

Comparative Effectiveness of Implementation Strategies for Blood Pressure Control in Hypertensive Patients

A Systematic Review and Meta-analysis

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Background: The prevalence of hypertension is high and is increasing worldwide, whereas the proportion of controlled hypertension is low.

Purpose: To assess the comparative effectiveness of 8 implementation strategies for blood pressure (BP) control in adults with hypertension.

Data Sources: Systematic searches of MEDLINE and Embase from inception to September 2017 with no language restrictions, supplemented with manual reference searches.

Study Selection: Randomized controlled trials lasting at least 6 months comparing the effect of implementation strategies versus usual care on BP reduction in adults with hypertension.

Data Extraction: Two investigators independently extracted data and assessed study quality.

Data Synthesis: A total of 121 comparisons from 100 articles with 55 920 hypertensive patients were included. Multilevel, multicomponent strategies were most effective for systolic BP reduction, including team-based care with medication titration

by a nonphysician (−7.1 mm Hg [95% CI, −8.9 to −5.2 mm Hg]), team-based care with medication titration by a physician (−6.2 mm Hg [CI, −8.1 to −4.2 mm Hg]), and multilevel strategies without team-based care (−5.0 mm Hg [CI, −8.0 to −2.0 mm Hg]). Patient-level strategies resulted in systolic BP changes of −3.9 mm Hg (CI, −5.4 to −2.3 mm Hg) for health coaching and −2.7 mm Hg (CI, −3.6 to −1.7 mm Hg) for home BP monitoring. Similar trends were seen for diastolic BP reduction.

Limitation: Sparse data from low- and middle-income countries; few trials of some implementation strategies, such as provider training; and possible publication bias.

Conclusion: Multilevel, multicomponent strategies, followed by patient-level strategies, are most effective for BP control in patients with hypertension and should be used to improve hypertension control.

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Hypertension is a major public health challenge because of its high prevalence and associated cardiovascular disease and premature death (1, 2). Randomized clinical trials have shown that pharmaceutical treatment and lifestyle modifications reduce blood pressure (BP) and risk for cardiovascular disease (3, 4). Despite the proven effectiveness of these interventions, only 13.8% of adults with hypertension and 37.1% of patients with treated hypertension worldwide had their BP controlled in 2010 (1). Barriers to hypertension control have been identified at the health care system, health care provider, and patient levels (5). Such barriers include limited health care resources, lack of performance standards, and limited reimbursement for health coaching at the system level; lack of adherence to clinical guidelines at the provider level; and lack of adherence to prescribed medications and lifestyle modifications at the patient level (5).

Implementation strategies to overcome the barriers to BP control, such as home BP monitoring, health

coaching, provider training, and team-based care, have been tested in randomized trials (6, 7). Most trials, however, have relatively small sample sizes and limited statistical power to reliably estimate intervention effects. Two previous reviews of implementation strategies for BP reduction included studies published up to 2003 and 2008 (6, 7). They showed that, compared with usual care, many implementation strategies, including team change and home BP monitoring, significantly improved BP control (6, 7). However, the effects of various implementation strategies on BP control were not directly compared in these meta-analyses. In addition, many implementation strategy trials have been published since 2008. In this meta-analysis, we aim to assess the comparative effectiveness of various implementation strategies on BP reduction in patients with hypertension by direct comparison. This information could be used by government and nongovernment organizations to select the most effective implementation strategies for hypertension control in communities.

METHODS

We developed and followed a protocol for all steps of the review and meta-analysis (Supplement, available at Annals.org).

Data Sources and Searches

We searched MEDLINE and Embase from inception to 11 September 2017 with search terms “hyper-

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Table 1. Descriptions of Implementation Strategy Categories*

Implementation Strategy Category	Description
Patient level	
Health coaching (10)	Multiple sessions for patient-centered health education and motivation delivered with the goal of facilitating lifestyle modification and/or medication adherence.
Home BP monitoring	Self-monitoring of patient BP and recording of measurements either manually or by automatic electronic transmission; BP readings given to providers.
Provider level	
Provider training	Education or training targeting providers on hypertension management, including guideline adherence (treatment goals, lifestyle intervention, and medication titrations), and/or patient communication.
Audit and feedback (11)	Repeated, periodic summaries of patient outcomes given to providers, such as BP values, so they can evaluate and improve patient care; could also include provider training.
Electronic decision-support system (11)	Computerized alerts, reminders, or order sets intended to aid providers in point-of-care decision making; could also include provider training.
Multilevel	
Multilevel strategy without team-based care	Interventions that target barriers to hypertension control at multiple levels but do not include team-based care, such as a combination of provider training and patient health coaching.
Team-based care with physicians titrating medications (12)	Collaborative provision of care for hypertension by ≥ 2 providers, including a primary care physician who titrates medications, working collaboratively with patients to accomplish shared treatment goals.
Team-based care with nonphysician providers titrating medications (12)	Collaborative provision of care for hypertension by ≥ 2 providers, including a nonphysician team member who titrates medications, working collaboratively with patients to accomplish shared treatment goals.

