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REVIEW ARTICLE

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Effect and efficacy of lifestyle interventions as secondary prevention

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Introduction: Improvements in health behaviour are often recommended as part of secondary prevention in patients with stroke and transient ischaemic attack. However, there is a lack of knowledge as to how this is applied in clinical practice.

Aim: In this systematic review and meta-analysis, we examined the effect of counselling or educational intervention directed at individual or multiple behavioural risk factors on blood pressure and other reported outcomes.

Methods: PubMed, Embase, PsycInfo, CINAHL, Scopus and Web of Science were systematically searched. Meta-analyses were conducted on all outcome measures if appropriate. A qualitative analysis of the content of the interventions was conducted to review which elements the interventions consisted of.

Results: Twenty-nine randomized controlled trials were identified. Fourteen reported effects on systolic blood pressure, and pooled results showed a significant beneficial effect (n = 2,222; −3.85 mmHg [95%CI −6.43; −1.28]). The effect was greatest in the four interventions which included supervised training (n = 174; −9.83 mmHg [95%CI −16.56; −3.09]).

Conclusion: Modifying health behaviour in stroke survivors might have a moderate beneficial effect on blood pressure, especially if the intervention includes supervised physical training.

KEYWORDS

adherence, exercise, health behaviour, health counselling, physical activity, smoking, stroke, transient ischaemic attack

1 | BACKGROUND

Stroke is one of the leading causes for morbidity, disability and death worldwide. The risk of recurrent stroke is 12%-13% within the first year of the index stroke and 4%-5% in the following year.[1] Recurrent stroke is an independent risk factor for loss of function, institutionalization and death.[2] Secondary and tertiary prevention are therefore important parts of stroke management.

The pathological mechanisms behind vascular diseases are complex. It is evident that hypertension and other modifiable risk factors, such as smoking, physical inactivity, unhealthy diet and abdominal obesity, are all contributors to the risk of both ischaemic and haemorrhagic stroke.[3,4]

Improved health behaviour is therefore widely recommended as part of the secondary prevention,[5] yet our knowledge as to how these recommendations are applied effectively in clinical practice is sparse.

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The results of previous systematic reviews have been inconsistent. In a meta-analysis of 42 randomized controlled trials (RCT) of stroke service-based secondary prevention interventions, Bridgwood et al[6] found no significant difference in any outcome measures, although there was a tendency towards a greater effect of organizational changes compared to educational/behavioural interventions. In a meta-analysis of 20 RCTs of multi-modal behavioural interventions, Lawrence et al[7] found a significant effect on systolic and diastolic blood pressure, waist circumference, but not on blood lipids, blood glucose, body composition, smoking or fruit/vegetable consumption. In a meta-analysis of 22 RCTs of lifestyle interventions in patients with stroke or transient ischaemic attacks (TIA), Deijle et al[8] found a significant effect on systolic blood pressure, but not on diastolic blood pressure, cardiovascular events or blood lipids. A greater effect on systolic blood pressure was found in interventions which included aerobic exercise training and with a duration > 4 months.

Most behavioural interventions are multi-modal and complex. The varying results in previous studies might imply that some elements contribute more to the effect than others. We therefore need to examine the content of the interventions in order to identify the most effective approaches to behavioural change after stroke or TIA.

2 | OBJECTIVES

The primary objective was to examine the effect of single- or multimodal counselling or educational intervention directed at individual

