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Adherence to a Mediterranean diet associated with lower blood pressure in a US sample: Findings from the Maine-Syracuse Longitudinal Study

Fayeza S. Ahmed PhD | Alexandra T. Wade PhD | Benjamin A. Guenther PhD | Karen J. Murphy PhD | Merrill F. Elias PhD, MPH

Abstract
Hypertension is a key modifiable risk factor for cardiovascular disease. The Mediterranean diet (MedDiet) may be associated with improvements in blood pressure. However, few studies have examined the association between MedDiet adherence and blood pressure in non-Mediterranean populations, and findings are mixed. We analyzed cross-sectional data (Wave 6) for 851 participants of the Maine-Syracuse Longitudinal Study. MedDiet adherence was calculated using food frequency questionnaire data and a literature-based MedDiet adherence score. Dependent variables included systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), and mean arterial pressure (MAP). Separate linear robust regression analyses revealed significant associations between MedDiet adherence and for SBP ($b = -0.69$, 95% CI $= [-1.25, -0.20]$), DBP ($b = -0.33$, 95% CI $= [-0.58, -0.04]$), and MAP ($b = -0.45$, 95% CI $= [-0.77, -0.11]$), but not for PP. These findings indicate that the MedDiet is associated with some metrics of blood pressure in a large, community-based, non-Mediterranean sample.

1 | INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide (World Health Organization [WHO], 2017), and according to the American Heart Association (AHA), the cost of medical care in the United States is expected to double by 2035.1

Notably, up to 90% of all CVD is preventable through risk factor modification.2,3 Hypertension (HTN) is one of the leading risk factors of CVD and a key target for intervention strategies.4 Predictive models indicate that small, population-wide reductions in blood pressure could significantly reduce the prevalence of CVD. For example, a 2 mm Hg reduction in systolic blood pressure (SBP) at the population level is associated with a 10% reduction in CVD,5 while a 7 mm Hg reduction could reduce CVD prevalence by 26%.5 Not surprisingly, the 2013 WHO Global Action Plan for the Prevention and Control of Non-Communicable Diseases listed reduction in blood pressure as one of its goals.7

Lifestyle interventions, with the potential to lower blood pressure, provide an alternate approach to medications and may be similarly effective at reducing risk of CVD.5,7 The Mediterranean diet (MedDiet) is characterized by the high consumption of extra-virgin olive oil (EVOO), fruits, vegetables, whole grain cereals, nuts and seeds; moderate consumption of fish, poultry, dairy, and red wine; and low consumption of red meat and processed foods.8 Observational studies conducted in Mediterranean countries demonstrate that higher adherence to a MedDiet is associated with reduced risk of CVD.9,10

Fayeza S. Ahmed and Alexandra T. Wade contributed equally to this manuscript.
The Prevención con Dieta Mediterránea (PREDIMED) conducted in Spain compared a MedDiet supplemented with EVOO, a MedDiet supplemented with nuts, and a low-fat control diet in a sample of adults at risk of CVD. After four years, investigators reported greater reductions in diastolic blood pressure (DBP) in those following a MedDiet. After adjusting for baseline anti-HTN medications, greater reductions were seen in both SBP and DBP. Researchers also found that reductions in blood pressure were seen as early as one year, with participants following the MedDiet showing significant improvements in 24-hour ambulatory systolic and diastolic blood pressure. Further, MedDiet adherence has been shown to independently relate to arterial stiffness in a sample of Greek children, indicating that the MedDiet can have an impact on blood pressure as early as age 12.

To date, the majority of MedDiet investigations have been conducted in Mediterranean populations. Studies from non-Mediterranean populations are currently limited, and findings are mixed. Cross-sectional studies conducted in the United States, including an investigation of the Coronary Artery Risk Development in Young Adults (CARDIA) cohort, have failed to find associations between MedDiet adherence and measures of blood pressure. Likewise, an investigation of the Framingham Heart Study Offspring Cohort (FHSOC) reported no longitudinal association between MedDiet adherence and SBP or DBP over a mean follow-up of seven years. Conversely, a prospective analysis of the Aerobics Centre Longitudinal Study (ACLS) cohort in the United States found inverse associations between MedDiet adherence and MAP. However, a recent pilot study in a younger sample (mean age = 26 years) did not find a statistically significant difference in MAP when comparing a MedDiet and a vegan diet.

