

# Dietary Fiber and Blood Pressure

## A Meta-analysis of Randomized Placebo-Controlled Trials

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**Background:** Dietary fiber is part of a healthy diet and may exert a protective effect in the cardiovascular system. The effect of fiber intake on blood pressure (BP) has not yet been established.

**Methods:** We performed a meta-analysis of randomized placebo-controlled trials to estimate the effect of fiber supplementation on BP overall and in population subgroups. Original articles published between January 1, 1966, and January 1, 2003, were retrieved for 24 trials that fulfilled criteria for meta-analysis. Data were abstracted on fiber dose, fiber type, BP changes, study design features, and study population characteristics. A random-effects model was used for meta-analysis.

**Results:** Fiber supplementation (average dose, 11.5 g/d) changed systolic BP by  $-1.13$  mm Hg (95% confidence interval:  $-2.49$  to  $0.23$ ) and diastolic BP by  $-1.26$  mm Hg ( $-2.04$  to  $-0.48$ ). Reductions in BP tended to be larger in older ( $>40$  years) and in hypertensive populations than in younger and in normotensive ones.

**Conclusion:** Increasing the intake of fiber in Western populations, where intake is far below recommended levels, may contribute to the prevention of hypertension.

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**O**BSERVATIONAL AND EXPERIMENTAL studies suggest a beneficial effect of dietary fiber intake on blood pressure (BP), in both normotensive and hypertensive subjects.<sup>1-3</sup> Subjects consuming a vegetarian diet are generally at lower risk of developing hypertension.<sup>1,2</sup> However, it is unknown whether this can be ascribed to the high fiber content of the diet because vegetarians—apart from differences in lifestyle—also have higher intakes of potassium, magnesium, and polyunsaturated fatty acids and a lower intake of saturated fat. Clinical trials of fiber supplementation have shown wide variation in BP response.<sup>3</sup> In trials with purified fiber supplements, reductions in BP tend to be larger than in trials with fiber-rich foods. This difference in BP response might be explained by fiber dose, type of fiber consumed, or better compliance with dietary supplements than with high-fiber diets.<sup>3</sup>

Daily intake of fiber in the United States and many other Western countries is around 15 g/d, which is only half the amount recommended by the American Heart Association (25 to 30 g/d from foods).<sup>4-6</sup> Given this large population seg-

ment with inadequate fiber intake, the demonstration of beneficial effects of fiber on BP may impact public health policy. Many clinical trials of dietary fiber and BP have been conducted in the past decades, but most lacked power to detect small, potentially meaningful BP effects. We aggregated data from 24 randomized placebo-controlled trials of fiber supplementation and BP by conducting a comprehensive meta-analysis. It is unknown whether BP response to fiber intake is related to type of fiber and subject characteristics such as age, sex, and hypertensive status. Therefore, we also obtained BP estimates in these specific subgroups and took potential confounders into account.

## METHODS

### SEARCH STRATEGY

A MEDLINE search (January 1, 1966, to January 1, 2003) was conducted using “(fiber OR fibre) AND (blood pressure OR hypertension) AND (trial OR intervention OR random\* OR study)” as words in the title or abstract. In addition, we performed a manual search using reference lists of original research and review articles. The search was lim-

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ited to studies in human subjects and English-language literature. For all trials, we retrieved the original publication, which in 2 cases were an abstract<sup>7</sup> and a letter,<sup>8</sup> respectively.

## SELECTION OF TRIALS

We selected any randomized controlled trial of fiber supplementation in human subjects with BP as a primary or secondary study outcome. Seventy-two trials were identified that met the inclusion criteria (**Figure 1**). Subsequently, 48 trials were excluded (reference list available from the authors) for the following reasons: lack of appropriate BP data (n=7), intentional cointervention from which the effect of fiber supplementation could not be separated (n=29), or lack of a concurrent placebo control group (n=12). In 1 trial, BP response to fiber supplementation was reported for different sources of fiber, which yielded 2 treatment strata with an identical placebo control group.<sup>9</sup> A total of 24 trials with 25 relevant strata remained for meta-analysis.<sup>7-29</sup> For 1 trial, data on diastolic BP were missing.<sup>25</sup>

## QUALITY ASSESSMENT

The internal validity of trials included in this meta-analysis is largely guaranteed by random assignment of fiber supplementation. Quality of studies was additionally quantified by scoring of blinding toward the type of treatment (ie, open, single blind, and double blind).

## DATA ABSTRACTION

Differences in systolic and diastolic BP and accessory variance measures were obtained for each trial according to a standardized procedure using a data abstraction form. In addition, data were collected on trial design (parallel vs crossover; double blind vs single blind or open); duration of the trial; type of fiber and fiber dose; and whether BP was a primary or secondary study outcome. Furthermore, we abstracted data on sample size and characteristics of the study population including mean age; sex (proportion of men); baseline BP; baseline body weight; baseline body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters; change in body weight during intervention; use of antihypertensive drugs (percentage treated); and baseline (habitual) fiber intake.