BP = blood pressure.

* Numbers in parentheses are references.

tension" and "blood pressure" and an extensive list of terms related to provider education, team-based care, patient education, provider feedback and guideline adherence, and home BP monitoring (Supplement Tables 1 and 2, available at Annals.org) (6-9). The search was restricted to clinical trials in human adults and had no language restrictions. Additional studies were identified by manual review of references cited in reviews, meta-analyses, and original articles. Finally, we searched ClinicalTrials.gov (September 2017), using the same terms as in the MEDLINE search, to find additional trials and assess publication bias by identifying completed trials without published results.

Study Selection

A study was eligible for inclusion if 1) it was a randomized controlled trial; 2) participants were adults with hypertension, defined as average systolic BP of at least 140 mm Hg, average diastolic BP of at least 90 mm Hg, or use of antihypertensive medication; 3) net change in systolic or diastolic BP was a main trial outcome; 4) the trial intervention targeted barriers to hypertension control at 1 or more of the patient, provider, and health care system levels; 5) the control group received usual care or minimal education; 6) the trial lasted at least 6 months; 7) variance of BP changes (or data to calculate it) was reported; and 8) clustering was accounted for in the analysis if the trial was cluster randomized. Two investigators independently screened abstracts for initial eligibility and reviewed full texts of eligible studies. Disagreements were resolved by consensus.

Data Extraction and Quality Assessment

Two investigators independently extracted data using a standardized form. Extracted data included study

design, participant characteristics, intervention descriptions, and study results. Data from the 2 investigators were compared, and discrepancies were resolved by consensus. For trials reporting results at more than 1 time point, the report closest to the end of the intervention was selected.

Trials were divided into 8 implementation strategy categories based on intervention descriptions (Table 1). Categories were created on the basis of prior literature and availability of trials meeting our inclusion criteria (6, 7). Two categories address only patient-level barriers to BP control: health coaching and home BP monitoring; 3 categories target only provider-level barriers: provider training, audit and feedback, and electronic decision-support systems; and 3 categories are multilevel strategies: multilevel strategies without team-based care, team-based care with physicians titrating medications, and team-based care with nonphysician providers titrating medications.

Health coaching strategies could be delivered in person or by telephone at several individual or group sessions during the intervention. The strategies were patient-centered, with a component of behavioral self-monitoring. A health coach (case manager, nurse, medical assistant, or community health worker) and patients worked together using self-discovery or active learning processes to improve medication adherence and lifestyle modification (10). Provider-level strategies aimed to improve the BP management performance of health care professionals primarily responsible for hypertensive patient care. Multilevel implementation strategies were aimed at overcoming barriers to hypertension control at 2 or more levels among patients, providers, health care systems, and communities. Team-based

care was characterized by interprofessional collaboration, a patient-centered approach, and an integrated care process (12). In this meta-analysis, implementation strategies for team-based care involved task shifting or task sharing from primary care physicians to nurses, pharmacists, or community health workers. Team-based care was divided into 2 categories depending on whether the nonphysician provider could titrate medications. Multilevel strategies without team-based care included any intervention targeting more than 1 level of barriers to BP control but did not include team-based care, such as patient health coaching combined with provider training. Multicomponent strategies were those that combined more than 1 approach regardless of barrier level.

We included trials if their control groups were either usual care or minimal education. Usual care was defined as hypertension management by patients' normal care providers with no trial intervention. Minimal education included the provision of educational materials or a brief educational session to either patients or providers.

To assess quality, we modified the Cochrane Risk of Bias Tool to make it applicable to cluster trials in implementation research (13). We focused on the following domains: random sequence generation, objective outcome assessment (blinding of BP observers or use of automatic BP cuffs), incomplete outcome data, and selective outcome reporting. Participant recruitment bias was also considered for cluster randomized trials, and funding sources were recorded for all trials. Two reviewers independently assessed risk of bias at the trial level.

Data Synthesis and Analysis

The Supplemental Methods section of the **Supplement** (available at Annals.org) describes the analysis and sample code in detail. For each trial, the net change in mean BP and associated SE were calculated from available data and defined as the difference (intervention minus control) in the changes of mean values (follow-up minus baseline). If BP was measured at several time points during follow-up, the measurements taken closest to the end of the intervention were used. In addition, the changes in mean BP and associated SEs in each randomized group were calculated separately for comparing effects among implementation strategies.

Random-effects models using the Sidik-Jonkman residual heterogeneity estimator with the Knapp-Hartung small-sample adjustment were used to calculate pooled mean differences within implementation categories using inverse variance weighting (14–16). In some trials, several intervention groups were compared with the same reference group. In these cases, robust variance estimation was used to account for nonindependent estimates (17). Heterogeneity was evaluated using the Cochran *Q* test and quantified with the *I*² index, and the 95% CI was calculated using the test-based method (18). Publication bias was assessed using the Begg rank correlation test and the Egger

weighted linear regression test for implementation strategies with at least 10 studies because of low statistical power with small sample sizes. When possible publication bias was observed, the trim-and-fill method was used to estimate the number of missing studies not published, augment the data to make the funnel plot more symmetrical, and calculate a summary estimate based on the augmented data (19).

