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Using syndemic theory to understand food insecurity and diet-related chronic diseases

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ABSTRACT

Syndemic Theory (ST) provides a framework to examine mutually enhancing diseases/health issues under conditions of social inequality and inequity. ST has been used in multiple disciplines to address interacting infectious diseases, noncommunicable diseases, and mental health conditions. The theory has been critiqued for its inability to measure disease interactions and their individual and combined health outcomes. This article reviews literature that strongly suggests a syndemic between food insecurity (FI) and diet-related chronic diseases (DRCDs), and proposes a model to measure the extent of such interaction. The article seeks to: (1) examine the potential syndemic between FI and DRCDs; (2) illustrate how the incorporation of Life History Theory (LHT), into a syndemic framework can help to highlight critical lifeperiods when FI-DRCD interactions result in adverse health outcomes; (3) discuss the use of mixed methods to identify and measure syndemics to enhance the precision and predictive power of ST; and (4) propose an analytical model for the examination of the FI-DRCD syndemic through the life course. The proposed model is more relevant now given the significant increase in FI globally as a result of the ongoing COVID-19 pandemic. The differential impact that the pandemic appears to have among various age groups and by other demographic factors (e.g., race, gender, income) offers an opportunity to examine the potential FI-DRCD syndemic under the lens of LHT.

During the 1990s, medical anthropologist Merrill Singer developed Syndemic Theory (ST) in response to the convergence of multiple epidemics (e.g., HIV/AIDS, substance abuse, and violence) taking place in Hartford, CT (Romero-Daza et al., 2003; Singer and Clair, 2003; Weeks et al., 1998). ST provides a framework to examine two or more mutually enhancing diseases or health conditions in socio-ecological settings where social inequality and inequities exist (Baer et al., 2013; Singer, 2009; Singer et al., 2017). ST has been used to examine infectious diseases (Freudenberg et al., 2006; Hill et al., 2019; Himmelgreen et al., 2009; Romero-Daza et al., 2003; Singer, 2000), non-communicable diseases (Chukwuma, 2017; Himmelgreen et al., 2017; Mendenhall, 2014; Mendenhall et al., 2017), and mental health conditions (Diderichsen and Anderson, 2019; Weaver and Mendenhall, 2014).

The interaction between food insecurity (FI) and diet-related chronic diseases (DRCDs) suggests a potential syndemic, as limited access and availability of food can result in compromised diets and DRCDs (Himmelgreen et al., 2012; Laraia, 2013; Page-Reeves et al., 2019; Savage et al., 2019; Tarasuk, 2005). This article aims to contribute to this topic by examining the FI-DRCD interaction through the life course under the lens of Life History Theory (LHT). The article proposes a model to ascertain whether the FI-DRCD interaction is, in fact, a syndemic, and to enhance the precision and predictive power of ST (Tsai and Burns, 2015; Tsai, 2018).

The goals of this paper are to:

- Examine the potential FI-DRCD syndemic drawing on existing literature
- Incorporate LHT to highlight critical life-periods (e.g., pregnancy) when the FI and DRCD interactions are especially detrimental
- Discuss the use of mixed methods to better understand and measure the potential FI-DRCD syndemic
- Propose a model of FI and DRCD interactions through the life course using ST

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1. FI and diet-related chronic diseases

While ST has mostly been applied to infectious diseases, it is now being used to examine non-communicable diseases including DRCDs such as type 2 diabetes, hypertension, cardiovascular disease (CVD), and obesity (Dressler, 2003; Mendenhall, 2014, 2016a; 2016b, 2019; Mendenhall et al., 2015, 2017; Swinburn et al., 2019). Broadly defined as limited access to food of enough quantity and quality, FI is an important determinant of health. Although FI stems from social inequalities and inequities, it is directly tied to biological processes in which diseases interact. Various definitions of FI exist, such as the limited or uncertain availability of nutritious and safe foods, the lack of access to sufficient amounts of safe and adequate foods for normal growth and development, and the inability to acquire acceptable foods in socially acceptable ways (Chilton et al., 2017; Coleman-Jensen et al., 2018). These definitions include four dimensions to determine whether individuals, households, and communities are food secure (Adhikari, 2018):

- **Availability:** Determined by the supply of food of sufficient quantity and quality. Availability depends on food production, food storage, and food assistance.
- **Access:** Determined by the ability of individuals and households to have adequate resources to obtain nutritionally adequate and safe food. Access is dependent on income, purchasing power, household production, market capacity, and food supply chains.
- **Utilization**: Determined by the consumption of nutritious food that can be adequately metabolized by the body. Utilization is affected by health status, feeding practices, food quality and safety, and access to health care, sanitation, and clean water.
- **Stability**: Determined by the interaction of Availability, Access, and Utilization. Stability is dependent on ecological factors (e.g., weather, seasonality, and soil quality) and on political and economic institutions and individual decision-making power. Instability on one or more of these dimensions increases the likelihood of FI.

1.1. FI and obesity

FI and chronic hunger contribute to under-nutrition, nutritional deficiencies, and DRCDs. FI may be also associated with an over-consumption of highly processed foods high in calories, fat, and refined carbohydrates increasing the risk for obesity (Franklin et al., 2012). Reliance on cheap, energy-dense foods contributes to adiposity and obesity which are associated with chronic disease (Vercammen et al., 2019). In adults, obesity is defined as a body mass index (BMI) equal to or greater than 30 (National Institutes of Health National Heart, Blood, and Lung Institute n. d.), while in children it is defined as a BMI at or higher than the 95th percentile for age (Barlow, 2007; Wang, 2001). The resulting FI-obesity paradox, a condition where individuals struggle with FI and obesity simultaneously, has been widely documented (Dinour et al., 2007; Franklin et al., 2012; Hernandez et al., 2017). Recently, the Lancet Commission examined the global syndemic of obesity, undernutrition, and climate change, asserting that "(m)alnutrition in all its forms, including obesity, undernutrition, and other dietary risks, is the leading cause of poor health globally" (Swinburn et al., 2019, 791).

Research demonstrates a positive association between FI and obesity among women, especially those from minority groups (Hernandez et al., 2017; Laraia, 2013). Similarly, Gooding et al. (2012) found FI to be more common among young women than young men, with women having a higher average BMI than their food secure counterparts. Dinour et al. (2007) found that FI was a significant predictor of overweight status for women, even after adjusting for socioeconomic status, sociodemographics, government assistance, environmental factors, and lifestyle factors.