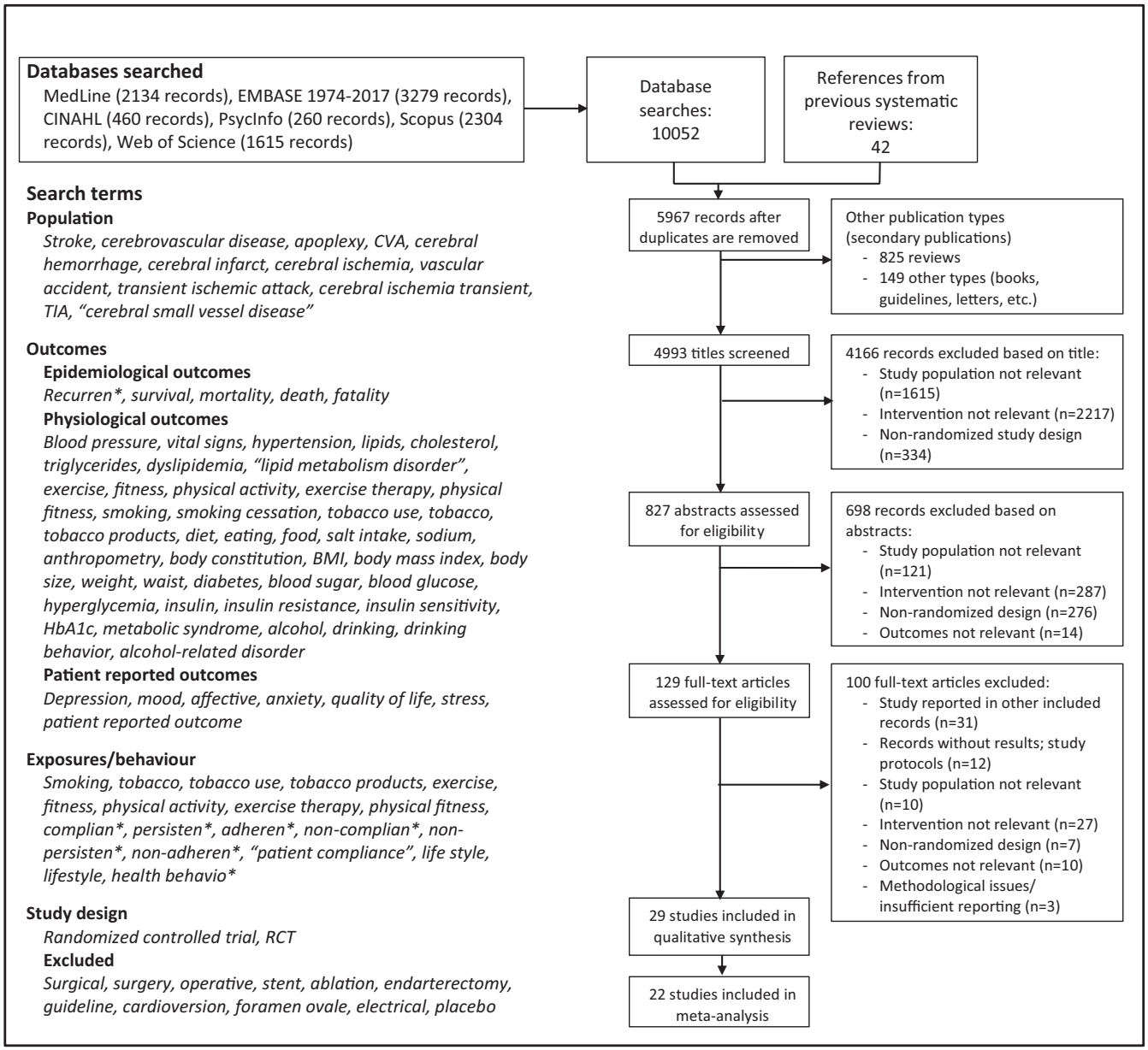


FIGURE 1 Search strategy and selection of reports

TABLE 1 Characteristics of the study participants

Study (Country)	Number of participants				Age (y)	Female (%)	Included diagnoses	Primary inclusion criteria
	Screened	Eligible	Randomized	Completed				
Adie 2010 (UK)[36]	*NA*	*NA*	56	56	72.5 ± 8.9	50%	TIA (43%)/minor stroke (57%)	Age ≥ 18 y, hypertension, living at home
Allen 2002 (USA)[20]	417	238	93	73	70.5 ± 11.0	56%	IS (70.5%), TIA (29.5%)	Admitted from home, Rankin scale ≤ 3
Allen 2009 (USA)[37]	*NA*	*NA*	380	319	65 ± 14.3	50%	IS (NIHSS ≥ 1)	Discharge to home
Barker-Collo 2015 (NZ)[21]	3487	*NA*	386	331	*NA*	*NA*	Stroke *(not specified)*	Age ≥ 16 y
Boss 2014 (NL)[38]	*NA*	*NA*	20	18	63 y (range 46-78)	30%	TIA (40%), minor stroke (60%) (NIHSS < 4)	Age ≥ 18 y, able to walk independently
Boysen 2009 (DK)[39]	2000	*NA*	314	276	69.7 y (IQR 60-78)	44%	IS	Age ≥ 40 y, able to walk unassisted
Brunner Frandsen 2012 (DK)[40]	*NA*	*NA*	94	88	53% 50-65 y/ 26% >65 y	42%	IS & TIA	Age < 76 y, current daily smoker
Chanruengvanich 2006 (TH)[41]	*NA*	*NA*	72	62	63 ± 7.2	68%	TIA & minor stroke	Age > 45 y, able to exercise safely
Cheng 2018 (USA)[22]	1476	*NA*	404	404	57.4 y	40%	IS & TIA	SBP ≥ 120 mmHg, English or Spanish speaker
Damush 2011 (USA)[23]	1017	*NA*	63	63	65.6 ± 10.5	2%	IS	Age ≥ 18 y, English speaker
English 2016 (AU)[42]	*NA*	72	33	33	67.3 ± 13.0	33%	IS (76%) & ICH (24%)	Living at home
Evans-Hudnall 2014 (USA)[43]	210	*NA*	60	52	53.0 ± 10.7	39%	IS & TIA	Age ≥ 18 y, discharged home
Faulkner 2014 (NZ)[24]	167	97	60	51	68.5 ± 10.4	48%	TIA/minor stroke	First ever TIA/ stroke
Flemming 2013 (USA)[44]	1083	110	41	36	71 ± 11.0	41%	Atherosclerotic IS (54%) & TIA (46%)	Age ≥ 55 y, at least one uncontrolled risk factor
Gillham 2010 (UK)[25]	91	*NA*	52	50	68.3 ± 12.5	*NA*	First time IS & TIA	First time stroke/ TIA
Holzemer 2011 (USA)[45]	274	*NA*	52	27	62.4 ± 12.0	*NA*	IS & TIA	Age ≥ 18 y
Hornnes 2009 (DK)[26]	917	470	349	303	69.3 ± 12.9	49%	IS, ICH, TIA	Relevant diagnosis
Irewall 2015 (SE)[27]	1102	*NA*	537	484	70.8 ± 10.8	43%	IS (60%), ICH (4%), TIA (37%)	Able to participate
Joubert 2006 (AU)[28]	421	224	97	80	66.5 ± 13.7	50%	IS, ICH, TIA	Age ≥ 20 y, discharged to GP management
Joubert 2009 (AU)[46]	*NA*	*NA*	233	186	65.9 ± 13.4	45%	IS, ICH, TIA	Age ≥ 20 y, discharged to GP management
Kim 2013 (KR)[29]	278	*NA*	36	34	65.7 ± 7.5	36%	IS	Living at home, access to the internet

(Continues)

TABLE 1 (Continued)

Study (Country)	Number of participants				Age (y)	Female (%)	Included diagnoses	Primary inclusion criteria
	Screened	Eligible	Randomized	Completed				
Kirk 2014 (UK)[30]	70	*NA*	24	24	67.2 ± 9.4	21%	Minor stroke (25%), TIA (75%)	Fit for exercise
Kono 2013 (JP)[31]	159	134	70	68	63.5 ± 9.4	31%	Minor stroke (non-cardioembolic)	Discharged home, mRS 0-1
McManus 2009 (UK)[47]	1804	*NA*	205	102	65.1 ± 9.3	48%	Stroke (63%), TIA (27%), amaurosis fugax (4%), TGA (1%), RAO (2%), MID (3%)	At least one relevant risk factor
Moren 2016 (SE)[32]	127	*NA*	88	56	71.1 ± 8.7	53%	TIA	Medically stable, able to communicate in Swedish
Nir 2004 (IL)[48]	*NA*	*NA*	155	*NA*	73.1 ± 7.3	48%	Stroke *(not specified)*	Relevant diagnosis
Peng 2014 (CN)[49]	*NA*	*NA*	3821	3330	60.9 ± 11.6	32%	IS & TIA	Age ≥ 18 y, clinically stable, habitually independent in ADL
Wan 2016 (CN)[33]	186	103	91	80	59.7 ± 12.4	29%	IS	Age > 35 y, habitually independent in ADL
Wolfe 2010 (UK)[34]	941	*NA*	523	487	21% >80 y	47%	IS (85.7%)	Registered with a study GP

Abbreviations: ADL, Activity of Daily Living; GP, General practitioner; ICH, Intracerebral haemorrhage; IS, Ischaemic stroke; MID, Multi-Infarct Disease; mRS, Modified Rankin Scale; NIHSS, NIH Stroke Scale; RAO, Retinal Artery Occlusion; TIA, Transient Ischaemic Attacks.

or multiple lifestyle risk factors on blood pressure and hypertension in patients with stroke or TIA.

