REVIEW

Healthy Food Prescription Programs and their Impact on Dietary Behavior and Cardiometabolic Risk Factors: A Systematic Review and Meta-Analysis

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ABSTRACT

The enormous burden of diet-related chronic diseases has prompted interest in healthy food prescription programs. Yet, the impact of such programs remains unclear. The aim of this study was to conduct a systematic review of healthy food prescription programs and evaluate their impact on dietary behavior and cardiometabolic parameters by meta-analysis. A systematic search was carried out in Medline, Embase, Scopus, and Cochrane Central Register of Controlled Trials databases since their inception to 3 January, 2020 without language restriction. A systematic search of interventional studies investigating the effect of healthy food prescription on diet quality and/or cardiometabolic risk factors including BMI, systolic (SBP) and diastolic blood pressure (DBP), glycated hemoglobin (HbA1c), or blood lipids was carried out. Thirteen studies were identified for inclusion, most of which were quasi-experimental (pre/post) interventions without a control group ($n = 9$). Pooled estimates revealed a 22% (95% CI: 12, 32; $n = 5$ studies, $n = 1039$ participants; $I^2 = 97\%$) increase in fruit and vegetable consumption, corresponding to 0.8 higher daily servings (95% CI: 0.2, 1.4; $I^2 = 96\%$). BMI decreased by 0.6 kg/m^2 (95% CI: 0.2, 1.1; $I^2 = 6.4\%$) and HbA1c by 0.8% (95% CI: 0.1, 1.6; $I^2 = 92\%$). No significant change was observed in other cardiometabolic parameters. These findings should be interpreted with caution in light of considerable heterogeneity, methodological limitations of the included studies, and moderate to very low certainty of evidence. Our results support the need for well-designed, large, randomized controlled trials in various settings to further establish the efficacy of healthy food prescription programs on diet quality and cardiometabolic health. *Adv Nutr* 2021;12:1944–1956.

Statement of Significance: This is the first systematic review and meta-analysis to evaluate the impact of healthy food prescription programs on dietary behavior and cardiometabolic parameters.

Keywords: food is medicine, chronic diseases, global burden of disease, food policy, nutrition, diet, food pharmacy, food insecurity, culinary medicine, public health

Introduction

A poor-quality diet is a leading risk factor for noncommunicable diseases worldwide (1, 2), with 1 of every 5 deaths across the globe attributable to a suboptimal diet (3). Furthermore, diet-related diseases including obesity, diabetes, and cardiovascular disease place a tremendous financial burden on healthcare systems (4–6), with costs projected to rise over the coming decades (7, 8). Food insecurity, defined as lack of access to nutritionally adequate food, is associated with the greater consumption of inexpensive nutrient-poor foods (9–14), lower intake of fruit and vegetables and other healthy foods (15, 16), and higher risk of cardiometabolic diseases. Food insecurity is also linked to lower self-efficacy in managing chronic diseases owing to mental and financial strains, such as high costs of medications and other out-of-pocket healthcare expenses (17–20).

Based on the critical roles of poor diet quality and food insecurity in chronic disease, there is a growing interest in incorporating "food is medicine" interventions into healthcare systems to provide healthy foods as a treatment of vulnerable patients (21). One approach gaining momentum is "produce prescription," whereby a physician or healthcare

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worker identifies patients, based on disease and/or food security criteria, eligible to receive free or discounted healthy produce. Eligibility criteria typically include a food insecurity or low-income criterion, and a diet-related health condition criterion such as the presence of diabetes, obesity, and/or hypertension. Patients are provided subsidized or free healthy foods, with uptake options including redemption of prescribed coupons at local food stores, or provision of fresh produce at the healthcare center or delivered to the home (22, 23).

Despite the rapidly growing interest in healthy food prescription programs by governments, payers, and healthcare providers, the impact of such programs on dietary behavior and cardiometabolic risk factors has not been systematically evaluated. Some individual studies have reported increases in participants' awareness of healthy dietary behaviors (24, 25), with mixed findings for actual dietary behaviors and/or cardiometabolic risk profiles (26–28). The aim of the present work was to perform a systematic review and meta-analysis of interventional studies that evaluated healthy food "prescription" programs to gain insight into study designs, intervention types, and their effects on participants' dietary behavior and cardiometabolic risk factors.

Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered on PROSPERO (CRD42020162553).

Search strategy

A systematic literature search up to 3 January, 2020 was conducted in Medline, Embase, Scopus, and Cochrane Central Register of Controlled Trials since their inception without language restriction using the following search terms: "fruit" and "vegetable" or "produce" or "food" adj3 "prescription" or "voucher" or "incentive" or "program" and "blood pressure" or "weight" or "body mass index" or "BMI" or "waist circumference" or "glucose" or "A1c" or "lipid" or "LDL" or "HDL" or "triglycerides" or "consum∗" or "intake." Reference lists of eligible studies were manually scanned to identify additional relevant publications.

