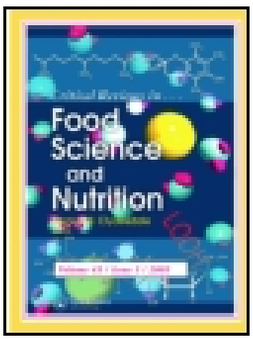

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REVIEW

Food insecurity and brain health in adults: A systematic review

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ABSTRACT

Food insecurity has been associated with adverse effects on physical health and well-being in both high and low-income countries, but effects on brain health are not clear. The purpose of this systematic review was to determine the relationship between food insecurity and important brain health outcomes in adults including depression, stroke, cognitive impairment and dementia. Electronic databases were searched to find studies which investigated relations between food insecurity and predefined brain health outcomes. Thirty studies met the inclusion criteria for review of which 23 were conducted in high income countries and seven in low- or middle-income countries. Most studies (n = 24) were cross-sectional, five were prospective and 1 was a case-control design. Seven studies reporting outcomes relating to cognitive performance and 24 relating to depression. No studies investigated relations between food insecurity and stroke or dementia. There was substantial heterogeneity in the populations studied as well as measures of food insecurity and outcomes which made comparisons between studies difficult. Overall, the findings highlighted that individuals who were food insecure had increased likelihood of depressive symptoms and poorer global cognition than those who were food secure. It is possible that social support and food aid programmes attenuate the effects of food insecurity on depressive symptoms. Future research is needed to determine whether interventions to alleviate food insecurity can benefit brain health in vulnerable populations.

KEYWORDS

Brain health; cognition; depression; food insecurity

Introduction

Food insecurity, or inadequate access to "sufficient, safe and nutritious food to meet dietary needs and food preferences for an active and healthy life," is a global public health challenge due to its increasing prevalence and adverse effect on health and well-being (World Food Summit 1996). Worldwide, one billion people are thought to be food insecure, with prevalence ranging from around 11% in high-income countries (HIC) to 57% in low and middle income countries (LMIC) (World Health Organization 2018). Furthermore, one in nine people suffer chronic food deprivation, hunger and undernourishment, with the most severely affected from poorer countries (Pérez-Escamilla 2017). Global food insecurity is expected to increase further as climate change, economic growth, urbanization and increasing life expectancy threaten the capability of food systems to feed the world's population (World Health Organization 2018; Godfray et al. 2010).

Across all regions, food insecurity is a determinant of poor diet quality and diet-related conditions, including undernutrition and obesity (Organization 2018; Farrell et al. 2018). In HIC, food insecurity has been associated with hypertension, diabetes, diminished quality of life and poor physical function (Gundersen and Ziliak 2015; Jackson et al. 2019; Russell et al. 2016) and is shown to be associated with increased healthcare utilization and cost (Berkowitz et al. 2018).

There is increasing interest in the role of food insecurity in conditions affecting the brain. Several putative mechanisms for a negative impact of food insecurity on brain health include the consumption of unhealthy and low quality diets, specific nutrient deficiencies (e.g. omega 3 fatty acids, zinc and folate) and stress pathways (Holben and Marshall 2017; Wong et al. 2016). Accumulating data suggest a greater risk of cognitive impairment and depression among food insecure individuals compared to those who are food secure (Holben and Marshall 2017; Wong et al. 2016; Maynard et al. 2018). However, studies have been extremely diverse in terms of the population, country, setting, as well as measures of food insecurity and brain health outcomes, making it difficult to draw firm conclusions.

To date, there have been limited comprehensive reviews of food insecurity in relation to brain health (Maynard et al. 2018; Arenas et al. 2019). A recent pooled analysis of observational studies demonstrated that food insecurity was associated with increased likelihood of depression (OR = 2.74 [95% CI 2.52–2.97]) (Arenas et al. 2019). However, this

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Table 1. Eligibility inclusion and exclusion criteria for review.

	Inclusion criteria	Exclusion criteria
Study design	Randomised controlled trial, controlled trial, cohort study, case-control study, systematic review, or meta-analysis	Case studies, case series, narrative reviews
Participants	Community dwelling adults >18 years	Persons <18 years old Pregnant women Participant with infectious disease e.g., HIV, Tuberculosis etc.
Exposure/Intervention	Studies that examine the association/effect of a suitable food insecurity measure on primary outcome(s)	Interventions/exposures that do not assess food insecurity.
Primary Outcomes	Dementia or dementia subtypes, cognitive function, cognitive decline, cognitive impairment stroke or depression measures	Studies where no results are provided and/or no primary outcome of interest is included Studies focusing on mental illness outcomes e.g., Schizophrenia

systematic review was limited to cross-sectional studies in US adults and did not consider evidence from other countries or populations.

Given that food insecurity is both preventable and reversible, there is a critical need to understand its relationship with brain health to inform prevention strategies. As most research into the relationship between food insecurity and brain health has been conducted with adults, we aimed to systematically review the evidence to assess the relationship between food insecurity and brain health in community-dwelling adults living in HIC and LMICs. We sought to examine specific brain health outcomes relating to dementia, depression and stroke, as these are major contributors to the global burden of disease (GBD 2016 Neurology Collaborators 2019; Rehm and Shield 2019).

Materials and methods

The methods for this systematic review were based on the Center for Reviews and Dissemination guidance for undertaking systematic reviews in health care (CRD 2009) and the protocol was registered on PROSPERO (PROSPERO 2018: CRD42018117419). The World Bank classification was used to determine whether a country was high-, middle- or low-income (World Bank 2018)

Search strategy and selection criteria

An electronic search was conducted using MEDLINE, EMBASE and PsychINFO databases for studies published up to May 03, 2021. A comprehensive search strategy was developed using key terms from published articles in the field of food insecurity and brain health and included: "food insecurity," "hunger," "brain health," "Alzheimer's disease," "cognitive function" "cognitive decline" and "cognitive impairment," "Depression," "Stroke" as shown in supplementary Table 1. We also conducted a manual literature search using citation lists of retrieved articles and the Cochrane Library database for studies not identified by electronic search.