For 1 trial, the change in fiber intake during intervention was calculated using a compliance table.<sup>17</sup> In 1 trial the intervention group received 2 different doses

of fiber during the intervention period, which we averaged.<sup>11</sup> Blood pressure measurements in the sitting position were abstracted. If those were not available, supine or awake ambulatory BP measurements were taken, in that order. For 2 trials, the change in BP had to be estimated from a graph in the article.<sup>13,23</sup>

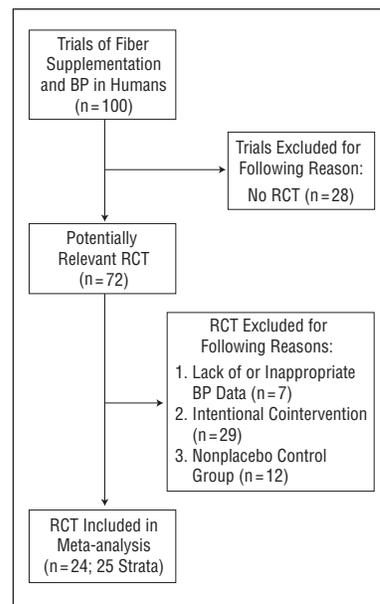
For description of study populations, the baseline values of age, proportion of men, systolic and diastolic BP, body weight, BMI, and fiber intake in the intervention and control groups were averaged. In 3 trials, age was given as a range, and minimum and maximum values were averaged.<sup>9,22,23</sup> Baseline BMI of the study population was reported in 13 trials, change in body weight in 21 trials, baseline fiber intake in 11 trials, and use of antihypertensive drugs in 15 trials. Study populations were assumed to be not undergoing antihypertensive treatment in 5 trials where use of diuretics was defined as an exclusion criterion.<sup>21,22,25,26</sup> In 1 trial, we imputed missing data on age (imputed value, 40 years, which was the median value for all other trials) and sex (imputed value, 50% male).<sup>8</sup> Populations were considered hypertensive if more than 50% of the subjects were undergoing antihypertensive treatment or if mean BP at baseline was 140/90 mm Hg or higher.

## QUANTITATIVE DATA SYNTHESIS

For parallel trials, BP change from baseline in the intervention group was subtracted from that in the control group to yield the net change in BP due to fiber supplementation. For crossover trials, the net change in BP was calculated as the final BP in the intervention period minus the final BP in the control period. Standard errors (SEs) for the net changes in systolic and diastolic BP were obtained. If not given, SEs were derived from confidence intervals, *P* values, or individual SEs for BP changes in intervention and control groups or intervention and control periods (crossover design). For parallel trials in which SEs for paired BP differences were reported, the pooled SE for net BP change was calculated by using the following equation:

$$SE_{\text{pooled}} = \sqrt{(SE^2_{\text{intervention group}} + SE^2_{\text{control group}})}$$

For parallel trials with lacking data on SEs for paired differences and for crossover trials, the pooled SE was estimated according to Follmann et al,<sup>30</sup> assuming a correlation of 0.50 between baseline and final BP values or BP in intervention and control periods (crossover design), as follows:



**Figure 1.** Selection of randomized controlled trials (RCTs) for meta-analysis of fiber supplementation and blood pressure (BP).

$$SE_{\text{delta BP}} = \sqrt{[SE^2_{\text{baseline}} + SE^2_{\text{final}} - (2 \times 0.50 \times SE_{\text{baseline}} \times SE_{\text{final}})]}$$

If only standard deviations (SDs) were given, the pooled SE was calculated by using this equation:

$$SE_{\text{pooled}} = \sqrt{[(SD^2_{\text{intervention}}/n_{\text{intervention}}) + (SD^2_{\text{control}}/n_{\text{control}})]}$$

where “n” is the number of subjects in the intervention and control group or intervention and control periods and

$$SD_{\text{delta BP}} = \sqrt{[SD^2_{\text{baseline}} + SD^2_{\text{final}} - (2 \times 0.50 \times SD_{\text{baseline}} \times SD_{\text{final}})]}$$

If variance was only reported at baseline, we assumed similar variance at the end of follow-up. The SAS statistical package was used for data analysis (version 8; SAS Institute Inc, Cary, NC). We first tested homogeneity of effect size by *Q* statistics<sup>31</sup> and found significant heterogeneity among trials (systolic  $\chi^2_{24} = 24.7$ , *P* = .002; diastolic  $\chi^2_{23} = 37.1$ , *P* = .03). We analyzed data according to Van Houwelingen et al,<sup>32</sup> using a random-effects model that accounted for both within- and between-study variation (SAS PROC MIXED statement). Blood pressure estimates were reported with 95% confidence intervals (CIs). Two-sided *P* values lower than .05 were considered statistically significant.

We performed a number of predefined stratified meta-analyses to examine between-group differences in BP response to fiber supplementation.<sup>32</sup> Subgroups were based on mean age ( $\leq 40$  years vs  $> 40$  years), hypertensive status (no vs yes), sex ( $< 50\%$  male vs  $\geq 50\%$  male), BMI ( $\leq 28$  kg/m<sup>2</sup> vs  $> 28$

**Table 1. Design and Study Population Characteristics of Randomized Controlled Trials of Fiber Supplementation and Blood Pressure**