Collectively, these results are indicative of a potential association between MedDiet adherence and blood pressure. However, further investigations are required in non-Mediterranean populations. The current study therefore aimed to examine the association between MedDiet adherence and blood pressure in a US sample from participants of the Maine-Syracuse Longitudinal Study cohort (USA). We hypothesized that study participants with higher MedDiet adherence would exhibit lower blood pressure values (as measured by multiple variables) than those who had a lower MedDiet adherence score.

2 | METHOD

2.1 | Participants

The Maine-Syracuse Longitudinal Study (MSLS) was approved by the University of Maine Institutional Review Board, and written informed consent was obtained from all volunteers.

The MSLS was a multi-wave longitudinal cohort study conducted on cardiovascular and cognitive function, with data collection occurring approximately every 5 years from 1975 (Wave 1) to 2010 (Wave 7) from community-dwelling adults living in Central New York. Exclusions at recruitment included diagnosis or treatment for psychiatric illness, alcoholism, and inability to read and see sufficiently to comprehend instruction. See www.mslsperspectives.net for description of study design.

Wave 6 (2001-2006) was the first and only wave of the MSLS to collect dietary data. Due to a change in study objectives dictated by grant support by the time Wave 7 began, the number of participants that could be followed from Wave 6 with regard to blood pressure and nutrition was significantly reduced. Thus, we confine our study to Wave 6 and employed a cross-sectional design.

Participants were excluded from the current analysis due to prevalent acute stroke (n = 28), prevalent probable dementia (n = 8), prevalent renal dialysis treatment (n = 5), inability to read English (n = 1), a history of diagnosed alcoholism (n = 1), and incomplete data for nutrition and health variables included in this study. This left 851 participants from Wave 6 with complete demographic, nutrition, and health data for reported variables.

Diagnosis of acute stroke was based on self-report, confirmed by hospitalization or medical records, or both. Stroke was defined as an acute onset focal neurological deficit persisting for more than 24 hours. Probable dementia was based on MSLS cognition data, diagnostic records, and medical review data, and was determined by a committee of neuropsychologists and social psychologists using the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRA) Alzheimer’s Criteria and confirmed with guidelines from the International Classification of Diseases, 10th edition (ICD-10).

2.2 | Procedure

At Wave 6, participants attended a laboratory visit following an overnight fast. Blood samples were drawn by a licensed phlebotomist. Following a light breakfast, participants underwent physical examination, including measures of blood pressure and anthropometry. Two weeks prior to the laboratory visit at Wave 6, participants recorded dietary intake. The remainder of the study session involved tests of cognitive function.

2.3 | Assessment of dietary intake and MedDiet adherence

Dietary intake was assessed using the Nutrition and Health Questionnaire (NHQ), developed for the European Prospective Investigation into Cancer (EPIC) study and validated against 24-hour recalls, urinary nitrogen, and total energy expenditure. The
NHQ establishes the frequency of food consumption across 37 food categories, including fruits, vegetables, legumes (beans and lentils), cereals, nuts, fish, dairy, and meat. Participants are instructed to indicate how regularly they consume each food by selecting "Never," "Seldom," "Once per week," "2-3 times per week," "5-6 times per week," or "Once or more per day."

A literature-based MedDiet score developed by Sofi et al (2014) was applied to dietary data to determine level of MedDiet adherence.9 The score allocates a score of 0, 1, or 2 across 9 food categories associated with the MedDiet: (1) fruit, (2) vegetables, (3) legumes, (4) cereals, (5) fish, (6) meat and meat products, (7) dairy products, (8) red wine, and (9) olive oil. For food categories associated with positive health outcomes (fruit, vegetables, legumes, cereals, fish, and olive oil), higher intake is awarded a higher score. For red wine, less than one serving per day is awarded a score of 1, between 1 and 2 serves per day is awarded a score of 2, and more than 2 servings per day is awarded a score of 0. A high total score is indicative of higher adherence to a MedDiet, and a low total score is indicative of low adherence.9

Consumption of MedDiet components is based on daily intake values. However, items from the Nutrition and Health Questionnaire include a mixture of daily and weekly quantities. Weekly quantities were determined for all relevant food items from the NHQ. The scoring framework of the MDS was then adjusted to match weekly intake data.

