Negative health outcomes associated with food insecurity status in the United States of America: *A systematic review of peer-reviewed studies*

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Abstract

Introduction: Social determinants of health, such as food security, are an important target for health providers, particularly in the care of patients from underserved populations, including the uninsured and socially marginalized. Preliminary research has shown that food insecurity status (FIS) is associated with negative health outcomes.

Objective: We aim to present a concise, yet comprehensive resource that lists the health outcomes associated with FIS. This guide is meant to provide innovative health providers with the tools needed to justify the importance of using FIS screening and treatment as a preventive medicine intervention.

Methods: We conducted a systematic review of peer-reviewed manuscripts that studied FIS in the United States of America (USA) and at least one health outcome. We searched PubMed, Embase, Web of Science, and Scopus and had multiple reviewers examine each abstract and manuscript. We only retained peer-reviewed studies that contained USA data, directly measured FIS, and directly compared FIS to a health outcome.

Results: The initial search yielded 1,817 manuscripts. After screening abstracts for duplicates and inclusion criteria, a total of 117 manuscripts were retained and fully examined. Several manuscripts showed significant association between FIS and neurologic, cardiac, endocrine, and pulmonary health outcomes. Studies in the USA population show robust associations between FIS and poor mental health (including depression, anxiety, sleep disorders, impaired cognitive functioning, and epilepsy), metabolic syndrome, hyperlipidemia, greater risk for bone fracture in children, higher risk of end-stage renal disease in patients with chronic kidney disease, self-reported poor health, and higher mortality in patients with the human immunodeficiency virus. Though other literature reviews show positive associations between FIS and health outcomes such as diabetes, body mass index, and hypertension, our systematic review showed mixed results.

Conclusions: FIS leaves underserved populations at risk for negative health outcomes. More research should be done to examine the effects of FIS alleviation as a preventative medicine intervention.

Introduction

Patients who live below the federal poverty line and hold minority-group status are more likely to have poorer outcomes in chronic yet common conditions such as diabetes(1), hypertension(2–4), hypercholesteremia(5–7), osteoporosis(8,9), and depression(10,11). Underserved populations also have a greater prevalence of poorer outcomes in complications such as kidney disease(12–14), neuropathy(15), strokes(16), cardiac failure(17,18), and atherosclerosis(19), as well as outcome imbalances in cancer diseases such as breast cancer, lung cancer, and colon cancer(20,21). Since preventive medicine can significantly reduce the burden of these diseases, increasing its access to impoverished or neglected populations is paramount(22).

Some innovative health-provider models target preventive medicine services to traditionally underserved populations(23,24). Provider models such as student-run clinics (SRCs) and mobile health clinics aim to increase availability and affordability to patients who fall within this category(25). Evidence suggests that the efforts of SRCs have resulted in high patient and provider satisfaction(26,27), as well as significant health and economic impacts(28). The interdisciplinary nature(23) of SRCs allows them to focus on services that alleviate the strain that a lack of affordable housing, food insecurity, substance addiction, and other conditions place on individuals. In order to enhance their services, it is advisable to incorporate socioeconomic questions and interventions into the general healthcare protocol utilized by SRCs and other innovative health providers.

It is important to validate why socioeconomic interventions belong in a health care setting. Resource allocation is an important concern because providers have limited capabilities and a limited amount of time with patients. Another concern is that patients deserve to know why health providers are screening for socioeconomic risks in a healthcare setting. Inquiries about food insecurity and housing stability are personal and potentially difficult to answer and are just two examples of the types of questions patients may not anticipate upon visiting a health clinic. Providers must be able to explain in a concise and clear matter the importance of socioeconomic interventions, as they pertain to the patient's health.

A common socioeconomic intervention in innovative health provision is the alleviation of FIS. All patients are screened for FIS and those who are found to be at risk are given information about local food assistance programs, food banks, and other resources. One important justification of this intervention is that several studies show that FIS is associated with negative health outcomes such as depression and diabetes(11,29). However, there are many studies but no systematic consolidation of all the health outcomes associated (and not associated) with FIS. Our rationale for conducting this review is that there have been some broad reviews of the association between FIS and various health outcomes, but they are not systematic(30–33), and they do not include insignificant associations. Furthermore, existing systematic reviews mainly focus on specific healthcare outcomes, and many non-physiological measurements [i.e. adherence for anti-retroviral therapy (ART) medication]. The objective of this study is to provide a resource in the form of a review, which consolidates the health outcomes (positive or negative) directly associated (or not associated) with FIS in the USA population.

Clearly, condensing and analyzing these studies would allow providers to make more accurate and compelling arguments when justifying the need for FIS screenings and/or interventions in clinical settings. This justification is important, whether it is aimed at management, donors, the community, or patients themselves.