An overview of the inclusion and exclusion criteria is shown in Table 1. Studies were considered eligible if they met *a priori* determined inclusion criteria: (i) examined food insecurity as exposure or intervention using an accepted measure, (ii) reported one or more primary outcomes related to brain health (dementia or dementia subtypes, cognitive function, cognitive decline, stroke or depression) based on neuropsychological tests, self-report and/or clinician diagnosis, and (iii) determined the association between food insecurity and brain heath outcome(s) or evaluated the effect of food insecurity interventions on brain health measures. We excluded narrative reviews, studies involving pregnant women or populations <18 years and those not published in the English language. We also excluded participants with infectious diseases given that unique behavioral pathways e.g., stigma, medication use and high-risk behaviors are implicated in relations between food insecurity and infectious disease that are difficult to disentangle (Weiser et al. 2011). Specified indicators of brain health were the primary outcomes (cognitive performance, incident dementia (any type) stroke or depression).

Article screening

Two reviewers (AJM, CME) independently assessed studies for eligibility for inclusion based on pre-defined criteria. Any disagreement among the reviewers was resolved by discussion with a third reviewer (BMG).

Data extraction

Data extraction was undertaken by the reviewers (AJM, CME). Data were extracted from the individual studies using a structured table that included information on: study design, country, country income (high, middle or low), population, sample size, food insecurity measure, outcome measure, follow up time (if applicable), main findings from adjusted results and covariates applied in adjusted models (if applicable).

Assessment of study quality

Two reviewers (AJM, CME) independently assessed the quality of studies using the Newcastle–Ottawa Scale (Wells et al. 2009.; Downes et al. 2016). A maximum of nine stars were awarded to each cohort study (eight for case-control studies): up to four stars were awarded for study selection (representativeness of the sample, sample selection, outcome

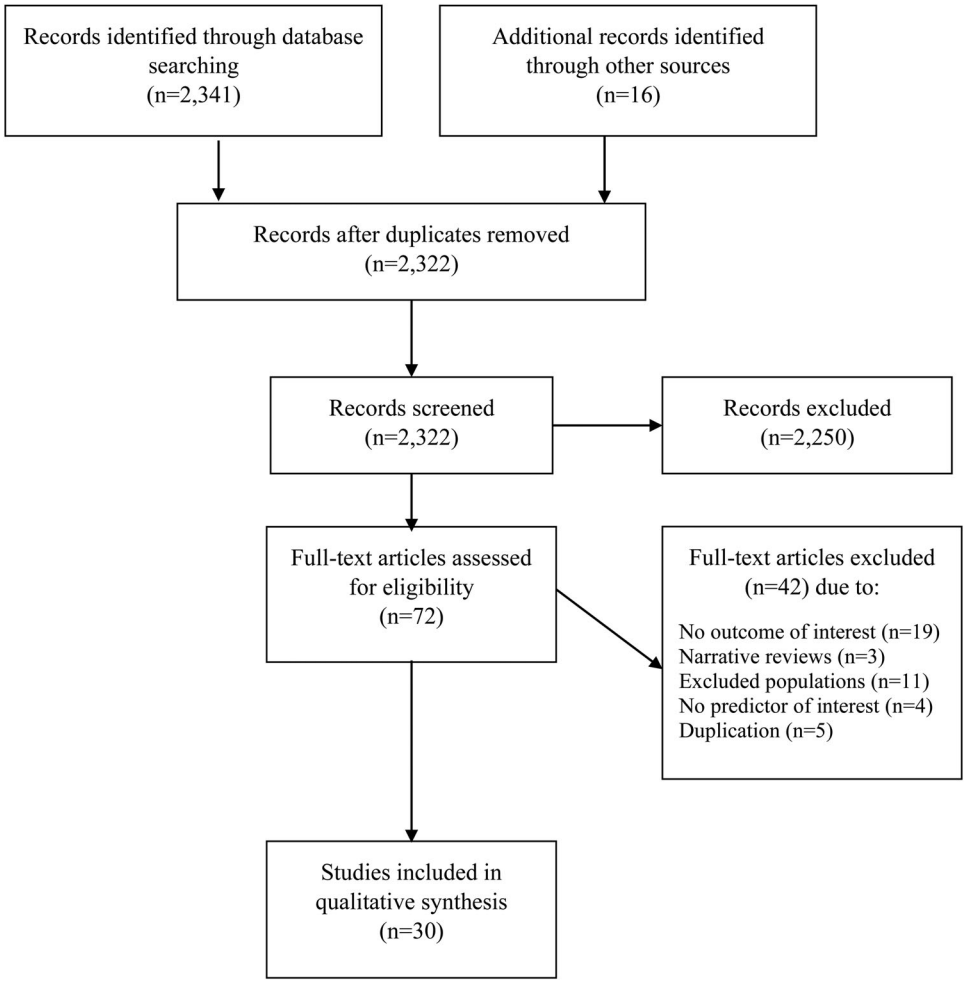

Figure 1. PRISMA (Moher et al. 2011) flow diagram showing the selection of eligible articles for inclusion in the review.

not present at start of study, and ascertainment of the exposure), up to two stars for comparability (controls for the effect or factors), and up to three stars for the outcome (assessment of the outcome and statistics applied). Studies were considered high-quality if they scored nine stars, medium quality if they scored seven to eight stars and low quality if they scored six and below.

Data analysis

Most of the eligible studies were cross-sectional designs and not considered suitable for meta-analysis due to substantial between study heterogeneity in terms of country, study populations, food insecurity measure, statistical analysis, adjustment for potential confounding, reporting of data and methods to determine outcomes. Therefore, a qualitative synthesis was used to summarize the findings.

Results

The PRISMA flowchart for the selection of studies is shown in Figure 1. The search yielded 2,322 potential articles, after removal of duplicates (n = 35). A total of 2,250 articles were excluded following title and abstract screen. From the remaining 72 full text articles, 42 were excluded for the reasons given in Figure 1, resulting in 30 eligible articles for qualitative synthesis.