The secondary objectives were to examine the effects on other outcomes, including recurrence of stroke and TIA, biochemistry, and health behaviour, and to examine the content and methodology of previous interventional studies.

3 | METHODS

A systematic review of RCTs of counselling and educational interventions with stroke patients was conducted in accordance with the PRISMA statement.[9]

3.1 | Search method and eligibility criteria

Database searches were made in PubMed, Embase, PsycInfo, CINAHL, Scopus and Web of Science (see Figure 1); citations in previous articles were screened for relevant references. The search strategy was designed in collaboration with an experienced research librarian. Studies were included if they were RCTs of counselling or educational interventions (individual or group) targeting single or multiple lifestyle risk factors in hospital, outpatient or community settings, including adult (≥18 years) patients with first or recurrent stroke or TIA. The primary outcome of interest was systolic blood pressure; secondary outcomes included stroke recurrence, vascular events, mortality, physiological outcomes (eg blood pressure, blood lipids, body composition), health behaviour (eg smoking habits, alcohol consumption, diet, physical activity) or patient-reported outcomes.

Studies were excluded if they were not randomized and if the intervention was a pharmacological treatment (eg nicotine replacement) or focused on neurological rehabilitation of physical function or everyday activity.

Titles were screened, and duplicates and non-original publications (reviews, editorials, guidelines etc) were excluded by JL. Titles and abstracts were assessed by JL in the remaining references excluding studies that clearly included patients without cerebrovascular diseases, if the intervention was not relevant, if the design was

non-randomized, or no relevant outcomes were reported. In case information in the abstract was insufficient for exclusion the full text article was assessed. Full-text assessment was performed by three reviewers independently (JL, MML, TM), and discrepancies were discussed until consensus was achieved.

Data extraction was done by two reviewers independently using a standardized extraction form. Extracted data included details of the study design, population, intervention (timing, setting, procedures, dosage, mode of delivery), comparator intervention and relevant outcomes.

Methodological quality and risk of bias were assessed by two reviewers independently using the Cochrane Risk of Bias tool (RoB),[10] and discrepancies were resolved by discussion. If agreement was not meet, a third reviewer was consulted.

3.2 | Qualitative analysis of the content of the intervention

A qualitative analysis of the reported interventions was conducted with the aim of gaining an overview of how the interventions attempted to modify the behaviour of the participants. Relevant parts of the articles, explaining the procedures of the interventions, were evaluated line by line and coded with explanatory expressions. Summaries of the interventions were constructed based on the codes, simple enough to give an overview but with enough details to be loyal to the original reports. The summaries were used to identify the main elements of the approaches and the targets of the intervention.

Each element of the intervention was categorized using the World Health Organization's ICF-model as a framework, categorizing the elements according to *body function & anatomy*, *activity*, *participation*, *personal factors* and *environmental factors*.

3.3 | Quantitative meta-analyses

Meta-analyses were performed to estimate the overall treatment effect on all outcome measures reported in a comparable manner in at least two studies using Review Manager 5.3.[11] As a result of variance in study populations, we used random effects models in all meta-analyses.[12] For continuous variables, we used mean differences if all studies reported the same scale of measurement; or standardized mean difference if the studies reported the same outcome with different measures or scales. For dichotomous variables, we used the Mantel-Haenszel method for the risk ratios with 95% CI. All tests were two-sided, and *P*-values < .05 were considered statistically significant.

Subgroup analyses were based on standardized mean differences in systolic blood pressure as it was the most commonly reported outcome measure. Kendall's rank correlation coefficient (Kendall's tau) was used to quantify the associations between study characteristics and standardized mean differences and completion rates, respectively.

4 | RESULTS

We identified 10 052 records through database searches and additionally 42 through citations in previous systematic reviews.[7,8,13] Of the 10 094 records, 4127 were duplicates, 825 were reviews, and 149 were other publication types (eg guidelines or editorials). The remaining 4993 records were screened for eligibility based on title and abstract, and 4864 records were excluded. All 129 remaining records were full text assessed by JL, MML and TM, and inclusion/exclusion

TABLE 2 Content of the interventions

Targets of the intervention
Looking after one's health (16 studies)
Modification of behaviour, such as smoking, alcohol use, diet, or adherence to medication[24-26,30,31,33,34,36,40,41,43-45,47-49]
Physical activity
Counselling in physical activity (8 studies)[24,30-32,38,39,41,42]
Supervised training (aerobic and strength training) (4 studies)[24,30,31,38]
Managing stress & anxiety (5 studies)[23,24,30,41,43]
Activities of daily living (2 studies)
Planning or training of everyday activities[23,48]
Knowledge about stroke and health
Knowledge about stroke, risk factors, lifestyle, or medication (21 studies)[20,22-26,29-31,34,36,37,39,41,43-47,49]
Increasing cognitive skills, such as motivation and self-management (10 studies)[21-25,32,33,36,42,44]
Specific skills such as goal setting or planning behaviour (7 studies)[23,33,41-44,48]
Approaches of the intervention
Communicating knowledge
Written material (4 studies)[36,43,45,47]
Computer-based patient education (4 studies)[29,31,34,49]
Patient education/group education (12 studies)[22,24,25,29-31,37,41,44,46,47,49]
Counselling
Counselling in health behaviour and behavioural change (20 studies[22,26,27,31,33,38-40,47,49]; of which 10 studies used a specific technic or theoretical framework[21,23,25,32,36,41-43,45,48])
Medication
Nicotine substitution (1 study) [40]
Self-monitoring
Monitoring of behaviour, physical activity, blood pressure (4 studies)[22,26,41,42]
Evaluation of needs
Evaluation of the participants' needs (6 studies)[20,27,28,37,46,48]
Support
Professional support (22 studies)[20-23,25,27,28,32,33,36-48]
Peer support from other patients (4 studies)[22-24,38]
Social support from family, friends or relatives (6 studies)[20,37,41,43,46,48]