There is also growing evidence of an association between FI and obesity among younger groups (Franklin et al., 2011). Gundersen et al. (2008) found that despite not being associated with one another, child specific FI and obesity often coexist, especially among low-income populations, with 25 percent of food insecure children also being overweight. Lohman et al. (2009) found that the interaction between FI and maternal stressors was linked to childhood obesity, as an increase in maternal stressors increased an adolescent's risk for obesity. Finally, a study among homeless youth in Minnesota (n = 202) found that 55 percent of participants did not have enough food in the house and 25 percent went to bed hungry (Smith and Richards, 2008). However, 45 percent of male participants and 50 percent of female participants were overweight or at risk for being overweight, leading the researchers to conclude that overeating, a coping mechanism for FI, increased the risk for obesity among this population.

Research has shown that FI and obesity may be causally related (Becerra et al., 2017; Weaver and Trainer, 2017). Himmelgreen and colleagues (2006; 2014) reported this in the Monteverde Zone, Costa Rica, where the growing tourism industry led to a shift away from coffee production and dairy farming. Despite efforts to grow the slow food movement in the Zone, the lack of time to prepare foods due to work demands outside the home led many residents to rely on energy-dense and nutritionally-inadequate purchased foods. High rates of FI were associated with high carbohydrate intake and adult overweight and obesity that correlated with high rates of diabetes and hypertension reported by the local clinic (Himmelgreen et al., 2006, 2014).

1.2. FI and CVD, hyperlipidemia, and hypertension

FI is associated with an increased likelihood of chronic disease, the number of chronic conditions suffered by individuals, and individuals' assessments of their own health. Food security status can be an even better predictor of chronic conditions than income (Gregory and Coleman-Jensen, 2017). A major threat to the health of food insecure individuals is CVD, which is defined as a disease affecting the heart or blood vessels and includes diseases such as coronary artery disease and congestive heart failure, both of which are of significant concern in the U.S. (National Cancer Institute, n. d.). The risk of developing CVD increases with smoking, high blood pressure or cholesterol, unhealthy diet, low levels of exercise, and obesity (Mendis et al., 2011). Similarly, "metabolic syndrome" refers to a condition "marked by extra fat around the abdomen, high levels of blood glucose when not eating, high levels of triglycerides in the blood, low levels of high-density lipoproteins, and high blood pressure" and is associated with an increased risk of developing diabetes and CVD (National Cancer Institute, n.d.).

As a DRCD, CVD has been linked to FI. Mendy et al. (2018) found that FI was associated with risk factors for CVD, including obesity, hypertension, and diabetes among adults in Mississippi. Using data from the 2015 Mississippi Behavioral Risk Factor Surveillance System (n = 5870), the study found that 42.9 percent of respondents were food insecure. Those who had hypertension were 51 percent more likely to be food insecure, and those with diabetes were 30 percent more likely to be food insecure. Although this is not conclusive evidence of synergy or interaction effects, it does suggest the need to study FI and CVD as co-occurring, and possible mutually reinforcing and interacting conditions.

CVD is a leading cause of mortality in the U.S. Although risk can be lowered with a healthy lifestyle, FI reduces the mitigating power of lifestyle changes. In a study by Vercammen and colleagues (2018), the least food secure households experienced a heightened ten-year risk of CVD, and reduced food security correlated to higher CVD risk and measures of adiposity. Adiposity and obesity are higher in food insecure populations than in food secure ones, indicating that FI is a significant factor in CVD risk (Myers et al., 2019). Given CVD's association with negative health outcomes including "all-cause mortality; CVD, coronary, stroke mortality; end stage renal disease; nonfatal CVD events; incident cancer, venous thromboembolism, depression, quality of life, compression of morbidity, overall cognitive function, and Medicare charges," (Saiz et al., 2016, 6), it is imperative to examine the association between CVD and FI thoroughly.

Other conditions associated with CVD, such as hyperlipidemia and hypertension, are influenced by dietary intake, and have also been implicated in a relationship with FI. Hyperlipidemia, as it pertains to low-density lipoproteins (LDL) is total cholesterol greater than the 90th percentile for a given patient's age, sex, and ethnicity (Frederickson, 1971). The CDC's NHANES III identifies 90th percentile cutoffs for various populations (262 mg/dL and 252 mg/dL, for non-Hispanic black men and women, respectively; 258 mg/dL and 242 mg/dL, for white men and women respectively; and 257 mg/dL and 258 mg/dL, for Mexican-American men and women, respectively) (CDC, 1994). The American College of Cardiology and the American Heart Association define adult hypertension as a systolic blood pressure greater than or equal to 130 mm Hg, and/or a diastolic blood pressure greater than or equal to 80 mm Hg (Whelton et al., 2018). Hypertension and hyperlipidemia are linked to increased risk for CVD as well as to FI. In their analysis of over 5000 NHANES adult participants, Seligman et al. (2010a) found that FI was associated with self-reported hypertension and hyperlipidemia as well as with lab-confirmed hypertension, thus suggesting increased risk for CVD.

1.3. Food insecurity and diabetes

Diabetes is another DRCD that poses a threat to those facing FI. According to the American Diabetes Association (2011), criteria for the diagnosis of diabetes include any of the following: (1) an A1C glycated hemoglobin greater than or equal to 6.5%; (2) a fasting plasma glucose level greater than or equal to 126 mg/dL; (3) a 2-h plasma glucose level greater than or equal to 200 mg/dL during an oral glucose tolerance test; or (4) a random plasma glucose level greater than or equal to 200 mg/dL in a patient with classic symptoms of hyperglycemia.

FI and type 2 diabetes often occur in tandem, as food insecure individuals are more likely to consume lower quality diets that consist of fewer fruits and vegetables and more processed, calorie-dense foods (Gucciardi et al., 2014; Seligman et al., 2007). While not a direct cause of the disease, these dietary factors increase an individual's risk for developing diabetes and may make its management more difficult. . A study in Canada found that the prevalence of household FI was higher among adults with diabetes (Gucciardi et al., 2009). In a study of 201 Latinas, Fitzgerald et al. (2011) found that individuals with very low food security were 3.3 times more likely to have type 2 diabetes, regardless of employment status, acculturation, waist circumference, and lifestyle. Seligman et al. (2010a) found that individuals from food-insecure households had a significantly higher risk for clinical diabetes than their food-secure counterparts. Moreover, FI was associated with inadequate control of the disease among those already diagnosed. Seligman and colleagues found that FI is an independent risk factor for poor glycemic control and hypoglycemia (Seligman et al., 2010b; Seligman et al., 2012). This is attributed in part to the difficulty of maintaining an appropriate diet for managing diabetes when food insecure (Gucciardi et al., 2014; Seligman et al., 2012).