### 2.4 | Assessment of blood pressure

Using hospital standard procedure, blood pressure (BP) measurements were conducted five times in standing, sitting, and recumbent positions; one-minute intervals occurred between each measurement. Averages were taken for each position. SBP and DBP were measured while pulse pressure (PP) and mean arterial pressure (MAP) were calculated at Wave 6. BP measurement in mmHg followed the same protocol as previous waves of the MSLS and has been described previously.25-27 In brief, after 15-minute reclining rest, automated blood pressure measurements were taken using GE DINAMAP 100DPC-120XEN (GE Healthcare), a hospital-grade blood pressure measurement device calibrated for accuracy. With an appropriately sized cuff, five measurements were taken from the right arm in each recumbent, sitting, and standing positions following a 15-minute supine rest period. A one-minute rest period separated each set of blood pressure measurements. Average SBP, DBP, PP, and MAP values were then calculated.

### 2.5 | Covariates

In addition to blood pressure, the MSLS assessed other markers of cardiovascular risk, including BMI, waist circumference, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), glucose, and plasma homocysteine (tHcy). Waist circumference was measured at the level of the iliac crest. Waist circumference was measured at the level of the iliac crest over light clothing using a non-extendable measuring tape. Standard assay methods are described elsewhere [29]. Cognition was a major outcome and results have been presented elsewhere.27-29

### 2.6 | Statistical analysis

Separate multiple linear regression analyses were conducted for each of the four measures: SBP (mm Hg), DBP (mm Hg), PP (mm Hg), and MAP (mm Hg). Covariates were organized into two models to capture demographic, health, and lifestyle variables. Covariates were informed by previous MSLS analyses and MedDiet literature.16,25,30

- **Model 1:** No covariates were included (MedDiet score only)
- **Model 2:** Sex, ethnicity, education (years), and age (years).
- **Model 3:** Model 2 + LDL cholesterol (mmol/L), HDL cholesterol (mmol/L), glucose (mmol/L), tHcy (µmol/L), BMI (weight (kg)/height (m)2), daily food intake (servings per day), physical activity (MET hours), smoking status (never, past, or current), and anti-hypertensive medication (yes/no).

All statistical analyses were performed in R.31 After fitting the OLS regression model for each measure, it was revealed that each suffered from heteroscedasticity, high leverage points, and heterogeneity of residual variance. Thus, the regression models were refit using robust regression with bootstrapped parameter estimates and confidence intervals. The robust regression was fit using the MASS package32 using M-estimation with Huber weighting. Bootstrapping of coefficients and confidence intervals was performed with 1000 repetitions using the car33 and boot34,35 packages. Significance of MedDiet score in each robust regression model was assessed via the Wald test using the sfsmisc package.36

### 3 | RESULTS

Demographic, lifestyle, and health characteristics according to level of MedDiet adherence are presented in Tables 1 and 2. The average MedDiet score at Wave 6 was 9 out of 18 across the entire sample. Participants with higher MedDiet adherence were older, completed more years of education, had lower BMI and DBP, had higher levels of HDL cholesterol, consumed more energy, and completed more physical activity. Out of the participants who had hypertension or were on anti-hypertensive medication (as defined as 140/90 or above), 90 were controlled (as defined as being on hypertensive medication with a BP of less than 140/90).

