 121 people refused to test for HIV, which is not uncommon in this context[46,47]. Third, and related to the previous, the data on medical comorbidities (along with, obviously, the data on stress and coping) were self-reported. While there is no practical way of understanding stress and coping without using self-reported measures, it is likely that some of the medical comorbidities, particularly HIV and tuberculosis, were subject to under-reporting given the stigma that has been attached to HIV and tuberculosis in this context[48]. Such underreporting could have biased our estimates of the association between quality of life and HIV. More generally, however, if people with higher quality of life were more likely to underreport medical comorbidities, this would have biased our estimates of the association between medical comorbidity and quality of life toward the null rather than away from the null. Fourth, the cross-sectional design prevented us from assessing both disease and coping trajectories, which could have provided a more nuanced understanding of living with multimorbidity. Indeed, such an approach could change how syndemics are framed: rather than focusing on individuals being subjects of syndemics, it would recenter their agency as individuals who respond, cope, and make sense of their illness, despite structural violence and social challenges.

This study illustrates the importance of grounding an epidemiological analysis of a syndemic in long-term ethnographic work. We argue that there is a need for more mixed-methods studies that draw from knowledge situated within contexts and developed with multi-disciplinary teams, so that the field can better understand how and why syndemics emerge, given local structural and social conditions. Our data emphasize the role of non-medical factors in explaining how people live well with, or suffer from, multiple chronic conditions. Although many people described some satisfaction with their care in the public system (despite common critiques of wait times for clinicians and drug stock-outs), it was very clear that not all health and healing could come from the public healthcare system. Moving some of this care from the clinic to the church or community, at scale, may be an effective way to promote social well-being, good mental health, and more effective management of physical conditions like diabetes and hypertension in Soweto and other similar contexts in urban South African neighborhoods.

How scholars measure syndemics will likely continue to change. Syndemics inherently differ from place to place. The roles of historical, ecological, political-economic, and sociocultural factors in shaping or perpetuating syndemics should be central to any investigation into what constitutes a syndemic. Untangling what factors are most relevant to disease concentration and disease interaction matters a great deal for a more precise and contextually relevant understanding of overlapping disease epidemics and future social interventions for public health, and can provide important contributions to future scholarship on syndemics.

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Methods

Setting

We conducted this study in collaboration with the Developmental Pathways for Health Research Unit (DPHRU), a research unit associated with the South African Medical Research Council and the University of the Witwatersrand (Wits) and based at Chris Hani Baragwanath Hospital in Soweto, South Africa. Research assistants were based at the DPHRU research station and fluent in multiple languages spoken in Soweto. Surveys for the Phase 1 epidemiological study were administered in people's homes. Interviews for the Phase 2 qualitative study were conducted at the research station. All research participants were residents of Soweto.

Soweto is an urban settlement within Johannesburg, the largest city in South Africa. More than one million people reside in Soweto; most are Black South Africans, representing various ethnic identities, including Zulu, Sotho, Tswana, Tsonga, and others. We use the term "Black" to describe the study participants while acknowledging a problematic history of this identity as a political category instituted by apartheid to distinguish "Black" from "Coloured" and "White"[49]. Soweto is diverse economically, with middle-class neighborhoods, working class communities, and informal settlements. Marginalization of Black South Africans and other non-white communities during apartheid and the decades afterward have contributed to poor housing, lack of sanitation, unhealthy food access, and deficient educational opportunities in the present day. These problems have been associated with the unequal burden of HIV and TB among Black compared with white South Africans, compounded by costly health care services in the private sector and systemic barriers in the public sector[49].

Sampling

The Phase 1 epidemiological study was embedded within the infrastructure of a larger study being conducted through the DPHRU. No statistical method was used to predetermine sample size. Given the size of Soweto ($200km^2$), we sampled study participants in clusters based on churches, which are widely distributed throughout Soweto. Starting with a list of geolocations of each church structure, fieldworkers visited each church and verified its existence. The churches were used to identify thirty community clusters, each with a 1-kilometre radius. For the purposes of our study, six clusters were randomly selected and then enumerated. Within each cluster, the research team walked down the streets, engaged potential participants, and interviewed available people in their homes who were willing to participate in the study. If the person approached did not fit the inclusion criteria (described in more detail below), another member of the household who did meet these criteria was then approached. Phase 1 epidemiological study participants were interviewed in their homes and were not provided with any compensation or study incentive. The University of the Witwatersrand Human Research Ethics Committee approved this study (M180544). All participants provided written informed consent before participating, and were free to stop the survey at any time.