Source	Design	No. of Subjects	Duration, wk	Mean Age, y	Men, %	Mean Baseline BP, mm Hg	BP Effect (SE), mm Hg*		Fiber Dose, g/d	Fiber Source† and Type
							Systolic	Diastolic		
Arvill and Bodin, <sup>10</sup> 1995	C-DB	63	4	47	100	140/85	-3.43 (1.39)	-0.27 (1.02)	3.9	S-Soluble
Birketvedt et al, <sup>11</sup> 2000	P-DB	53	24	40	0	130/82	0.60 (3.81)	-2.30 (2.82)	4.7	S-Insoluble
Brussaard et al, <sup>9</sup> 1981a	P-O	31	5	23	65	125/61	3.50 (2.94)	3.90 (2.94)	10.0	S-Soluble
Brussaard et al, <sup>9</sup> 1981b	P-O	32	5	23	65	126/64	3.60 (3.43)	1.00 (3.73)	19.0	S-Insoluble
Burke et al, <sup>12</sup> 2001	P-O	36	8	57	50	133/76	-6.50 (1.30)	-1.90 (1.00)	12.0	S-Soluble
Eliasson et al, <sup>13</sup> 1992	P-DB	63	12	48	62	149/100	-0.34 (3.48)	-4.30 (1.95)	6.0	S-Insoluble
Fehily et al, <sup>14</sup> 1986	C-SB	201	4	37	73	132/80	-0.40 (0.67)	0.20 (0.61)	12.0	D-Soluble
Hagander et al, <sup>15</sup> 1989	C-O	12	8	62	58	150/83	-3.00 (5.22)	2.00 (2.18)	25.6	S-Soluble
He et al, <sup>7</sup> 2004	P-DB	102	12	48	40	128/80	-1.79 (1.27)	-1.24 (0.89)	10.0	S-Soluble
Keenan et al, <sup>16</sup> 2002	P-SB	18	6	44	50	139/91	-8.80 (5.95)	-6.00 (2.72)	5.5	D-Soluble
Little et al, <sup>17</sup> 1990	P-SB	78	8	58	51	138/77	-0.30 (3.30)	-0.40 (1.85)	36.4	D-Mixed
Margetts et al, <sup>18</sup> 1987	C-SB	88	6	39	58	132/80	-1.20 (0.90)	-1.10 (0.75)	42.6	D-Mixed
Nami et al, <sup>19</sup> 1995	P-DB	16	2	46	38	157/99	-14.3 (5.95)	-5.40 (1.53)	3.5	S-Mixed
Önning et al, <sup>20</sup> 1999	C-DB	52	5	63	100	141/88	-1.60 (1.82)	-1.50 (1.28)	6.8	S-Soluble
Rigaud et al, <sup>21</sup> 1990	P-DB	52	24	37	21	127/77	-1.30 (3.20)	2.50 (2.18)	6.0	S-Insoluble
Rössner et al, <sup>22</sup> 1987a	P-DB	54	8	39	0	134/84	3.00 (4.68)	0.00 (2.80)	5.0	S-Mixed
Rössner et al, <sup>22</sup> 1987b	P-DB	41	12	39	0	135/86	0.00 (7.19)	-5.00 (3.74)	7.0	S-Mixed
Rössner et al, <sup>23</sup> 1988	P-DB	62	12	40	0	124/75	1.00 (2.29)	-3.00 (1.16)	6.5	S-Mixed
Ryttig et al, <sup>24</sup> 1989	P-DB	97	11	39	0	131/85	0.10 (3.78)	-2.90 (2.09)	7.0	S-Insoluble
Ryttig et al, <sup>25</sup> 1990	C-DB	19	2	25	53	109/NR	3.00 (1.87)	NR	7.0	S-Soluble
Schlamowitz et al, <sup>8</sup> 1987	P-DB	46	12	NR	NR	153/96	-11.00 (4.39)	-3.00 (2.18)	7.0	S-Mixed
Solum et al, <sup>26</sup> 1987	P-DB	60	12	35	0	133/90	-9.00 (6.56)	-5.00 (4.77)	5.0	S-Insoluble
Swain et al, <sup>27</sup> 1990	C-DB	20	6	30	20	112/68	3.00 (2.90)	2.00 (1.93)	20.5	S-Soluble
Törrönen et al, <sup>28</sup> 1992	P-DB	28	8	41	100	129/81	6.00 (5.52)	1.00 (3.81)	15.1	S-Soluble
Van Horn et al, <sup>29</sup> 1991	P-O	80	8	42	50	128/80	0.50 (3.53)	-1.40 (2.14)	4.2	S-Soluble

Abbreviations: a and b, separate strata within the same study; BP, blood pressure; C, crossover; DB, double blind; NR, not reported; O, open; P, parallel; SB, single blind.

\*Values are net BP effects of fiber supplementation.

†S indicates from supplement; D, from diet.

kg/m<sup>2</sup>), and type of fiber (soluble vs insoluble vs mixed). Analyses by age and BMI were based on the median of the frequency distribution of these variables. In addition, the associations of fiber dose and duration of intervention with BP response were examined by means of linear regression analysis, for which we reported intercepts and  $\beta$  regression coefficients with 2-sided *P* values. Analyses in subgroups were repeated using a multivariate model to adjust for the potential confounders of age, proportion of men, hypertensive status, study design (parallel vs crossover), duration of intervention, and fiber dose.

Publication bias was visually examined after construction of a funnel graph, in which weight factors (1/SE<sup>2</sup>) were plotted against net changes in BP.<sup>33</sup> In addition, a nonparametric “trim and fill” method was used to adjust for publication bias.<sup>34</sup>

## RESULTS

### STUDY CHARACTERISTICS

An overview of the 24 randomized controlled trials of fiber and BP in-

cluded in our meta-analysis is given in **Table 1**. A total of 1404 subjects were included, and sample sizes ranged from 12 to 201 subjects. Trials had a mean duration of 9.0 weeks (median, 8 weeks; range, 2-24 weeks). Sixteen trials were double-blind, and 15 had BP as a primary study outcome. The mean age of trial populations was 42 years (median, 40 years; range, 23-63 years). Three trials included only men, 6 trials only women, and the remainder both men and women. Average baseline BP was 133/82 mm Hg, and populations in 8 trials were considered hypertensive. Baseline BMI was reported for 12 trial populations, 11 (92%) of which appeared to be overweight (ie, BMI  $\geq$  25 kg/m<sup>2</sup>). Net mean change in body weight during fiber supplementation was available for 21 trials and ranged from -2.5 kg to +1.0 kg (mean, -0.39 kg; *P* = .13). Baseline fiber intake was reported in 11 trials and ranged from 12.8 to 44.1 g/d (mean, 24.8 g/d). Soluble fiber was given in 11 trials, insoluble fiber in

7 trials, and a mixture of soluble and insoluble fiber in the remaining trials. In 4 trials, fiber intake was increased by dietary intervention.<sup>14,16-18</sup> Fiber doses varied between 3.5 and 42.6 g/d, with a mean dose of 11.5 g/d (median dose, 7 g/d). The unweighted average BP change in all trials combined for systolic BP was -1.54 mm Hg (95% CI, -3.48 to 0.39) and for diastolic BP, -1.34 mm Hg (95% CI, -2.41 to -0.27).