A summary of the results is presented in Table 3. Bootstrapped raw regression coefficients (β), standardized regression coefficients (β̂), and 95% confidence intervals (CI) represent associations between MedDiet adherence score and the blood pressure measures. After controlling for all covariates (Model 3), significant negative
linear associations were observed for SBP ($b = -0.69, CI = [-1.25, -0.20]$), DBP ($b = -0.33, CI = [-0.58, -0.04]$), and MAP ($b = -0.45, CI = [-0.77, -0.11]$) but not PP ($b = -0.36, CI = [-0.72, 0.03]$) with MedDiet adherence. The same analysis was conducted on only those participants who had hypertension and yielded similar results (see Table 4).

4 | DISCUSSION

These findings extend the current body of literature and provide new evidence for the association between MedDiet adherence and blood pressure in a large, non-Mediterranean sample. Linear robust regression analyses adjusting for demographic, lifestyle, and cardiovascular variables revealed statistically significant relationships between MedDiet adherence and SBP, DBP, and MAP. Specifically, in Model 3, for every 1 unit increase in a participant’s MedDiet score, there was a corresponding decrease of 0.69 units on SBP, a decrease of 0.33 on DBP, and a decrease of 0.45 on MAP. Though seemingly small, this change can have notable impact at the population level. A reduction of 2mmHg in SBP could lead to a population decrease of 10%. To our knowledge, this study is the first to identify a cross-sectional association between MedDiet adherence, SBP, DBP, and MAP in a US sample. Inconsistencies across previous studies conducted in the United States may be due to the scoring of MedDiet adherence. For example, the observational investigation of the Aerobics Centre Longitudinal cohort employed a scoring system dependent on the median intake of the study sample. Specifically, participants are awarded points if they consumed greater than the median for foods characteristic of a MedDiet (eg, olive oil, fruits, vegetables, nuts, fish) and lower than the median for discretionary foods (eg, red meat and dairy). As the median intake of an American sample is likely to be lower than the median intake of a Mediterranean sample, this scoring system may not accurately classify MedDiet adherence. In contrast, the current study employed a MedDiet scoring system with predetermined values for intake across food categories, based on traditional dietary guidelines and empirical evidence.

Previous studies may also be limited by sample characteristics. For example, the participants of the Framingham Offspring Cohort had a mean SBP of 122 mm Hg, while participants of the CARDIA Study had mean SBP of 110 mm Hg. In contrast, mean SBP in the current study was 131 mm Hg which may be more likely to respond to dietary factors.

It is not uncommon to find significant relationships among some but not all indices of blood pressure. For example, Toledo and
colleagues reported significant changes in DBP but not SBP following four-year MedDiet adherence. Similarly, a meta-analysis examining the association between olive oil and blood pressure found effects for DBP but not SBP. The relationship between MedDiet adherence and PP was not found to be statistically significant in this study. However, it is noteworthy that the change in PP was still in the same direction as SBP and DBP; as MedDiet adherence increased, there was a trend of decreasing PP. It is possible that the small effect accounted for the lack of statistical significance in the PP variable.

MAP is considered a marker of cardiac output and peripheral resistance. In our study, we found a statistically significant decrease in MAP with increasing MedDiet score. To our knowledge, our study is one of very few that have examined the impact of MedDiet adherence to MAP.

Our findings are supported by previous studies conducted in Mediterranean populations, as well as randomised controlled trials in non-Mediterranean populations. For example, the MedLey study, conducted in an older Australian population, reported that a Mediterranean intervention significantly improved systolic blood pressure but not diastolic blood pressure over 6 months. Adding more dairy to a typical MedDiet has also been found to significantly decrease SBP. Our findings are also consistent with the mechanisms of the MedDiet, which is rich in bioactive nutrients with the potential to reduce blood pressure. For example, EVOO and green leafy vegetables contain high levels of polyphenols which increase nitric oxide synthesis to relax endothelial muscles and reduce blood pressure. Further, fish, nuts, and seeds are rich in monounsaturated and polyunsaturated fatty acids which reduce inflammation to promote healthy endothelial functioning. The MedDiet is also low in processed foods and therefore low in sodium. Modest reductions in sodium intake have been associated with statistically and clinically significant reductions in blood pressure. Further, sodium has been identified as a mediating factor in the association between MedDiet adherence and blood pressure. More importantly, as one does not consume foods in isolation, the MedDiet promotes a pattern of eating a variety of foods that, together, provide a whole diet rich in bioactive ingredients, polyphenols, and unsaturated fatty acids that reduce chronic inflammation.