Generalized estimating equations (with an exchangeable correlation matrix between estimates within a study) were used to compare BP reductions associated with each implementation strategy after important covariate adjustment and for pairwise comparisons between implementation strategies. Indicator variables were used for each implementation strategy category, with the common control group as the reference. Weights for these models were exported from a random-effects meta-analysis, including all changes in mean BP and associated SEs from all treatment groups. As such, these weights take into account within- and between-trial variance. Each trial was treated as a cluster to maintain randomized comparisons, and the following trial-level baseline characteristics were adjusted: logit-transformed proportion male, centered mean age, centered mean systolic BP, centered trial duration, and whether the control group was usual care or minimal education. A sensitivity analysis was done including only trials where all participants had uncontrolled hypertension at baseline.

Analyses were done using packages *metafor*, *robustmeta*, and *forestplot* in R, version 3.3.2 (R Project for Statistical Computing), and PROC GENMOD in SAS, version 9.4 (SAS Institute).

Role of the Funding Source

This work was supported in part by the National Institute of General Medical Sciences and the National Heart, Lung, and Blood Institute. The funding sources had no role in the design, conduct, or reporting of the study or the decision to publish the manuscript.

RESULTS

After duplicates were excluded, our search strategy identified 6697 references, of which 958 underwent full-text review (**Figure 1**). In total, we included 100 articles reporting 121 comparisons with 55 920 participants (**Supplement Table 3**, available at Annals.org). The median of the study-specific mean ages was 60 years (range, 33 to 77 years), and the medians of the study-specific mean systolic and diastolic BPs at baseline were 148 mm Hg (range, 124 to 190 mm Hg) and 86 mm Hg (range, 70 to 105 mm Hg), respectively. Trial durations ranged from 6 months to 5 years (median, 6 months). The number of comparisons per implementation category ranged from 39 for health coaching to 2 for audit and feedback (**Table 2**). We identified no trials at high risk of bias for random sequence generation; some were considered to have high risk of bias for objective outcome assessment (*n* = 3), incomplete outcome data (*n* = 13), selective reporting (*n* = 2), or re-

cruitment bias ($n = 1$) (Supplement Tables 4 and 5, available at Annals.org). Of the 88 studies reporting funding information, 17% received full or partial funding from pharmaceutical firms. The rest were funded by federal, state, and local governments; foundations; and universities.

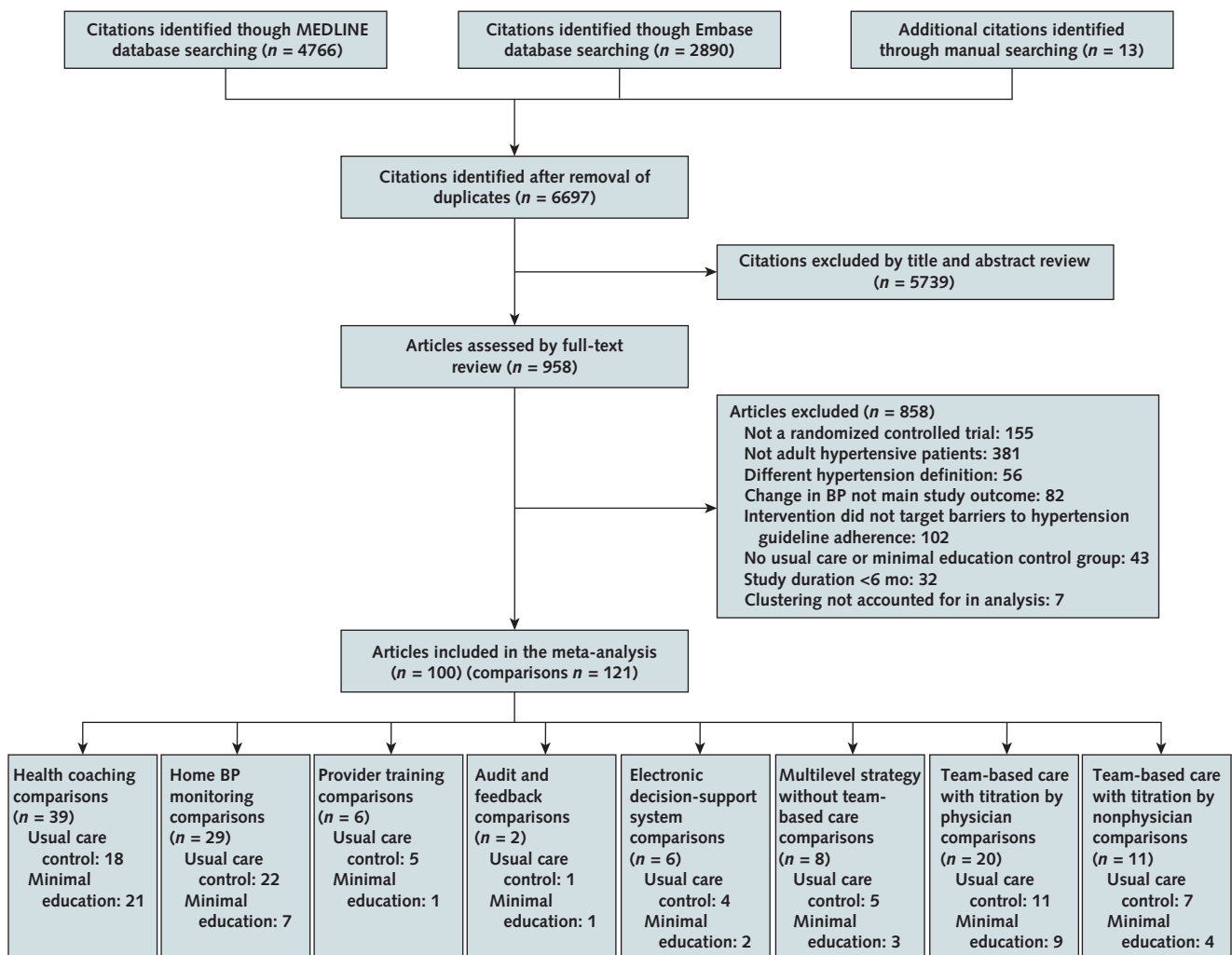
The search of ClinicalTrials.gov identified 31 eligible trials. Of these, 8 of 9 published trials had been identified in our other searches, 19 were either ongoing or recently completed (defined as date of data collection completion for the primary outcome within the past 2 years), and 3 (1 of home BP monitoring and 2 of health coaching) with data collection completed more than 2 years ago were not published.