1.4. FI as cyclical and structurally implicated

The behavioral and biological modifications that occur under conditions of FI speak to the severity of the issue and its link to chronic disease, including DRCDs. The FI and DRCD relationship is cyclical and perpetuates negative health outcomes, primarily affecting minority, lower income populations with lower levels of education (Saiz et al., 2016). Food insecure households are more likely to cycle in and out of periods of food scarcity on a monthly or yearly basis, leading to poor metabolic regulation and an increased desire for nutrient-poor, energy-dense food items (Vercammen et al., 2018). When combined with patterns of scarcity/abundance and long-term FI, the financial dependence on, and biological cravings for, inexpensive and unhealthy foods contribute to physiological shifts of these metabolic pathways. When this occurs, biological functions are fundamentally altered by FI. For instance, the severe stress of food insecure conditions can change the cortisol and neuropeptide release patterns that are regulated by the hypothalamus-pituitary-adrenal axis (HPA axis), leading to the accumulation of visceral fat, which is linked to a number of chronic diseases (Laraia, 2013).

This cycle of FI and DRCDs is further complicated by the difficulty of chronic disease management under significant financial constraints, which negatively impact self-care and health practices (Gucciardi et al., 2009). Medication underuse due to cost, impaired self-monitoring of glucose levels, poor mental health, and gaps in food intake can lead to unregulated glycemic levels—all of which augment health issues (Vercammen et al., 2018). In a study of a home-based diabetes self-management intervention, Silverman et al. (2015) found that FI was associated with depression, diabetes distress, low medication adherence, and poor glycemic control (Silverman et al., 2015). Household FI is also associated with an increased likelihood of unhealthy coping behaviors such as smoking and overeating, increased blood pressure, increased psychological distress, and overall poorer physical health (Gucciardi et al., 2009, 2014; Vercammen et al., 2018).

The interaction between FI and DRCDs is mediated, in part, by dietary intake (Hanson and Connor, 2014; Mello et al., 2010; Seligman et al., 2010a), which is often influenced by other socio-economic determinants (e.g., education, income, employment, place of residence, transportation, access to healthcare, and level of stress). The mutually enhancing effects of FI and DRCDs are likely more complicated in areas where availability and access to nutritionally adequate foods are limited. A food desert is an area devoid of access to fresh fruits and vegetables and other healthy foods (Gallagher, 2010) while a food swamp is characterized by an overabundance of fast-food restaurants and convenience stores (Khazan, 2017). Food deserts and food swamps are commonly found in inner cities and rural areas, especially in the U.S. These conditions likely exacerbate the cycle in which reduced food budgets hinder self-management capacity, which consequently increases healthcare expenditures, thereby further reducing food budgets (Seligman et al., 2010a).

Weaver and Fasel (2018) have argued that the pathways linking FI and DRCDs may include the systematic effects of poverty, micronutrient deficiencies, and environmental factors (e.g., toxins). This suggests that a FI-DRCD syndemic may exist; however, the co-occurring factors that interact with FI synergistically to exacerbate DRCD health outcomes have not yet been identified. As such, ST provides a framework to explore the relationship between FI and DRCDs and to disentangle and measure the effects of the FI dimensions (i.e., availability, access, utilization, and stability) on dietary intake and DRCD risk.

2. Conceptualizing the FI-DRCD syndemic using Life History Theory (LHT)

The concept of FI has been applied at different levels (e.g., individual, household, community, national, regional, and global) and throughout the life course (Frongillo, 2019). There are social inequalities and inequities and biological needs experienced at particular stages during the life course (e.g., pregnancy, adolescence, older age) when FI can have more consequential effects on physical and mental health. LHT can be employed to examine and address the ill effects of syndemics at each life stage.

LHT posits that there are similarities between humans and other primates in the growth that occurs through the four main stages of the life course: gestation, infancy, juvenility and childhood, and adulthood (Trevathan, 2018). LHT examines the evolution and function of these life stages, as well as the behaviors related to each of them (Stinson et al., 2012). Likewise, LHT is used to examine the food energy and nutrients available in the ecosystem, the energy and nutrients needed for survival (growth, development, maintenance, reproduction), and the trade-offs that occur when there is an imbalance between availability and requirements. LHT has been used to explore issues including the FI-obesity paradox. For example, Schlüssel et al. (2013) examined the impacts of the paradox among adult women, female adolescents, and young children. Their findings indicate that female adolescents who were food insecure were twice as likely to be obese as compared to their food secure peers (Schlüssel et al., 2013). Household FI has been linked to increased obesity risk throughout the life course and researchers have hypothesized that childhood FI may increase the risk for long-term ill health (Frongillo and Bernal, 2014). Miller (2014) studied the relationship among dietary intake, fat deposition, and nutritional status among breastfeeding Ariaal infants in northern Kenya, finding that infants who experienced chronic nutritional stress also accumulated fat deposits, which indicated reduced oxidation of fat.

Given the synergistic social and biological systems involved in DRCDs and FI, the precision and predictive power of ST is enhanced by the use of LHT, which adds the elements of time, trajectory, and life stages. This enables the examination of the interaction of diseases/ health conditions during the life course. Unterberger (2018, 107) underscores this by pointing to the "intersecting and synergistic effects of place/environment, timing, timelines, and equity on health over the life span." This is important as "traumas and illnesses continue to add and build up over time," creating exponential, not merely additive or linear effects (Unterberger, 2018, 109).

Different life stages present different health issues as well as specific needs (e.g., growth and development, immunity, reproduction). Early-life adverse experiences can have health implications later in life. For example, Horton and Barker use LHT to disentangle how early-life health issues among farm workers' children produce childhood oral caries, which are linked with stigma, speech pathologies, and low self-esteem, and with later-life heart disease, stroke, and pancreatic cancer (Horton and Barker, 2016, 137-8). Here, LHT highlights the role of the environment through life course experiences. The authors found that many caregivers' rural environments in Mexico were relatively uncariogenic—involving few processed and refined foods, and thus producing few dental caries—however upon migration to the U.S., a broader bio-cultural transition took place (Horton and Barker, 2010, 205). For many mothers, being exposed to different diets and infant feeding practices, entering the workforce for the first time, and having easy availability of relatively low-cost formula, led to a transition in diet, and in oral health. Here, "life course" includes a variety of changes including biological (the measurable health effects), knowledge and culture-based (psychosocial contexts influencing how agency in enacted), and environmental (ecological contexts and changes experienced) ones that occur throughout an individual's life. ST is noteworthy for its ability to draw in a psycho-biosocial analysis of such phenomena.

Studies among adolescents suggest that, depending on the timing and extent of FI, the onset of puberty may be delayed or accelerated (Belachew et al., 2011, 2013). For example, Burris (2018) examined the relation between FI and menarche among a low-income urban group in the U.S., finding that food insecure teens experienced earlier menarche than their food secure counterparts. There was a dose response with increasing severity of FI associated with earlier menarche. These findings are relevant, given the association between early menarche and obesity in teens and with diseases like breast cancer later in life. The results are contrary to those of studies showing an association between FI and delayed menarche due to undernutrition and micronutrient deficiencies in resource-poor settings (Cordeiro et al., 2012; Hoffman and Klein, 2012).