Eligibility criteria, search strategy, and data extraction

Interventional studies that investigated the impact of healthy food prescription programs on dietary behavior and/or cardiometabolic risk factors including BMI, systolic (SBP) and diastolic blood pressure (DBP), glycated hemoglobin (HbA1c), or blood lipids in participants aged 18 y or older were eligible for inclusion. Our preliminary literature review revealed that patient populations that were often the target of healthy food prescription programs were those with type 2 diabetes mellitus, hypertension, and/or cardiovascular disease. We therefore wanted to assess how healthy food prescription interventions would impact well-established clinical markers of cardiometabolic disease risk that were most commonly reported by studies in the field. Included studies were either quasi-experimental (pre/post with or without an external control group) or randomized controlled trials (RCTs). In addition, healthy food prescription programs had to be integrated into the healthcare system, with patients identified and referred by a healthcare provider or other allied health staff member (e.g., dietitian). Studies involving pregnant or breastfeeding women, those investigating only financial or economic implications, and those only examining patient knowledge and attitudes, or ethical considerations were excluded. Observational studies, school-based food programs and government-led food security programs not linked to healthcare systems and workers and not administered with the primary purpose of tackling health outcomes were excluded. Qualitative studies that did not measure changes in dietary behavior or cardiometabolic risk factors were excluded, as were commentary or opinion pieces. Two reviewers (SB and either KT or DC) independently screened studies for eligibility and extracted the following data into prepiloted forms: period of data collection, study location and setting, study design, inclusion criteria, sample size, average participant age, proportion of female participants, duration of follow-up, program details, participation rate, effect size estimates, and data required to calculate variance of effect estimates (CIs, SEs, or *P* values). As studies were conducted in different countries and years, the value of the reported incentive offered to participants was converted into a standardized United States Dollar (USD)-equivalent amount adjusted for inflation to January 2020. We assessed the quality of RCTs using version 2 of Cochrane's Risk of Bias tool (RoB2) (29) and nonrandomized studies using Cochrane's Risk of Bias in Non-Randomised Studies-of Intervention (ROBINS-I) tool (30). Disagreements were resolved by consensus or via involvement of a third reviewer (JHYW). The overall certainty of evidence was evaluated using the Grades of Recommendation, Assessment, Development, and Evaluation Working Group (GRADE) framework (31).

Statistical analysis

The primary outcomes were changes in dietary behavior and cardiometabolic risk factors due to healthy food prescription programs, standardized as percent differences from either study baseline or compared with external control groups. For studies without a separate comparison group, we evaluated the pre/post difference. For RCTs (including parallel intervention and crossover studies) and studies with a separate comparison group, we evaluated the difference at the end

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MM and JHYW contributed equally to this project.
Address correspondence to JHYW (e-mail: jwu1@georgeinstitute.org.au).
Abbreviations used: DBP, diastolic blood pressure; GRADE, Grades of Recommendation, Assessment, Development, and Evaluation Working Group; HbA1c, glycated hemoglobin; RCT, randomized controlled trial; SBP, systolic blood pressure; USD, United States Dollar equivalent.

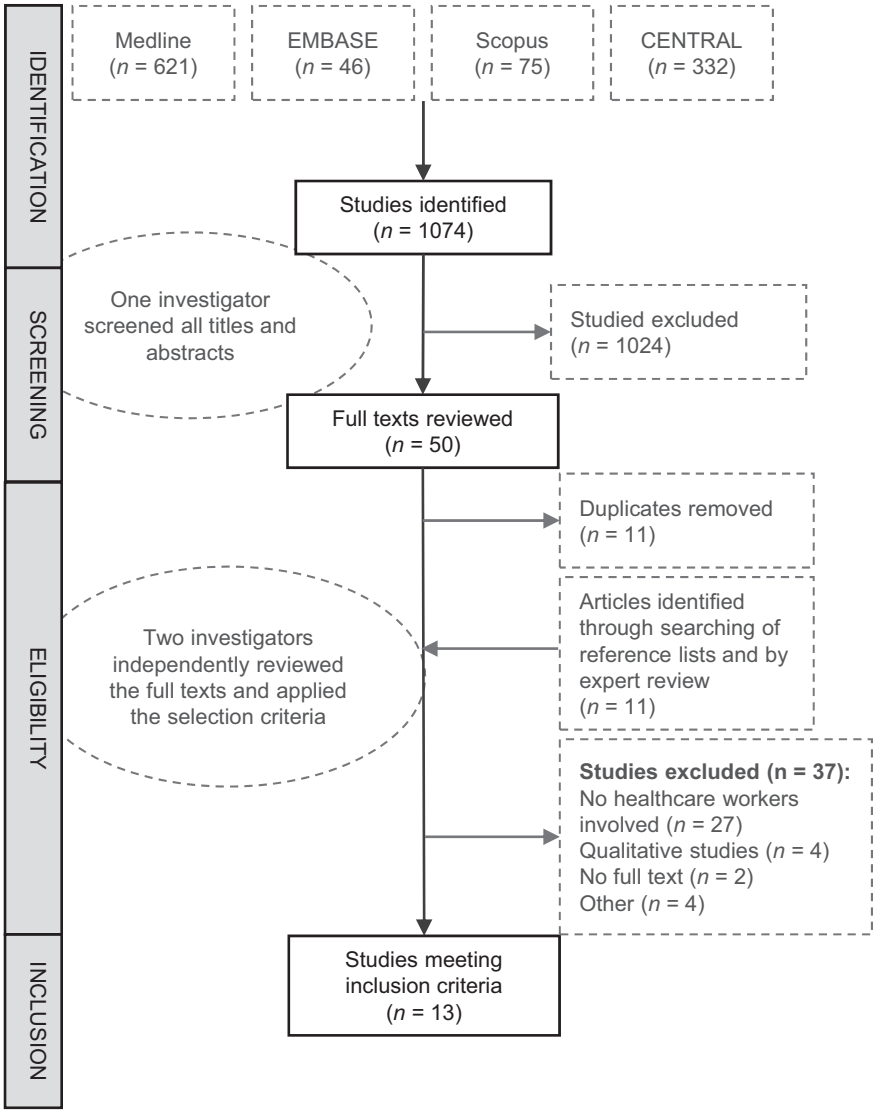

FIGURE 1 Flow diagram for the screening and inclusion of publications in the systematic review.