Effects of Implementation Strategies

All 5 patient-level and multilevel implementation strategies were associated with reductions in systolic BP (Supplement Figure 1, available at Annals.org). Health coaching reduced systolic BP by 4.3 mm Hg (95% CI, 2.6 to 5.9 mm Hg) ($P < 0.001$), and home BP

monitoring reduced it by 2.2 mm Hg (CI, 1.0 to 3.5 mm Hg) ($P = 0.001$). The multilevel strategies without team-based care reduced systolic BP by 3.9 mm Hg (CI, 1.3 to 6.5 mm Hg) ($P = 0.003$). Team-based care with physicians and nonphysician providers titrating medications had the largest reductions in pooled mean systolic BP of 5.7 mm Hg (CI, 3.6 to 7.9 mm Hg) ($P < 0.001$) and 6.6 mm Hg (CI, 4.2 to 9.0 mm Hg) ($P < 0.001$), respectively. Strategies targeting provider-level barriers to BP control did not statistically significantly reduce BP compared with the control group. Some evidence of publication bias was observed for health coaching (Egger $P = 0.27$; Begg $P = 0.051$) and team-based care with physicians titrating medications (Egger $P = 0.146$; Begg $P = 0.020$). However, trim-and-fill analysis showed that publication bias did not account for the observed associations for health coaching (change, -4.3 mm Hg [CI, -6.1 to -2.6 mm Hg]; $P < 0.001$) or for team-based care with physicians titrating medications (change, -4.2 mm Hg [CI, -6.5 to -1.8 mm Hg]; $P < 0.001$).

Figure 1. Evidence search and selection.



BP = blood pressure.

Table 2. Summary Characteristics of Trials, by Implementation Strategy

Implementation Strategy	Studies, n*	Participants, n	Range of Mean Ages, y	Range of Men, %	Range of Mean Baseline BP, mm Hg		Duration	Study Design, %
					Systolic	Diastolic		
Patient level								
Health coaching	39	10 656	33-74	0-100	124-181	70-105	6 mo-2 y	Parallel RCTs: 97 (cluster randomized: 30) Factorial RCTs: 3
Home BP monitoring	29	7966	47-77	21-92	126-170	72-104	6 mo-2 y	Parallel RCTs: 100 (cluster randomized: 8)
Provider level								
Provider training	6	17 642	53-67	35-47	127-153	74-96	6 mo-2 y	Parallel RCTs: 100 (cluster randomized: 100)
Audit and feedback	2	2121	61-62	54-64	133-146	73-89	6 mo-2 y	Parallel RCTs: 100 (cluster randomized: 100)
Electronic decision-support system	6	8229	54-69	22-97	136-158	75-89	6-18 mo	Parallel RCTs: 100 (cluster randomized: 100)
Multilevel								
Multilevel strategy without team-based care	8	3436	53-67	30-100	133-169	73-95	6 mo-2 y	Parallel RCTs: 100 (cluster randomized: 75)
Team-based care with physicians titrating medications	20	6680	47-68	21-99	127-162	76-93	6-18 mo	Parallel RCTs: 100 (cluster randomized: 30)
Team-based care with nonphysician providers titrating medications	11	3417	41-68	31-100	136-174	76-99	6 mo-5 y	Parallel RCTs: 100 (cluster randomized: 18)

BP = blood pressure; RCT = randomized controlled trial.