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Phase 1: Epidemiological Survey Data Collection and Analysis

For the Phase 1 study, we visited the six neighborhood clusters over a period of one year (April 2019-March 2020). We finished 783 complete surveys before the study was shut down due to the pandemic of severe coronavirus disease 2019 (COVID-19). The response rate was 86 percent. Measurements were taken from this sample at a single time point. No data were excluded from the analyses. We enrolled participants 25 years of age or older who lived within each identified cluster and who considered themselves to be a regular member of the household (i.e., spent most nights in the home during the three months preceding the interview). Participation was limited to people 25 years of age and older because of our focus on chronic multimorbidity and because we wished to avoid interfering with recruitment for a concurrent study that was enrolling young adults. Exclusion criteria included: people younger than 25 years of age; people who did not consider themselves to be residents of Soweto; and individuals who could not meaningfully communicate with the study team, such as people with cognitive impairments, people who were acutely intoxicated upon approach, people who were too ill, or people who threatened our team with harassment or violence.

Our field teams collected survey data using tablets programmed with Research Electronic Data Capture (REDCap). The primary outcome was quality of life, which we measured using the 26-item World Health Organization Quality of Life-BREF (QOL-BREF)[50]. The primary explanatory variables of interest were multimorbidity (namely, the sum score of the most commonly reported medical comorbidities, including type 2 diabetes, hypertension, chronic pain, high cholesterol, and cancer) and stress (measured using the 21-item Soweto Stress Scale, a locally developed and validated *emic* scale based on our ethnographic work conducted in Soweto over the past decade[51]).

Model 1 specifies a multivariable linear regression model to estimate stress and medical comorbidities as correlates of quality of life. We then added a vector of additional covariates (Model 2): age; sex; household asset wealth, measured using a 13-item checklist of assets in the household; perceived lack of neighborhood safety, measured using two questions about feeling safe during the day and night; perceived neighborhood social cohesion [52]; HIV status, measured by an at-home rapid test kit; coping, measured using the 14-item Soweto Coping Scale, an *emic* scale designed to measure different aspects of problem/emotion-focused and religious coping, also based on our ethnographic work conducted in Soweto; and neighborhood cluster. In the final regression model, we added a product term to assess for an interaction between multimorbidity and stress (Model 3).

We used multiple specifications to probe for this hypothesized interactive relationship. First, we treated the stress scale as binary, with caseness denoted as a stress scale value greater than or equal to the 75^{th} percentile. Second, because an arbitrary 75^{th} percentile threshold for the locally derived stress scale has no empirical precedent, we substituted for the Soweto Stress Scale the 28-item General Health Questionnaire (GHQ-28)[53,54] in the regression model. The GHQ-28 is a nonspecific measure of psychological distress but has been used in global health studies for decades with well-established thresholds for caseness. Third, because a dichotomous variable may mask variability in quality of life at more granular levels of stress, we examined the interaction between multimorbidity and the stress scale

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split into quintiles, where each group represented 20% of the sample, ranging from the least stressed (first quintile) to the most stressed (fifth quintile). Fourth, we eliminated possible high leverage points to assess whether the estimated associations were dependent on extreme values. Lastly, to compare the estimates associated with the multimorbidity sum score variable vs. the individual conditions that comprise it, we disaggregated the sum score and analyzed the individual conditions separately[55].

Statistical analyses were conducted using R version 3.6.3. Two-sided tests were used throughout.

Phase 2: Qualitative Data Collection and Analysis

Next we conducted in-depth/semistructured qualitative interviews with 88 participants from the epidemiological survey. The aim of these qualitative interviews was to explore major life events, disease-related stress, challenges associated with living with one of the co-morbidities of focus, major barriers or facilitators to health, challenges associated with care-seeking and co-morbidity, systemic barriers to or facilitators of health care, and self-care regimens. These individuals were purposively sampled based on their membership in one of several comorbidity clusters: Group 1 (diabetes, hypertension, low stress; n=19), Group 2 (diabetes, hypertension, high stress; n=15), Group 3 (diabetes and either HIV or tuberculosis; n=7), and Group 4 (people living healthy lives without any medical diagnoses; n=47). Phase 2 qualitative interviews were conducted at the DPHRU research station, and each participant was reimbursed 150 South African Rand (approximately 12 USD at the time the study was conducted) for transportation to the research station. A handful of in-home qualitative interviews were conducted for participants who could not travel.