of the study between the intervention and control group if only postintervention data were available, and the difference-in-difference (end-study differences between the treatment and control group accounting for baseline) if both baseline and follow-up data were available. The SEs of the percent differences in outcome data were calculated as described previously (32).

Meta-analysis

Study-specific effect estimates were pooled using inverse-variance weighted random effects meta-analysis, according to the method of DerSimonian and Laird (33). Pooled effects are presented as percent difference (PD), indicating percentage change compared with baseline (for pre/post study design) or compared with a control group (for RCT or crossover study design), or as absolute change in the respective outcome measures. For the 1 study (34) that did not report measures of uncertainty (SD or SE) or statistics to derive these parameters, the SD was imputed from the pooled SD of the other studies included in the meta-analysis (35). Sensitivity analysis was performed by excluding this study from the meta-analysis to ascertain the impact of such an approach to the overall results. The I^2 statistic was used to assess the heterogeneity of included studies, with values <25%, 25 to 50%, and >50% corresponding to low, moderate, and high degrees of heterogeneity, respectively (36). Publication bias was assessed by visual inspection of funnel plots and statistically using Egger's and Begg's tests. Too few studies were identified to allow stratified analyses and investigation of sources of heterogeneity by metaregression. Data are presented as mean ± SD or mean (95% CI) unless stated otherwise. All statistical analyses were conducted in STATA version 16 (Stata Corp), with 2-tailed α of 0.05.

Results

Study characteristics

Of 1074 studies identified by our search strategy, 13 met inclusion and exclusion criteria and were included for analysis (**Figure 1** and **Table 1**) (24–27, 34, 37–44).

TABLE 1 Characteristics of the healthy food prescription studies included in the systematic review[1]

Study	Country	Setting	Design	Medical inclusion criteria	Food insecurity criteria	*n*	Age,[2] y	% Female	Follow-up (mo)	RoB[3]
Bihan (37)	France	Healthcare center	RCT	None	Yes	135	44.6 ± 8.1	56.3	3	Some concerns
Buyuktuncer (24)	UK	Primary care clinics	Pre/post	None	No	124	≥ 16	71.8	5	Serious
Weinstein (38)	USA	Primary care or diabetes clinics	RCT	Diabetes mellitus, BMI >25 kg/m^2 and HbA1c >7%	No	79	55 ± 10.8	69	3	High
Seligman (43)	USA	Primary care clinics	Pre/post	HbA1c ≥ 6.5% or previously diagnosed diabetes	Yes	687	56.6	74	6	Critical
Bryce (26)	USA	Healthcare center	Pre/post	Diabetes mellitus and HbA1c >6.5%	No	65	52.5 ± 10.6	70.8	3.25	Serious
Cavanagh (27)	USA	Healthcare center	Retrospective case-control	Diabetes mellitus, BMI >30 kg/m^2 and/or hypertension	No	108	NR	NR	18	Serious
Feinberg (34)	USA	Healthcare center	Pre/post	Diabetes mellitus and HbA1c > = 8%	Yes	95	NR	NR	18	Critical
Izumi (39)	USA	Healthcare center	Pre/post	None	No	9	NR	100	5.75	Serious
Trapl (40)	USA	Healthcare center	Pre/post	Hypertension	Yes	137	60.3 ± 10.9	71.1	6	Serious
Emmert-Aronson (41)	USA	Healthcare center	Pre/post	Diabetes mellitus, prediabetes, cardiac disease, hypertension, dyslipidemia, obesity, anxiety, and/or depression	Yes	49	59.1 ± 10.6	63.3	6	Serious
Forbes (25)	USA	Healthcare center	Pre/post	At risk of chronic illness or metabolic disease, as determined by primary care physicians	Yes	9	NR	55.6	1.5	Serious
Orsega-Smith (42)	USA	Pediatrician clinics	Pre/post	Overweight	Yes	41	NR	NR	12	Serious
Ferrer (44)	USA	Primary care clinic	RCT	HbA1c >9%	Yes	58	54	62	7	High

[1] HbA1c, glycated hemoglobin; NR, not reported; RCT, randomized controlled trial; RoB, risk of bias.
[2] Values are mean ± SD.
[3] Detailed derivation of the overall risk of bias is provided in Supplemental Table 1.