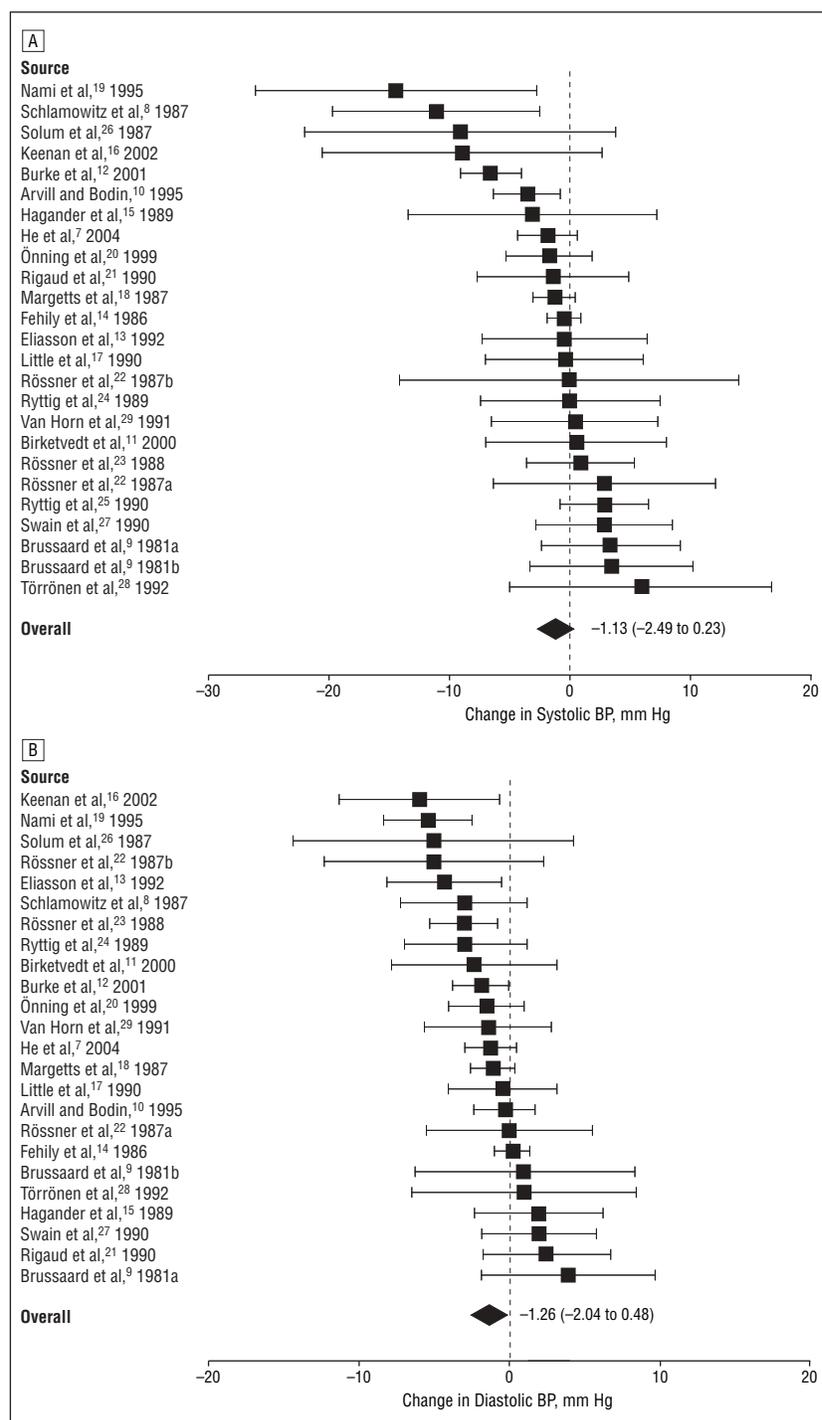
### QUANTITATIVE DATA SYNTHESIS

Meta-analysis yielded a weighted overall effect of fiber supplementation on systolic BP of -1.13 mm Hg (95% CI, -2.49 to 0.23) and on diastolic BP, -1.26 mm Hg (95% CI, -2.04 to -0.48) (**Figure 2**). Blood pressure responses to fiber supplementation in strata of population characteristics are summarized in **Table 2**. Blood pressure reductions were larger in older popula-

tions (mean age, >40 years) than in younger populations, but the difference was only statistically significant for systolic BP ( $P=.001$ ). Hypertensive populations had significantly larger BP reductions than normotensive populations, both systolic ( $P<.001$ ) and diastolic ( $P=.019$ ). Sex and BMI of trial populations did not significantly modify BP response to fiber supplementation.

Changes in BP became less pronounced with increasing fiber dose in linear regression analysis, but  $\beta$  coefficients were small and not statistically significant (regression equation for systolic BP,  $-1.55+0.032$  mm Hg/g of fiber,  $P=.60$ ; diastolic BP,  $-1.89+0.047$  mm Hg/g of fiber,  $P=.16$ ). Blood pressure response was also not related to duration of intervention (regression equation for systolic BP,  $-0.77-0.046$  mm Hg/wk,  $P=.73$ ; diastolic BP,  $-1.15-0.013$  mm Hg/wk,  $P=.88$ ). With regard to type of intervention, soluble fiber changed BP by  $-1.32$  mm Hg systolic (95% CI,  $-3.19$  to  $0.55$ ) and  $-0.82$  mm Hg diastolic (95% CI,  $-1.83$  to  $0.18$ ); insoluble fiber by  $-0.23$  mm Hg systolic (95% CI,  $-2.88$  to  $2.42$ ) and  $-0.57$  mm Hg diastolic (95% CI,  $-1.86$  to  $0.72$ ); and the mixture of soluble and insoluble fiber by  $-1.74$  mm Hg systolic (95% CI,  $-4.49$  to  $1.02$ ) and  $-2.22$  mm Hg diastolic (95% CI,  $-3.40$  to  $-1.03$ ).