Methods

1. Databases Search

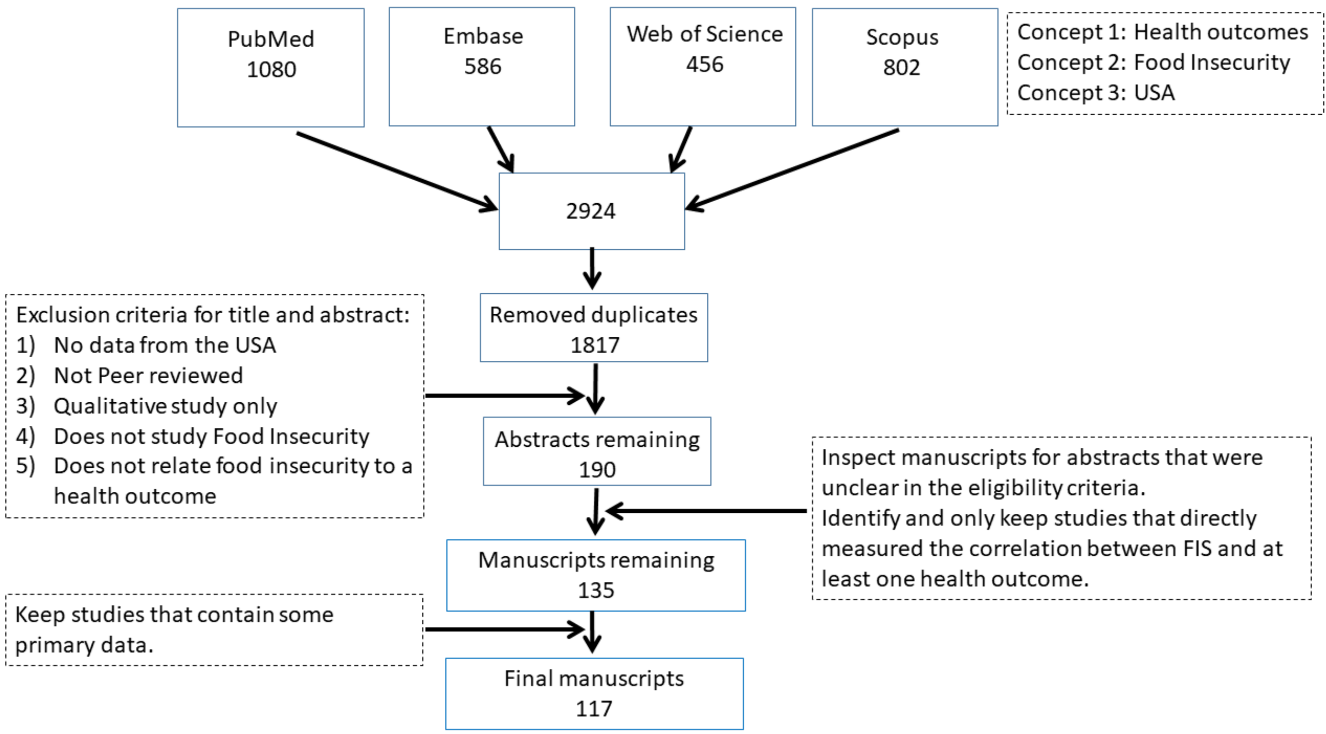
Information sources were the four databases: PubMed, Scopus, Web of Science, and Embase. We searched for abstracts that included the three concepts: Health outcomes, FIS, and USA. Search terms were tailored for each database and the details of the electronic search strategy are offered in S1 of the supplementary documents. Duplicates were removed using RefWorks and by subsequent manual inspection. Table 1 shows an outline of the results. The search was conducted on September-4th-2017 and yielded 1,817 abstracts.

2. Abstract Exclusion

We used the program Abstrackr(34) to conduct the abstract exclusion process. A study was deemed relevant if it satisfied all the following eligibility criteria: 1) The study contained USA data, 2) it was peer-reviewed, 3) it was quantitative, 4) it measured FIS, and 5) it studied a health outcome. We decided to exclusively use manuscripts that contain data from the USA because our target audience consists of innovative health providers and social workers who reach vulnerable and underserved populations in this country. Only articles written in English were considered, and all publication dates were accepted.

Since health outcome is a broad definition that merits discussion among the reviewers, we first ran a pilot of the study selection process. During which, four investigators reviewed the same 200 abstracts with three possible options: “inclusion”, “exclusion”, and “maybe”. The pilot was also helpful to assess agreement in the other criteria areas. We counseled reviewers to conduct a sensitive search: they would keep the study if it was not clear from the abstract that a criterion was met, and the reviewers were made aware that the next step, reading the text manuscript, would offer an opportunity to exclude unclear abstracts. After the abstract exclusion pilot, 76 percent of the 200 abstracts had complete ratings-agreement between the four graders. The inter-rater reliability of the four graders was quantified using a Fleiss kappa value of 0.49 [0.32, 0.66], which yielded moderate agreement. The disagreements in the pilot exclusion were reviewed with a fifth new reviewer, and then multiple reviewers met to discuss these disagreements. The discussion resulted in choosing that food environment would not be considered as food insecurity, and that we would not treat diet quality nor food environment as health outcomes. We also decided to keep self-reported physical and mental health, and cognitive development as health outcomes. From the discussion, we also decided to disregard manuscripts that solely linked food environment and poor health outcomes. FIS and poor food environment are linked, but they are not equal. In this manuscript we decided to focus on FIS because it is more straightforward to screen a patient for FIS than for their food environment.

Figure 1. Flow of identification of manuscripts for the systematic review.



After the pilot and subsequent discussion, we randomly distributed the remaining 1,617 abstracts to four reviewers in such a way that at least two reviewers examined each abstract. Ninety-four percent of the abstracts had complete-agreement between the two raters, and the Fleiss kappa inter-reliability was 0.62 [CI: 0.55, 0.69], suggesting 'substantial agreement'. At the end, we retained 190 abstracts out of the original 1,817.

3. Manuscripts examination

This step only included the 190 abstracts that remained after the previous step. We randomly distributed the 190 abstracts to five reviewers so that at least two reviewers examined each manuscript. Reviewers read the text of the manuscript to fulfill two goals: one, ascertain that the manuscript satisfied the inclusion criteria (which may have not been clear from the abstract). In this step reviewers also had to identify and exclude abstracts from poster sessions that did not have full text associated with it. At this point, we also removed duplicates that were missed by the automated program earlier.

The second, and possibly the most challenging, step of the manuscript examination was identifying studies that directly measured the correlation between FIS and a health outcome. The objective was to approve only the papers that investigated the possibility of a direct association between FIS and a health outcome. This research project defines “investigation of direct association” as having directly measured the correlation between FIS and a health outcome. This means that papers that correlate FIS to a health outcome via another variable (i.e. food prices, food environment) are not acceptable. It was equally valid if the direct correlation was discussed in the text, or if data was presented in a table comparing the prevalence of the health outcome with or without FIS. It was clearly communicated to all reviewers that positive and negative results (significant or non-significant) were equally important.

There was 85% agreement between the reviewers in exclusion of the manuscripts. The two-rater kappa was 0.60. We automatically excluded the 32 abstracts for which both reviewers agreed were not appropriate. We then maximized the sensitivity of the search by further exploring (by a third reader) manuscripts for which only one reviewer voted to exclude, then 15 more manuscripts were excluded by the third reviewer. After this point, reviewers met to discuss disagreements and to revisit which health outcomes would be included. The conclusion was that studies that measured smoking rate, illegal drug use rate, and medication adherence were excluded if they did not present another health outcome [such as chronic obstructive pulmonary disease (COPD) exacerbation, or neurologic complications]. Eight studies were subsequently removed.