The impact of FI among young adults is a burgeoning area of research indicating higher odds of chronic disease risk among those who are food insecure. For instance, Nagata et al. (2019) used data from the National Longitudinal Study of Adolescent to Adult Health to construct a multiple logistic regression model among young adults 24–32 years of age (n = 14,786). They found that 11 percent of participants were food insecure, self-reporting increased incidences of diabetes, hypertension, and "very overweight" status. Using this same data set, Gooding et al. (2012) evaluated differences between young adult women (n = 7116) and men (n = 6604), finding that women (14%) experienced higher rates of FI than men (9%). Thus, there appears to be a dynamic where FI is associated with adverse health outcomes and where gender also plays a role increasing risk for FI and its accompanying health risks among women.

Young adults who experienced FI during their adolescence have higher BMI and waist-to-hip ratio than those who were not food insecure in their younger years, indicating links between different stages in the life course (Darling et al., 2017; Laraia, 2013). Given the social, economic, and life transitions occurring during this stage of life, the health impacts are likely both diachronically cumulative and situationally contextual. Recent studies among college students indicate that up to 59 percent experience FI at some point in their college career (Chaparro et al., 2009). Henry (2020) offers an important insight into these complex issues by exploring the feelings, motivations, and challenges faced by 92 young adults, many of whom had experienced FI before college. Henry examines how FI is tied with issues of negative physical health outcomes, as well as with feelings of stigma and shame that tend to overlap with one another. Several participants expressed a desire for a shift in cultural norms around how communities discuss FI and its consequences.

As described previously, FI is associated with DRCDs such as type 2 diabetes, hypertension, metabolic syndrome, and CVD among adults. For those with chronic diseases such as diabetes, FI is especially detrimental as it impacts the management of the condition and increases the risk for complications such as peripheral neuropathy, kidney disease, and retinopathy, among others (Banerjee et al., 2017; Cettomai et al., 2013; Marjerrison et al., 2011). For older adults, FI can exacerbate health problems that are part of the natural aging process. Studies indicate that seniors who are food insecure have higher risk for diabetes, hypertension, heart conditions, congestive heart failure, gum disease, and asthma (National Council on Aging, 2019).

Given the increasing evidence of the comorbidity of FI and DRCDs, it stands to reason that a syndemic may exist as plausible biological interactions may occur on the nutritional and health status of individuals that may exacerbate the burden and prognosis of both FI and DRCDs. *Thus, we propose a dynamic model where upstream changes in the socio-ecological environment (*e.g., *FI) can modify both behaviors (*e.g., *eating highly processed foods) and biology (*e.g., *weight gain and fat-deposition), and result in adverse health outcomes (*e.g. *type 2 diabetes). LHT can be added to the model to help contextualize and evaluate the energy and nutrients required at different stages during the life course in order to prevent or mitigate adverse health outcomes in the short- and long-term (Himmelgreen* et al., *2012)*. Finally, concepts such as Chronicity, the personal and social changes that chronic illnesses pose to an individual, and Syndemic Vulnerability, those social inequalities and inequities that increase susceptibility to the ill effects of syndemics (Weaver and Mendenhall, 2014), can be included in the model to examine syndemic interactions at the macro-, meso-, and micro-levels (Carnes, 2016; Gilbert et al., 2013; Pollard et al., 2018).

Fig. 1 presents the conceptual model proposed to examine the FI-DRCD syndemic through the life course. Reading from left to right, social inequality and inequity determine FI, which affects the availability, access, and utilization of food. This leads to food instability where there are nutritionally inadequate foods that may be unsafe and/ or socially inappropriate. The stress (e.g., worry, anxiety, depression) over FI has an amplification effect that varies through the life course depending on nutritional and other needs. Depending on the life course stage, the macro- and the micro-nutrient budget affects nutritional status and health, which can ultimately result in one or more DRCDs, especially, but not exclusively, in adulthood. Finally, the DRCDs create a feedback loop that can become a vicious cycle affecting the life-history trade-offs and changes in nutritional status and health, thereby

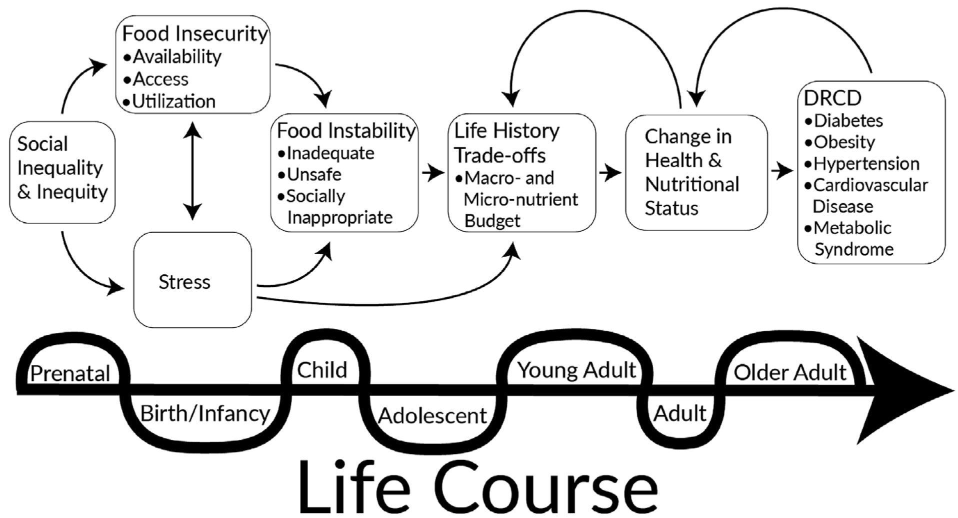

Fig. 1. Conceptual model of the FI-DRCD syndemic.

amplifying adverse health outcomes. This model is a heuristic device for the research design (e.g., mixed methodology), analysis (e.g., SEM), programming (e.g., food prescription programs), and policies (e.g., rezoning for local urban food production) to address the FI and DRCD syndemic.

3. Mixed methods for understanding and measuring the potential FI-DRCD syndemic

ST postulates that the interaction of two or more epidemics results in a multiplying (rather than simply an additive) effect. However, there has been criticism related to the inability to differentiate between comorbidities and true syndemics, to operationalize the specific level of interaction between the epidemics at play, and to quantify this multiplying effect. What follows is a discussion on the methods, variables, and analytical tools that can be used to examine the potential FI and DRCD syndemic and to increase the precision and predictive power of syndemic studies. Here we present an initial postulation of a model to determine whether, and to what extent, there is a syndemic between FI and DRCDs.