Study characteristics

All 30 articles included in the review were observational studies comprising five prospective studies (Wong et al. 2016; Hadley and Patil 2008; Huddleston-Casas, Charnigo, and Simmons 2009; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007), 24 cross-sectional studies (Koyanagi et al. 2019; Portela-Parra and Leung 2019; Shafiee et al. 2021; Lee, Lee, and Cho 2021; Loh, Oddo, and Otten 2020; Mesbah et al. 2020; Smith et al. 2021; Frith and Loprinzi 2018; Tong et al. 2019; Onadja et al. 2013; Gao et al. 2009; Montgomery et al. 2017; Maharaj et al. 2017; Chung et al. 2016; Pryor et al. 2016; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006; Weigel et al. 2007; Okechukwu et al. 2012; Siefert et al. 2001; Ramsey et al. 2012) and one case control study (Fitzgerald et al. 2011). As shown in Table 2, seven studies (one prospective (Wong et al. 2016) and six cross-sectional (Koyanagi et al. 2019; Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Tong et al. 2019; Onadja et al. 2013; Gao et al. 2009) examined food insecurity in relation to cognitive outcomes. Table

Table 2. Summary of observational studies examining the association between food insecurity and cognitive outcomes (n = 7).

References	Study design	Country	Country income	Population	**Sample (n) F:M** (%)	Food insecurity measure	Outcome measures	Primary outcome of interest	Main findings from adjusted results (where applicable)	Covariates	Newcastle-Ottowa score
(Koyanagi et al. 2019)	Cross-sectional SAGE	South Africa	Middle	Adults ≥50 years	3672 F: 56% M: 44%	2-items based on US HFSSM	National Institute on Aging-Alzheimer's Association definition of cognitive impairment no dementia	Mild Cognitive Impairment	Moderate or severe food insecurity associated with increased odds for MCI. OR 2.82; 95% CI 1.65, 4.84 and OR 2.51; 95% CI 1.63, 3.87 respectively for adults with moderate and severe food insecurity compared to food security	Age, sex, education, wealth, race, physical activity, smoking, alcohol use, BMI, diabetes, stroke, hypertension, depression	5
(Portela-Parra and Leung 2019)	Cross-sectional 2011-2014 NHANES	USA	High	Older adults ≥60 years with incomes ≤300% of the federal poverty level	1823 F: 54% M:46%	10-item US FSSM	Digital Symbol Substitution Test CERAD word learning/ recall Animal Fluency Test	Cognitive function z-score	Food insecurity was associated with a lower score on the cognitive function *z* score ($\beta = -0.15$, 95% CI: −0.26, −0.05)	Age, age as a quadratic term, sex, race/ethnicity, highest education level, marital status, household income, smoking status	6
(Frith and Loprinzi 2018)	Cross-sectional 1999-2002 NHANES	USA	High	Older adults 60-85years	1851 F: 59% M:41%	18-item US FSSM	Digital Symbol Substitution Test	Cognitive performance	Older adults who were marginally food secure (β=-7.7; 95% CI: −11.9,-3.5), food insecure without hunger (β= −7.0; 95% CI: −11.4, −2.6) and food insecure with hunger (β=-14.4; 95% CI: −23.9, −4.5) had significantly worse cognitive performance Compared to those who were food secure	Age, gender, race-ethnicity, body mass index, C-reactive protein, smoking, diabetes, blood pressure, physical activity, social support, education, energy intake	7
(Tong et al. 2019)	Cross- sectional HOPE HOME study	USA	High	Homeless adults ≥50 years	350 F: 23% M: 77%	6-item Short form US HFSSM	Modified MMSE	Cognitive impairment (MMSE below the seventh percentile)	Those experiencing very low food insecurity had increased odds for cognitive impairment relative to those with low food security (OR 2.21; 95% CI 1.12, 4.35)	Not clear - variables with P ≤ 0.05 after backward elimination were retained in the final model	3
(Onadja et al. 2013)	Cross sectional The Ouagadougou Health and Demographic Surveillance Survey	Burkina Faso	Low	Adults ≥50 years	918 F: 53% M: 47%	Food Insecurity Score (0-100) 1-item question "having experienced hunger in the first	Leganes´s cognitive Test (LCT) battery (0-32)	Cognitive impairment LCT score ≤22	No association between food insecurity and cognitive impairment (OR 1.00; 95% CI 1.00 (0.99–1.01). Childhood hunger	Age, gender, education level during childhood, ethnicity, childhood hunger, health status, marital status, household food insecurity,	6

						15 years of life"			associated with higher odds of cognitive impairment (OR 1.80; 95% 1.06, 3.06).	high blood pressure, BMI	
(Gao et al. 2009)	Cross-sectional The Boston Puerto Rican Health Study	USA	High	Under privileged Boston Puerto Ricans 45-75 years	1358 F: 86% M: 14%	10-item US HFSSM	Cognitive test battery: MMSE, 16-word list learning, digit span forward and backward, Stroop, verbal fluency, clock drawing and figure copying tests	Cognitive performance; Cognitive impairment	Very low food insecurity was associated with greater odds for impairment on the MMSE (<24) OR: 2.28; 95% CI: 1.26, 4.12). Food insecurity was inversely associated with executive function (P_{Trend} 0.003), but there was no significant association with the memory or attention	Age, sex, BMI, education, smoking, poverty, acculturation, plasma homocysteine, alcohol, diabetes, hypertension	6
(Wong et al. 2016)	Prospective (2-year follow-up) The Boston Puerto Rican Health Study	USA	High	Under privileged Puerto Ricans living in Boston 40-75years	597 F: 67% M: 33%	3 items from the Cornell-Radimer Hunger Scale and the 10-item US HFSSM	Cognitive test battery (7 tests)	Global cognitive decline (composite z-score)	Food insecurity was significantly associated with faster decline in global cognitive function ($p = 0.03$) and particularly in executive function ($p = 0.02$)	Age, sex, education, baseline cognition, BMI, poverty, acculturation, smoking status, alcohol, physical activity, diabetes, hyper-tension, APOE-4, homocysteine, healthy eating index, time between baseline and follow-up	4

F = Female; M = Male; SAGE = Study on global Aging and adult health; FSSM = Food Security Survey Module; (US) HFSSM = (US) Household Food Security Survey Module; BMI = Body Mass Index; NHANES = National Health and Nutrition Examination Survey; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; HOPE HOME = Health Outcomes in People Experiencing Homelessness in Older Middle age, MMSE = Mini Mental State Exam.