The 18 review studies found(31–33,35–50) were examined to see if they provided primary data, otherwise they were discarded. The final number of manuscripts was 117.

4. Data extraction and organization into systems

The data collection process for the final 117 manuscripts consisted of two reviewers independently reading each manuscript and cataloguing the health outcomes that were measured and directly compared to the FIS measurement. The main summary measures sought in each manuscript were the health outcome studied and whether the association with FIS was significant or not. These associations were obtained from tables of odd ratios, statements in the text, *p*-values, and/or confidence intervals. We concluded that the paper showed significant association based on the *p*-values and their confidence interval, and we noted if there was a discrepancy with the text. Other data items extracted from each manuscript were: The methods for measurement of FIS and health outcomes, the populations studied, and the study size. Each health outcome was separated into the following categories: Brain and Behavior, Cardiovascular, Endocrine, Infectious Disease, Pulmonology, Renal, Musculoskeletal, and General Health. Some manuscripts related multiple health outcomes measurements to FIS and therefore the studies were mentioned more than once. All manuscripts and their summary measures are presented for each health outcome and synthesized in tables in the Results section.

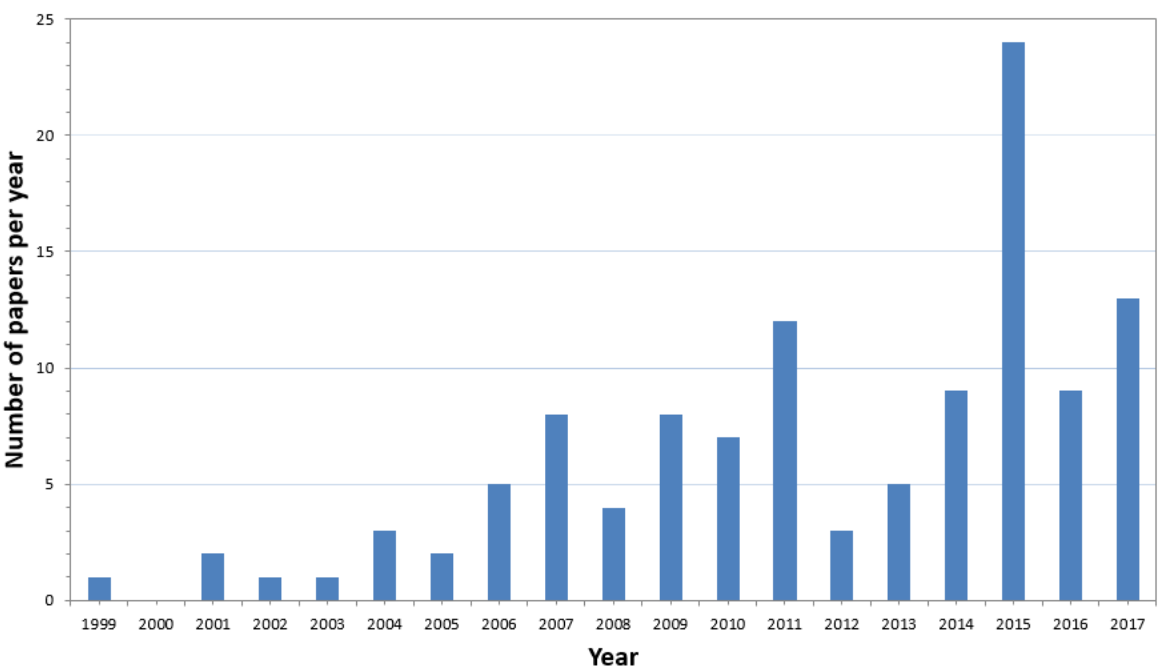
Results and Discussion

Figure 1 shows the number of studies screened along with the intermediate results and the final result of 117 studies. All 117 manuscripts were published after 1999, and the results clearly show (Figure 2) that the scientific community has experienced a sharp increase in the interest of the health effects of FIS.

For each health outcome, the results are synthesized in a table that is presented in the main text, or S2 of the supplementary documents, that lists for each study the following: population characteristics, type of measurement for both FIS and the healthcare outcome, study size, and citations.

The two most common surveys that were used to measure FIS were the United States Department of Agriculture Food Security Survey Module (USDA FSSM) and the National Health and Nutrition Examination Survey (NHANES). The USDA FSSM survey is sometimes referred by different names such as US Adult Food Security Survey Module, Bickel's Household Food Security Survey, USDA Household Food Security Scale, among others. The survey consists of screeners asking the individual questions about the prevalence of FIS and hunger in their household within the span of a year. The NHANES is a general population survey that combines information from interviews and physical examinations and includes information about an individual's nutrition and health status. Another common FIS and health outcome measurement tool were custom surveys conducted during patient interviews.

Figure 2. Publications by year of the final 117 studies.



Legend: Of the final 117 studies, all were published after 1999. The graph shows the increasing interest in the health repercussions of FIS in the last decades.

1. Brain and Behavior

Anxiety

Out of the 117 manuscripts, there were seven (Table 1) with data that directly compares stress/anxiety to FIS. All of the articles found a significant association between the two variables. The studies used a diverse group of questionnaires for measuring FIS and anxiety, with one study directly measuring cortisol levels. The effect of FIS on anxiety was shown in preschool children(51), pregnant women(52,53), general public visiting the emergency department (ED)(54), diabetic patients(55,56), Hispanic adults(57), and college freshmen(58).

The mechanism between food insecurity and anxiety is straightforward: members of the family worry about the household's family food supply(58,59). This is not only unfortunate for the obvious impact on the patient and family, but to society in general, since anxiety has a well-known economic burden associated with both medical and general productivity costs(60).