Thirty-seven studies were excluded after reviewing the full texts (23, 28, 45–79). Most studies ($n = 11$) were conducted in the USA, 1 was conducted in France, and 1 in the UK. About half ($n = 8$) of the recruited participants experiencing food insecurity, and three-quarters ($n = 9$) of the patients had specific existing cardiometabolic conditions including overweight or obesity, hypertension, or type 2 diabetes mellitus. The most common study designs were pre/post intervention studies without a control group ($n = 9$) and pre/post intervention study with an externally matched control group ($n = 1$), followed by RCTs ($n = 3$). Most studies recruited middle-aged to older participants (mean age ranged between 45 and 60 y) and had a median sample size of 79 (range, n from 9 to 687). The median follow-up duration was 6 mo, and 3 studies had extended follow-up ranging from 12 to 18 mo. Amongst the 10 nonrandomized studies, 7 were deemed to have serious risk of bias and the remaining 3 were deemed to have critical risk of bias due to confounding **(Supplemental Table 1)**. Of the 3 RCTs, 2 were deemed to have high risk of bias whereas the other was categorized as having some methodological concerns **(Supplemental Table 2)**. The primary sources of funding were academic grants ($n = 5$), not-for-profit organizations ($n = 3$), government social support programs including food banks ($n = 2$), insurance companies ($n = 2$), and pharmaceutical companies ($n = 1$).

Key design features of the intervention programs

Primary care physicians were the exclusive referring healthcare providers in 5 studies; the remaining studies employed other members of the healthcare team, with or without primary care providers, to prescribe healthy food interventions (**Table 2**). Most studies ($n = 9$) utilized food subsidies as the means to provide access to healthy foods, although the amount subsidized varied widely from USD 14 to 189 per month, lasting from 1 to 6 mo. Four studies gave participants varying amounts of food supplies at no cost. For studies that provided subsidies, participants were able to redeem vouchers at various locations, most commonly at local supermarkets or farmers' markets ($n = 7$), although other studies chose less conventional settings such as mobile fresh food produce vans or food pantries located within a healthcare center ($n = 4$). The most commonly prescribed foods were fruits and/or vegetables ($n = 10$); 3 studies further incorporated other foods such as whole grains and lean proteins into their list of redeemable products. In addition to monetary incentives, most studies incorporated other intervention components into their programs such as dietary education classes ($n = 9$). Completion rate, calculated as the proportion of individuals who agreed to participate in the program and completed it, ranged from 15 to 100% with a median completion rate of 68%.

Effect of healthy food prescription on dietary outcomes

Nine studies reported dietary outcomes. Three did not report significant changes in dietary behavior following healthy food prescription programs whereas 6 reported an increase in fruit and/or vegetable intake as a result of the prescription program (**Table 3**). Raw pre- and postintervention data, where available, are provided in **Supplemental Table 3.** When results were pooled across studies, healthy food prescription programs increased daily combined fruit and vegetable intake by 22% (95% CI: 12, 32), and fruit intake by 39% (95% CI: 12, 67), with a similar but nonsignificant change in vegetable intake of 29% (95% CI: −8, 65) (**Figure 2** and **Table 4**). This translated to an increase in combined fruit and vegetable intake of 0.8 servings/d (95% CI: 0.2, 1.4) and fruit consumption by 0.6 servings/d (95% CI: 0.3, 0.9), with a trend towards an increase in vegetable consumption by 0.5 servings/d (95% CI: −0.0, 1.1) (Table 4). There was no evidence of publication bias by Egger's and Begg's tests or by visual inspection of the funnel plots. A high level of heterogeneity was observed for each outcome ($I^2 > 50\%$) but we were unable to meaningfully explore potential sources of heterogeneity due to the limited number of studies available. Excluding the study with imputed SD (34), based on pooled SD of other studies from the meta-analyses, had no substantial impact on the overall pooled estimates (data not shown). The detailed GRADE assessment for each studied outcome is presented in **Supplemental Table 4**. Based on the GRADE criteria, the overall certainty of evidence was rated "moderate" for treatment effect on fruit intake, "very low" for vegetable intake, and "low" for fruit and vegetable intake combined.

Effect of healthy food prescriptions on cardiometabolic outcomes

The effect of healthy food prescriptions on plasma lipids was evaluated in 2 studies, BMI in 3 studies, blood pressure in 4 studies, and HbA1c in 5 studies (Table 3 and Table 4). Pooled results identified a modest change in BMI of –1.6% (95% CI: –2.8, –0.3), which corresponded to an absolute change of –0.6 kg/m^2 (95% CI: –1.1, –0.2). Likewise, a percent change in HbA1c of –8.6% (95% CI: –16.9, –0.4), corresponding to an absolute change of –0.8% (95% CI: –1.6, –0.1), was observed across studies. No significant treatment effects were observed for SBP, DBP, LDL, HDL, or triglycerides (Table 4). There was no evidence of publication bias by Egger's and Begg's tests or by visual inspection of the funnel plots. Based on the GRADE criteria, the certainty of evidence for treatment effects on cardiometabolic outcomes was rated "low" or "very low."