Results from multivariate, stratified meta-analyses with adjustment for age, hypertensive status, proportion of men, duration of intervention, study design, and fiber dose are also summarized in Table 2. Change in body weight during intervention appeared not to be significantly associated with systolic and diastolic BP ( $P=.65$  and  $P=.38$ , respectively) and was therefore left out of the multivariate model. Again, age was a significant modifier of the effect on systolic BP. The reduction in systolic BP remained significantly larger in older than in younger populations ( $P=.04$ ). Blood pressure effects were also larger in hypertensive than normotensive populations after adjustment for confounders, but the difference was no longer statistically significant (Table 2).



**Figure 2.** Blood pressure (BP) response to fiber supplementation in randomized controlled trials. Effects on systolic BP (A) and diastolic BP (B) in individual trials are depicted as open squares; error bars indicate 95% confidence intervals. Meta-analysis yielded pooled estimates of  $-1.13$  mm Hg ( $-2.49$  to  $0.23$ ) for systolic BP and  $-1.26$  mm Hg ( $-2.04$  to  $-0.48$ ) for diastolic BP, which are depicted as black diamonds. Data on diastolic BP were missing for the trial by Ryttig et al.<sup>25</sup>

Exclusion of 8 nonblinded trials yielded essentially similar effects of fiber on systolic BP ( $-1.14$  mm Hg [95% CI,  $-2.37$  to  $0.08$ ]) but a larger effect on diastolic BP ( $-1.71$  mm Hg [95% CI,  $-2.61$  to  $-0.81$ ]). Exclusion of the trial by Fehily et al<sup>14</sup> with a relatively large sample

size ( $n=201$ ) did not change the overall BP estimates (data not presented). Exclusion of 4 dietary trials did not change the estimate for systolic BP ( $-1.06$  mm Hg [95% CI,  $-2.80$  to  $0.67$ ]) but yielded a larger effect of fiber supplementation on diastolic BP ( $-1.43$  mm Hg

**Table 2. Blood Pressure Response to Fiber Supplementation in Strata of Study Population Characteristics**

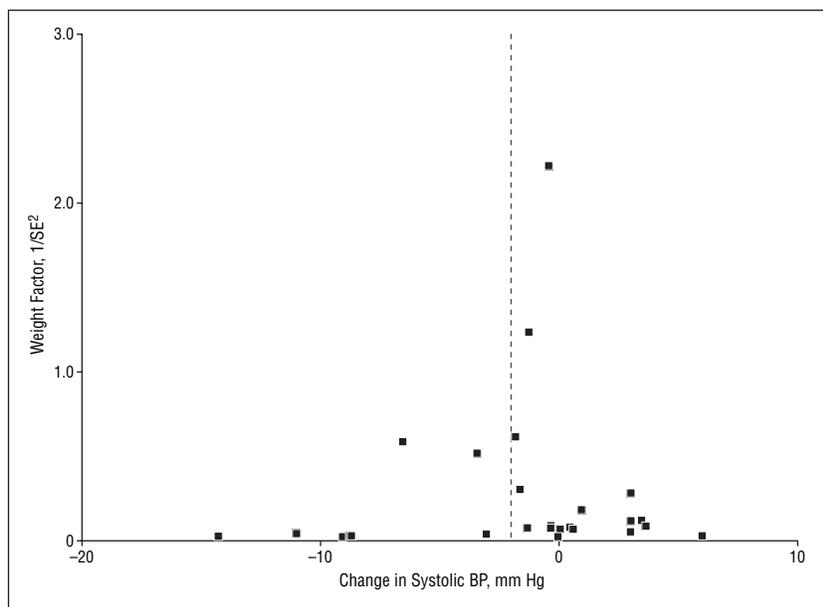
Characteristic	No. of Strata (No. of Subjects)	Systolic BP*				No. of Strata (No. of Subjects)	Diastolic BP*			
		Univariate Model	P Value	Multivariate Model†	P Value		Univariate Model	P Value	Multivariate Model†	P Value
Age, y										
≤40	13 (810)	0.35 (-1.00 to 1.69)	.001	-0.19 (-1.39 to 1.01)	.04	12 (791)	-0.64 (-1.70 to 0.42)	.16	-0.74 (-1.85 to 0.38)	.53
>40	11 (548)	-3.08 (-4.61 to -1.56)		-3.04 (-4.99 to -1.09)		11 (548)	-1.70 (-2.72 to 0.68)		-1.41 (-2.68 to -0.14)	
Sex										
<50% Male	10 (557)	-0.71 (-3.11 to 1.70)	.81	-0.51 (-3.43 to 2.40)	.65	10 (557)	-1.87 (-3.07 to -0.67)	.16	-1.93 (-3.39 to -0.48)	.19
≥50% Male	14 (801)	-1.06 (-2.65 to 0.53)		-1.32 (-2.28 to -0.36)		13 (782)	-0.81 (-1.67 to 0.05)		-0.67 (-1.47 to 0.13)	
Hypertension‡										
No	17 (1083)	-0.23 (-1.43 to 0.98)	<.001	-1.00 (-1.94 to -0.06)	.41	16 (1064)	-0.68 (-1.44 to 0.09)	.02	-0.81 (-1.60 to -0.02)	.35
Yes	8 (321)	-4.53 (-6.69 to -2.38)		-2.42 (-5.28 to 0.45)		8 (321)	-2.37 (-3.56 to -1.19)		-1.83 (-3.52 to -0.14)	
BMI, kg/m <sup>2</sup>										
≤28	6 (433)	-1.04 (-2.48 to 0.41)	.32	-0.54 (-2.54 to 1.46)	.25	6 (433)	-1.63 (-2.72 to -0.54)	.50	-1.81 (-3.16 to -0.47)	.43
>28	6 (309)	-2.13 (-3.74 to -0.53)		-2.75 (-5.11 to -0.39)		6 (309)	-1.11 (-2.16 to -0.07)		-0.95 (-2.22 to 0.32)	

Abbreviations: BMI, body mass index; BP, blood pressure.