Table 1. Anxiety and FIS

Year	Authors	FIS measurement	HO measurement	Population characteristics	Study size	Significant association with FIS?
2002	Weinreb et al.(51)	7-item custom questions	NHIS Child Behavior Checklist	Preschool children in MA	152	Yes
2006	Laraia et al.(52)	USDA FSSM	Spielberger's Trait Anxiety Inventory	Pregnant women	606	Yes
2011	Sullivan et al.(54)	USDA FSSM	Custom question	Boston ED patients	496	Yes
2015	Becerra et al.(57)	3-item custom questions	Kessler 6-scale	Low income Hispanic adults	10,966	Yes
2015	Borders et al.(53)	USDA FSSM	ACTH levels	Pregnant women	112	Yes
2016	Bermudez-Millan et al.(56)	6 items from USDA FSSM	PHQ, Problem Areas in Diabetes Questionnaire	Diabetic adults	121	Yes
2017	Darling et al.(58)	USDA FSSM	DASS	College freshmen	98	No

NHIS: National Health Interview Survey

MA: Massachusetts

ACTH: Adrenocorticotrophic hormone

PHQ: Patient Health Questionnaire

DASS: Depression, Anxiety, and Stress Scale

Cognitive Development

Out of six papers reviewed(51,61–65), five manuscripts reveal a significant association between FIS and cognitive impairment (Table S2-1). This association is observed among USA children(51,62), Mexican migrant farm workers' children(61), Puerto Rican adults(65), and older adults(64). Cognitive development is measured through various tests, including surveys, in-person interviews, the Mini-Mental State Examination (MMSE), the 22-item Adult Lifestyles and Function Interview Mini-Mental State Examination (ALFI MMSE), and Parents' Evaluations of Developmental Status (PEDS).

A rather surprising result from the studies reveals that the association between FIS and cognitive impairment seems to not only affect children but also adults, and even older adults. For example, in a study with Mexican migrant farm workers' children, food insecure households are significantly more likely to have at least one child suffering from a physician-diagnosed learning disability(61). In addition, a longitudinal study with Puerto Rican subjects ages 40-75 in the Boston region demonstrates a 2-year decline in global cognitive function in association with FIS at the baseline level(65). Lastly, a recent nationally representative study of kindergarten children shows that FIS results in lower hyperactivity, conduct problems, and lower reading and math scores(66).

The diverse range of age cohorts and methodologies in these studies suggest a robust correlation between FIS and cognitive impairment. Further investigation in the directionality of this relationship may provide greater insights.

Depression

Thirty manuscripts studied the association between FIS and depression(51,52,55,56,58,59,61,63,64,67–87), and twenty-eight of them show a significant association (Table S2-2). The association between FIS and depression is strong and is demonstrated in the general public(68), college students(58,59,83), minorities(55,76,80), geriatric patients(64), migrant farm workers(61), diabetic(55,56,87), and patients with the human immunodeficiency virus (HIV)(75,79,87). Additionally, FIS increases the risk of prenatal depression(52,72,73), and increases depression rates later in life for individuals who experience FIS as children(51).

The association was robust to the choice of depression measurement used by the studies. This included several questionnaires such as the Center for Epidemiological Studies Depression Scale (CESD)(88,89), Patient Health Questionnaire (PHQ)(90,91), Geriatric Depression Scale (GDS)(92,93), Depression Anxiety and Stress Scale (DASS)(94), as well as custom questions. These studies also used different questionnaires for FIS measurement and were conducted in several locations across the USA.

The association between FIS and depression is important, and worth the multitude of studies, because the effects of depression are devastating and well-documented(95). Depression increases the risk of suicide(96), and affects society with absenteeism and reduced productivity at work(97). In geriatric patients, depression can be detrimental to functioning and self-care, and it is as detrimental as heart and lung conditions(98,99). Depression during pregnancy is damaging to fetal health, increases the risk of pre-term delivery, and results in poorer maternal practices after birth(100). In all, the effects of depression are detrimental to all of society; in 1990 it was estimated that depression created an economic burden of over $40 billion in the USA(95). Although it is not the scope of this paper, future work can be done to estimate the cost efficiency of food insecurity interventions and the burdens that could be prevented on depression alone.

Epilepsy

A recent manuscript represents the first comprehensive study to investigate the relationship between FIS and epilepsy among USA children(101) (Table S2-3). The researchers review the electronic health record data of children ages 2-17 years old, who receive care from an academic pediatric hospital. The measured health outcomes are divided into two portions: 1) acute care utilization and 2) assessments of quality-of-life and epilepsy medication side effects. The former is determined by emergency department visits and hospitalizations, and the latter is measured via formalized questionnaires: the health-related quality-of-life (HRQOL) and Pediatric Epilepsy Side-Effects Questionnaire (PESQ), which evaluates the side effects of anti-epileptic drugs (AEDs). Overall, the results show that 14% of the children in the study suffered from FIS. The results also found that children who experience FIS experience greater utilization of healthcare facilities, lower quality of life, and higher AED side effects(101).

This study is significant because it demonstrates a positive correlation between epileptic symptoms and FIS. Lastly, the results expand the notion that FIS may be particularly influential among children with long-term health management needs. Epilepsy epitomizes such a need and represents an ideal area for further research.

Sleep

A significant association is observed between FIS and poor sleep in all seven manuscripts reviewed(54,56,102–106) (Table S2-4). This correlation is demonstrated among USA veterans(104,105), diabetic Latinos(56), ED patients in Boston(54), as well as the general adult population in the USA(102,103,106). In these studies, sleep quality, duration, complaints, insomnia, and latency are measured through subjects’ self-reported surveys(54,56,103,104,106). A 2013 study conducted by Grandner et al. measured a more comprehensive breadth of symptoms linked to common sleep disorders like insomnia and sleep apnea: sleep latency, difficulty falling and staying asleep, waking in the morning, non-restorative sleep, and sleepiness during the day, snorting or gasping, and snoring(102).

This positive association between FIS and poor sleep is important because sleep defects are often linked to many other health problems, including; injury, cardiovascular disease, obesity, diabetes, hypertension, general poor health, and mental health issues(105). Moreover, FIS afflicts more adverse effects on sleep than any other measured sociodemographic or socioeconomic variable(102). This finding demonstrates that FIS holds unique effects on sleep symptoms and warrants more investigation. Furthermore, Bermudez et al.'s 2016 study of diabetic Latinos reveals that the direct relationship between FIS and poor sleep quality is mediated by psychological distress(56). This suggests the association between FIS and sleep exists within the context of other health variables, especially mental illnesses.