3 summarizes the 24 studies (four prospective (Craig Hadley and Patil 2008; Huddleston-Casas, Charnigo, and Simmons 2009; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007), 19 cross-sectional (Shafiee et al. 2021; Lee, Lee, and Cho 2021; Loh, Oddo, and Otten 2020; Mesbah et al. 2020; Smith et al. 2021; Tong et al. 2019; Montgomery et al. 2017; Maharaj et al. 2017; Chung et al. 2016; Pryor et al. 2016; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006; Weigel et al. 2007; Okechukwu et al. 2012; Siefert et al. 2001; Ramsey et al. 2012) and one case-control (Fitzgerald et al. 2011) that examined relations between food insecurity and depression outcomes. One study investigated food insecurity in relation to both cognitive impairment and depressive symptoms among homeless US older adults (Tong et al. 2019). None of the studies reported dementia or stroke outcomes.

Most studies (n = 23) were conducted in HICs, three studies were conducted in middle-income countries (Maharaj et al. 2017; Koyanagi et al. 2019; Mesbah et al. 2020), three studies (Onadja et al. 2013; Hadley et al. 2008; Hadley and Patil 2008) in a low-income country, one study involved six low-middle income countries (Smith et al. 2021). Among the HICs, 19 studies (83%) were conducted in the USA and several were performed in different subsamples of USA cohorts, for example NHANES (Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Montgomery et al. 2017; Leung et al. 2015) and The Boston Puerto Rican Health Study (Wong et al. 2016; Gao et al. 2009). The sample size of the included studies ranged from 100 (Weigel et al. 2007) to 34,129 (Smith et al. 2021). Study populations were diverse. Among the seven studies conducted in LMICs, one focused on immigrants and refugees (Maharaj et al. 2017), four in older adults (50 years and over) (Koyanagi et al. 2019; Onadja et al. 2013; Smith et al. 2021; Mesbah et al. 2020) and two among households living in rural communities (Hadley et al. 2008; Hadley and Patil 2008). The HIC study populations involved older adults (Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Tong et al. 2019; Kim and Frongillo 2007), younger adults [18–35 years old] (Pryor et al. 2016), adults ≥18 years (Shafiee et al. 2021; Lee, Lee, and Cho 2021), low income populations (Portela-Parra and Leung 2019; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Okechukwu et al. 2012), Latinos (Wong et al. 2016; Gao et al. 2009; Kollannoor-Samuel et al. 2011; Fitzgerald et al. 2011), migrant workers (Weigel et al. 2007), low paid workers (Loh, Oddo, and Otten 2020) those with pre-diabetes or diabetes (Montgomery et al. 2017; Kollannoor-Samuel et al. 2011), new mothers (Whitaker, Phillips, and Orzol 2006), women living in rural areas (Huddleston-Casas, Charnigo, and Simmons 2009), and mothers or single women receiving welfare (Siefert et al. 2001; Heflin, Siefert, and Williams 2005). Across studies, the most common measure of food security, used was the 18-Item US Household Food Security Survey Module (HFSSM) (Shafiee et al. 2021; Lee, Lee, and Cho 2021; Frith and Loprinzi 2018; Montgomery et al. 2017; Chung et al. 2016; Leung et al. 2015; Weigel et al. 2007; Ramsey et al. 2012; Huddleston-Casas, Charnigo, and Simmons 2009), or a modified shortened version of the HFSSM (Mesbah et al. 2020; Portela-Parra and Leung 2019; Loh, Oddo, and Otten 2020; Wong et al. 2016; Tong et al. 2019; Gao et al. 2009; Pryor et al. 2016; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006; Ramsey et al. 2012). In seven studies, food security was assessed using one to three questions largely around experiencing hunger and or having enough food to eat (Smith et al. 2021; Koyanagi et al. 2019; Maharaj et al. 2017; Okechukwu et al. 2012; Siefert et al. 2001; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007).

A summary of the main findings for food insecurity and brain health are summarized in Tables 2 and 3 and discussed in more detail below.

Observational studies investigating association between food insecurity and cognition

Cross-sectional studies

Six cross-sectional studies examined relations between food insecurity and cognitive outcomes, as shown in Table 2 (Koyanagi et al. 2019; Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Tong et al. 2019; Onadja et al. 2013; Gao et al. 2009). In US populations, food insecurity was associated with poorer cognitive test performance, particularly in domains of global cognition and executive function, after adjustment for potential confounders (Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Gao et al. 2009). Food insecurity was also associated with over twice the odds of cognitive impairment among homeless older adults (Tong et al. 2019) and underprivileged Latinos (Gao et al. 2009) in the USA, and older adults in South Africa (Koyanagi et al. 2019) but not among older adults from West Africa (Onadja et al. 2013). In the latter study, early life hunger was more strongly associated with higher likelihood of cognitive impairment than a food insecurity score (Onadja et al. 2013).

Case control study

One study used a case control design (Fitzgerald et al. 2011). In a sample of 201 Latinas, with and without type 2 diabetes, participants who were food insecure were 3.3 times (OR = 3.3: 95%CI = 1.36–7.57) more likely to have T2D. However, regardless of T2D diagnosis, participants who were food insecure also reported elevated levels of depressive symptoms (Fitzgerald et al. 2011).

Prospective studies

Only one study investigated the relationship between food insecurity and cognitive decline (Wong et al. 2016). Among 597 Latinos in the Boston Puerto Rican Health Study, food insecurity was significantly associated with accelerated cognitive decline, particularly in domains of global cognition and executive function over a 2-y period (Wong et al. 2016).

Table 3. Summary of observational studies examining the association between food insecurity and depression outcomes (n = 24).