Discussion

This systematic review and meta-analysis identified 13 healthy food prescription programs integrated into the healthcare system, which provided either monetary subsidies for or direct provision of fruits and vegetables as a treatment for patients, most often those experiencing food insecurity and/or with specific cardiometabolic conditions. The pooled findings suggest that these programs increase fruit and vegetable consumption and reduce BMI and HbA1c, without significant identified effects on other cardiometabolic risk

TABLE 2 Key design features of the healthy produce prescription studies included in the systematic review

Study	Referrer	Type	Intervention					Completion rate (%)
			Description	Duration	Foods included	Location	Additional components	
Bihan (37)	Dietitian	Subsidy	17 to 67 USD[1]/mo[2]	3 mo	Fruits and vegetables	Supermarkets	Dietary advice	45
Buyuktuncer (24)	General practitioners, nurses, health visitors, and midwives	Subsidy	Discount of 3 USD for every 8 USD spent per transaction	1 mo	Fruits and vegetables	Supermarket	Dietary advice and cooking sessions	43.5
Weinstein (38)	Primary care physicians	Subsidy	30 USD/mo	3 mo	Fruits and vegetables	Farmers' market	Dietary advice	98.7
Seligman (43)	Primary care physicians	Food provision	Prepacked boxes of food equivalent to 18 USD per box, every 1–2 wk	6 mo	Whole grains, lean meats, beans, fruit, vegetables, milk, yogurt, cheese, and bread	Food bank	Dietary advice and recipes	58
Bryce (26)	Community health and social services	Subsidy	14 USD/mo	1 mo	Fruits and vegetables	Farmers' market	None	29
Cavanagh (27)	Nutritionist	Subsidy	35 USD/mo	6 mo	Fruits and vegetables	Mobile fresh produce van	None	100
Feinberg (34)	Primary care physicians	Food provision	Food supplies to make 10 meals/wk for the entire family	18 mo	Fruits and vegetables, whole grains, and lean proteins	Food pantry in a clinical center	Diabetes education	NR[3]
Izumi (39)	Community health worker	Subsidy	Subsidized membership cost of 95 USD per share per month of community supported agriculture program	6 mo	Vegetables	Farmers' market	Dietary advice	36
Trapl (40)	Nonphysician healthcare providers	Subsidy	44 USD/mo	3 mo	Fruits and vegetables	Farmers' market	None	61
Emmert-Aronson (41)	Primary care physicians, dietitians, pharmacists, social workers, and medical assistants	Subsidy	44 USD/mo	4 mo	Vegetables	Food pantry in a clinical center	Physical activity, mindfulness meditation general health education, nutrition education, plant-based snacks, and group coaching	100
Forbes (25)	Primary care physicians	Subsidy	189 USD/mo	6 mo	Fruits and vegetables	Farmers' market	Dietary advice	90
Orsega-Smith (42)	Pediatricians	Food provision	15–25 pounds/mo of fresh produce	12 mo	Fruits and vegetables	Mobile fresh produce van	None	100
Ferrer (44)	Primary care physician	Food provision	10 pounds of fresh produce biweekly	6	Fruits, vegetables, canned food, fish, chicken	Food pantry in clinical centre	Dietary advise and home visits by community health workers	74

[1] United States Dollar equivalent inflation adjusted to January 2020.
[2] The value of subsidy was adapted to family composition and depended on number of children and their caregivers.
[3] Not reported.

TABLE 3 Summary of changes in dietary and cardiometabolic outcomes in the healthy food prescription studies included in the systematic review[1]

Study	Design	Changes in outcomes evaluated					Details[2]
		Dietary behavior	BMI	BP	Plasma lipids	HbA1c	
Buyuktuncer (24)	Pre/post	ND	NR	NR	NR	NR	Fruit consumption (portions/d) did not differ between baseline (median 3; range 0 to 7) and follow-up (median 2.5; range 0 to 6). Vegetable consumption (portions/d) did not differ between baseline (median 2; range 0 to 7) and follow-up (median 2; range 0 to 4).
Izumi (39)	Pre/post	ND	NR	NR	NR	NR	Change in frequency of vegetable intake ≥2 cups/d = 25%.
Trapl (40)	Pre/post	+	NR	NR	NR	NR	Change in fruit intake = 0.8 (0.6 to 1.0) servings/d. Change in vegetable intake = 0.8 (0.6 to 1.0) servings/d.
Forbes (25)	Pre/post	+	NR	NR	NR	NR	Change in frequency of fruit intake ≥ 1/d = 25%. Change in frequency of dark green vegetables ≥ 1/wk = 25%. Change in frequency of orange-colored vegetables ≥1/wk = 50%. Change in frequency of other vegetables ≥ 1/wk = 25%. Statistical significance not tested
Orsega-Smith (42)	Pre/post	+	NR	NR	NR	NR	Change in fruit intake = 0.4 (0.1 to 0.7) servings/d. Change in vegetable intake = 0.2 (−0.1 to 0.6) servings/d.
Bihan (37)	RCT	ND	ND	ND	ND	NR	Change in fruit and vegetable intake = 0.12 (−0.42 to 0.66) servings/d.
Weinstein (38)	RCT	+	NR	ND	ND	ND	Change in fruit intake = 0.5 (0.1 to 0.9) servings/d.
Seligman (43)	Pre/post	+	NR	NR	NR	+	Change in fruit and vegetable intake = 0.3 servings/d. Change in HbA1c = −0.15%.
Emmert-Aronson (41)	Pre/post	+	+	+	NR	NR	Change in fruit and vegetable intake = 1.2 (1.1 to 1.4) servings/d. Change in SBP = −6.7 (−7.5 to −6.0) mmHg. Change in BMI = −0.4 (−0.9 to 0.1) kg/m^2.
Ferrer (44)	RCT	NR	ND	NR	NR	+	Change in HbA1c = −1.4% (−2.7, −0.1).
Bryce (26)	Pre/post	NR	NR	ND	NR	+	Change in HbA1c = −0.7%.
Cavanagh (27)	Pre/post with externally matched controls	NR	+	NR	NR	NR	Change in BMI = −1.1 (−2.0 to −0.2) kg/m^2.
Feinberg (34)	Pre/post	NR	NR	NR	+	+	Change in HbA1c = −2.1%.