We transcribed all interviews verbatim. Audio from vernacular languages was transcribed and translated into English, while maintaining consistency with their original meaning. We used an inductive method that involved reading and rereading transcripts and field notes while comparing the two to ensure no data were misinterpreted. The study team designed a codebook based on this inductive analysis, which included 30 main codes. These codes were well-defined and collectively agreed upon, and were reflected in the interview guide, field notes, selected transcripts, and in-depth discussions. Each code was identified, defined, applied, revised, and discussed among five core members of the research team. We attached the codes to each transcript using Dedoose software (SocioCultural Research Consultants, Los Angeles, Calif.), with a primary coder and two secondary coders reviewing and applying codes to each transcript. Further information about the methods and findings of the qualitative study are described elsewhere[44].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability:

The data that support the findings of this study cannot be shared publicly due to the risk of patient identification where small numbers of patients per neighborhood cluster are included (i.e., clusters 2 and 3). Researchers interested in inquiring about access to confidential data should contact the corresponding author.

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Table 1.

Characteristics of the sample (n=783)

	Women (n=541)	Men (n=242)	Total sample (n=783)
Age (mean±SD)	46.6±12.6	45.0±13.1	46.1±12.7
Number of assets in home (mean±SD)	7.9±1.8	8.2±2.2	8.0±1.9
Perceived lack of safety (n, %)	356 (65.8)	109 (45.0)	465 (59.4)
Perceived social cohesion (n, %)	452 (83.5)	193 (79.8)	645 (82.4)
Soweto Stress Scale (mean±SD)	48.9±12.9	44.5±12.5	47.6±12.9
Soweto Coping Scale (mean±SD)	45.4±9.3	45.5±9.0	45.4±9.2
General Health Questionnaire-28, caseness (n, %)	66 (12.2)	14 (5.8)	80 (10.2)
Quality of Life	57.6±18.9	60.1±19.6	58.3±19.1
Number of medical conditions (mean±SD)	0.71±0.87	0.50±0.78	0.65±0.85
None (n, %)	275 (50.8)	153 (63.2)	428 (54.7)
One (n, %)	171 (31.6)	65 (26.9)	236 (30.1)
Two (n, %)	72 (13.3)	17 (7.0)	89 (11.4)
Three or more (n, %)	23 (4.3)	7 (2.9)	30 (3.8)
Self-reported hypertension (n, %)	222 (41.0)	63(26.0)	285 (36.4)
Self-reported type 2 diabetes (n, %)	39 (7.2)	13 (5.4)	52 (6.6)
Self-reported chronic pain (n, %)	76 (14.0)	31 (12.8)	107 (13.7)
Self-reported hyperlipidemia (n, %)	41 (7.6)	14 (5.8)	55 (7.0)
Self-reported cancer (n, %)	8 (1.5)	1 (0.4)	9 (1.1)
HIV-positive, based on either self-report or test (n, %)	120 (22.2)	36 (14.9)	156 (19.9)
Neighborhood cluster (n, %)			
Cluster 1	145 (26.8)	63 (26.0)	208 (26.6)
Cluster 2	12 (2.2)	4 (1.7)	16 (2.0)
Cluster 3	31 (5.7)	17 (7.0)	48 (6.1)
Cluster 4	111 (20.5)	65 (26.9)	176 (22.5)
Cluster 5	94 (17.4)	32 (13.2)	126 (16.1)
Cluster 6	148 (27.4)	61 (25.2)	209 (26.7)

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Note: The columns present the summary characteristics of the subsample of women (column 1), the subsample of men (column 2), and the total sample. Cell numbers correspond to mean±SD for continuous variables or N (%) for categorical variables.

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Table 2.

Correlates of quality of life as assessed using the 26-item World Health Organization Quality of Life-BREF (n=783)