2. Cardiovascular

Dyslipidemia

Seven manuscripts studied the association between FIS and hyperlipidemia in the USA, and six of them show a significant association(29,107–112) (Table 2). The association between FIS and hyperlipidemia was shown among diabetic adults(111), low-income adults(109), and the general public (107,110), particularly in male adults(29). One paper suggested that FIS can lead to hyperlipidemia due to poor dietary choices, such as choosing to eat energy-dense foods with fewer nutrients(109). Another paper proposed that dyslipidemia is related to poor glycemic control and metabolic disorders, which is also associated with FIS(111).

Table 2. Dyslipidemia and FIS

Year	Authors	FIS measurement	HO measurement	Population characteristics	Study size	Significant association with FIS?
2006	Holben et al.(29)	USDA FSSM	Total cholesterol	Adults in Athens, Hocking, Meigs, Perry, Pike, and Vinton counties in Ohio	808	Yes
2008	Stuff et al.(107)	USDA FSSM	Self-reported survey, cholesterol	Adults in the lower Mississippi Delta	1,457	Yes
2009	Tayie et al.(108)	10 items from USDA FSSM	LDL cholesterol	Adults across the USA in NHANES	5,400	No
2009	Tayie et al.(108)	10 items from USDA FSSM	Total cholesterol	Adults across the USA in NHANES	5,400	No
2010	Seligman et al.(109)	USDA FSSM	Total cholesterol, self-reported and clinical diagnoses	Low-income adults in the USA in NHANES	1,930	Yes
2013	Ford(110)	USDA FSSM	HDL cholesterol	Adults across the USA in NHANES	10,455	Yes
2015	Berkowitz et al.(111)	USDA FSSM	LDL cholesterol	Adults in MA receiving treatment for diabetes mellitus	411	Yes
2015	Moreno et al.(112)	6 items from USDA FSSM	LDL cholesterol	Latinos with diabetes	250	Yes

LDL: Low-Density Lipoprotein

HDL: High-Density Lipoprotein

Hypertension

Twelve manuscripts studied the association between FIS and hypertension(29,61,63,107,109–116), and seven manuscripts showed a significant association (Table S2-5). The association between FIS and hypertension was demonstrated in minorities(63,115), pregnant women(113), low-income adults(109,113), older adults(116), and the general public(107,110). The association was not found in some adult populations such as Mexican immigrants(61) and adults living in certain parts of Massachusetts(29) and Ohio(111). One manuscript suggested that these results are mixed due to hypertension's sensitivity to medication adherence rather than diet(109). Another suggested that, unlike hyperlipidemia, hypertension is not reliant on the same metabolic pathways that are affected by FIS(111).

Other Cardiovascular Health Outcomes

There were three manuscripts that studied the association between FIS and anemia(29,61,113,117), and only one of the papers shows a significant association between the two variables (Table S2-6). This association was found in children of low-income families,(117) but not adults(29,113). Younger children were more likely to be anemic than older children(117). The mechanism by which FIS may lead to anemia is unknown. However, in the manuscript that found a significant association between FIS and anemia, the authors acknowledge that the families that were food insecure had a family history of anemia(117).

Two manuscripts showed significant association between FIS and cardiovascular disease(107,110). This association was found in the general public(107,110), particularly in adults age 30-59.(110) Both manuscripts used previous diagnoses of cardiovascular disease as a major health outcome associated with FIS. Furthermore one manuscript concluded that very low FIS is correlated with increased predicted ten-year cardiovascular disease risk(110).

Two studies showed significant association between FIS and risk for heart attack. Both papers showed that adults across the USA who are FIS have higher levels of C-reactive protein, a marker that is caused by inflammation in the arteries, which leads to a higher risk of heart attack(110,118).

One paper showed significant association between FIS and peripheral artery disease (PAD) in older adults(119). Peripheral artery disease was measured through the ankle-brachial index. The mechanism by which FIS can lead to PAD is unknown, but the authors suggested that a low-nutrient diet causes inflammation in endothelial walls, which may damage arteries(119).

One paper showed significant association between FIS and previous diagnosis of stroke(107). The mechanism between FIS and stroke is unknown and was not discussed in the paper.

It should also be mentioned that there are reviews in the literature that conclude that there is a significant association between FIS and the following cardiovascular disorders: hyperlipidemia(32,36,40,43), hypertension(32,40,43), childhood iron deficiency anemia(33,47), and risk for cardiac disease(33). Though these studies conclude that there is a positive association between FIS and the health outcome, this systematic review shows that the results are mixed, particularly amongst manuscripts that discussed hypertension and anemia. Therefore, it is unclear whether there is a positive association or no association between FIS with hypertension and anemia.

3. Endocrine

Body Mass Index

We found 37 manuscripts that directly measured the association between FIS and body mass index (BMI)(30,54,58,61,63,67,71,83–85,87,107,108,112–116,118,120–137). Only 18 manuscripts report a statistically significant association (Table 3). The diverse group of results merits careful inspection of the different methodologies used in the manuscripts.

In this group of studies, a subset (25/37) involve designs where researchers measure the weight and height of the patients, a subset (3/37) where the parameters were extracted from clinical documents, and another (9/37) where height and weight are self-reported by patients. For the studies where researchers measure the height and weight, 11/25 studies found a significant association; while the self-report methodology yielded 6/9 studies with significant association. One concern of the self-report measurements is that response bias may make it more likely for these studies to go towards a conclusion for positive FIS association, and this concern is based on the percentage of papers that show significant association. A difference of 6/9 versus 11/25 suggests that the self-reported papers are more likely to have report-bias that results in obtaining an association between FIS and BMI; however, this is still a distribution with a high probability that the null hypothesis (no difference in likelihood of observing a positive FIS association) is true (p = 0.20). These studies are also very diverse in the populations' studies. It's also possible that the difference in conclusions arise from the fact that the studies present data on diverse populations (children, women, patients above 50 years old, women, underserved populations, etc.) and that the association is complex.