High BP is one of the leading risk factors for CVD. Raw beta coefficients from our cross-sectional analyses indicate an SBP reduction of 0.69 mm Hg per 1 unit increase in MedDiet score, a DBP reduction of 0.33 mm Hg per 1 unit increase in MedDiet score, and a 0.45 decrease in MAP per 1 unit increase in MedDiet score. Although these values are clinically small, the MedDiet could have a significant impact on CVD prevalence at the population level. For example, if MedDiet adherence is increased by 4 units, this
could potentially reduce SBP by ≥ 2 mm Hg, subsequently reducing the number of CVD cases by 10%. Further, studies using an Australian population have shown that non-Mediterranean samples can incorporate a MedDiet and that slight deviations (such as incorporating more dairy) are still more beneficial for health than a simple low-fat diet.

The current study has a number of strengths. We examined a sample with higher ranges of blood pressure, which are more likely

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Robust raw regression analysis of associations of Mediterranean diet score and blood pressure outcomes (n = 851)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Model</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.32</td>
</tr>
<tr>
<td>2</td>
<td>-0.92</td>
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<tr>
<td>3</td>
<td>-0.69</td>
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<tr>
<td>Diastolic Blood Pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.52</td>
</tr>
<tr>
<td>2</td>
<td>-0.37</td>
</tr>
<tr>
<td>3</td>
<td>-0.33</td>
</tr>
<tr>
<td>Pulse Pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.23</td>
</tr>
<tr>
<td>2</td>
<td>-0.49</td>
</tr>
<tr>
<td>3</td>
<td>-0.36</td>
</tr>
<tr>
<td>Mean Arterial Pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.46</td>
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<tr>
<td>2</td>
<td>-0.56</td>
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<tr>
<td>3</td>
<td>-0.45</td>
</tr>
</tbody>
</table>

Note: Regression coefficients represent change in 1 mm Hg units. Bootstrapped regression coefficients and bootstrapped confidence intervals are presented for each robust regression model.

*a* Model 1: MedDiet score; Model 2: Model 1 + sex, ethnicity, education (years), and age (years); Model 3: Model 2 + LDL cholesterol (mmol/L), HDL cholesterol (mmol/L), glucose (mmol/L), homocysteine (µmol/L), BMI (weight (kg)/height (m)²), daily food intake (servings per day), physical activity (MET hours), smoking status, and anti-hypertensive medication (yes/no).

*b* The Wald test was used to test for the significant contribution of MedDiet score in each model.

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Robust regression analysis of associations of Mediterranean diet score and blood pressure outcomes for participants with hypertension (n = 498)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-0.25</td>
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<tr>
<td>2</td>
<td>-0.85</td>
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<tr>
<td>3</td>
<td>-0.74</td>
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<tr>
<td>Diastolic Blood Pressure (mm Hg)</td>
<td></td>
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<tr>
<td>1</td>
<td>-0.67</td>
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<tr>
<td>2</td>
<td>-0.42</td>
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<tr>
<td>3</td>
<td>-0.40</td>
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<td>Pulse Pressure (mm Hg)</td>
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<td>2</td>
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<td>3</td>
<td>-0.33</td>
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<tr>
<td>Mean Arterial Pressure (mm Hg)</td>
<td></td>
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<tr>
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<td>-0.53</td>
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<tr>
<td>2</td>
<td>-0.60</td>
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<tr>
<td>3</td>
<td>-0.50</td>
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</tbody>
</table>

Note: Hypertension was defined as a SBP ≥ 140, a DBP ≥ 90, or taking anti-HTN medication. Regression coefficients represent change in 1 mm Hg units. Bootstrapped regression coefficients and bootstrapped confidence intervals are presented for each robust regression model.