TABLE 3 Characteristics of the interventions

Study (Country)	Time of recruitment	Length of intervention	Time of follow-up	Main elements of the intervention	Theoretical framework	Targets
Adie 2010 (UK)	<1 mo	4 mo	6 mo	Individual counselling; written educational material; telephone follow-up	Social-cognitive theory	Medication, blood pressure, lipids, smoking, diet, exercise
Allen 2002 (USA)	Before discharge	3 mo	3 mo	Home visits; evaluation of need for care and support; plan for primary physician		Health, psycho social well-being
Allen 2009 (USA)	Before discharge	6 mo	6 mo	Home visits; evaluation of need for rehabilitation, care and support; plan for primary physician	The chronic illness model	
Barker-Collo 2015 (NZ)	28 d	9 mo	12 mo	Individual counselling; support in goal setting; telephone follow-up	Motivational interviewing	
Boss 2014 (NL)	<1 wk	8 wk	6 + 12 mo	Supervised exercise; individual counselling	Motivational interviewing	Physical activity
Boysen 2009 (DK)	<90 d	24 mo	24 mo	Individual counselling; repeated encouragement for physical activity; inpatient follow-up		Physical activity
Brunner Frandsen 2012 (DK)	*Unclear*	4 mo	6 mo	Individual counselling; telephone follow-up; nicotine substitution		Smoking
Chanruengvanich 2006 (TH)	*Unclear*	12 wk	12 wk	Individual counselling; patient education; self-regulation training; home visits; telephone follow-up	Self-regulation theory (Bandura, Pender)	Stroke knowledge, diet, weight, stress management
Cheng 2018 (USA)	<90 d	12 mo	12 mo	Group & individual counselling; telephone follow-up; blood pressure monitoring	The chronic care model	Blood pressure, medication adherence, smoking, physical activity, depression
Damush 2011 (USA)	<1 mo	12 wk	6 mo	Patient education; individual counselling in goal setting; telephone or face-to-face follow-up	Self-efficacy theory (Bandura)	Risk factor management
English 2016 (AU)	>6 mo	7 wk	7 wk	Individual counselling; monitoring of physical activity; telephone follow-up	Motivational interviewing	Physical activity
Evans-Hudnall 2014 (USA)	Before discharge	4 wk	4 wk	Individual counselling; training in self-management skills; written material; out-patient follow-up		Risk factor management
Faulkner 2014 (NZ)	<2 wk	8 wk	12 mo	Supervised exercise; individual counselling; patient education; group exercise	The health belief model	Vascular risk factor control, diet, blood pressure, medication adherence, stress management
Flemming 2013 (USA)	<12 wk	1 y	1 y	Patient education; individual counselling; summary to the primary physician; out-patient and telephone follow-up	Motivational interviewing	Diet, exercise

(Continues)

TABLE 3 (Continued)

Study (Country)	Time of recruitment	Length of intervention	Time of follow-up	Main elements of the intervention	Theoretical framework	Targets
Gillham 2010 (UK)	*Unclear*	3 mo	3 mo	Individual counselling; patient education; face-to-face or telephone follow-up	Motivational interviewing, the transtheoretical model	Risk factor control
Holzemer 2011 (USA)	Before discharge	3 wk	3 mo	Individual counselling; face-to-face and telephone follow-up	Self-determination theory	Smoking, diet, exercise, stroke knowledge, medication
Hornnes 2009 (DK)	*Unclear*	10 mo	1 y	Home visits; individual counselling; monitoring of blood pressure		Medication adherence, lifestyle factors
Irewall 2015 (SE)	1 mo after discharge	12 mo	12 mo	Individual counselling; evaluation of preventive treatment; telephone follow-up		Medication, lifestyle factors
Joubert 2006 (AU)	Before discharge	12 mo	12 mo	Shared care between hospital and primary physician; regular outpatient follow-up; telephone reminders		Physical activity, smoking, alcohol, medication, depression, blood pressure, lipids, risk factors
Joubert 2009 (AU)	Before discharge	12 mo	12 mo	Shared care between hospital and primary physician; regular outpatient follow-up; telephone reminders		Physical activity, smoking, alcohol, medication, depression, blood pressure, lipids, risk factors
Kim 2013 (KR)	1-12 mo	9 wk	3 mo	Web-based patient education		
Kirk 2014 (UK)	<1 mo	6 wk	6 mo	Supervised exercise; group education		Physical activity, medication, alcohol, exercise, diet, stroke knowledge, well being
Kono 2013 (JP)	Before discharge	24 wk	3.3 y	Supervised exercise; computer-based patient education		Exercise, salt intake
McManus 2009 (UK)	<3 mo	3 mo	3.6 y	Individual counselling; written material; patient education; out-patient follow-up		Lifestyle, medication, stroke knowledge
Moren 2016 (SE)	<2 wk	Unclear	6 mo	Individual counselling; exercise prescription; outpatient follow-up	Motivational interviewing	Physical activity
Nir 2004 (IL)	<13 d	12 wk	3 + 6 mo	Individual counselling; evaluation of self-care agency; regular home visits	The self-care model (Orem)	Self-care (incl. lifestyle management)
Peng 2014 (CN)	<30 d	Unclear	12 mo	Implementation of standard guidelines; individual counselling; web-based patient education		Smoking, diet, exercise, stroke knowledge
Wan 2016 (CN)	Before discharge	3 mo	6 mo	Individual counselling; training of self-management skills; telephone follow-up		Self-management, health behaviour
Wolfe 2010 (UK)	<6 mo	6 mo	12 mo	Algorithm-based prevention plan sent by mail; enhanced corporation with the primary physician		

was based on agreement between all three authors. Ultimately, 29 studies were included in the review (Figure 1 and Table 1).

4.1 | Description of the studies

4.1.1 | Targets of the intervention

Table 2 provides an overview of study rationales and contents of the interventions. In 16 studies, the aim was to enable the participants to take care of their own health, for example facilitate modification of lifestyle factors or adherence to preventive medication. In eight studies, the primary aim was to increase the participants' level of physical activity, and in additionally four studies physical activity was a minor part of the counselling. Four studies included supervised strength and aerobic exercise. Studies including physical activity also included other elements, such as patient education or health counselling (Table 2).

Counselling on anxiety or stress management was included in five studies, and two studies included counselling on participation in everyday life. Twenty-one studies aimed at providing participants with knowledge on their disease, lifestyle and vascular risk factors, or preventive medication. Nine studies aimed at providing participants with the cognitive skills and know how to modify their health behaviour, such as motivation, self-efficacy or self-management skills, while seven studies aimed at providing specific behavioural skills, such as self-monitoring, goal setting and planning behavioural change.