* A total of 121 comparisons from 100 publications and 55 920 participants are included. Sixteen publications contributed >1 comparison because they had multiple treatment groups.

Results were similar for diastolic BP (Supplement Figure 2, available at Annals.org). Significant reductions in diastolic BP compared with the control group were seen for health coaching (change, -1.9 mm Hg [CI, -2.8 to -1.0 mm Hg]; $P < 0.001$), home BP monitoring (-1.5 mm Hg [CI, -2.0 to -1.0 mm Hg]; $P < 0.001$), team-based care with titration by a physician (-2.5 mm Hg [CI, -3.9 to -1.1 mm Hg]; $P = 0.002$), and team-based care with medication titration by a nonphysician provider (-3.5 mm Hg [CI, -4.6 to -2.5 mm Hg]; $P < 0.001$). Multilevel strategies without team-based care were not associated with a significant diastolic BP reduction (change, -2.7 mm Hg [CI, -6.0 to

0.6 mm Hg]; $P = 0.114$). Provider training, audit and feedback, and electronic decision-support systems were also not associated with significant reductions in diastolic BP.

Comparative Effectiveness of Implementation Strategies

After adjustment for important covariates and all implementation strategies simultaneously using generalized estimating equations, the 3 multilevel strategies were the most effective for reducing systolic BP (Figure 2). Team-based care with medication titration by a nonphysician had the greatest reduction in systolic BP

Table 2—Continued

BP Measurement Methods, n		Control Categories, %
Comparisons	Type of Device	
1 visit, 2–6 measurements: 20 2 visits, 2 measurements each: 1 Unknown: 18	Automated: 16 Standard mercury: 8 Automated or standard mercury: 1 Random 0: 2 Unknown: 12	Usual care: 46 Minimal education: 54
1 visit, 2–6 measurements: 17 2 visits, 3 measurements each: 1 9 visits, 1 measurement each: 1 Daytime ambulatory: 1 Routine clinic measurements: 1 Unknown: 8	Automated: 13 Standard mercury: 4 Random 0: 1 Aneroid: 1 Ambulatory: 1 Device used in clinic: 3 Unknown: 6	Usual care: 76 Minimal education: 24
1 visit, 3 measurements: 2 24-h ambulatory: 1 Routine clinic measurements: 1 Unknown: 2	Automated: 2 Ambulatory: 1 Device used in clinic: 1 Unknown: 2	Usual care: 83 Minimal education: 17
2 visits, 2 measurements each: 1 Unknown: 1	Automated: 1 Unknown: 1	Usual care: 50 Minimal education: 50
1 visit, 2 measurements: 1 Routine clinic measurements: 4 Unknown: 1	Automated: 3 Device used in clinic: 2 Unknown: 1	Usual care: 67 Minimal education: 33
1 visit, 2–3 measurements: 5 2 visits, 2 measurements each: 1 Unknown: 2	Automated: 6 Standard mercury: 1 Unknown: 1	Usual care: 63 Minimal education: 37
1 visit, 2–4 measurements: 9 2 visits, 3 measurements each: 1 24-h ambulatory: 1 Routine clinic measurements: 3 Unknown: 6	Automated: 8 Standard mercury: 5 Random 0: 2 Aneroid: 1 Device used in clinic: 3 Unknown: 1	Usual care: 55 Minimal education: 45
1 visit, 1 measurement: 1 1 visit, 2–3 measurements: 8 2 visits, 3 measurements each: 1 Routine clinic measurements: 1	Automated: 6 Standard mercury: 2 Random 0: 1 Device used in clinic: 1 Unknown: 1	Usual care: 64 Minimal education: 36

(change, -7.1 mm Hg [CI, -8.9 to -5.2 mm Hg]; $P < 0.001$), followed by team-based care with medication titration by a physician (-6.2 mm Hg [CI, -8.1 to -4.2 mm Hg]; $P < 0.001$) and multilevel strategies without team-based care (-5.0 mm Hg [CI, -8.0 to -2.0 mm Hg]; $P = 0.001$). The patient-level strategies of health coaching (change, -3.9 mm Hg [CI, -5.4 to -2.3 mm Hg]; $P < 0.001$) and home BP monitoring (-2.7 mm Hg [CI, -3.6 to -1.7 mm Hg]; $P < 0.001$) were also associated with reductions in systolic BP. After multivariate adjustment, the electronic decision-support systems strategy was associated with a statistically significant reduction in systolic BP (change, -3.7 mm Hg [CI, -5.2