	Model 1			Model 2			Model 3		
	b	**95% CI**	**P-value**	**b**	**95% CI**	**P-value**	**b**	**95% CI**	**P-value**
Multimorbidity count	−4.803	(−6.242 to −3.364)	<0.001	−3.862	(−5.389 to −2.334)	<0.001	4.084	(−1.662 to 9.829)	0.163
Soweto Stress Scale	−0.529	(−0.623 to −0.435)	<0.001	−0.575	(−0.671 to −0.480)	<0.001	−0.475	(−0.593 to −0.356)	<0.001
Age				−0.179	(−0.281 to −0.077)	<0.001	−0.191	(−0.293 to −0.089)	<0.001
Male				−1.689	(−4.296 to 0.919)	0.204	−1.744	(−4.341 to 0.852)	0.188
Number of assets in home				0.534	(−0.088 to 1.157)	0.092	0.534	(−0.085 to 1.154)	0.091
Perceived lack of safety				−0.493	(−2.988 to 2.001)	0.698	−0.525	(−3.008 to 1.959)	0.678
Perceived social cohesion				−1.224	(−4.301 to 1.853)	0.435	−0.993	(−4.061 to 2.075)	0.525
HIV				−0.533	(−3.511 to 2.444)	0.725	−0.597	(−3.562 to 2.367)	0.693
Soweto Coping Scale				0.454	(0.323–0.585)	<0.001	0.445	(0.314–0.576)	<0.001
Neighborhood cluster									
Cluster 1				Ref			Ref		
Cluster 2				4.215	(−4.264 to 12.694)	0.329	3.370	(−5.091 to 11.832)	0.434
Cluster 3				0.167	(−5.145 to 5.478)	0.951	0.427	(−4.864 to 5.718)	0.874
Cluster 4				4.301	(0.900–7.702)	0.013	4.447	(1.060–7.835)	0.010
Cluster 5				2.309	(−1.472 to 6.090)	0.231	2.296	(−1.468 to 6.060)	0.232
Cluster 6				−1.772	(−4.973 to 1.429)	0.277	−1.657	(−4.845 to 1.530)	0.308
Multimorbidity count x Soweto Stress Scale product term							−0.161	(−0.274 to −0.049)	0.005
Constant term	86.772	(82.116–91.427)	<0.001	72.549	(61.984–83.113)	<0.001	68.488	(57.597–79.380)	<0.001

Note: Each column represents the output of a single multivariable linear regression model specifying quality of life as the dependent variable and the row variables as multiple explanatory variables. Model 1 includes medical comorbidities and the Soweto Stress Scale. Model 2 additionally includes age, sex, number of assets in home, perceived safety, perceived social cohesion, HIV, the Soweto Coping Scale, and neighborhood cluster. Model 3 additionally includes a product term to assess for an hypothesized interaction between multimorbidity and stress.

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Table 3.

Correlates of quality of life as assessed using the 26-item World Health Organization Quality of Life-BREF, with alternative specifications for the measurement of stress (n=783)

	Caseness for stress measured with the Soweto Stress Scale			Caseness for stress measured with the General Health Questionnaire-28			Soweto Stress Scale categorized into quintiles		
	b	**95% CI**	**P**	**b**	**95% CI**	**P**	**b**	**95% CI**	**P**
Multimorbidity count	−3.361	(−5.197 to −1.525)	<0.001	−4.464	(−6.169 to −2.759)	<0.001	−1.844	(−5.182 to 1.493)	0.278
Caseness for stress[†]	−9.831	(−13.438 to −6.224)	<0.001	−10.546	(−16.051 to −5.041)	<0.001			
Soweto Stress Scale quintiles									
Least stressed (quintile 1)							Ref		
Less stressed							−5.119	(−9.535 to −0.704)	0.023
Middle							−10.018	(−14.691 to −5.346)	<0.001
More stressed							−13.012	(−17.674 to −8.350)	<0.001
Most stressed (quintile 5)							−16.831	(−21.664 to −11.997)	<0.001
Age	−0.155	(−0.261 to −0.049)	0.004	−0.139	(−0.248 to −0.031)	0.012	−0.188	(−0.291 to −0.084)	<0.001
Male	−1.195	(−3.897 to 1.508)	0.386	−0.465	(−3.238 to 2.309)	0.742	−1.532	(−4.173 to 1.108)	0.255
Number of assets in home	0.806	(0.163–1.450)	0.014	0.841	(0.179–1.503)	0.013	0.495	(−0.135 to 1.125)	0.123
Perceived lack of safety	−1.986	(−4.544 to 0.572)	0.128	−2.806	(−5.425 to −0.188)	0.036	−0.815	(−3.334 to 1.704)	0.525
Perceived social cohesion	−0.707	(−3.900 to 2.486)	0.664	−0.980	(−4.272 to 2.311)	0.559	−0.972	(−4.099 to 2.155)	0.542
HIV	−0.528	(−3.619 to 2.563)	0.738	−1.282	(−4.454 to 1.891)	0.428	−0.599	(−3.630 to 2.432)	0.698
Soweto Coping Scale	0.446	(0.310–0.582)	<0.001	0.358	(0.215–0.501)	<0.001	0.444	(0.312–0.577)	<0.001
Neighborhood cluster									
Cluster 1	Ref			Ref			Ref		
Cluster 2	2.299	(−6.490 to 11.088)	0.608	2.323	(−6.726 to 11.373)	0.614	1.380	(−7.195 to 9.956)	0.752
Cluster 3	−0.506	(−6.016 to 5.005)	0.857	−2.688	(−8.326 to 2.950)	0.350	0.525	(−4.869 to 5.918)	0.849
Cluster 4	3.592	(0.068–7.116)	0.046	2.429	(−1.183 to 6.042)	0.187	4.188	(0.749–7.627)	0.017
Cluster 5	2.133	(−1.791 to 6.056)	0.286	1.748	(−2.295 to 5.791)	0.396	2.166	(−1.665 to 5.998)	0.267
Cluster 6	−0.677	(−3.985 to 2.632)	0.688	−0.539	(−3.944 to 2.866)	0.756	−1.422	(−4.666 to 1.821)	0.389
Multimorbidity count x stress[†] product term	−3.682	(−6.865 to −0.499)	0.023	−1.990	(−7.027 to 3.047)	0.438			