The dimensions of FI include limited food availability and access along with biological utilization of food and nutrients, which can result in compromised diets and increased risk for DRCDs. The timing and severity of FI during the life course can have multiplicative effects where DRCD rates are higher than expected. In order to assess these interactions in a comprehensive way, research should employ qualitative and quantitative methods. Qualitative methods offer in-depth knowledge about how people experience the realities of FI and about the overall impact it has on their well-being. In turn, this provides insight into the complex social, economic, and behavioral forces that explain the phenomena. For instance, qualitative methodologies have been used to investigate critical life-periods that are implicated in the life course while also serving as the primary methods used to first investigate syndemic interactions occurring within ecologically disadvantaged contexts. For example, the convergence of substance abuse, violence, and AIDS in Hartford, CT (Singer and Clair, 2003) and of violence, depression, diabetes, immigration, and abuse (Mendenhall, 2016b) were primarily investigated using qualitative, methods.

Quantitative methods allow for the collection of generalizable information from population-based data to assess the interactions among mutually reinforcing conditions (FI, DRCDs). Innovative methods are needed to assess the synergistic epidemics beyond just assessment of dependent variables (e.g., FI level), contextual factors or modifying variables (e.g., dietary intake, psychometric indicators of stress and depression) and health outcome variables (e.g., BMI, HbA1c levels, blood pressure, and cortisol). It should be noted that while none of these methods is unique to ST, they are all necessary tools for the systematic collection of information needed to test the proposed model.

3.1. Qualitative methods: interviews, focus groups, and photovoice

Qualitative methods offer an ideal tool for the collection of rich data on the lived-experience of people affected by FI and related conditions. Free listing, pile sorting, and ranking serve to examine the way in which individuals (especially those of diverse cultural backgrounds) conceptualize issues related to diet and FI (Bernard and Gravlee, 2014). For example, to assess perceptions related to diet quality in Costa Rica, Himmelgreen and colleagues (2012; 2014) first asked participants to list all the foods they commonly consumed (free listing) and then to categorize them into those they considered “healthy,” “unhealthy,” “prestigious,” etc. (pile sorting). By analyzing the way individuals classified food items, and their rationale for doing so, researchers obtained a culturally nuanced understanding of food preferences and choices.

Another method often combined with free listing involves the ranking of items. For example, to assess how the types of foods consumed vary depending on level of FI, researchers can elicit a ranking of food items in terms of “desirability,” from most to least preferred foods, along with an explanation of when the least desirable items are consumed. When combined with dietary recalls, this ranking allows for the identification of strategies used to cope with FI. Ranking is also useful when exploring how individuals prioritize competing needs such as food/nourishment, health care, rent, transportation, etc. Similarly, these methods can be used to explore the interaction between FI and associated conditions, through the use of prompts to list, categorize, and rank the impact FI has on overall health in general, and on DRCDs specifically.

Data collected through open-ended and semi-structured interviews and focus groups serve to contextualize statistical data and “put a face” to the numbers. When working with children or teens, visual methods such as photovoice are especially useful. In photovoice, participants take pictures that show what a given issue means to them and engage in discussion with peers about the topic. They then create a public exhibit to raise awareness about the issue at hand and to advocate for action from various stakeholders. Burris et al. (2020) used photovoice in their study of adolescent FI in Florida. Their research highlighted strategies teenagers adopt to deal with FI such as shoplifting at convenience stores and skipping meals so that their younger siblings can eat. The study also elucidated the stigma of participating in school-based reduced-lunch initiatives, which leads teenagers to avoid using this much-needed program. Importantly, the exhibit generated from this project helped the school district modify the way in which it provided food assistance.

Interviews, focus groups, and photovoice are especially suited for the study of syndemics since they yield rich in-depth data to illustrate the impact health conditions have on one another. An inductive approach to qualitative data analysis is most appropriate for these methods. Open coding allows themes to emerge naturally from the data, reducing the risk of confining qualitative data to predetermined categories and misrepresenting participants' experiences. Ryan and Bernard (2003) identify numerous ways to effectively analyze qualitative data, each best-suited for specific research goals. A number of techniques are relevant for coding textual data collected from free lists, interviews, and focus groups. Applicable scrutiny techniques include looking for repetitions, similarities and differences, and metaphors and analogies in text.

Processing techniques such as word lists, key words in context (KWIC), and word co-occurrence are also useful for identifying major themes. As photovoice generates non-textual data in the form of pictures, analysis should rely on an examination of similarities/differences, repetitions, and/or what is missing from the collected photographs and accompanying narratives (Ryan and Bernard, 2003). The themes generated from coding will be useful for developing an understanding of the FI-DRCD syndemic by unearthing the major and overlapping life experiences. Qualitative methods are important in FI-related and syndemic-focused research because of their ability to capture powerful narratives that provide insight into the embodied experiences of participants.

3.2. Quantitative methods: measurements and analytic frameworks

Syndemics are unobservable factors or constructs that represent latent variables or latent traits. Thus, it is important to utilize reliable measures for such constructs. There are several evidence-based scales that have been validated to measure FI, including: the USDA Household Food Security Survey Module (HFSSM), the Household Food Insecurity Access Scale (HFIAS), the Latin American and Caribbean Food Security Scale (ELCSA), and the Food Insecurity Experience Scale (Tuholske et al., 2018). These scales measure uncertainty in the ability to obtain food, compromises regarding the quality and variety of food, reductions in food quantity (including skipping meals), and lack of food consumption for a day or more. Together with other methods, these scales can examine and measure the FI dimensions of limited food access, availability, biological utilization, and stability as previously discussed. The HFFSM module is used widely and is administered nationally in the US; it provides data that can be scored to categorize individuals and households into four levels of food security (USDA, 2019).

3.2.1. Measures of dietary intake

Dietary intake at the individual and household levels can be examined using 24-hour food recalls, food frequency questionnaires (FFQ), and Food Accounts. The first two provide individual-level data, while the latter give a daily record of all the food entering the household (Gibson, 2005). Abbreviated FFQs can be used to identify which nutritionally adequate, safe, and socially appropriate foods are uncertain or limited. There is an array of scales to assess whether a set of foods aligns with national and international dietary guidelines. For instance, the Healthy Eating Index (HEI-2-16) measures dietary quality and assesses individual and group compliance with the U.S. Dietary Guidelines for Americans (NCI, 2019).

3.2.2. Assessment of other social determinants of health (SDoH)

Typically, surveys are used to measure SDoH associated with DRCDs. SDoH variables include place of residence, race and ethnicity, socioeconomic status, education, and employment, among others. Multiple variables can be clustered in order to measure economic stability (e.g., employment, income, expenses), neighborhood and physical environment (e.g., housing, transportation), education (e.g., literacy, language), community and social context (e.g., social connectedness, social support systems), and health care (e.g., health coverage, provider availability, and quality of care) (Artiga et al., 2019). Individual level indicators of SDoH such as social support, loneliness, and self-efficacy can be measured as well. The Multidimensional Scale of Perceived Social Support (MSPSS) and the modified Rasch-based de Jong Gierveld (DJ) loneliness scale have been used in studies of FI, health, and social connectedness among older adults (Burris et al., 2019).