\*Mean BP effects with 95% confidence interval obtained from random-effects model. P values are given for difference in BP response between strata.

†Adjusted for age, proportion of men, hypertensive status, study design, duration of intervention, and fiber dose.

‡Hypertension defined as average baseline BP of trial population ≥140/90 mm Hg or >50% of subjects undergoing antihypertensive treatment.



**Figure 3.** Funnel plot of trial weights against change in systolic blood pressure (BP). Blood pressure effects in individual trials are depicted as squares scattered around the pooled BP estimate of -1.13 mm Hg. A nonparametric “trim and fill” method<sup>34</sup> indicated that 1 trial might have been missing owing to publication bias. After adjustment for putative missing data, the overall effect on systolic BP was attenuated to -0.94 mm Hg (95% confidence interval, -2.34 to 0.46).

diastolic BP [95% CI, -2.36 to -0.50]).

From visual examination of the funnel plot it was concluded that small trials with large systolic BP reductions are possibly overrepresented in meta-analysis (**Figure 3**). A nonparametric “trim and fill” method revealed that 1 trial might have been missing. After adjustment for putative missing data, the overall effect on systolic BP was attenuated to -0.94 mm Hg (95% CI, -2.34 to 0.46).

### COMMENT

In this meta-analysis of 24 randomized controlled trials, fiber supplementation (mean dose, 11.5 g/d) caused a nonsignificant change in systolic BP of -1.13 mm Hg (95% CI, -2.49 to 0.23) and a significant change in diastolic BP of -1.26 mm Hg (95% CI, -2.04 to -0.48). The effects of fiber supplementation on BP were larger in older (>40

years) than in younger populations in multivariate analysis, although this was only statistically significant for systolic BP. Furthermore, BP reductions tended to be larger in hypertensive populations, but after adjustment for the older age of hypertensive populations (mean age, 52 years vs 37 years in normotensive populations), this difference lost statistical significance. Body weight and sex did not modify the effect of fiber supplementation on BP.

The effect of fiber on BP was estimated only from randomized placebo-controlled trials that had a high internal validity. Studies in which other dietary factors were modulated at the same time were excluded, and the BP effects are therefore likely to be causal and primarily attributable to changes in fiber intake. An advanced statistical approach for meta-analysis of continuous outcomes was used that accounted for both within- and between-study variability, which yielded accurate BP estimates and confidence intervals.<sup>32</sup>

This meta-analysis also has several limitations. First, we might not have been able to completely rule out BP effects by magnesium and potassium in the studies of fiber supplementation that we examined. A meta-analysis by Jee et al<sup>35</sup> showed a small, nonsignificant change in BP of -0.6 mm Hg systolic (95% CI, -2.2 to 1.0) and -0.8 mm Hg diastolic (95% CI, -1.9 to 0.4) after

magnesium supplementation. A meta-analysis by Whelton et al<sup>36</sup> showed a significant BP change of -3.11 mm Hg systolic (95% CI, -1.91 to -4.31) and -1.97 mm Hg diastolic (95% CI, -0.52 to -3.42) after potassium supplementation. In 1 of the 4 dietary intervention trials in our meta-analysis, a concomitant increase in magnesium and potassium intake occurred.<sup>18</sup> Moreover, fiber supplementation may also increase magnesium intake, as reported in 2 other trials,<sup>9,19</sup> and potassium intake, as reported in 1 trial.<sup>9</sup> For the remaining trials, no data on magnesium or potassium intake were available.

Second, publication bias could have occurred in that trials with large systolic BP reductions might be somewhat overrepresented. However, these trials had small weights in meta-analysis, and adjustment for putative missing data caused only a small attenuation of the effect on systolic BP. Sutton et al<sup>37</sup> empirically assessed the effect of publication bias on meta-analyses, which is a common phenomenon in systematic reviews, and found that the impact of publication bias on final conclusions is generally small.

Dietary fiber or nonstarch polysaccharide is a collective term for a variety of plant substances that are resistant to digestion by human gastrointestinal enzymes. The structural fibers (cellulose, lignin, and hemicelluloses) are insoluble, whereas the natural gel-forming fibers (pectins, gums, and mucilages) are soluble.<sup>38</sup> In the human diet, insoluble fiber is mainly derived from whole-grain products and soluble fiber from fruits, vegetables, pulses, and oats.<sup>38</sup> Little is known about the potential mechanisms through which dietary fiber might lower BP. Dietary fiber reduces the glycemic index of foods, thereby attenuating insulin response.<sup>39</sup> Insulin may play a role in BP regulation,<sup>40</sup> and dietary fiber has been shown to enhance insulin sensitivity and improve vascular endothelial function.<sup>39,41</sup> Furthermore, there is evidence that fiber, especially soluble types, improves mineral absorption in the gastrointestinal system,<sup>42,43</sup> which may have an indirect favorable effect on BP. In the

Dietary Approaches to Stop Hypertension (DASH) trial,<sup>44</sup> the effect of dietary patterns on BP was assessed. The fruits-and-vegetables diet provided potassium, magnesium, and high amounts of fiber and resulted in BP reductions of 2.8/1.1 mm Hg compared with a typical US diet. Data from our meta-analysis provide some support for a larger effect of soluble than insoluble fiber on BP.

Few prospective studies have examined the relationship between fiber intake and the risk of hypertension. In the Health Professionals' Follow-up Study<sup>45</sup> of 30 681 US male subjects, dietary fiber was independently associated with a reduced risk of hypertension. In the Nurses' Health Study<sup>46</sup> of 41 541 predominantly white US women, a significant inverse association of fiber intake with self-reported BP was found although not with risk of hypertension.