[1] BP, blood pressure; HbA1c, glycated hemoglobin; ND, no difference; NR, not reported; RCT, randomized controlled trial; +, indicates beneficial change in the measured parameters.

[2] Shows raw data corresponding to outcomes that showed a beneficial change (+). For RCTs and nonrandomized trials with pre- and postmeasurements in both treatment and control groups, we assessed group differences in change (mean, $\bar{x}_{change}$; SE_{change}), using formulae [1] and [2]:

$$\bar{x}_{change} = \frac{\bar{x}_d - \bar{x}_c}{\bar{x}_c} - \frac{\bar{x}_b - \bar{x}_a}{\bar{x}_a} \quad [1]$$

$$SE_{change} = SE_{\frac{\bar{x}_d - \bar{x}_c}{\bar{x}_c} - \frac{\bar{x}_b - \bar{x}_a}{\bar{x}_a}} = \sqrt{SE^2_{\frac{\bar{x}_b - \bar{x}_a}{\bar{x}_a}} + SE^2_{\frac{\bar{x}_d - \bar{x}_c}{\bar{x}_c}}} \quad [2]$$

where $\bar{x}_a$ = control group mean at baseline, $\bar{x}_b$ = control group mean at study end, $\bar{x}_c$ = intervention group mean at baseline, and $\bar{x}_d$ = intervention group mean at study end. For pre/post study designs without control groups, we assessed change over time with formulae [3] and [4]:

$$\bar{x}_{change} = \frac{\bar{x}_d - \bar{x}_c}{\bar{x}_c} \quad [3]$$

$$SE_{change} = SE_{\frac{\bar{x}_d - \bar{x}_c}{\bar{x}_c}} = \frac{\bar{x}_d}{\bar{x}_c}\sqrt{SE_d^2 + SE_c^2 - 2 \cdot r \cdot SE_d \cdot SE_c} \quad [4]$$

where r is the correlation coefficient within individuals, assumed to be 0.5 (80). For RCTs or nonrandomized trials with control group and measurements only at study end, we assessed group differences at the end of the study, using formulae [5] and [6]:

$$\bar{x}_{change} = \frac{\bar{x}_d - \bar{x}_b}{\bar{x}_b} \quad [5]$$

$$SE_{change} = SE_{\frac{\bar{x}_d - \bar{x}_b}{\bar{x}_b}} = \frac{\bar{x}_d}{\bar{x}_b}\sqrt{SE_b^2 + SE_d^2} \quad [6]$$