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	Caseness for stress measured with the Soweto Stress Scale			Caseness for stress measured with the General Health Questionnaire-28			Soweto Stress Scale categorized into quintiles		
	b	**95% CI**	**P**	**b**	**95% CI**	**P**	**b**	**95% CI**	**P**
Multimorbidity count x Soweto Stress Scale quintile 1 product term							Ref		
Multimorbidity count x Soweto Stress Scale quintile 2 product term							−0.362	(−5.025 to 4.302)	0.879
Multimorbidity count x Soweto Stress Scale quintile 3 product term							−1.309	(−5.788 to 3.169)	0.566
Multimorbidity count x Soweto Stress Scale quintile 4 product term							−2.093	(−6.456 to 2.270)	0.347
Multimorbidity count x Soweto Stress Scale quintile 5 product term							−5.396	(−9.894 to −0.898)	0.019
Constant term	45.360	(35.673–55.047)	<0.001	48.209	(38.069–58.348)	<0.001	54.972	(45.058–64.887)	<0.001

[†]Note: Each column represents the output of a single multivariable linear regression model specifying quality of life as the dependent variable and the row variables as multiple explanatory variables. The first column displays the results of a multivariable regression model in which caseness for “stress” is specified as a binary variable equal to 1 if the study participant’s Soweto Stress Scale score was greater than or equal to the 75th percentile. This binary variable was also interacted with the multimorbidity sum score variable. The second column displays the results of a multivariable regression model in which caseness for “stress” is identified using the 28-item General Health Questionnaire, also interacted with the multimorbidity sum score variable. The third column displays the results of a multivariable regression model in which the Soweto Stress Scale values were used to partition the sample into quintiles, ranging from least stressed to most stressed, also interacted with the multimorbidity sum score variable.

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Table 4:

Primary themes from the qualitative interviews (n=88)