References	Study design	Country	Country income	Population	Sample (n) F:M (%)	Food insecurity measure	Outcome measure	Primary outcome of interest	Main findings from adjusted results (where applicable)	Covariates	Newcastle-Ottowa score
(Shafiee et al. 2021)	Cross-sectional Canadian Community Health Survey	Canada	High	Adults aged ≥18 years	19118 F: 51% M:49%	18-item HFSSM	Patient Health Questionnaire-9 (PHQ-9)	Depressive symptoms	Food security was associated with increased odds of depressive symptoms (OR 2.87; 95% CI: 2.33, 3.55)	Not clear - variables with P < 0.2 from simple logistical regression or those with clinical importance were included in a multivariate logistic model	3
(Lee, Lee, and Cho 2021)	Cross-sectional 2014 Korean NHANES	Korea	High	Adults 20-64 years	3102 F: 61% M: 39%	18-item HFSSM	PHQ-9	Depressive symptoms	Moderate-severe food insecurity was associated with increased odds of depressive symptoms (OR 4.0; 95% CI: 1.7, 9.0) compared to food security	Sex, age, income, marital status, education, chronic disease, physical disabilities, and menopausal status (in women)	4
(Loh, Oddo, and Otten 2020)	Cross-sectional	USA	High	Adults ≥18 years working in Early Childhood Education Centers	313 F:94% M:6%	6-item US HFSSM	20-Item Center for epidemiological studies depression scale (CES-D)	Depressive symptoms	Very low and low food Insecurity was associated with OR 4.95 (95% CI: 2.29, 10.67) and OR 2.69 95% CI: 1.29, 5.63) higher odds of depression, respectively, compared to food security	Age, marital status, birth country, race/ethnicity, number of children, job title, average paid hours of work per week, highest level of education, total household income, study site	3
(Mesbah et al. 2020)	Cross-sectional	Malaysia	Middle	Adults ≥60 years	220 F: 58% M: 42%	6-item US HFSSM	15-item Geriatric Depression scale (GDS-15)	Depressive symptoms	Food insecurity was associated with increased odds of depressive symptoms (OR 3.54; 95% CI: 1.35, 9.28)	Not clear	3
(Smith et al. 2021)	Cross-sectional SAGE	China, Ghana, India, Mexico, Russia, and South Africa	Low-Middle	Adults ≥50 years	34129 F: 52% M:48%	2-items based on US HFSSM	World Mental Health Survey version of the Composite International Diagnostic Interview	Depression	Severe food insecurity was associated with increased pooled odds of depression (OR 2.43; 95% CI: 1.65, 3.57) across countries, compared to food security	Age, sex, wealth, education, physical activity, smoking	5
(Tong et al. 2019)	Cross- sectional HOPE HOME study	USA	High	Homeless adults ≥50 years	350 F: 23% M: 77%	6-item Short form US HFSSM	20-Item CES-D	Depressive symptoms	Very low food insecurity was associated with increased odds of depressive symptoms (OR 3.01; 95% CI: 1.69, 5.38)	Not clear - variables with P ≤ 0.05 after backward elimination were retained in the final model	3
(Montgomery et al. 2017)	Cross-sectional 2011-2014 NHANES	USA	High	Adults aged ≥20 years	11441 F: 51% M: 49%	18-Item US HFSSM	PHQ-9	Depressive symptoms	Among diabetics, mild food insecurity and severe food	Age group, sex, race, income, education,	5

(*continued*)

Table 3. Continued.

References	Study design	Country	Country income	Population	Sample (n) F:M (%)	Food insecurity measure	Outcome measure	Primary outcome of interest	Main findings from adjusted results (where applicable)	Covariates	Newcastle-Ottowa score
					Diabetes (1724); pre-diabetes (2004); normo-glycemia (7713)				insecurity were associated with higher odds (OR 2.6; 95% CI: 1.0, 6.6, and OR 3.5; 95% CI: 1.9, 6.3, respectively) of depressive symptoms relative to being food secure. Results were similar for those with pre-diabetes. Among those with normoglycaemia, severe food insecurity was associated with elevated depressive symptoms (OR 2.0; 95% CI: 1.0, 3.9)	smoking, physical activity	
(Maharaj et al. 2017)	Cross-sectional	South Africa	Middle	Immigrants and refugees >18 years	335 F: 47% M: 53%	2 questions from the Short Form of the 12-month Food Security Scale	Hopkins Symptom Checklist-25	Depressive symptoms	Not eating enough (OR 4.51; 95 % CI: 2.01, 10.09) and eating less (OR 2.88; 95 % CI: 1.54, 5.39) were significantly associated with depression symptoms	Not clear	4
(Chung et al. 2016)	Cross-sectional 2012-2013 Korean NHANES	Korea	High	Adults 20-64 years	5862 F: 61% M: 39%	18-item US HFSSM	Self-reported depressive symptoms	Depressive symptoms	Food insecure household with hunger had significantly greater odds of depressive symptoms (OR 3.64; 95% CI 2.17, 6.08) compared to food secure households,	Age, sex, education, income, smoking, alcohol, physical activity, marital status, receiving food assistance	6
(Pryor et al. 2016)	Cross-sectional TEMPO cohort	France	High	Young adults 18-35 years	1109 F: 62% M: 38%	Cornell-Radimer Hunger Scale and 10-item US Food Security Survey Module to derive Food Insecurity propensity score	Mini-International Neuropsychiatric Interview	Depression	Food insecurity propensity score was associated with increased risk of depression (RR 2.01; 95% CI: 1.01, 4.02)	Multi-variable analysis weighted by inverse probability weight	4
(Leung et al. 2015)	Cross-sectional NHANES	USA	High	Adults 20-65 years with incomes ≤300% of the federal poverty level	3518 F: 54% M: 46%	18-item US HFSSM and short form of the US household food security supplement	PHQ-9	Depressive symptoms	Very low food security was associated with increased odds of depressive symptoms (OR 5.10; 95% CI: 3.09, 8.41). Those with very	Age, sex, race/ethnicity, education, marital status, household size, poverty,	7