4.1.2 | Approaches of the interventions

Of the 21 studies, which included communication of knowledge, twelve included direct patient education, of which two were provided in a group setting. Four studies employed written educational material and four employed computer-based education. Patient counselling was part of the invention in twenty of the studies, and in ten of them, the counselling was based in a specific technic or theoretical framework. Most of them employed face-to-face counselling the first time, while the following sessions were provided either face-to-face or by telephone. Only one study provided nicotine substitution as a medical aid for smoking cessation.

Four studies used self-monitoring; either of physical activity, behaviour or blood pressure as a part of the intervention. Additionally, six studies had a regular assessment of the participants need for assistance or help.

Systematic support in relation to behavioural change or handling own health was a part of the intervention in 23 of the studies. In 22 of the studies, the support was provided by health professionals affiliated with the intervention team, in some cases in addition to other types of support, and in a single study, the support was provided by the participants' primary physician. Four studies employed group elements or activities to facilitate peer support from other participants, and in six studies, the participants' own social network was used as support, either by directly including the relatives in activities or by encouraging participants to seek support from friends and relatives.

In nine studies, the intervention or part of the intervention comprised changes to the organization of the care, for example home visits, implementation of clinical guidelines, or changes in the communication or collaboration between the hospital and the primary physicians.

4.1.3 | Time of recruitment and length of intervention

In eight studies, participants were recruited before hospital discharge; in ten studies, they were recruited within the first month; and in seven studies, they were recruited between 1-12 months after admission. In four studies, the time of recruitment was not reported (Table 3).

The length of the interventions varied between three weeks and two years, with seven studies in each interval of 3-12 weeks, 12-13 weeks, 13-52 weeks and ≥ 52 weeks. One study did not report the length of the intervention (Table 3).

4.2 | Risk of bias in included studies

Random allocation of participants was an inclusion criterium in this review, and all studies therefore stated that they were RCTs. In 25 of the studies, the method of randomization was clearly reported, but in three studies this was unclear, and in one study, the method was not adequately described. In 19 studies, measures to conceal future allocations were clearly stated; in nine studies, it was unclear, and in one study, measures were inadequate. None of the studies had adequate blinding of participants and personal delivering the intervention; although one study used "placebo" counselling, it was unclear if this blinding was effective as the personnel was not blinded. In 13 studies, the outcome assessments were adequately blinded, but in the remaining studies outcome measurements were performed by unblinded study personal. In 22 of the studies outcome, data were either complete or the incompleteness was clearly accounted for. In four studies, the completeness of data was unclear, and in three studies, outcome data were clearly missing and not adequately accounted for. In 24 of the studies, results of all outcome measures were clearly reported; in four studies, the results were not clearly reported in the secondary outcomes measures, and in one study, the results were reported in an ambiguous and unclear manner. Other potential biases were found: Five studies had baseline imbalances of

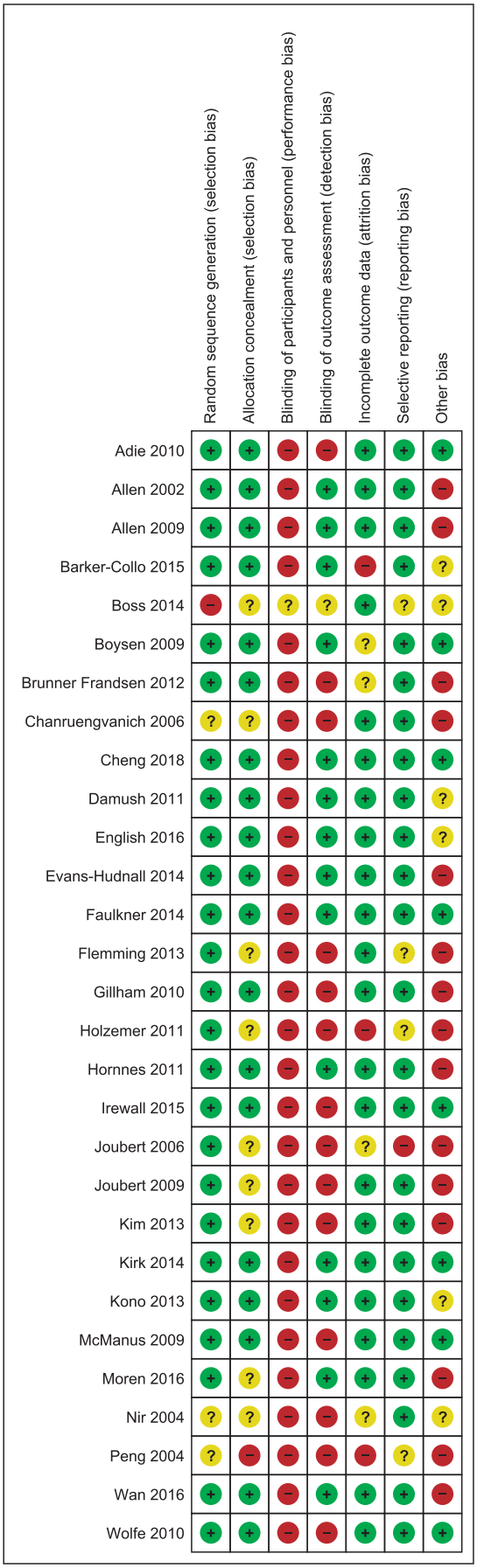


FIGURE 2 Risk of bias summary: the authors' judge-ments about each risk of bias item for each included study

potential clinical importance; two studies were stopped early without a clear reason stated; and several studies used block randomization with fixed block sizes potentially resulting in study personal being able to foresee the allocation of some participants before recruitment (Figure 2).

4.3 | Effects of interventions

The most frequent outcome reported were systolic and diastolic blood pressure, which were both significantly lower among participants in the interventions (Tables 4 and 5, Figure 3). Six studies reported the number of participants with a systolic blood pressure < 140 mmHg at follow-up. In a random effects model, the pooled risk ratio was 1.14 (95%CI 1.03-1.25), equivalent to a number needed to benefit of 13.83 (95%CI 8.25-42.84) (Table 5, Figure 3).

Sub-analyses of the studies reporting systolic blood pressure showed that both interventions with and without supervised physical training had a significant effect, but the effect was greater in interventions including supervised training (9.4 (95%CI 3.1-16.6) vs. 2.6 (95%CI 1.0-4.3) mmHg). The inter-strata differences were not significant for time of recruitment, length of the intervention, intervention based on a specific theoretical framework or family support (Table 5).