3.2.3. Psychosocial and biometric methods and measures of health outcomes

Psychometric instruments such as the Perceived Stress Scale (PSS) can measure the degree to which situations in an individual's life are stressful (Cohen, 1986; Lee, 2012), and have been used in FI and mental health studies (Laraia et al., 2006: Jilcott et al., 2011a). Likewise, c-reactive protein tests are useful to measure inflammation, while cortisol has been measured as an indicator of stress in at least one study examining the relationship between household FI and insulin resistance in Latinos with type 2 diabetes (Bermudez-Millan et al., 2019). In another study, hair cortisol levels were associated with FI status in low-income mother-child dyads (Ling et al., 2019).

Common indices to assess nutritional status include BMI, waist-to-hip ratio, weight-for-age, height-for-age, and weight-for-height, among others (Gibson, 2005). In addition to anthropometric measures such as weight, height, and skinfolds, other methods including densitometry, bioelectrical impedance analysis, dual-energy X ray absorptiometry, computed tomography, and magnetic resonance can be employed when more exact measures of body composition are desired (Fosbøl and Zerhan, 2015). With all of these methods, feasibility and appropriateness need to be taken into account before they are administered. Nutrient and other indicators of DRCDs include hemoglobin and hematocrit, blood glucose and HbA1c, cholesterol (total cholesterol, low-density lipoproteins, high-density lipoproteins, triglycerides), doubly labeled water (caloric intake), and blood pressure.

4. Analytical tools to measure FI-DRCD syndemic interactions

There are useful analytical tools to compare individuals, households, regions, and countries when examining interactions between FI and DRCDs. When planning syndemic analyses, two concepts must be considered: disease concentration and disease interactions. *Disease concentration* implies testing the hypothesis that two or more diseases co-occur in particular temporal or geographical contexts due to harmful social conditions (e.g., associated with each other or co-variation, and/or mediated by harmful conditions). Demonstrating co-occurring epidemics is just a partial picture of the theory of syndemics; interaction must be present for synergistic effects. Statistical interaction occurs when the effect of one explanatory variable depends on the particular level or value of another explanatory variable (Fitzmaurice, 2000). *Disease interaction* implies that epidemics must also interact at the level of populations and individuals, with mutually enhancing deleterious consequences for health risks. Interactions may be additive or multiplicative. Additive interaction refers to the interdependent action of two or more factors to produce or prevent a joint effect and assesses whether the combined effect of two exposures is more or less than the sum of their separate effects. Thus, additive interaction may be expressed as increasing or decreasing joint effects.

On the other hand, multiplicative interaction (relative risk) indicates the degree to which the likelihood of a particular exposure is multiplied (amplified beyond the sum of parts) in individuals with a given risk factor compared to those without it. Thus, syndemic analysis must measure the extent to which the effect of the two factors together exceeds the effect of each considered individually either additive or multiplicative for the joint effects of the two syndemic factors. It is also necessary to determine the size and the statistical significance of interactions to quantify how large the mutually reinforcing relationship between epidemics is. Also, syndemic factors may affect health outcomes in direct and/or indirect ways due to the effects of intermediate (mediation) or contextual (confounding) factors. Clearly, testing ST in tandem with LHT presents several challenges that cannot be easily addressed with simple bivariate analyses. Very important effects may be missed if single factors are examined independently.

Researchers need a collection of tools and techniques to study synergistic relationships. The attributable proportion due to interaction and the synergy index are two measures that have been used to assess simple interactions and are readily applicable to categorical outcomes with observed variables (e.g., odds ratios, logistic models) (Rothman, 1976, 1974). Assessing interactions with covariates is also possible with multiple factors using generalized linear models. This can be done by introducing interaction terms or by conducting moderation analyses using stratified models. However, if syndemics are conceptualized as latent variables (with continuous scales) that influence each other, the simpler indexes and conventional regressions will not be appropriate as they cannot assess multiple dependent variables and the co-variation of a large number of determinants at multiple levels (e.g., SDoH at individual, household, and community levels) simultaneously. Also, principles of the LHT need to be considered to identify disease interactions during critical periods of human development (i.e., vulnerability), with a longitudinal view (latency of exposure/outcomes) and considering cumulative exposures (chronicity) over the lifespan. Because ST assumes the presence of factors as underlying mechanisms, rather than simple bivariate relationships of observed measures or indicators, more complex analyses are needed to assess interactions with latent variables.

4.1. Modeling syndemic interactions using structural equation modeling

One useful set of techniques is *structural equation modeling (SEM)*, which is a collection of multivariate statistical techniques (i.e., parametric regression, confirmatory factor analysis, path analysis, and latent growth curve modeling) especially suited to assess structural relations of multiple independent variables with multiple dependent variables, including latent variables and latent classes. We argue that SEM, also known as simultaneous equations or covariance structure models, can be effectively utilized to model complex relationships between directly observed and indirectly observed (latent) variables, which is precisely the inquiry under ST constructs. SEM simultaneously solves systems of both linear and non-linear equations.

Recently, SEM has gained popularity in syndemic research applications in diverse fields such as public health, epidemiology, medicine, and the social sciences. A variety of proprietary and open-source software choices are available, such as MPLUS, EQS, SAS PROC CALIS, SPSS/AMOS, STATA, LISREL, OpenMx, and others (Stein et al., 2012). Estimation methods allow for the assessment of categorical and continuous variables and non-normally distributed variables (Kline, 2015).

SEM Steps. The first step needed to use SEM with ST would be to conceptualize syndemic factors as latent variables (unobserved variables) and identify their corresponding indicators (measured variables) (Diamantopoulos and Siguaw, 2000). Such conceptual models should be represented in a diagram that specifies the variables and the relations among them (Kline, 2015).

Because SEM enables us to utilize latent variables and their interactions, it also permits the assessment of psychometric properties of LHT domains such as physical growth, sexual maturation, and sexual, social, and parental behaviors (Richardson et al., 2017). For instance, when we utilize psychometric scales to measure growth or even parent styles, we can use a special case of SEM called confirmatory factor analysis (CFA) to determine the measurement validity (factorial validity) of each latent variable. The model specified must be assessed to determine if it has sufficient number of parameters for estimation, or if it has so many that estimation cannot be determined (Kline, 2015).

The next step when using SEM consists of modeling the relationship between latent variables (called structural model). This step consists of path analyses where the relationships among latent factors are examined as simultaneous linear regressions. Here, SEM researchers estimate the parameters (Beta coefficients) and test their significance. One advantage of using SEM for ST and LHT is that measurement errors are accounted for and the pathways or effects can be separated from the influence of error or unmeasured confounding. Therefore, the pathways are more precisely measured (Helle, 2018).