						module [US-HFSSM] module			low food security and in the federal Supplementary Nutrition Assistance Programme also had higher odds of depression but at a lower magnitude (OR 2.21; 95% CI: 1.54, 3.17)	smoking, and BMI categories.	
(Kollannoor-Samuel et al. 2011)	Cross-sectional	USA	High	Low-income Latinos with Type 2 diabetes (T2DM)	211 F: 74% M: 26%	6 item short form US HFSSM	20-Item CES-D	Depressive symptoms	Food insecurity was associated with depressive symptoms which was attenuated by higher levels of social support ($p < .05$)	Gender, ethnicity, marital status, smoking, income, employment, social support, BMI, number of clinical symptoms, self-reported health, interference score, HbA1c, insulin use	4
(Silverman et al. 2015)	Cross-sectional	USA	High	Low-income Adults with T2DM 30-70 years	287 F: 49% M: 51%	6-item short form US Food Security Survey Module	PHQ-8	Depressive symptoms	Food insecurity was associated with higher odds of depressive symptoms (OR 2.82; 95 % CI: 1.50, 5.31) compared to food security	Age, gender, education, race/ethnicity, language, marital status, BMI and insulin use	3
(Hadley et al. 2008)	Cross-sectional	Ethiopia	Low	Parents from rural households	902 (451 husband-wife pairs)	7-item validated Food Insecurity Instrument based on US Food Security Survey Module.	Hopkins Symptom Checklist-25 (HSCL)	Depressive symptoms	Food insecurity was significantly associated with depressive symptoms ($p = <0.01$)	Not clear	5
(Whitaker, Phillips, and Orzol 2006)	Cross-sectional	USA	High	New mothers >18 years	2870 F: 100%	10-item US HFSSM	World Health Organization Composite International Diagnostic Interview Short Form	Major depressive episode	Mothers who were marginally or severely food insecure were more likely to experience a major depressive episode in comparison to mothers who were food secure (OR 1.4; 95% CI: 1.1, 1.8, and OR 2.2; 95% CI: 1.6, 2.9, respectively)	Mother's education, race/ethnicity, relationship status, employment in previous year, binge drinking, illicit drug use, global health, prenatal smoking, and prenatal physical domestic violence; household's income/poverty ratio, number of children, and material hardship (non–food	5

(*continued*)

Table 3. Continued.

References	Study design	Country	Country income	Population	**Sample (n) F:M** (%)	Food insecurity measure	Outcome measure	Primary outcome of interest	Main findings from adjusted results (where applicable)	Covariates	Newcastle-Ottowa score
										related), whether father was ever in jail.	
(Weigel et al. 2007)	Cross-sectional	USA	High	Migrant and seasonal farmworkers living on the U.S – Mexico border >18 years	100 F: 43% M: 57%	18-item US HFSSM	California Agricultural worker health survey (CAWHS)	Self-reported depression in the past 12 months	Food insecure adults had increased odds for reported depression (OR 6.0; 95% CI: 1.28, 27.6) compared to those who were food secure	Children living in household, maternal education, US residence time, age, sex	5
(Okechukwu et al. 2012)	Cross sectional Work, Family and Health Network Study	USA,	High	Lower income employees at nursing homes in Boston	416 F: 83% M: 17%	2-item Food Insufficiency	11-Item CES-D	Depressive symptoms	Food insufficiency was associated with depressive symptoms (OR 2.10; 95% CI: 1.10, 4.18) and the relationship was stronger among household primary earners compared to non-primary earners (OR 3.60; 95% CI: 1.42, 9.1)	Age, gender, education, adjusted household income, marital status, race/ethnicity, immigrant status, presence of a child younger than 19 years in the household	6
(Siefert et al. 2001)	Cross-sectional Women's Employment Study	USA,	High	Mothers receiving cash assistance living in Michigan 18-54 years	753 F:100%	Single Item question. "Which of the following describes the amount of food your household has to eat–enough to eat, sometimes not enough to eat, or often not enough to eat?"	World Health Organization Composite International Diagnostic Interview	Depression	Food insufficiency associated with higher odds of depression (OR 2.21; 95% CI: 1.48, 3.29).	Age group, race/ethnicity, , education, poverty status, employment status, exposure to domestic violence number of children in the household, stressful life circumstances, race/gender discrimination	6
(Ramsey et al. 2012)	Cross-sectional	Australia	High	Disadvantaged suburbs of Brisbane adults ≥20 years	505 F: 56% M: 45%	18-item US HFSSM	Depression domain extracted from the short form (SF-12) healthcare survey	Depression risk	Food insecurity was associated with higher odds for depression (OR 5.77; 95% CI: 2.88, 11.54)	Indigenous status equivalised household structure household income	5
(Fitzgerald et al. 2011)	Case control	USA	High	Latinas with and without type 2 diabetes 35-60 years	201	6-item US HFSSM	20-Item CES-D	Depressive symptoms	Low food security and very low food security were associated with elevated depressive symptoms (OR 2.51; 95% CI: 1.26, 5.00, and OR 3.21; 95% CI: 1.36, 7.57, respectively)	Waist circumference	6

(Hadley and Patil 2008)	Prospective (6 months follow up) Gilgel Gibe Growth and Development Study	Tanzania	Low	Women caretakers living in rural Tanzania	173 F: 100%	7-item Household Food Security measure based on US HFSSM	HSCL	Depressive symptoms	Food insecurity was associated with elevated HSCL score. Changes in food insecurity across the dry and wet seasons predicted changes in symptoms of anxiety and depression ($\beta = 0.79$; SE 0.21, $p < 0.0001$	Ethnicity, material wealth, household production, animal ownership	3
(Huddleston-Casas, Charnigo, and Simmons 2009)	Prospective (2-year follow-up) Rural Families Speak Study	USA	High	Low-income rural women $\geq$18 years and their families	413 F:100%	18-item Core Food Security Module	20-item CES-D	Depressive symptoms	Structural equation models indicated that the causal relationship between household food insecurity and depressive symptoms is bidirectional for causation	N/A	4
(Heflin, Siefert, and Williams 2005)	Prospective (3-year follow-up) Women's Employment Study	USA	High	Single women welfare recipients living in Michigan 18-54 years	753 F: 100%	Single-Item Question "Which of the following describes the amount of food your household has to eat—enough to eat, sometimes not enough to eat, or often not enough to eat?"	World Health Organization Composite International Diagnostic Interview	Depression	Change in food insecurity status was positively associated with a change in major depression status.($\beta = 0.75$; SE 0.24, $p < 0.01$)	Number of children, household income, neighborhood hazards, stressful life circumstances, domestic violence, sex/race discrimination	4
(Kim and Frongillo 2007)	Prospective (7-year follow-up) HRS and AHEAD studies	USA	High	Older adults 51 − 61 years HRS $\geq$70 years AHEAD	15835 N = 9481 HRS F: 48% M: 52% N = 6354 AHEAD F: 60% M: 40%	Two questions from the US HFSSM	8-Item CES-D	Depressive symptoms	Food-insecure older adults had higher depression scores than those who were food-secure in both HRS ($\beta = 0.27$, $p = 0.001$) and AHEAD ($\beta = 0.18$, $p = 0.05$). Previous food-insecure older adults also had a greater increase in depression score than previous food-secure older adults in HRS ($p = 0.01$).	Age, race, marital status, education, income, number of chronic diseases, physical activity, activities of daily living, instrumental activities of daily living	3

F = Female; M = Male; NHANES = National Health and Nutrition Examination Survey; BMI = Body Mass Index; SAGE = Study on global Aging and adult health; TEMPO = Trajectoires epidemiologiques en population; (US) HFSSM = (US) Household Food Security Survey Module; HRS = Health and retirement study; AHEAD = Asset and Health Dynamics among the Oldest Old.