Table 3. BMI and FIS

Year	Authors	FIS measurement	HO measurement	Population characteristics	Study size	Significant association with FIS?
1999	Olson, C. M.(30)	Radimer/Cornell questionnaire	BMI measured by researchers	Childbearing-age women from upstate New York	193	Yes
2003	Sharkey et al.(67)	4 custom questions	BMI measured by researchers	Senior women who receive home-delivered meals	281	No
2004	Kaiser et al.(120)	USDA FSSM	BMI measured by researchers	Low-income Latino women	559	Yes
2005	Jyoti et al.(121)	USDA FSSM	BMI measured by researchers	Children from ECLS-K Database	10,869	No
2006	Whitaker et al.(122)	USDA FSSM	BMI measured by researchers	Study cohort of pre-school children across USA	2452	No
2006	Rose et al.(123)	USDA FSSM	BMI measured by researchers	Children from ECLS-K Database	16,889	Yes
2006	Jones et al.(121)	USDA FSSM	Self-reported height and weight	Pregnant women across USA in PSID	5,503	Yes
2007	Weigel et al.(61)	USDA FSSM	BMI measured by researchers	Mexican immigrants in the USA Farm workers.	100	No
2007	Martin et al.(125)	USDA FSSM	BMI measured by researchers	Parents and children from Connecticut	412	Yes
2007	Kim et al.(71)	USDA FSSM	Self-reported height and weight	Adults between 51-61 years old from across the USA	9,481	No
2007	Jones, S. J. et al.(126)	USDA FSSM	Self-reported height and weight	Adult women across USA in PSID	5,595	No
2008	Stuff et al.(107)	USDA FSSM	Self-reported height and weight	Adults in Lower Mississippi Delta	1,457	Yes

2009	Gao et al.(63)	USDA FSSM	BMI measured by researchers	Puerto Rican community in Boston	1,358	No
2009	Widome et al.(127)	2 questions from USDA FSSM	BMI measured by researchers	High school students in Minneapolis	4,746	No
2009	Tayie et al.(108)	10 items from USDA FSSM	BMI measured by researchers	Adults across the USA in NHANES	5,400	Yes
2010	Laraia, B. A.(113)	USDA FSSM	Pregravid BMI self-reported height and weight	Pregnant women in PIN cohort	810	Yes
2010	Hendrickson et al.(128)	USDA FSSM	Review of hospital documents	Asthma children patients visiting ED	127	No
2010	Sullivan et al.(54)	USDA FSSM	Self-reported height and weight	Boston ED patients	520	Yes
2011	Karnik et al.(129)	2 custom questions	BMI measured by physician	Primary care clinic patients	558	Yes
2012	Gowda et al.(118)	USDA FSSM	BMI measured by researchers	NHANES database	12,191	Yes
2013	Robaina et al.(130)	USDA FSSM	BMI measured by researchers	Food Pantry clients in Connecticut	212	No
2014	Sirotin, N. et al.(131)	USDA FSSM	BMI measured by researchers	HIV infected women in the Bronx	350	Yes
2015	Asfour, L. et al.(132)	CDC Prevention Survey	BMI measured by researchers	2-5-year-old in Miami	1,211	No
2015	Cheung et al.(133)	2 custom questions	BMI measured by researcher	Patients in community health center in MA	457	Yes
2015	McCurdy et al.(135)	USDA FSSM	Self-reported height and weight	Mothers using day care centers	166	Yes
2015	Moreno et al.(112)	6 items from USDA FSSM	BMI from chart reviews	Latinos with diabetes	250	Yes
2015	Millimet et al.(134)	USDA CFSM	BMI measured by researchers and assessing future childhood obesity	Children in ECLS-K Database	10,700	No
2016	Sharpe et al.(85)	6 items from USDA FSSM	BMI measured by researchers	25-50-year-old women	202	No
2016	Bruening et al.(83)	USDA FSSM	BMI measured by researchers	College freshmen in Southwestern USA	206	No
2016	Burke, Frongillo, et al.(84)	USDA FSSM	BMI measured by researchers	Children in ECLS-K Database	15,800	Yes
2017	Vaccaro et al.(116)	USDA FSSM	BMI measured by NHANES researchers	Patients > 55 years old across USA	3,781	Yes
2017	Palar et al.(87)	USDA FSSM	BMI measured by researchers	Patients with HIV and/or T2DM in San Francisco, CA	52	No
2017	Darling et al.(58)	Hager's questionnaire	BMI measured by researchers	College freshmen	983	No
2017	Kral et	6 items from	Measured in-site by	Mothers, and their	50	No

	al.(136)	USDA FSSM	patients themselves	children in Philadelphia, PA		
2017	Shalowitz et al.(137)	USDA FSSM	Review of clinical documents	Underserved diabetic patients	336	No
2017	Jernigan et al.(115)	2 items from USDA FSSM	Self-reported height and weight	Chickasaw and Choctaw Nations of Oklahoma	513	Yes
2017	Banerjee et al.(114)	Custom question	BMI measured by researchers	Adults with CKD below 400% of the federal poverty line	12,700	No

ECLS-K: Early Childhood Longitudinal Program

PSID: Panel Study of Income Dynamics

PIN: Pregnancy, Infection, and Nutrition Study

CDC: Center for Disease Control

T2DM: Type 2 Diabetes Mellitus

CA: California

PA: Pennsylvania

CKD: Chronic Kidney Disease

Diabetes

We identified seventeen peer-reviewed USA articles studying the association between FIS and diabetes(29,55,61,82,107,109,111–116,137–140). Of those manuscripts, twelve of them show a significant association (Table S2-7). Articles assess both the report of a diabetes diagnosis and measurements including Hemoglobin A1C and the oral glucose tolerance test (OGTT). These associations are studied in a wide group of populations including rural communities(29,107), Hispanic adults(55,109,112), pregnant women(113), Native Americans(115), geriatric patients(116), adults in the general population(109), and adults with other chronic illnesses, including HIV(87). While not all studies show significant results, the mechanism underlying associations between FIS and poor diabetes control is easily conceivable, as proper diabetes management requires implementation of healthy eating patterns which may be difficult for FIS individuals(141).

The association between diabetes and FIS is of particular interest due to the extensive healthcare and economic implications of diabetes. Type 2 diabetes mellitus (T2DM) is known to be associated with several debilitating conditions, such as kidney disease and retinopathy(36). Economically, the estimated cost of diagnosed diabetes is $245 billion(142).

Furthermore, studies by Seligman et al. show evidence that adults with T2DM and FIS are more likely to suffer severe hypoglycemic episodes than those with food security(138) – this is also important and worthy of future research since hypoglycemic episodes can be devastating to patients(143), and are costly to society(144).