4.4 | Feasibility

The number of potential participants screened for eligibility was reported in 20 studies; of 16,227 screened, 3545 were included for participation. The inclusion rates ranged from 3.8%-69.3% with a weighted mean of 22% (95%CI 21.2-22.5). The rate of inclusion from the number of patients eligible for participation was reported in eight studies; out of 1448 eligible patients, 836 were included for participation. Inclusion rates ranged from 37.3%-88.3% with a weighted mean of 58% (95%CI 55.2-60.3). Completion rates of participants were reported in 28 studies. Of 8254 participants randomized, 7173 were retained until the final follow-up. Completion rates ranged from 49.8%-100% with a weighted mean of 86.9% (95%CI 86.2-87.6). Five studies achieved a completion rate of 100% (Table 1).

There was a significant correlation between completion rate and the timing of recruitment (tau = 0.377; $P = .018$), an indication of a more complete follow-up in studies with late recruitment. No significant correlation was found between completion rate and the length of the intervention (Kendall's tau = −0.07; $P = .63$) or time of follow-up (Kendall's tau = −0.08; $P = .59$), respectively.

TABLE 4 Outcomes reported in each study as either primary, secondary, or part of a compound outcome measure

	Adie 2010	Allen 2002	Allen 2009	Barker-Collo 2015	Boss 2014	Boysen 2009	Brunner Frandsen 2012	Chanruengvanich 2006	Cheng 2018	Damush 2011	English 2016	Evans-Hudnall 2014	Faulkner 2014
Vital signs	1			1	2			2	1				1
Biochemistry	2			1	2			2	2				2
Body composition	2												2
Adverse events		c	c		1	2					1		
Function	2	c	c			2		1					
Medication adherence					2				2	2		c	
Patient activation	2		c							2			
PROM	2	c	c	2				2		1	2	2	
Risk factors		c	c		2		1		2	2		1	
Physical activity	2					1			2		2		

Note: 1: Primary outcome, 2: secondary/tertiary outcomes, c: part of a composite outcome, PROM Patient Reported Outcome Measure.

5 | DISCUSSION

In this systematic review, we have explored the effects of health behaviour counselling and behavioural modification in patients with cerebrovascular diseases, and potential mediators of the effects. We found that, although the effect sizes are modest, supportive behavioural interventions might have some additional effect on systolic and diastolic blood pressure, the prevalence of hypertension and low-density lipoprotein in the blood compared to usual care. Including supervised exercise as part of the intervention seems to enhance the effect on systolic blood pressure. Besides that, we did not find any intervention elements capable of mediating the effectiveness.

Interventions were applied as add-on to usual care though the exact definitions and components of usual care seldom were elucidated. Consequently, we are not able to determine the causal mechanism and effects related to the intervention as the effect on, for example systolic blood pressure might have been mediated by enhanced adherence to medication rather than an isolated interventional effect.

We identified a range of different intervention element, which might all contribute to the overall effect of the interventions, but only blood pressure and total blood cholesterol were reported in ≥ 10 studies, and the lack of uniformly reported outcomes made it difficult to compare the effectiveness of the elements.

The inclusion and completion rates varied considerably between studies. Approximately half of eligible patients consented to participation, and the rate of successful follow-up ranged from 50%-100%. We found some association between the timing of recruitment and the completion rates, implying that participants are more likely to leave the study if they are recruited early. A reason for this might be that studies with late recruitment primarily approached patients in outpatient clinics, hence including patients who are more motivated to participate in additional treatment, if offered. In contrast, the time of recruitment did not seem to impact the effect of the intervention. Recruiting participants at an early stage is therefore feasible, but a higher rate of attrition should be expected.

Previous systematic reviews of behavioural interventions in patients with stroke have arrived at different conclusions. Deijle et al[8] found an effect on systolic blood pressure; Lawrence et al[7] found an effect on waist circumference, compliance to preventive medication, anxiety, cardiac events, and systolic and diastolic blood pressure, while Bridgwood et al[6] found no effect of behavioural interventions, but minor effects on TIA recurrence and cardiovascular risk scores in organizational changes. Different statistical approaches might explain the varying results: Lawrence et al used fixed effect models, assuming that "all studies were functionally identical," whereas Bridgwood et al used random effects models and Deijle et al different models depending on the degree of heterogeneity. We used random effects models in all our meta-analyses, assuming that clinical diversity in study populations, settings and interventions contributed to variation between studies,[12] and therefore, we did not find the assumptions of a fixed effect model to be justified.

In a systematic review of qualitative interviews with participants in secondary stroke prevention interventions and their family members, Lawrence et al[14] found that the participants experienced the interventions as meaningful. The informants highlighted the importance of support from health professionals, family and other stroke survivors, and that the interventions helped them acquire the knowledge and confidence needed to change behaviour.

Several interventions incorporated formal support from health professionals and informal support from peers and the participants' family and social network; patient education or other means of communicating knowledge; or counselling in goal setting,

Flemming 2013	Gillham 2010	Holzemer 2011	Hornnes 2009	Irewall 2015	Joubert 2006	Joubert 2009	Kim 2013	Kirk 2014	Kono 2013	McManus 2009	Moren 2016	Nir 2004	Peng 2014	Wan 2016	Wolfe 2010
2		2	1	1	2	1		2	2	2					
2		2		2	2	2	2	2	2	2					
2						2		2	2						
									1	2			2		
						2					2	2		2	
			2				2			2			2	2	2
	1		2	2		2	2					2		2	
2	2					2		2		2		2			
1	2	1		2	2	2	2	1	2	1		2	1	1	1
											1				

planning and confidence to change behaviour. Although the formal effects of the behavioural interventions might be vague, they could be meaningful and beneficial to the patients. Cognitive difficulties and fatigue are prevalent, even among patients with minor stroke[15] and for some having a stroke can be a considerable change in their life.[16]

Health behaviour is regulated by a multitude of biological, psychological and social factors.[17] Interventions to modify patient behaviour are therefore complex in nature. At this point, we are not able to recommend any specific approach to behavioural modification. The evidence supports that the interventions should include physical exercise. Previous research indicates that behavioural interventions should address several domains[8] and have multiple points of follow-up over at least a month.[8,18]

Several potential biases were identified in the included studies. All included studies were randomized, and most of them reported the procedure of randomization and measures to conceal the allocation of future participants. Blinding measure such as assessor blinding was only reported in less than half of the studies. Furthermore, the use of self-reported outcome measures might be sensitive to rapport between the participant and the assessor.

In five studies, the results were reported in an inadequate manner: one study only reported results from a model adjusted for baseline imbalances. The remaining four lacked necessary details, for example. standard deviations, confidence intervals or exact p-values. Such inaccuracies made it difficult to assess the risk of selective reporting.