Dietary fiber may, apart from its effect on BP, also favorably influence other cardiovascular risk factors. A meta-analysis by Brown et al<sup>47</sup> showed that soluble fiber had a favorable effect on blood lipids: for each gram increase in dietary fiber, the concentration of blood low-density lipoprotein cholesterol was lowered by about 2 mg/dL (about 0.052 mmol/L). Furthermore, high intake of fiber, although mainly insoluble types from cereals, has been associated with lower risk of diabetes mellitus type 2.<sup>48,49</sup>

In the Cardiovascular Health Study,<sup>50</sup> a population-based multicenter study among 3588 elderly men and women, an inverse association between the consumption of fiber from cereal sources (insoluble fiber) and the risk of incident cardiovascular disease has recently been reported. As a biologically plausible mechanism for the beneficial effects of cereal fiber intake on cardiovascular risk in the elderly, the authors suggested a BP lowering effect of dietary fiber. In the large National Health and Nutrition Examination Survey I (NHANES I) Epidemiologic Follow-up Study,<sup>51</sup> a higher intake of dietary fiber appeared to be associated with a reduced risk of coronary heart disease. Beneficial effects in NHANES I were related to water-soluble types of fiber rather

than insoluble fiber, as was also the case in our meta-analysis of BP trials.

Intake of fiber in Western countries is low, with less than half of the US population meeting the recommended levels.<sup>4-6,51</sup> The present meta-analysis shows that dietary fiber has a small BP-lowering effect. Increasing fiber intake in the general population may contribute to the prevention of hypertension.

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## REFERENCES

1. Beilin LJ. Vegetarian and other complex diets, fats, fiber, and hypertension. *Am J Clin Nutr.* 1994; 59(5; suppl):1130S-1135S.
2. Rouse IL, Beilin LJ, Armstrong BK, Vandongen R. Blood-pressure-lowering effect of a vegetarian diet: controlled trial in normotensive subjects. *Lancet.* 1983;1:5-10.
3. He J, Whelton PK. Effect of dietary fiber and protein intake on blood pressure: a review of epidemiologic evidence. *Clin Exp Hypertens.* 1999; 21:785-796.
4. Van Horn L. Fiber, lipids, and coronary heart disease: a statement for healthcare professionals from the Nutrition Committee, American Heart Association. *Circulation.* 1997;95:2701-2704.
5. Marlett JA, McBurney MI, Slavin JL; American Dietetic Association. Position of the American Dietetic Association: health implications of dietary fiber. *J Am Diet Assoc.* 2002;102:993-1000.
6. Alaimo K, McDowell M, Briefel R, et al. Dietary intake: vitamins, minerals and fiber of persons age two months and over in the United States: Third National Health and Nutrition Examination Survey: phase 1, 1988-91. *Adv Data.* 1994;258:1-28.
7. He J, Streiffer RH, Whelton PK. Effect of dietary fiber supplementation on blood pressure: a randomized, double-blind placebo-controlled trial. *J Hypertens.* 2004;22:73-80.
8. Schlamowitz P, Halberg T, Warnoe O, Wilstrup F, Rytting K. Treatment of mild to moderate hypertension with dietary fibre. *Lancet.* 1987;2:622-623.
9. Brussaard JH, van Raaij JM, Stasse-Wolthuis M, Katan MB, Hautvast JG. Blood pressure and diet in normotensive volunteers: absence of an effect of dietary fiber, protein, or fat. *Am J Clin Nutr.* 1981; 34:2023-2029.
10. Arvill A, Bodin L. Effect of short-term ingestion of konjac glucomannan on serum cholesterol in healthy men. *Am J Clin Nutr.* 1995;61:585-589.
11. Birketvedt GS, Asseth J, Florholmen JR, Rytting K. Long-term effect of fibre supplement and reduced energy intake on body weight and blood lipids in overweight subjects. *Acta Medica (Hradec Kralove).* 2000;43:129-132.
12. Burke V, Hodgson JM, Beilin LJ, Giangulioi N, Rogers P, Puddey IB. Dietary protein and soluble fi-