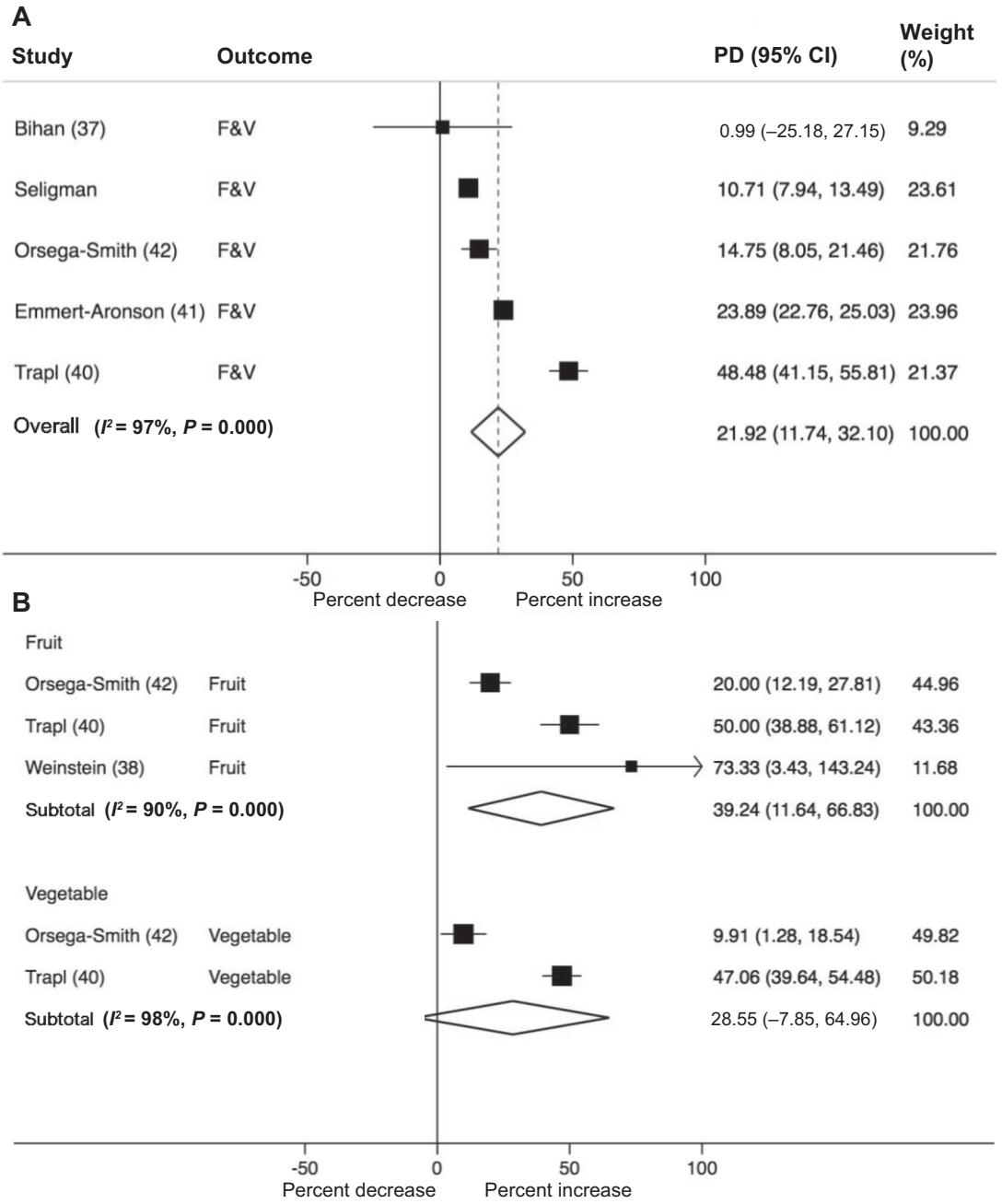

FIGURE 2 Forest plot illustrating the change in fruit and/or vegetable intake per day (percentage difference, PD) following participation in healthy food prescription programs. Fruit and vegetable (F&V) intake was reported both as a composite variable (A) and separately (B). Data were pooled using random effects meta-analysis.

factors. However, our systematic review also highlights that the findings are mostly based on nonrandomized study designs, with significant heterogeneity in the amount and duration of the food prescriptions, and with only a small number of studies evaluating cardiometabolic outcomes. Overall, these findings provide encouraging evidence that healthy food prescription programs may lead to improvements in diet quality and, even over a few months, BMI and HbA1c, with the magnitude of effect on HbA1c comparable to that achieved with commonly prescribed glucose lowering medications (81, 82). Our novel results strongly support the need for additional appropriately designed and adequately powered RCTs to test the impact of food prescription programs.

A key finding from this review is the heterogeneity in criteria pertaining to food security, household income, medical comorbidities, monetary value of subsidies or amount of fresh produce supplied, and duration of interventions. For

TABLE 4 Pooled change in cardiometabolic outcomes as a result of healthy produce prescription programs[1]

Outcome	Studies (*n*)	Reference	Participants (*n*)	Percent change			Absolute change			Certainty of evidence (GRADE)
				Estimate (95% CI)	P^2	I^2 (%)	Estimate (95% CI)	P^2	I^2 (%)	
Fruit and vegetable intake, servings/d[3]	5	(37, 40–43)	1039	22 (12, 32)	<0.001	97	0.79 (0.23, 1.35)	0.004	96	LOW[4,5] ⊕⊕⊖⊖
Fruit intake, servings/d	3	(38, 40, 42)	257	39 (12, 67)	0.005	90	0.59 (0.32, 0.87)	<0.001	59	MODERATE[6] ⊕⊕⊕⊖
Vegetable intake, serving/d	2	(40, 42)	178	29 (−8, 65)	0.124	98	0.53 (−0.04, 1.10)	0.068	87	VERY LOW[7,8,9] ⊕⊖⊖⊖
SBP, mmHg	4	(26, 37, 38, 41)	328	−1.8 (−5.9, 2.3)	0.383	86	−2.39 (−7.77, 2.99)	0.383	85	VERY LOW[10,11,12] ⊕⊖⊖⊖
DBP, mmHg	4	(26, 37, 38, 41)	328	0.0 (−1.2, 1.3)	0.966	15	0.02 (−0.95, 0.99)	0.964	13	LOW[10,12] ⊕⊕⊖⊖
HbA1c, %	5	(26, 34, 38, 43, 44)	1064	−8.6 (−16.9, −0.35)	0.041	99	−0.81 (−1.56, −0.06)	0.035	92	VERY LOW[10,13,14] ⊕⊖⊖⊖
LDL, mM	2	(37, 38)	214	−1.1 (−12.4, 10.3)	0.855	58	−0.03 (−0.33, 0.27)	0.856	50	LOW[15,16] ⊕⊕⊖⊖
HDL, mM	2	(37, 38)	214	2.9 (−4.9, 10.8)	0.468	0	0.04 (−0.06, 0.14)	0.463	0	LOW[15,16] ⊕⊕⊖⊖
TG, mM	2	(37, 38)	214	22.5 (−44.2, 89.2)	0.509	52	0.23 (−0.44, 0.90)	0.502	49	LOW[15,16] ⊕⊕⊖⊖
BMI, kg/m^2	3	(27, 41, 44)	215	−1.6 (−2.8, −0.3)	0.013	27	−0.61 (−1.06, −0.16)	0.008	6.4	LOW[17,18] ⊕⊕⊖⊖