We did not identify any study from LMICs examining prospective relations between food insecurity and cognition.

Observational studies investigating association between food insecurity and depression or depressive symptoms

Cross-sectional studies

A total of 20 cross-sectional studies examined the relationship between food insecurity and depression outcomes (Shafiee et al. 2021; Lee, Lee, and Cho 2021; Loh, Oddo, and Otten 2020; Mesbah et al. 2020; Smith et al. 2021; Tong et al. 2019; Montgomery et al. 2017; Maharaj et al. 2017; Chung et al. 2016; Pryor et al. 2016; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006; Weigel et al. 2007; Okechukwu et al. 2012; Siefert et al. 2001; Ramsey et al. 2012; Fitzgerald et al. 2011). Sixteen studies were conducted in HIC (Shafiee et al. 2021; Lee, Lee, and Cho 2021; Loh, Oddo, and Otten 2020; Tong et al. 2019; Montgomery et al. 2017; Chung et al. 2016; Pryor et al. 2016; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Whitaker, Phillips, and Orzol 2006; Weigel et al. 2007; Okechukwu et al. 2012; Siefert et al. 2001; Ramsey et al. 2012; Fitzgerald et al. 2011) with 11 of these in US populations (Loh, Oddo, and Otten 2020; Tong et al. 2019; Montgomery et al. 2017; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Whitaker, Phillips, and Orzol 2006; Weigel et al. 2007; Okechukwu et al. 2012; Siefert et al. 2001; Fitzgerald et al. 2011). A further four studies were in LMICs (Mesbah et al. 2020; Smith et al. 2021; Maharaj et al. 2017; Hadley et al. 2008). Data from all regions indicated a consistent association between food insecurity and increased likelihood of depressive symptoms(Montgomery et al. 2017; Maharaj et al. 2017; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006)Adults who reported food insecurity had between two and five times higher likelihood of elevated depressive symptoms compared to those who were food secure (Shafiee et al. 2021; Loh, Oddo, and Otten 2020; Lee, Lee, and Cho 2021; Tong et al. 2019; Montgomery et al. 2017; Chung et al. 2016; Leung et al. 2015; Silverman et al. 2015; Okechukwu et al. 2012; Fitzgerald et al. 2011; Maharaj et al. 2017; Silverman et al. 2015; Whitaker, Phillips, and Orzol 2006)) and risk estimates were greatest among those experiencing severe food insecurity (Loh, Oddo, and Otten 2020; Lee, Lee, and Cho 2021; Montgomery et al. 2017; Leung et al. 2015; Fitzgerald et al. 2011), those who were diabetic (Montgomery et al. 2017; Silverman et al. 2015), on low income (Leung et al. 2015; Silverman et al. 2015; Okechukwu et al. 2012) or homeless (Tong et al. 2019). A dose-response relationship between food insecurity and depressive symptoms was demonstrated among low-income US adults, which was attenuated by receipt of a food assistance programme (Leung et al. 2015). Food insecurity was associated with higher risk of depression among young French adults (Pryor et al. 2016), US mothers receiving welfare (Siefert et al. 2001), Australian adults living in disadvantages areas (Ramsey et al. 2012) and migrant farmworkers on the US-Mexican border (Weigel et al. 2007) and was also independently associated with higher risk of a depressive episode among US new mothers (Whitaker, Phillips, and Orzol 2006). Furthermore, severe food insecurity was associated with more than double the risk of depression in a pooled analysis involving six LMICs (Smith et al. 2021).

Prospective studies

Four studies investigated the prospective relationship between food insecurity and depression outcomes (Hadley and Patil 2008; Huddleston-Casas, Charnigo, and Simmons 2009; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007), with three of these conducted in HIC (USA) (Huddleston-Casas, Charnigo, and Simmons 2009; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007) and one in a LMIC (Tanzania) (Hadley and Patil 2008). Similar to the findings from cross-sectional studies, food insecurity was related to future increased risk of depressive symptoms (Hadley and Patil 2008; Huddleston-Casas, Charnigo, and Simmons 2009; Kim and Frongillo 2007) or risk of depression (Heflin, Siefert, and Williams 2005). Food insecure US adults in receipt of food assistance were also less likely to report the development of depressive symptoms than those with food insecurity without assistance (Kim and Frongillo 2007). Furthermore, a bidirectional relationship was demonstrated between household food insecurity and depressive symptoms, with food insecurity increasing the risk of depressive symptoms and depressive symptoms predicting food insecurity among US low-income women living in rural households (Huddleston-Casas, Charnigo, and Simmons 2009).

Discussion

The findings of this review support a link between food insecurity and poor brain health among community-dwelling populations in high- and low-income countries. We did not identify outcomes for stroke or dementia therefore only evidence relating to depression and cognitive performance was reviewed.

A consistent relationship was found between food insecurity and elevated depressive symptoms or depression risk in both HIC (Shafiee et al. 2021; Loh, Oddo, and Otten 2020; Lee, Lee, and Cho 2021; Tong et al. 2019; Maharaj et al. 2017; Leung et al. 2015; Silverman et al. 2015; Okechukwu et al. 2012; Ramsey et al. 2012; Fitzgerald et al. 2011; Hadley and Patil 2008; Huddleston-Casas, Charnigo, and Simmons 2009; Heflin, Siefert, and Williams 2005; Kim and Frongillo 2007) and LMIC (Mesbah et al. 2020; Smith et al. 2021; Gao et al. 2009; Kollannoor-Samuel et al. 2011; Siefert et al. 2001) even though the magnitude of association varied between populations and by different measures of depression. Overall, food insecure participants were between two and five times more likely to report elevated depressive