Metabolic Syndrome

There were three manuscripts investigating the association between FIS and metabolic syndrome, and two found a significant association(107,145) (Table S2-8). Parker et al.(145) studied this association across the USA adult population using NHANES, resulting in a large study with over 9,000 entries. Stuff et al. reached a similar conclusion studying adults in Mississippi(107). Both articles use the Adult Treatment Panel III guidelines for metabolic syndrome diagnosis, considering waist circumference, triglycerides, HDL levels, blood pressure, and blood glucose.

4. General Health

Children Anthropometric Measurements

Seven studies explored the association between FIS and children's anthropometric measurements (Table 4). Several manuscripts showed that there was no significant association between FIS and children's height(128), weight-for-length(70,146), weight-for-age(62,78), and probability of pre-term birth(147). Although one study did find an association between proxy-reported low birth weight and FIS(51).

Table 4. Children Anthropometric Measurements and FIS

Year	Authors	FIS measurement	HO measurement	Population characteristic	Study Size	Significant association with FIS?
2002	Weinreb et al.(51)	Custom question	Proxy-reported low-birth weight	Preschool children in MA	203	Yes
2007	Bronte-Tinkew et al.(70)	USDA FSSM	Length/Age Survey	ECLS-B	8,693	Yes
2007	Bronte-Tinkew et al.(70)	USDA FSSM	Weight/Length survey	ECLS-B	8,693	Yes
2008	Rose-Jacobs et al.(62)	USDA FSSM	Weight-for-age z score	ACP clinics and ED patients	2,010	No
2012	Cook et al.(78)	USDA FSSM	Weight/age < 5%	Across USA	41,515	No
2010	Hendrickson et al.(128)	USDA FSSM	Children's height	Asthma children patients visiting ED	127	No
2015	Tucker et al.(147)	Not specified	Preterm birth	Medicaid patients in NC	15,428	No
2016	Barroso et al.(146)	2 custom questions	Weight-for-length	Hispanic families from Southwestern USA	240	No

ACP: Asthma Care Pathway

ECLS-B: Early Childhood Longitudinal Survey-Birth Cohort

NC: North Carolina

Self-reported and Proxy-reported Health

Our search found 16 manuscripts with data that directly compared self-reported health to FIS(64,86,112,116,148–159), from which 14 studies found a significant association between the two variables (Table S2-9). These studies included, among others, older adults(64,148,151), caregivers(149), immigrants(152), college students(156), and the general public(116). The utility of self-reported health has been demonstrated by its strong association with mortality(160–162). Benjamin et al. showed that self-reported health is strongly associated with death from diabetes, infectious diseases, heart disease, and other chronic conditions(163).

Similarly, seven manuscripts had data on the association between the health of the child, reported by parents or guardians, and FIS in the household(49,70,78,128,164–166); and six studies found a significant association (Table S2-10).

5. Infectious Disease

Unsuppressed HIV (High Viral Load)

Nine manuscripts investigated the effects of FIS on HIV viral loads(79,167–174). Most of them established HIV viral loads to be elevated and unsuppressed if the level were greater than 500 ribonucleic acid (RNA) copies/mL. All the studies established a significant correlation between FIS and an unsuppressed HIV viral load (Table 5). Multiple pathways have been proposed to explain this relationship, some of them include nutrient deficits, poor coping strategies and behaviors, psychological distress, and substance abuse(167,174). Psychological and behavioral changes can lead to missed HIV clinic visits and decreased ART medication adherence. In particular, ART medication is typically taken with food for maximal processing and absorption(172,173). Therefore, HIV patients who are FIS may either take ART medication without following directed use, or they may skip taking medication altogether.

Table 5. HIV Viral Load and FIS

Year	Authors	FIS measurement	HO measurement	Population characteristics	Study Size	Significant association with FIS?
2009	Weiser, S. D. et al.(167)	USDA FSSM	Viral Load Blood Test	Homeless HIV individuals receiving ART in San Francisco, CA	104	Yes
2011	Wang, E. A. et al.(168)	1 item from USDA FSSM	Viral Load Blood Test	HIV veteran	2,353	Yes
2013	Mendoza, J. A. et al.(169)	USDA FSSM	Viral Load Blood Test	HIV individuals in Houston, TX	62	Yes
2014	Kalichman, S. C. et al.(79)	4-item Coates, Swindale, and Bilinsky	Viral Load Blood Test	HIV individuals receiving ART in Atlanta, GA	197	Yes
2015	Feldman, M. B. et al.(170)	3 items from Adaptation to US Census Current Population Survey	Viral Load Blood Test	HIV individuals in NYC enrolled in a nutrition service program	2,118	Yes
2015	Kalichman et al.(171)	Custom questions	Self-reported Viral Load	HIV individuals in Atlanta, GA recruited from clinical and community services	671	Yes
2015	Kalichman et al.(172)	USDA FSSM	Viral Load from medical records	HIV adults from Atlanta, GA	418	Yes
2015	Kalichman et al.(173)	Custom questions	Self-reported Viral Load	HIV individuals in Atlanta, GA recruited from clinical and community services	759	Yes
2015	Surratt, H. L. et al.(174)	1 custom question	Self-reported Viral Load	Documented HIV adults with current ART prescription	503	Yes

TX: Texas

GA: Georgia

NYC: New York City

Unsuppressed HIV (Low Cluster of Differentiation 4 Count)

A similar correlation is established with cluster of differentiation 4 (CD4) cell counts. Out of the 4 of manuscripts that study the effects of FIS on CD4 counts(168–170,172), 3 studies report a statistical correlation between FIS and low CD4 counts. These papers set the threshold for low CD4 counts as anything less than 200 cells/mL. Only one paper stated there was no significant correlation. (Table S2-11).

Other Infectious Disease Outcomes

Table S2-12 in the supplementary documents shows the additional health outcomes in this section. A prospective cohort study by McMahon et al.(175) evaluated overall mortality in HIV patients versus different socioeconomic variables. The results showed a significant association between mortality and FIS. This is an unfortunate result that furthers emphasizes the importance of FIS interventions in these patients.