- ber reduce ambulatory blood pressure in treated hypertensives. *Hypertension*. 2001;38:821-826.
13. Eliasson K, Ryttig KR, Hylander B, Rossner S. A dietary fibre supplement in the treatment of mild hypertension: a randomized, double blind, placebo-controlled trial. *J Hypertens*. 1992;10:195-199.
  14. Fehily AM, Burr ML, Butland BK, Eastham RD. A randomised controlled trial to investigate the effect of a high fibre diet on blood pressure and plasma fibrinogen. *J Epidemiol Community Health*. 1986;40:334-337.
  15. Hagander B, Asp NG, Ekman R, Nilsson-Ehle P, Lundquist I, Schersten B. Dietary fibre enrichment, blood pressure, lipoprotein profile and gut hormones in NIDDM patients. *Eur J Clin Nutr*. 1989;43:35-44.
  16. Keenan JM, Pins JJ, Frazel C, Moran A, Turnquist L. Oat ingestion reduces systolic and diastolic blood pressure in patients with mild or borderline hypertension: a pilot trial. *J Fam Pract*. 2002;51:369.
  17. Little P, Girling G, Hasler A, Trafford A, Craven A. A controlled trial of a low sodium, low fat, high fibre diet in treated hypertensive patients: the efficacy of multiple dietary intervention. *Postgrad Med J*. 1990;66:616-621.
  18. Margetts BM, Beilin LJ, Vandongen R, Armstrong BK. A randomized controlled trial of the effect of dietary fibre on blood pressure. *Clin Sci (Lond)*. 1987;72:343-350.
  19. Nami R, Gallo V, Pavese G, Panza F, Gennari C. Antihypertensive activity of a vegetable fibre preparation: a preliminary, double-blind, placebo-controlled study. *Eur J Clin Nutr*. 1995;49(suppl 1):S201-S206.
  20. Önnings G, Wallmark A, Persson M, Akkeson B, Elmstahl S, Öste R. Consumption of oat milk for 5 weeks lowers serum cholesterol and LDL cholesterol in free-living men with moderate hypercholesterolemia. *Ann Nutr Metab*. 1999;43:301-309.
  21. Rigaud D, Ryttig KR, Angel LA, Apfelbaum M. Overweight treated with energy restriction and a dietary fibre supplement: a 6-month randomized double-blind, placebo-controlled trial. *Int J Obes*. 1990;14:763-769.
  22. Rössner S, von Zweigbergk D, Ohlin A, Ryttig K. Weight reduction with dietary fibre supplements: results of two double-blind randomized studies. *Acta Med Scand*. 1987;222:83-88.
  23. Rössner S, Andersson IL, Ryttig K. Effects of a dietary fibre supplement to a weight reduction programme on blood pressure: a randomized, double-blind placebo-controlled study. *Acta Med Scand*. 1988;223:353-357.
  24. Ryttig KR, Tellnes G, Haegh L, Boe E, Fagerthun H. A dietary fibre supplement and weight maintenance after weight reduction: a randomized double-blind, placebo-controlled long-term trial. *Int J Obes*. 1989;13:165-171.
  25. Ryttig KR, Lammert O, Nielsen E, Garby L, Poulsen K. The effect of a soluble dietary fibre supplement on 24-hour energy expenditure during a standardized physical activity programme. *Int J Obes*. 1990;14:451-455.
  26. Solum TT, Ryttig KR, Solum E, Larsen S. The influence of a high-fibre diet on body weight, serum lipids and blood pressure in slightly overweight persons: a randomized, double-blind, placebo-controlled investigation with diet and fiber tablets (Dumo Vital). *Int J Obes*. 1987;11 (suppl 1):67-71.
  27. Swain JF, Rouse IL, Curley CB, Sacks FM. Comparison of the effects of oat bran and low-fiber wheat on serum lipoprotein levels and blood pressure. *N Engl J Med*. 1990;322:147-152.
  28. Törrönen R, Kansanen L, Uusitupa M, et al. Effects of an oat bran concentrate on serum lipids in free-living men with mild to moderate hypercholesterolaemia. *Eur J Clin Nutr*. 1992;46:621-627.
  29. Van Horn L, Moag-Stahlberg A, Liu KA, et al. Effects on serum lipids of adding instant oats to usual American diets. *Am J Public Health*. 1991;81:183-188.
  30. Follmann D, Elliot P, Suh I, Cutler J. Variance imputation for overviews of clinical trials with continuous response. *J Clin Epidemiol*. 1992;45:769-773.
  31. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177-188.
  32. van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. *Stat Med*. 2002;21:589-624.
  33. Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. *BMJ*. 1997;315:1533-1537.
  34. Duval S, Tweedie R. Trim and fill: a simple funnelplot based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*. 2000;56:455-463.
  35. Jee SH, Miller ER III, Guallar E, Singh VK, Appel LJ, Klag MJ. The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. *Am J Hypertens*. 2002;15:691-696.
  36. Whelton PK, He J, Cutler JA, et al. Effects of oral potassium on blood pressure: meta-analysis of randomized controlled clinical trials. *JAMA*. 1997;277:1624-1632.
  37. Sutton AJ, Duval SJ, Tweedie RL, Abrams KR, Jones DR. Empirical assessment of effect of publication bias on meta-analyses. *BMJ*. 2000;320:1574-1577.
  38. Spiller A. *CRC Handbook of Dietary Fiber in Human Nutrition*. 3rd ed. Boca Raton, Fla: CRC Press; 2001.
  39. Bessesen DH. The role of carbohydrates in insulin resistance. *J Nutr*. 2001;131:2782S-2786S.
  40. Landsberg L. Insulin-mediated sympathetic stimulation: role in the pathogenesis of obesity-related hypertension (or, how insulin affects blood pressure, and why). *J Hypertens*. 2001;19:523-528.
  41. Cleland SJ, Petrie JR, Ueda S, Elliott HL, Connell JM. Insulin as a vascular hormone: implications for the pathophysiology of cardiovascular disease. *Clin Exp Pharmacol Physiol*. 1998;25:175-184.
  42. Coudray C, Demigne C, Rayssiguier Y. Effects of dietary fibers on magnesium absorption in animals and humans. *J Nutr*. 2003;133:1-4.
  43. Greger JL. Nondigestible carbohydrates and mineral bioavailability. *J Nutr*. 1999;129:1434S-1435S.
  44. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med*. 1997;336:1117-1124.
  45. Ascherio A, Rimm EB, Giovannucci EL, et al. A prospective study of nutritional factors and hypertension among US men. *Circulation*. 1992;86:1475-1484.
  46. Ascherio A, Hennekens C, Willett WC, et al. Prospective study of nutritional factors, blood pressure, and hypertension among US women. *Hypertension*. 1996;27:1065-1072.
  47. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr*. 1999;69:30-42.
  48. Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. *N Engl J Med*. 2000;342:1392-1398.
  49. Willett W, Manson J, Liu S. Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr*. 2002;76:274S-280S.
  50. Mozaffarian D, Kumanyika SK, Lemaitre RN, Olsen JL, Burke GL, Siscovick DS. Cereal, fruit, and vegetables fiber intake and the risk of cardiovascular disease in elderly individuals. *JAMA*. 2003;289:1659-1666.
  51. Bazzano LA, He J, Ogden LG, Loria CM, Whelton PK. Dietary fiber intake and reduced risk of coronary heart disease in US men and women. *Arch Intern Med*. 2003;163:1897-1904.