to -2.2 mm Hg]; $P < 0.001$), but provider training and audit and feedback were not. Likewise, team-based care with medication titration by a nonphysician had the greatest reduction in diastolic BP (change, -3.1 mm Hg [CI, -4.1 to -2.2 mm Hg]; $P < 0.001$), followed by multilevel strategies without team-based care (-2.9 mm Hg [CI, -5.4 to -0.4 mm Hg]; $P = 0.025$) and team-based care with medication titration by a physician (-2.7 mm Hg [CI, -3.8 to -1.5 mm Hg]; $P < 0.001$). The patient-level strategies of health coaching (change, -2.1 mm Hg [CI, -2.9 to -1.3 mm Hg]; $P < 0.001$) and home BP monitoring (-1.5 mm Hg [CI, -2.3 to -0.8 mm Hg]; $P < 0.001$) were also associated with reductions in diastolic BP. Use of electronic decision-support systems was the only provider-level strategy associated with a statistically significant reduction in diastolic BP (change, -1.5 mm Hg [CI, -1.9 to -1.1 mm Hg]; $P < 0.001$). Results were similar for patient-level and multilevel interventions when analyses included only trials where all participants had uncontrolled BP at baseline (Supplement Figure 3, available at Annals.org). Insufficient studies met this criterion to estimate summary effects for audit and feedback and provider training.

Pairwise Comparison of Implementation Strategies

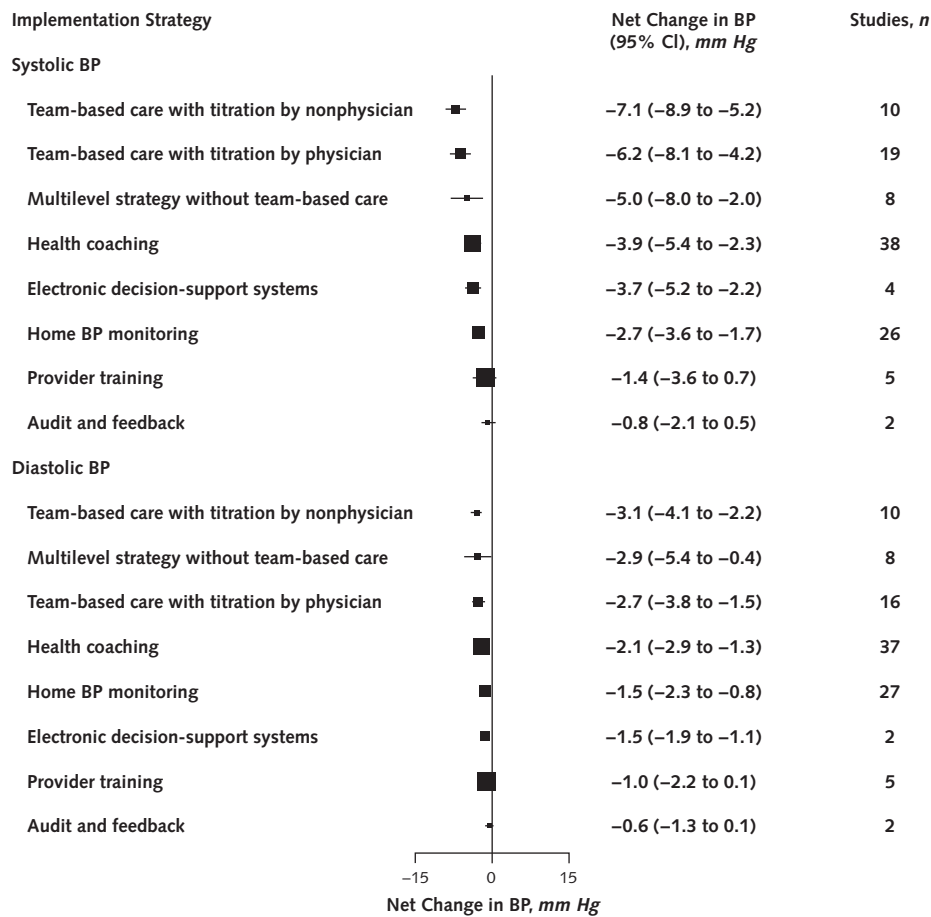
Figure 3 provides a pairwise comparison of the intervention strategies, ordered by effect sizes of systolic BP reduction and adjusted for covariates. Team-based care with titration by a nonphysician resulted in greater systolic BP reductions (range, -3.22 to -6.29 mm Hg) than any patient-level or provider-level strategy and greater diastolic BP reductions (range, -1.60 to -2.52 mm Hg) than home BP monitoring or any provider-level strategy. Team-based care with titration by a physician also resulted in greater reductions in systolic BP compared with all patient-level and provider-level strategies except health coaching.

DISCUSSION

Our findings indicate that implementation strategies targeting multilevel or patient-level barriers are effective for BP reduction. Specifically, team-based care with and without a nonphysician team member titrating medications and multilevel strategies without team-based care were the most effective implementation strategies for hypertension control. Patient health coaching and home BP monitoring were also effective.

These findings have important public health implications. Despite strong evidence that antihypertensive medications and lifestyle modifications reduce BP and subsequent morbidity and mortality from cardiovascular disease, hypertension control rates are low worldwide (5). The National Academy of Medicine and the National Heart, Lung, and Blood Institute have both called for research focusing on integrating evidence-based strategies into routine health care for hypertension control (20, 21). Our findings provide evidence that multilevel, multicomponent implementation strategies are most useful and should be recommended in

Figure 2. Adjusted mean net reduction in BP associated with implementation strategies.