Lastly, there are two USA studies that explore FIS effects on other interesting infectious disease outcomes. Weigel et al. investigated the association between FIS and previous diagnosis of tuberculosis and hepatitis. The study stated that no significant association was found(61). Similarly, Naenifard et al. used the 2009-2010 NANHES survey to extract Epstein-Barr viral capsid antigen measurements in FIS populations, and found no significant association(176).

6. Pulmonary, Musculoskeletal, and Renal Health Outcomes

The musculoskeletal, pulmonary, and renal systems are shown in Table S2-13 of the supplementary documents. There were three manuscripts that measured the association between asthma and FIS(61,128,177). Two of the studies did not find significant association between FIS and asthma in migrant seasonal farm workers(61), or children who were hospitalized for asthma(128). Only one manuscript found a significant association with asthma in kindergarteners across the USA(177). This study may have found significant results because of its large sample size. In the study that assessed hospitalized children(128), the authors mention that their convenience sample may not be representative of the whole population due to the seasonal nature of asthma.

The only paper that measured bone mineral density found a significant association between FIS and low bone mineral density in male children, which places them at risk for bone fractures(178).

Banerjee et al.(114) investigated the renal effects of FIS by correlating it with glomerular filtration rate. Their results show that patients with CKD that experience FIS were more likely to develop end stage renal disease (ESRD) compared to non-FIS patients. Their results also show that for the non-CKD population there is no significant association between FIS and ESRD(114).

There was one manuscript that measured self-reported diagnosis of lung disease in older adults. The study found that there is no significant association between lung disease and FIS. However being food secure, and having normal waist circumference, were both protective of lung disease(116).

Summary of Evidence

The association between FIS and negative health outcomes in the USA has been investigated by at least 117 studies up until September 2017. They investigate FIS association with more than 30 health outcomes. These associations range from general perceived health to health conditions affecting several different organ systems. Behavior and cognitive function are one area that seems to have a particularly robust association to FIS. Debilitating conditions such as depression, anxiety, and sleep disorders are found to be associated with FIS in the vast majority of papers identified by this systematic review. Cardiovascular conditions such as hypertension and dyslipidemia are also associated with FIS in several reviewed manuscripts, although these associations may be influenced by comorbidity between cardiovascular conditions and diabetes. Other endocrine conditions, such as metabolic syndrome, have been identified as well. It is of note that there is not a consistent association between BMI and FIS across the literature. Though we do not hypothesize why certain authors find an association in certain populations, these mixed results suggest that further research—perhaps with a more consistent and rigorous methodology across studies—are needed to determine if there is a true association between FIS and certain healthcare outcomes. Overall, the findings of this review emphasize the value of targeted approaches for alleviating FIS, especially in patients suffering from cognitive and behavioral disorders. These findings will be particularly relevant for providers looking to better understand the breadth of negative outcomes associated with FIS, and also to those looking to justify FIS-based interventions.

Limitations

This study is limited mainly due to the scope of our search. The search protocol is designed to be sensitive for health outcomes, but not to be sensitive and specific for a particular health outcome. The purpose was to identify the plethora of health outcomes associated with FIS, and not to conduct a meta-analysis for each outcome. For example, our protocol is not designed to yield all the papers that investigate FIS and depression, but is designed to find as many of the psychiatric and neurologic health outcomes associated with FIS such as depression, sleep disorders, etc. Although this study does not identify every manuscript investigating FIS and a specific outcome, it elucidates the multitude of negative health consequences of FIS across several different organ systems. We did not include specific health outcomes (i.e. depression, hypertension) in the original search so that we would not bias the search towards the health outcomes known to the researchers to be associated with FIS, and to avoid an immense number of search terms and subsequent false positives. A meta-analysis for each health outcome and FIS would require a more specific search and is not in the scope of this manuscript. This study however would be a convenient starting point for those interested in conducting a meta-analysis for specific health outcomes.

Additionally, our study is not designed to arbitrate disagreements in the conclusions from different studies. In other words, we cannot offer concrete evaluation on the superiority, in risk of individual bias, of some studies over others. One main reason is that the association between FIS and a health outcome is complex and may be dependent on the population studied. Another is that many of these studies focused on convenient sample groups.

Furthermore, it is important to reiterate that association is not the same as causation. We are reporting health outcomes that are associated with FIS, and this association may be caused by a third variable. For example, since FIS measurements do not elucidate the length of exposure to FIS, it is difficult to determine whether FIS precedes diagnosis of chronic diseases or if FIS status is acquired after living with chronic disease. Nonetheless, the association is still useful even if only as a marker for higher risk of other morbidities.

Finally, publication bias is certainly possible and a concern. Performing a meta-analysis and statistically quantifying the publication bias is complicated by the fact that different populations are studied in different manuscripts. It is worth mentioning however that our search yielded many negative results – and this shows the utility of systematic reviews.

Conclusions

A multitude of studies have shown the association between FIS and devastating negative health outcomes. This is a strong justification for screening patients for FIS because these patients are clearly at risk of developing many complications. Although we cannot determine the causality of this relationship, FIS is often a strong marker for high risk of poor physical and mental health. All these associations should also inspire further research to investigate the cost-efficiency of alleviation of FIS as a preventive medicine intervention.

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Author Contributions

Daniel J. Arenas led the project along with Sara Zhou and Arthur Thomas.

Daniel J. Arenas, Sara Zhou, Arthur Thomas, and Gilberto Vilá-Arroyo designed the systematic review methodology.

All authors participated in the systematic review and edited the paper.

Sara Zhou and Arthur Thomas contributed equally to this work and their order was chosen randomly.

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Supplemental Information Captions

S1: Specific terms used for searching manuscripts in each database.

S2-1 Table: Cognitive Development and FIS

S2-2 Table: Depression and FIS

S2-3 Table: Epilepsy and FIS

S2-4 Table: Sleep and FIS

S2-5 Table: Hypertension and FIS

S2-6 Table: Other Cardiovascular Outcomes and FIS

S2-7 Table: Diabetes and FIS

S2-8 Table: Metabolic Syndrome and FIS

S2-9 Table Self-reported Health and FIS

S2-10 Table: Proxy-reported Health and FIS

S2-11 Table: HIV Control (CD4 cell count) and FIS

S2-12 Table: Other Infectious Disease Outcomes and FIS

S2-13 Table: Other Organ Systems Health Outcomes and FIS