*a* Model 1: MedDiet score; Model 2: Model 1 + sex, ethnicity, education (years), and age (years); Model 3: Model 2 + LDL cholesterol (mmol/L), HDL cholesterol (mmol/L), glucose (mmol/L), homocysteine (µmol/L), BMI (weight (kg)/height (m)²), daily food intake (servings per day), physical activity (MET hours), smoking status, and anti-hypertensive medication (yes/no).

*b* The Wald test was used to test for the significant contribution of MedDiet score in each model.
to exhibit change over time. This study is also one of the first to use a literature-based MedDiet adherence score to characterize and more accurately capture MedDiet adherence in a non-Mediterranean population.

The following limitations should also be considered. Firstly, our cross-sectional design limits our ability to infer causation from these findings. The MSLS collected dietary intake data through self-report, which may have limited accuracy of results. Further, the NHQ does not elicit information regarding serving sizes. The conversion of dietary intake to MedDiet adherence therefore relied on assumptions which, although consistent, may have influenced our results. Further, as the NHQ did not capture sodium intake, we were unable to explore the influence of sodium consumption. Finally, the cohort was relatively healthy at Wave 6, which may have limited our ability to detect associations across other measures of cardiovascular risk. Though relatively healthy, many participants were being treated for hypertension. This may be considered a limitation to our study; however, this may be considered a strength as many individuals who are treated for hypertension seek out additional BP lowering via diet. In this study, we learn that this additional treatment improves BP very little in clinical terms, but we argue that these findings are important because in a large population leads to BP reduction in terms of population risk.

In conclusion, the current study provides new evidence for cross-sectional associations between MedDiet adherence and blood pressure in a non-Mediterranean population. On an individual basis, or from a strictly clinical perspective, the effect sizes were small. However, given that blood pressure is one of the leading modifiable risk factors for CVD, these results have significant implications at a population level. More data are needed in non-Mediterranean samples to support our findings. This includes examination with similar diets, such as DASH and the Nordic diets, which also emphasize consumption of similar food groups.49,50

5 | CONCLUSIONS

Hypertension is a major risk factor for other cardiovascular diseases. Fortunately, it is modifiable with lifestyle changes, such as diet. The MedDiet has shown promise as a way to lower blood pressure. However, the impact of the MedDiet in non-Mediterranean populations has been understudied. In our analyses of 851 US older adults (Maine-Syracuse Longitudinal Study), we found that those who adhered to a MedDiet achieved lower systolic, diastolic, and mean arterial pressure values. Though a small effect, this finding has important implications for reducing risk at the population level.

ACKNOWLEDGEMENTS

The Maine-Syracuse Longitudinal Study was supported by grants from the National Heart, Lung, and Blood Institute (USA; R01HL067358 and R01HL081290) and the National Institutes of Health (USA; R01AG03055). ATW was supported by an Australian Government Research Training Programme Scholarship. The funding sources had no involvement in the study design, data collection, writing, or decision to submit for publication. The conclusions reached are those of the authors and not conclusions by the funding sources.

CONFLICT OF INTEREST

The authors declared no conflicts of interest.

AUTHOR CONTRIBUTIONS

Note: Both F.S.A. and A.T.W. are joint first authors. F.S.A. is the associate director of the Maine-Syracuse Longitudinal Study (MSLS) and an assistant professor at the University of Maine. Her contributions to this manuscript involved conceptualization, data analysis, and primary writing of this manuscript. A.T.W. is a postdoctoral fellow at the Alliance for Research in Exercise at the University of South Australia. Her contributions included conceptualization, calculation of MedDiet scores, and primary writing of this manuscript. B.A.G. is the lead in-house Statistician for the MSLS and a lecturer at the University of Maine. His contributions included data analysis (primary role), writing of Results section, and creation of tables and figures. K.J.M. is a professor at the University of South Australia. She is A.T.W.’s research advisor, and her contribution included guidance in the field of nutrition and editing. M.F.E. is the director of the MSLS, principal investigator since its inception, and a professor emeritus at the University of Maine. His contributions to this manuscript involved guidance in conceptualization, data analysis, interpretation, and editing.

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