[1] DBP, diastolic blood pressure; GRADE, Grades of Recommendation, Assessment, Development, and Evaluation Working Group; HbA1c, glycated hemoglobin; RCT, randomized controlled trial; SBP, systolic blood pressure; TG, triglycerides.
[2] *P* value of *Z*-test for significance of pooled change and 95% CI.
[3] Where possible, fruit and vegetable intake (in servings/d) reported separately within a study was converted to combined fruit and vegetable intake by methods described previously (83) and meta-analyzed using the method described in the footnote of Table 3.
[4] Downgraded by 1 for risk of bias: ≥4 studies non-RCTs; ≥3 studies with >10% loss to follow-up (risk of selection bias and attrition bias).
[5] Downgraded by 1 for inconsistency: significant unexplained heterogeneity.
[6] Downgraded by 1 for risk of bias: ≥2 studies non-RCTs; ≥1 study with >10% loss to follow-up (risk of selection and attrition bias).
[7] Downgraded by 1 for risk of bias: ≥2 studies non-RCTs; 1 study with >10% loss to follow-up (risk of selection bias and attrition bias).
[8] Downgraded by 1 for inconsistency: significant unexplained heterogeneity.
[9] Downgraded by 1 for imprecision: does not meet optimal information size criterion.
[10] Downgraded by 1 for risk of bias: ≥2 studies non-RCTs; ≥2 studies with >10% loss to follow-up (risk of selection bias and attrition bias).
[11] Downgraded by 1 for inconsistency: significant unexplained heterogeneity.
[12] Downgraded by 1 for imprecision: does not meet optimal information size criterion.
[13] Downgraded by 1 for inconsistency: significant unexplained heterogeneity.
[14] Downgraded by 1 for imprecision: does not meet optimal information size criterion.
[15] Downgraded by 1 for risk of bias: ≥1 study with >10% loss to follow-up (risk of attrition bias).
[16] Downgraded by 1 for imprecision: does not meet optimal information size criterion.
[17] Downgraded by 1 for risk of bias: ≥2 studies non-RCTs (risk of selection bias).
[18] Downgraded by 1 for imprecision: does not meet optimal information size criterion.

some studies, the input of the healthcare professional(s) to the intervention and interaction with the healthcare system were not clearly described. Likewise, details of the nutrition education component of the programs were often not fully reported. Although it is possible that nutrition education acts to enhance the efficacy of food subsidies (84–86), there were insufficient data to tease out the independent or interactive effect of different components of the healthy food prescription interventions on dietary outcomes. Future studies are needed to evaluate the effectiveness of such programs in enhancing the nutritional knowledge of participants.

We also identified considerable methodological limitations and variable quality of the healthy food prescription studies. Most were quasi-experimental (nonrandomized) and did not have a control group, increasing the risk of bias and chance of overestimated findings, and precluding strong causal interpretations. Several studies were small, short-term pilot programs that were not powered to detect clinically meaningful changes in dietary or especially cardiometabolic outcomes, a limitation that could underestimate the positive impacts. These limitations are reflected in the serious or critical risk of bias identified in the nonrandomized studies and the high or concerning risk of bias in the randomized trials, and the moderate to very low strength of evidence for outcomes as determined by the GRADE assessment. These evaluations highlight the need for more rigorously designed and adequately powered RCTs to further evaluate the impact of healthy food prescription on dietary behavior and cardiometabolic outcomes. Future studies should also investigate potential sources of heterogeneity that were observed in our pooled estimates. Many of the studies did not simultaneously assess change in dietary behavior and cardiometabolic risk factors, making it difficult to ascertain whether a sufficiently large change in dietary behavior had occurred to alter the cardiometabolic parameters studied. Self-reporting of fruit and vegetable intake is subject to significant recall bias (which could overestimate effects) and measurement error (which could underestimate effects). All studies were conducted in high-income Western nations (particularly the USA), and therefore findings may not be applicable to other countries with different medical and social security systems. Finally, more food prescription studies in different countries with varying healthcare systems and dietary contexts are needed to further understand the impact of food prescription programs on diet and cardiometabolic health.

The focus of most healthy food prescriptions so far has been on fruit and vegetables. Other dietary components, including nuts, beans, whole grains, and fish are recognized as important for cardiometabolic health (87, 88), and the impact of including these dietary components remains to be evaluated. Of note, healthy food prescription programs could be more effective if they were combined with policies to address other barriers to healthy eating such as limited access to food stores, lack of cooking skills, and/or access to high-quality kitchens (80, 89–92, 93). We note that other "food is medicine" initiatives such as "medically tailored meal" programs are also being evaluated and seek to overcome these food security barriers by delivering preprepared meals to participants (76). The impact of "medically tailored meal" programs on dietary behavior and cardiometabolic outcomes also requires further evaluation.

The strengths of our investigation include its comprehensive search strategy and standardization of the reported change in dietary and cardiometabolic outcomes that enabled meta-analysis. The moderate to long durations of many of the included studies were comparable to prior evaluation of community-based nutrition intervention programs (94), and suggest healthy food prescription programs may enable sustained change in dietary behavior. Two-thirds of the individual studies, including 1 of the randomized trials, reported a positive effect on dietary outcomes over this time frame.

In conclusion, this systematic review and meta-analysis suggests that healthy food prescription programs may be beneficial in increasing consumption of fruit and vegetables and modestly reduce BMI and HbA1c. This investigation also identified substantial heterogeneity and varying methodological limitations of these studies. Our results support the need for future RCTs in a range of settings that are adequately designed and powered with appropriate comparison groups to assess robustly the efficacy of healthy food prescription programs on diet quality and cardiometabolic well-being.

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