Next, we evaluate the goodness of fit of the SEM to determine whether the measurement and structural parts of a model fit well with the theory-based hypothesis (Diamantopoulos and Siguaw, 2000). Syndemics under a life course approach (ST combined with LHT) will invariably call for the inclusion of multifaceted factors (risk and protective factors over the life trajectories); it is important that researchers find the models that are more useful (predictive power and with goodness of fit to the data) and parsimonious (fewer factors and pathways possible) (Grace et al., 2010). Thus, SEM fit can be assessed by fit indices, including absolute fit-, incremental (relative, comparative) fit-, parsimonious-, and predictive fit-indexes (Kline, 2015). If the goodness of fit for a specified model is poor, researchers can modify their models. Such a decision must be based on theory and evidence, not just on parameter statistics. Finally, researchers must follow the published guidelines for reporting results in SEM to ensure quality (McDonald and Ho, 2002; Schreiber et al., 2006).

The application of SEM is becoming more common in recent studies, demonstrating its usefulness for the analysis of complex latent models (Gonzalez-Guarda et al., 2011). SEM can be used to analyze the relationships between correlated variables (synergistic relationship and co-variation), to model risk and protective factors as latent variables as a function of multiple observed variables, to assess the association between multiple syndemic factors and multiple correlated outcomes of interest, and interactions among variables and factors. It is a valuable tool to advance the state of ST and inquiry.

SEM can be used to assess longitudinal associations and distinct pathways (syndemic risks - additive and multiplicative) that are considered in LHT (Gibbons et al., 2012). In particular, this can be assessed with latent growth and dynamic SEM (Grimm and Ram, 2018). Longitudinal SEM methods can be used to study within-person change, such as how a specific DRCD progresses, how FI differs across individuals, what its determinants are, and what its consequences over time are (Grimm and Ram, 2018). Latent growth methods have been applied in many domains to examine average and differential responses to interventions and treatments.

In this review, we introduce the growth modeling approach to studying change by presenting different models of change and interpretations of their model parameters. Therefore, the analysis of syndemic through SEM techniques can contribute to the evolutionary analysis of human life trajectories (Belsky et al., 2012; Ullman et al., 2005). Finally, through SEM, we can examine latent variable interactions that operationalize the complexities of LHT (Maslowsky et al., 2015). For instance, we can examine latent interactions of trauma and social support and how they affect FI during critical periods and life stages. Although there are different approaches to assess moderated SEM (Schumacker, 2002), they are widely available in current commercial software (Muthen and Muthen, 2016). Some special cases need to be considered when we examine interactions between latent and measured variables, in which a two-step procedure is needed (Klein and Moosbrugger, 2000).

Using the approach described above, the SEM representation shown in Fig. 2 of our proposed FI-DRCD Syndemic would be as follows:

f BY y1 y2 y3; where f is a latent factor (Social inequality)
f1 BY y4 y5 y6; where f1 is a second latent factor (Food Insecurity)

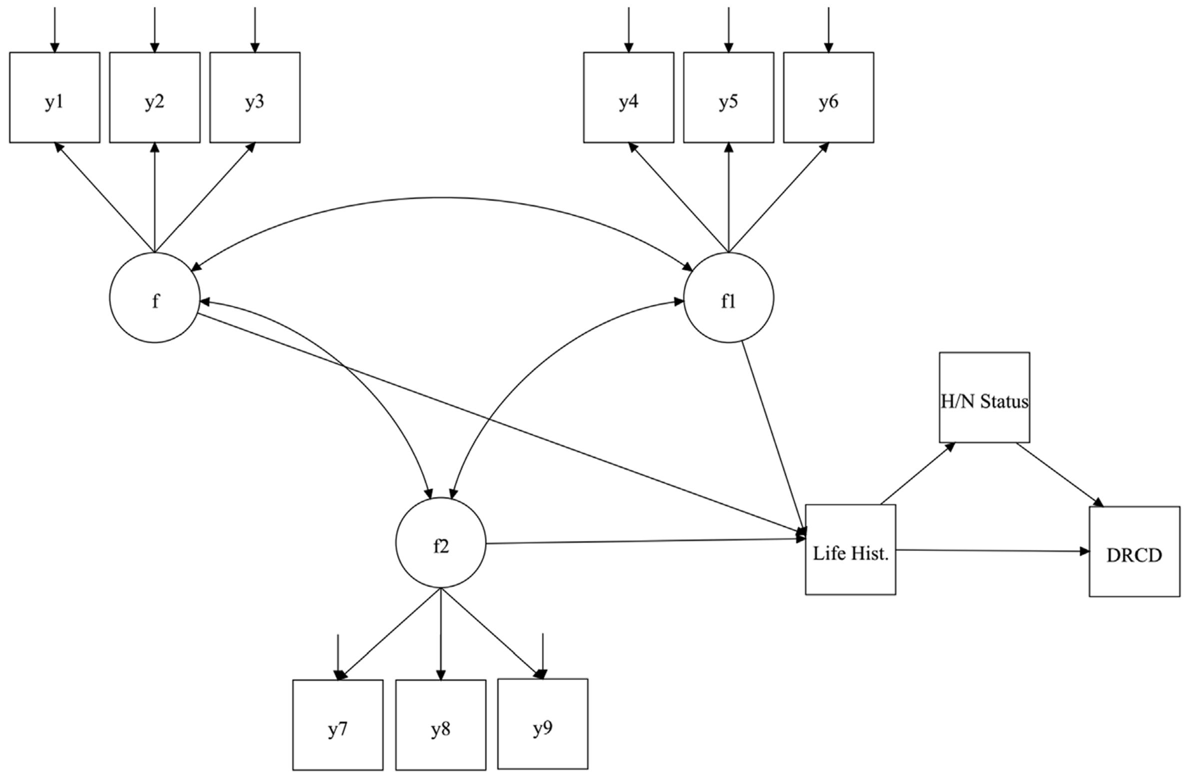

Fig. 2. SEM representation of proposed FI-DRCD syndemic.

f2 BY y7 y8 y9; where f2 is the third factor that researchers may be interested in (e.g., Stress or Violence or other)
where the statement BY means a confirmatory factor analysis and estimation of factor loadings.
Life Hist. ON f f1 f2; where the statement ON means regression estimation.
H/N Status ON Life Hist.;
DRCD ON Life Hist. H/N Status; “H/N Status” is a change in health status and nutrition and “Life Hist.” is life history trade-offs.
f1 WITH f; where the statement WITH means covariance.
f2 WITH f;
f1 WITH f2

The use of these and other analytical tools holds great promise for measuring the syndemic interactions of two or more mutually enhancing diseases or health conditions. Some challenges still remain when assessing the interaction of latent variables, particularly with models seeking multiplicative interaction (X*Y) as co-variances may be negative and models do not converge (Maslowsky et al., 2015). It is not a failure of the theory, but a limit of the methods. Fortunately, in recent years new methods for latent moderated structural equations have been developed and built in available software (e.g., MPLUS), which consist of two-step estimation procedures (Maslowsky et al., 2015).