Mean net reductions were estimated using generalized estimating equations and adjusted for sex, age, baseline systolic (or diastolic) BP, trial duration, type of control group, and all other intervention strategies. Boxes are weighted by sample size. BP = blood pressure.

clinical practice and public health policy for hypertension control in communities.

Two previous meta-analyses of intervention strategies for BP reduction reviewed studies published up to 2003 and 2008 and showed that some implementation strategies, including team-based care and home BP monitoring, improved hypertension control compared with the control group (6, 7). Between February 2008 and September 2017 (MEDLINE search), meta-analyses for some individual strategies have been published (8, 22-25), but none that included all implementation strategies for BP control. Our study expanded on the previous meta-analyses by including many trials published since 2008. Moreover, our meta-analysis is the first to our knowledge to directly compare the effect of various implementation strategies on BP control after adjustment for key trial and participant characteristics. Generalized estimating equations using studies as clusters allowed intervention strategies to be compared while preserving individual study randomization.

Team-based care strategies, in which hypertension management responsibilities are shared among team members (nurses, pharmacists, medical assistants, or

community health workers) in addition to primary care physicians, were found to be most effective for BP control in our analyses. Santschi and colleagues reported that compared with usual care, pharmacist-led interventions showed greater reductions in systolic BP (change, -7.6 mm Hg [CI, -6.3 to -9.0 mm Hg]) and diastolic BP (-3.9 mm Hg [CI, -2.8 to -5.1 mm Hg]) in a meta-analysis of randomized controlled trials (22). In addition, Clark and colleagues reported that compared with usual care, nurse-led interventions with a nurse prescribing medications showed greater reductions in systolic BP (change, -8.9 mm Hg [CI, -5.3 to -12.5 mm Hg]) and diastolic BP (-4.0 mm Hg [CI, -2.7 to -5.3 mm Hg]) in a meta-analysis of 4 trials (23). Team-based care is particularly effective because it frees physicians to focus on urgent and complex cases while allowing patient-centered care that is tailored, frequent, and collaborative (26). Taken together, our findings and those from previous research provide strong evidence that team-based care is effective for BP control in hypertensive patients (24, 26, 27).

Among the included trials reporting positive findings, pharmacist-led team-based care often included

provider training, health coaching, and home BP monitoring in addition to task-sharing by pharmacists (28–33). Likewise, nurse-led team-based care usually included health coaching and home BP monitoring (34, 35). Team-based strategies led by community health workers typically included health coaching, home BP monitoring, and provider training (36). Multilevel implementation strategies without team-based care commonly consisted of health coaching, home BP monitoring, and provider training (37, 38). In some multilevel intervention trials, pharmacists did medication titration, health coaching, and home BP monitoring independent of the primary care team (39). Multilevel, multi-component strategies combining team-based care, health coaching, home BP monitoring, and provider training are clearly the most effective for BP control among patients with hypertension.

Our findings also showed that health coaching and home BP monitoring alone resulted in significant BP reduction among hypertensive patients. Health coaching is effective for behavioral change, including lifestyle modification and antihypertensive medication adherence (40). Especially when combined with home BP monitoring, it may therefore be an effective alternative for BP control in settings where multilevel strategies are not feasible because resources are limited. Future studies testing whether health coaching plus home BP monitoring provides a cost-effective approach could help inform BP control strategies in populations with health disparities.

A few trials tested strategies targeting only physician-level barriers to hypertension control (that is, provider training, audit and feedback, and electronic decision-support systems), and only the electronic decision-support systems strategy was significantly associated with BP reduction after multivariate adjustment, despite contributing only 4 trials to the analysis. Although the effects of provider-level strategies were limited on their own, they were commonly part of multilevel, multicomponent strategies shown to be effective. For example, Veterans Affairs medical centers and Kaiser Permanente have seen improvements in BP control among their patients after adopting multilevel strategies that included audit and feedback and electronic decision-support systems (41–43). Because of the limited number of trials available in this category, the positive findings for electronic decision-support systems after adjustment, and the effective use of these interventions as part of multicomponent interventions, future clinical trials are needed to test additional physician-targeted implementation strategies (such as physician-patient communication), which could improve patient engagement and adherence to hypertension treatment (44, 45).

Our analyses have several limitations. First, despite the inclusion of many trials in this meta-analysis, some implementation strategies did not have enough studies. For example, provider training, audit and feedback, electronic decision-support systems, and multilevel strategies without team-based care all had fewer than

Figure 3. Comparison of systolic and diastolic BP reduction among implementation strategies.