	Key themes	Sub-themes	Exemplar quotations
Group 1: Diabetes, hypertension, low stress (n=15)	Acceptance Positive attitude	† Many accepted their illnesses and coped well Many demonstrated flourishing	"I don't dwell on it a lot, if you dwell on a sickness that is when you get sicker." "When you are happy, there is no way your BP can be high." "A lot of people hide the fact that they have diabetes. This may be because they are afraid of dying."
	Support mechanisms	Family and religion were key sources of support Hospital provided support through information	"My family is very supportive. They help me with the things that I can't do myself, for instance, my son, he can sit with me in hospital until I have recovered." "I am diabetic, and I am hypertensive, so I go to the chronic clinic and tell them what is going on and they tell me what to do."
	Self-care	Many took charge of their own self-care Taking medication Taking over the counter medication Five participants mentioned taking traditional medication	"I do exercise and take my medications to be well." "If I feel pain or anything, I take aspirin and I just tell myself that aspirin makes my blood flow and that's my pain killer and I don't have nothing prescribed."
Group 2: Diabetes, hypertension, high stress (n=19)	Diabetes-related stress	† Participants prioritized diabetes stress over other stressors, including other illnesses: diabetes management, fear of stroke, amputation, or death	"With diabetes, if you have not eaten, it is a problem. You eat, your sugar levels increase. You eat the right things, and your levels decrease, they decrease too much, and you die!"
	Other stressors	Multiple morbidity stress Disease interaction Pill burden Financial stress Family conflicts, children stress, death of family members	"You can feel as your blood pressure goes up, even when you eat atchaar or snoekfish, you can feel that you are eating wrong foods. Blood pressure also affects my diabetes because I am not supposed to be angry, I must always be calm." "I do get stressed; sometimes you find that I owe people money because at home there's no one that's employed."
	Access to care	Visiting different hospitals or clinics Doctors'/nurses' negative attitudes Drug stock-outs Long queues/waiting times Over the counter medication Lack of or limited access to mental health care † Many reported distrust in hospital care	"I go to Tshepisong [clinic], I started in Orlando [hospital] but I it was far, so they gave me a transfer letter, I go there [Orlando] once every 3 months." "I had to sit for 4 days without medication, and when I got back my diabetes had gone up, so those are the type of things that are happening in these clinics." "For me to feel better I have to take pills and I buy [over the counter medication] Grand-Pa or Panados and I will feel better."
	Self-care	Many used a glucometer to check their blood sugar Self-care: exercise, sleep, reading a book or reading the Bible, visiting friends or family, and/or prayer † Seven participants mentioned that they skipped taking medication	"I exercise in the house. Also, the work in the house, to walk around, where I live until Bara [hospital] is part of exercise." "Sometimes I forget and skip taking my pills, they hurt taking pills every day."
	Support mechanisms	Family and friends' support Religion Counselling/psychotherapy	"The most important people in my life are my children. They support me, lots of support on my illnesses." "They [nurses] gave me counselling and after that, I did not stress again."
Group 3: Diabetes and infection (n=7)	Access to care	† Visiting primary health clinics for care/ management Participants mentioned having received support	"I am the type of person that believes that when you go to the clinic and take the medication that the doctor has prescribed for you, then you will be fine. When I or my wife are sick, we go to the clinic."

	Key themes	Sub-themes	Exemplar quotations
		from the clinics † Hospital is a key source of information	"Yes, I eat more veggies. I was told at the clinic to eat more veggies and that I should refrain from consuming sugar and using fish oil to cook."
	Self-care	Taking pills/medication Sleep, finding a quiet space, taking walks, or taking time to calm down and think	"I like walking so when I feel tired, I sleep to just relax a bit." "I take my pills. One in the evening and this one at night before supper."
	Stressors	Skip taking medication Disease interaction Negative attitudes from providers, drug stock-outs, lack of transport to the hospital Financial stress, unemployment	"Sometimes, I skip the medication. You take advantage because you feel like you are feeling better knowing very well that you could get attacked again."
	Alternative medicine	Reluctance to use alternative medicines (due to fear of side effects)	"I'm scared to drink it [traditional medicine] because I don't know if it'll increase my diabetes." "I am scared of traditional medicine because, I don't want to cause further damage."
	Social support	Family, friends, religion, clinic Received counselling	"I pray and go to church often. There's a lady at church who also offers counselling."
Group 4: No diagnoses (n=47)	Feeling healthy	† Generally, participants in this category described feeling healthy Many did not go to the hospital including for check-ups, but only presented at the clinic when ill	"No, not for me, nothing like that. As long as I do the house chores, I take that as my daily exercise, I feel healthy." "I am also well because I go and sleep and when I wake up I am fresh and I am all right, I don't have pain, I don't have anything." "When I'm sick I go to the clinic so that I can find out how I am, I get the medication I need so I can use it."
	Stressors	† Emphasis on financial stress, unemployment or underemployment, and family conflict/stress rather than health related stress	"The thing I can say makes me sick, it was just money, it was just that." "I feel so stressed at the end of the month. During that time, I'm stressed because I have just been paid and I don't earn a lot of money but have a lot of responsibilities. So, the money that I get is not enough to cover everything I need to pay for." "I do have stress; like now my husband and I are stressed because he's the only child at home, his parents died and so the family, the aunt's children; they're fighting with us for that house where we live. the house is my husband's mother; they want to rent it out for themselves."
	Access to care	Distrust in hospital care Self medication - Med-Lemon (for nausea), Panado (for gastrointestinal distress), and Grandpa (for headache)	"I self-medicate when I have a headache, I'll buy Grandpa for that." "I'll use Med-Lemon and Disprin to sweat it out and get better; but for now there's nothing else that infects me."
	Self-care	Socializing, relaxation, reading, prayer	"I like going out. Two weeks back I went out with the ladies to spoil myself at a spa; and I said it is all about me. When you talk to someone you know, you feel much better." "I do exercise, gardening and walking and avoid grudges because they can also have a negative effect in my life."

Note:

† denotes dominant sub-theme

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