Additionally, incorporating mixed methods increases the understanding of the experiential nature of the FI-DRCD syndemic, and will serve to enhance the precision and predictive power of ST. Although the integration of qualitative and quantitative data is necessary, it can be challenging because its application depends heavily on researchers' skill sets and study design. Creswell and Clark (2007) identify four major typologies of mixed-method data integration: the triangulation design, the embedded design, the explanatory design, and the exploratory design. Given the focus of ST and simultaneous qualitative and quantitative approaches, the triangulation design is most practical. This design seeks to find complementary yet distinct data from qualitative and quantitative methods addressing the same research question; each type of data is analyzed in its own right by researchers with expertise in each methodology, and then examined in conjunction with the other in order to complement or verify findings (Creswell and Clark, 2007; Mengshoel, 2012). The triangulated results can speak holistically and with more clarity about research findings, integrating both lived and quantifiable experiences.

4.2. *One experience with applications to FI*

Himmelgreen and colleagues (2006; 2012) employed bivariate tests (e.g., Student t, Kruskal-Wallis, Spearman's Rho) and multivariate tests (Multiple Logistic Regression) when looking at socio-demographics, household FI, diet, and overweight and obesity in children and adults in Costa Rica. The results suggest a syndemic, but the analysis did not measure the strength of the interactions or their direction. In an unpublished study, Himmelgreen and colleagues examined household FI status, nutritional status, food choices, knowledge and utilization of food programs, and psychometric measures of stress among 100 randomly chosen households in Florida. Multivariate regression, factor analysis, and SEM were used to test if household coping behaviors mediated the effects of FI on stress. The results show that adults buffered children from FI but that this came at a cost, as they had higher stress levels. Though there was not enough evidence to conclude that coping behavior was a mediator of FI and stress, the SEM provided insight into the dynamics among FI, coping, and mental health (Hall, 2014).

5. Public health and clinical applications

While the literature offers substantial evidence of the syndemic interaction between FI and infectious diseases such as HIV/AIDS (Himmelgreen et al., 2009; Okafor et al., 2018; Ostrach and Singer, 2012; Reddi et al., 2012; Singer, 2011; Singer et al., 2017; Talman et al., 2013; Tsai and Venkataramani, 2016), syndemics pertaining to FI and other chronic conditions are not as well-documented. As the literature indicates, there exists a clear comorbidity between FI and DRCDs; however, the issue remains as to whether this comorbidity also represents a true syndemic as originally postulated by Singer (2000). That is, does the interaction between FI and DRCDs result in the multiplying, rather than additive, cascade of detriments to individuals and groups living under social inequity? If that is indeed the case, what is the extent to which these epidemics reinforce each other? Are the effects of this syndemic manifested differently or to a different extent among people at different stages of life? How can researchers document such syndemic interaction to ensure their research is translational? The model presented in this paper represents an attempt to address the above-mentioned issues in a way that combines quantitative and qualitative methods and is firmly anchored in LHT.

The model relies on the integration of qualitative and quantitative methods through all stages of the process. During the initial research, data from observations, free listing, pile sorting, and informal interviews can inform the creation of research instruments and the identification of variables to be included in the SEM analysis. Likewise, the use of in-depth interviews, focus groups, and observations along with surveys, scales, anthropometry, and biomarkers, provide a comprehensive picture of the FI-DRCD interaction in a way that neither approach could do by itself. The data can then be quantified (even if qualitative in nature) for SEM analysis to determine whether a syndemic in fact exists and to measure the extent of the interaction among different variables. The interpretation of results must rely on the combination of both types of data to obtain a comprehensive picture that acknowledges statistical patterns as well as individual experiences. Finally, specific qualitative methods such as photovoice can be used for the dissemination of data to various stakeholders through public exhibits that represent the issues under study through the photos and narratives of those most affected. The use of LHT allows researchers to gain a more nuanced understanding of the differential impact that the potential FI-DRCD syndemic has on individuals/groups at different stages of life. These data can then be used to inform programming that directly responds to the specific needs of different developmental groups. For example, initiatives to alleviate FI among pregnant and lactating women will necessarily be different than those designed for elderly adults who are facing complications related to aging with chronic diseases.

The authors will soon have the opportunity to test the proposed model by applying it to their evaluation of a local initiative to decrease FI. The sample will include 300 randomly selected adults who present to a medical clinic with chronic diseases and who are found to be food insecure. In addition to medical data provided by the clinic for each participant, the researchers will use a battery of instruments to collect data on level of FI, demographics, dietary practices, anthropometry, self-reported illness, stress levels, etc. The project will involve three waves of data collection, thus resulting in a considerable amount of qualitative and quantitative data to statistically determine if the relationship between FI and DRCDs among this low-income population constitutes a true syndemic. If the sample is sufficiently diverse, the researchers may also be able to test the differential impact of the FI-DRCD interactions among younger adults and those of advanced age.

The goal of this evaluation is to inform the design and implementation of programming that alleviates FI in efforts to curtail the detrimental effects of hypertension, diabetes, obesity, depression, and hypercholesterolemia, the most frequent health problems in this clinic. We are certain that the nuanced understanding that will result from this evaluation (regardless of whether it involves a syndemic) will aid in efforts to improve the health of this underserved community. For example, this may lead to changing local ordinances and creating incentives for opening brick and mortar and mobile markets that offer more fresh produce and healthier food options.

By postulating a model for the identification of syndemics and the analysis of their impact we hope to provide a framework that other researchers can use to increase the precision of syndemic theory and strengthen its application to address pressing public health issues. The proposed model for the identification of the potential FI-DRCD syndemic becomes more relevant at the present moment, given the significant increase in FI globally as a result of the ongoing COVID-19 pandemic. The differential impact that the pandemic appears to have among various age groups and by other demographic factors (e.g., race, gender, income) offers an opportunity to examine the potential FI-DRCD syndemic under the lens of LHT.

Author credit

Himmelgreen: Conceptualization, Writing –Original draft, Writing –Review and editing, Supervision, Visualization. Romero-Daza: Conceptualization, Writing –Original draft, Writing –Review and editing, Supervision. Heuer: Writing –Original draft, Writing –Review and editing. Lucas: Writing –Original draft, Writing –Review and editing, Visualization. Salinas-Miranda: Writing –Original draft, Writing –Review and editing, Visualization. Stoddard: Writing –Review and editing.

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