		Adjusted Difference in Mean Systolic BP Reduction (95% CI), mm Hg							
		Team-based care with titration by nonphysician	Team-based care with titration by physician	Multilevel strategy without team-based care	Health coaching	Electronic decision-support system	Home BP monitoring	Provider training	Audit and feedback
Adjusted Difference in Mean Diastolic BP Reduction (95% CI), mm Hg		-0.88 (-3.58 to 1.80)	-2.05 (-5.53 to 1.43)	-3.22 (-5.72 to -0.72)†	-3.35 (-5.75 to -0.96)‡	-4.41 (-6.50 to -2.32)§	-5.63 (-8.57 to -2.69)§	-6.29 (-8.52 to -4.05)§	
		-0.48 (-1.95 to 0.99)	-1.16 (-4.73 to 2.41)	-2.34 (-4.86 to 0.18)	-2.47 (-4.42 to -0.52)†	-3.52 (-5.56 to -1.49)§	-4.74 (-7.66 to -1.83)‡	-5.40 (-7.71 to -3.09)§	
		-0.29 (-2.84 to 2.26)	0.19 (-2.55 to 2.93)	-1.17 (-4.47 to 2.13)	-1.30 (-4.60 to 1.99)	-2.36 (-5.48 to 0.76)	-3.58 (-8.02 to 0.86)	-4.24 (-6.26 to -2.22)§	
		-1.08 (-2.29 to 0.14)	-0.60 (-2.03 to 0.84)	-0.79 (-3.26 to 1.69)	-0.13 (-2.28 to 2.02)	-1.19 (-3.00 to 0.63)	-2.41 (-4.71 to -0.11)†	-3.06 (-5.04 to -1.09)‡	
		-1.68 (-2.64 to -0.72)§	-1.19 (-2.09 to -0.30)‡	-1.39 (-3.85 to 1.08)	-0.60 (-1.48 to 0.28)	-1.06 (-2.78 to 0.66)	-2.28 (-4.93 to 0.38)	-2.93 (-4.81 to -1.06)‡	
		-1.60 (-2.71 to -0.48)‡	-1.12 (-2.50 to 0.27)	-1.31 (-3.87 to 1.25)	-0.52 (-1.62 to 0.58)	0.08 (-0.76 to 0.91)	-1.22 (-3.61 to 1.18)	-1.88 (-3.48 to -0.28)†	
		-2.12 (-3.57 to -0.68)‡	-1.64 (-3.28 to 0.00)	-1.83 (-4.61 to 0.95)	-1.04 (-2.35 to 0.27)	-0.44 (-1.65 to 0.77)	-0.52 (-1.90 to 0.85)	-0.66 (-3.60 to 2.28)	
		-2.52 (-3.54 to -1.51)§	-2.04 (-3.40 to -0.67)‡	-2.23 (-4.21 to -0.25)†	-1.44 (-2.36 to -0.53)‡	-0.84 (-1.57 to -0.12)†	-0.92 (-1.92 to 0.07)	-0.40 (-1.73 to 0.93)	

Adjusted for sex, age, baseline systolic BP (or diastolic BP), trial duration, and type of control group. Strategies are ordered by rankings of net reduction in mean systolic BP. Differences in BP reduction are located in the cell in common between the row- and column-defining implementation strategies. For the mean difference in systolic BP, the difference is the row strategy BP reduction minus the column strategy BP reduction. For the mean difference in diastolic BP, the difference is the column strategy minus the row strategy BP reduction. For example, the differences in mean systolic and diastolic BP reduction between team-based care with titration by a nonphysician and health coaching are -3.22 mm Hg (95% CI, -5.72 to -0.72 mm Hg) and -1.08 mm Hg (CI, -2.29 to 0.14 mm Hg), respectively. BP = blood pressure.

† P < 0.050.
‡ P < 0.010.
§ P < 0.001.

10 comparisons. Second, few multilevel intervention trials addressed system-level barriers (that is, lack of performance standards, leadership commitment, and reimbursement of physician-patient health coaching). These factors could have a substantial effect on BP control among patients with hypertension and should be evaluated in future studies. Third, few clinical trials tested the effect of implementation strategies for free or low-cost medications or financial incentives on BP control. They did not meet our inclusion criteria and were not included in this meta-analysis. Fourth, an insufficient number of studies were done in subgroups of interest, such as patients with diabetes or chronic kidney disease, to estimate associations within these groups. Fifth, searches of ClinicalTrials.gov identified a few trials with data completion dates more than 2 years ago that were not yet published. Finally, only 20% of included trials were from low- and middle-income countries, where uncontrolled hypertension is a serious public health problem. However, many were done in low-income, ethnic minority, and other populations with health disparities in the United States and other high-income countries. Furthermore, 16 studies funded by the Global Alliance for Chronic Diseases will partially fill this knowledge gap (36, 46).

To translate these findings into routine clinical practice through scale-up and dissemination at the health care system level, additional research is needed on cost-effectiveness and sustainability of implementation strategies for BP control (20, 47). Although some trials included in this meta-analysis did cost-effectiveness analyses (30, 32, 33, 36, 37, 48–52), data were insufficient for a systematic review. In addition, no long-term follow-up studies after trial completion assessed intervention sustainability.

In conclusion, multilevel, multicomponent implementation strategies with and without team-based care are most effective for BP control among patients with hypertension. Health coaching and home BP monitoring that target barriers at the patient level are also effective. These strategies should be disseminated and scaled up in clinical practices and public health programs to improve hypertension control in communities.

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