symptoms compared to those who were food secure. However, deciphering relations between food insecurity and depression is not straightforward. Food insecure individuals are likely to be living in poverty with unmet basic needs, low social capital and poor access to healthcare that can increase depression risk (Patel and Kleinman 2003). Furthermore, chronic stress and anxiety caused by not knowing if there is enough food to feed the family can act as a primer for depression among parents who are food insecure (Kessler 1997). Conversely, depression may increase vulnerability to food insecurity by reducing employment stability, decreasing income and increasing medication and healthcare costs (Patel and Kleinman 2003; Lund et al. 2010). Hence, a cyclical relationship likely exists between food insecurity and depression that may be influenced by socioeconomic factors including poverty, income and social capital (Patel and Kleinman 2003). Indeed poverty was controlled for in several of the analyses in our qualitative synthesis, with studies finding that the combination of both poverty and food insecurity affect global cognition (Gao et al. 2009; Wong et al. 2016) and elevate depressive symptoms (Leung et al. 2015; Whitaker, Phillips, and Orzol 2006). It has been suggested that social support provides a buffer against the adverse effects of food insecurity on brain health (Siefert et al. 2007). As a case in point, among low income Latinos with and without T2D, food insecurity predicted these higher levels of depressive symptoms, the association was attenuated by higher levels of social support (Kollannoor-Samuel et al. 2011). However, these findings need to be replicated in other studies and among other populations. Furthermore, nutrition programmes to alleviate food security may reduce depression risk among food insecure individuals (Leung et al. 2015).

In regards to cognitive performance, there were negative associations between food insecurity and cognitive impairment in US populations (Portela-Parra and Leung 2019; Frith and Loprinzi 2018; Onadja et al. 2013; Montgomery et al. 2017; Maharaj et al. 2017; Pryor et al. 2016) and South African older adults (Koyanagi et al. 2019) but not in West African older adults (Chung et al. 2016), likely owing to the small number of studies conducted especially in LMIC and between-study heterogeneity in the methods used to assess food insecurity and cognition. For example, the US studies used variations of the HFSSM to determine food insecurity whereas the West African study examined a population-specific food insecurity score, which limits the comparability of findings between these studies.

Interestingly, early life hunger rather than food insecurity was a predictor of cognitive impairment in older West African adults. Other studies in LMIC have also reported associations between early life hunger or childhood food insufficiency and increased risk of cognitive impairment (Galler et al. 2012; Zhang, Gu, and Hayward 2008) and dementia in later life (Momtaz et al. 2014). It is likely that infants and children in LMIC have greater exposure to suboptimal maternal diet and more extreme forms of food insecurity including chronic lack of food, hunger and malnutrition than their HIC counterparts. However, early life experience of hunger (0–4 years) but not at 12 years has been associated with poor cognitive function among Europeans ages 65 years and over (Cohn-Schwartz 2020). Childhood malnutrition can result in suboptimal cognitive development, low educational attainment during childhood (Prado and Dewey 2014) and increased risk of obesity, diabetes and depression, all of which are risk factors for dementia risk in later life (Livingston et al. 2020).

Several pathways can help to explain an adverse impact of food insecurity on the brain. First, chronic stress triggers the release of glucocorticoids that have been implicated in the pathogenesis of depression and accelerated cognitive decline via oxidative stress and neuroinflammation (Marsland et al. 2008). Chronic stress has also been associated with lower gray matter volume, particularly in the frontal cortex and hippocampal regions that are vulnerable to depression and dementia (Souza-Talarico et al. 2011). Second, food insecurity limits food choice and drives the consumption of poor quality diets, characterized by low intake of essential vitamins and minerals and high intake of saturated fat, sugar and salt (Holben and Marshall 2017; Wong et al. 2016). Dietary sources of vitamins, minerals and other plant bioactive constituents have important physiological roles in brain health by inhibiting oxidative stress and neuroinflammation, promoting neurogenesis, neuronal cell signaling and neuronal integrity (McGrattan et al. 2019). In contrast, saturated fat and sugar have been shown to trigger neuroinflammatory processes, particularly in the hippocampus, and can impair memory (Spencer et al. 2017). Mounting data lend support to an association between high quality diets and a slower rate of cognitive decline and late life dementia (Chen et al. 2019) and potentially reduced risk of depression (Molendijk et al. 2018).

The findings of this review should be interpreted with caution given that all studies were observational and unable to determine causality, and the majority of studies were rated as low quality with a Newcastle-Ottowa Score of six or less. None of the included studies were assessed as "high quality." There was substantial variation between studies in the adjustment for confounders in multivariable models including household income, poverty status, social support and comorbidities that can affect both food insecurity and brain health, however, the associations remained significant even after controlling for these covariates (Montgomery et al. 2017; Maharaj et al. 2017; Leung et al. 2015; Kollannoor-Samuel et al. 2011; Silverman et al. 2015; Hadley et al. 2008; Whitaker, Phillips, and Orzol 2006). Given the nature of observational data we cannot exclude the possibility of residual confounding from unmeasured or unadjusted covariates in the individual studies. Furthermore, a quantitative meta-analysis was not possible, given the heterogeneity in measures of food insecurity, depression and cognitive performance that made it difficult to compare findings across studies. Importantly, the US HFSSM/FSSM is the most widely used quantitative measure of household food deprivation but does not capture the multidimensional and graded experience of food insecurity at an individual level (Jones et al. 2013). It is possible that broader aspects of the

experience of food insecurity that are not measured by this tool, such as having to go without food, running out of food or the social implications of not having enough food (Jones et al. 2013), have implications for brain health.

In summary, the available observational evidence suggests that food insecure adults are at increased risk of depression and cognitive impairment. The extent and duration of food insecurity is likely to influence brain health, however this can only be elucidated in future longitudinal cohort studies with repeated measures of food insecurity and clinical measures of brain health in diverse populations. Food insecurity, depression and dementia rates are disproportionately increasing in LMIC, but surprisingly few studies have been conducted in this setting. There is a clear need for future research to determine relations between food insecurity and dementia particularly among high-risk populations. While preliminary evidence from HIC suggests that new mothers, those on low incomes or homeless or diabetic may be most vulnerable to adverse effects of food insecurity on brain health, this requires confirmation in long-term cohort studies. We did not identify interventions that target food insecurity for brain health. Therefore, further high-quality research is warranted to identify strategies that can effectively address food insecurity for neurocognitive benefit among those who will benefit most.

Disclosure statement

The authors have no potential competing interests.

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