To assess the risk of publication bias, we attempted to match preliminary reports to subsequent full-text publications. We identified 23 conference proceedings, 18 study protocols and one academic thesis that were potentially relevant. Of these records, 10 did not fulfil all inclusion criteria and 20 were matched to publications already included in the search results. Of the remaining 12 reports, we managed to find trial registrations on 10 studies. This might indicate that there is a risk of publication bias, although this was less than observed in other research areas.[19]

Generalizability of the results might be limited by selection bias. The number of patients screened for eligibility was reported in 19 studies, and the number of eligible patients was reported in nine studies (Table 1). The number of refusals was reported in 15 studies[20-34] with proportions ranging from 0.6%-66.7% (median 36.8%). Only two studies[25,30] reported reasons for refusal (eg lack of time, work commitments, transportation problems, lack of interest).

Although this review was designed to be comprehensive, there is still a risk that relevant research was not included. We searched several different medical databases and searched references of previous studies, and we attempted to find full publications of preliminary reports. Due to language restrains, we could only include literature in English and Scandinavian languages. We only included study results as they were reported in the full-text articles or supplementary material-supplementary material. But we did not attempt to obtain the original datasets or any missing data.

6 | CONCLUSIONS

Interventions to modify health behaviour in patients with stroke and prevent stroke recurrence might have a modest effect; but may still be meaningful to the patient. Recruiting patients at an early stage after stroke does not seem to affect the effect, but a higher attrition rate should be expected. Supervised exercise most likely enhances the effect of the interventions on blood pressure. However, we need further research on how other approaches, including health counselling, support from professionals, relatives, or peers, patient education, monitoring of behaviour and health status, and primary and secondary sector collaboration, could benefit the patients and their relatives.

TABLE 5 Results of the meta-analyses

Outcomes	Studies	Participants	Effect Estimate	*P*-value	I^2	Quality of evidence (GRADE)
Vital signs						
Systolic blood pressure (mmHg)[21,22,24,26-28,30,31,36,38,41,45-47]	14	2222	MD −3.85 [−6.43, −1.28]	.003**	53%	⊕⊕◯◯ Low[A, B]
Diastolic blood pressure (mmHg)[21,24,26,27,30,31,36,38,41,45-47]	12	1711	MD −1.60 [−3.09, −0.11]	.04*	40%	⊕⊕◯◯ Low[A, B]
SBP < 140 mmHg[22,27,28,37,38,46]	6	1546	RR 1.14 [1.03, 1.25]	.01**	23%	⊕⊕◯◯ Low[A, B]
Heart rate (Beats per minute)[24,41]	2	113	MD −2.87 [−6.34, 0.61]	.11	0%	⊕◯◯◯ Very low[A, B, C]
Biochemistry						
Total cholesterol[21,24,28-30,36,41,45-47]	10	925	MD −4.25 [−9.27, 1.22]	.13	9%	⊕⊕◯◯ Low[A, B]
HDL[21,24,30,31,41,45]	6	552	MD 1.64 [−1.12, 4.40]	.24	0%	⊕⊕◯◯ Low[A, B]
LDL[22,27,31,38,45]	5	1003	SMD −0.23 [−0.41, −0.05]	.01**	36%	⊕⊕◯◯ Low[A, B]
Triglycerides[29,45]	2	63	MD −14.71 [−43.07, 13.56]	.31	0%	⊕◯◯◯ Very low[A, B, C]
Fasting blood glucose[24,30]	2	75	MD −0.19 [−0.47, 0.10]	.20	0%	⊕◯◯◯ Very low[A, B, C]
HbA1c[31,47]	2	170	MD 0.12 [−0.46, 0.70]	.69	63%	⊕◯◯◯ Very low[A, B, C]
TC/HDL-ratio[24,30]	2	75	MD 0.0 [−0.49, 0.49]	.99	0%	⊕◯◯◯ Very low[A, B, C]
Body composition						
Body mass index[24,30,31,46]	4	329	MD −0.44 [−1.38, 0.51]	.37	0%	⊕◯◯◯ Very low[A, B, C]
Body weight [24,31,36,44]	4	175	MD −0.53 [−4.09, 3.03]	.77	0%	⊕◯◯◯ Very low[A, B, C]
Waist-hip ratio[24,30]	2	75	MD 0.0 [−0.04, 0.03]	.83	0%	⊕◯◯◯ Very low[A, B, C]
Adverse events						
Death (All causes)[20,24,37,39,49]	5	4668	RR 0.97 [0.58, 1.61]	.37	0%	⊕⊕◯◯ Low[A, B]
Recurrent stroke/TIA[20,39,47,49]	4	4330	RR 1.08 [0.78, 1.50]	.77	0%	⊕⊕◯◯ Low[A, B]
Adverse events (All)[20,31,37,39,42,47,49]	7	4813	RR 0.77 [0.56, 1.08]	.83	0%	⊕⊕◯◯ Low[A, B]
Functional level						
Modified Rankin scale[33,36,39,46]	4	606	SMD −0.26 [−0.58, 0.05]	.11	69%	⊕◯◯◯ Very low[A, B, C]
Patient reported outcomes						
Quality of life[21,23,30,46,47]	6	1546	SMD −0.09 [−0.53, 0.34]	.67	85%	⊕◯◯◯ Very low[A, B, D]
Sub-analyses	**Studies**	**Participants**	**Effect Estimate**	***P*-value†**	**I^2**	**References**
Time of recruitment	**11**	**1777**	**SBP (mmHg)**	.19	40%	⊕⊕◯◯ Low[A, B]
Early recruitment[31,38,45,46]	4	303	MD −0.54 [−0.98, −0.10]			
1-4 wk[21,24,27,30,36]	5	968	MD −0.16 [−0.31, −0.00]			
Late recruitment[22,47]	2	506	MD −0.03 [−0.40, 0.33]			
Length of the intervention	**13**	**2142**	**SBP (mmHg)**	.99	0%	⊕⊕◯◯ Low[A, B]
3-12 wk[24,30,38,41,45]	5	193	MD −0.21 [−0.55, 0.13]			
13-51 wk[21,26,31,36,47]	5	875	MD −0.19 [−0.51, 0.12]			
≥52 wk[22,27,46]	3	1074	MD −0.21 [−0.33, −0.09]			
Training interventions	**13**	**2142**	**SBP (mmHg)**	.04*	76%	⊕⊕◯◯ Low[A, B]
Training[24,30,31,38]	4	174	MD −9.83 [−16.56, −3.09]			
No training[21,22,26,27,36,41,45-47]	9	1968	MD −2.61 [−4.26, −0.96]			
Theory-based intervention	**13**	**2142**	**SBP (mmHg)**	.71	0%	⊕⊕◯◯ Low[A, B]
Theory based[21,22,24,36,38,41,45]	7	973	MD −3.99 [−6.36, −1.61]			
Non-theory based[26,27,30,31,46,47]	6	1169	MD −3.35 [−5.67, −1.03]			
Family support	**13**	**2142**	**SBP (mmHg)**	.74	0%	⊕⊕◯◯ Low[A, B]
Family/relative support[41,46]	2	248	MD −2.44 [−11.26, 6.38]			
No family support[21,22,24,26,27,30,31,36,38,45,47]	11	1894	MD −4.00 [−6.91, −1.10]			

Note: All meta-analyses are based on random effects models. Mean difference (MD) was used for parametrical outcomes when all studies reported the same unit; standardized mean difference (SMD) was used for parametrical outcomes when different units were reported; risk ratio (RR) was used for binominal outcome measures.

Abbreviations: HDL, High-density Lipoprotein; LDL, Low-density lipoprotein; MD, Mean difference; RR, Risk ratio; SBP, Systolic blood pressure; SMD, Standardized Mean Difference; TC/HDL ratio, Total cholesterol/HDL ratio.

*$P < .05$,

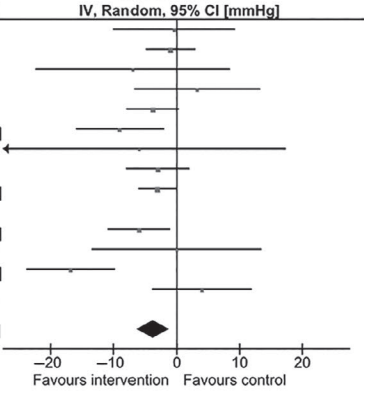
**$P < .01$,

†*P*-value for the overall effect of the model. GRADE [**50**]: A, Down-graded due to insufficient blinding, B, Down-graded due to indirectness caused by substantial different intervention, C, Down-graded because the analysis is based on limited data (few studies or few participants), D, Down-graded due to the use of indirect outcome measures.

(A) Systolic blood pressure (mmHg)

Study or Subgroup	Intervention Mean [mmHg]	SD [mmHg]	Total	Control Mean [mmHg]	SD [mmHg]	Total	Weight	Mean Difference IV, Random, 95% CI [mmHg]
Adie 2010	142	19.3	29	142.4	17.2	27	5.2%	−0.40 [−9.96, 9.16]
Barker-Collo 2015	137.41	18.79	172	138.42	17.69	172	12.7%	−1.01 [−4.87, 2.85]
Boss 2014	120	12.6	10	127	21.3	10	2.4%	−7.00 [−22.34, 8.34]
Chanruengvanich 2006	141.19	16.77	31	137.94	22.74	31	4.9%	3.25 [−6.70, 13.20]
Cheng 2018	132.3	20.5	204	136.1	20.8	200	12.4%	−3.80 [−7.83, 0.23]
Faulkner 2014	129	12	30	138	15	30	7.8%	−9.00 [−15.87, −2.13]
Holzemer 2011	138.7	31	12	144.7	30.2	15	1.1%	−6.00 [−29.26, 17.26]
Hornnes 2011	139.4	21.3	145	142.4	22.2	158	10.8%	−3.00 [−7.90, 1.90]
Irewall 2015	131.9	15.7	241	135	17.5	243	14.3%	−3.10 [−6.06, −0.14]
Joubert 2006	132.34	0	35	136.58	0	45		Not estimable
Joubert 2009	128.5	13.7	91	134.5	19.4	95	10.9%	−6.00 [−10.81, −1.19]
Kirk 2014	131.92	15.2	12	131.92	18.1	12	3.1%	0.00 [−13.37, 13.37]
Kono 2013	122.1	15.9	35	138.9	13.8	35	7.7%	−16.80 [−23.77, −9.83]
McManus 2009	143	18.8	49	139	21.6	53	6.7%	4.00 [−3.84, 11.84]
Total (95% CI)			**1096**			**1126**	**100.0%**	**−3.85 [−6.43, −1.28]**

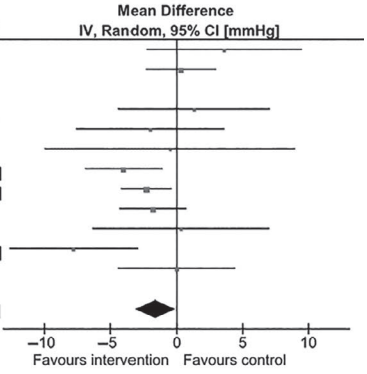
Heterogeneity: $\tau^2 = 9.78$; $\chi^2 = 25.36$, df = 12 ($P = 0.01$); $I^2 = 53\%$
Test for overall effect: $Z = 2.93$ ($P = 0.003$)



(B) Diastolic blood pressure (mmHg)

Study or Subgroup	Experimental Mean [mmHg]	SD [mmHg]	Total	Control Mean [mmHg]	SD [mmHg]	Total	Weight	Mean Difference IV, Random, 95% CI [mmHg]
Adie 2010	75.7	10.1	29	72.1	12.1	27	5.2%	3.60 [−2.26, 9.46]
Barker-Collo 2015	77.77	12.58	163	77.46	11.66	165	14.5%	0.31 [−2.32, 2.94]
Boss 2014	71	0	10	75	0	10		Not estimable
Chanruengvanich 2006	77.13	11.34	31	75.81	11.54	31	5.4%	1.32 [−4.38, 7.02]
Faulkner 2014	78	9	27	80	11	24	5.7%	−2.00 [−7.56, 3.56]
Holzemer 2011	78.4	13.6	12	78.9	10.8	15	2.3%	−0.50 [−9.94, 8.94]
Hornnes 2011	82	13.1	145	86	12.3	158	13.4%	−4.00 [−6.87, −1.13]
Irewall 2015	77.3	10.3	241	79.6	10.5	243	18.8%	−2.30 [−4.15, −0.45]
Joubert 2009	77.3	8.3	91	79.1	8.9	95	15.3%	−1.80 [−4.27, 0.67]
Kirk 2014	75	7.9	12	74.67	8.7	12	4.2%	0.33 [−6.32, 6.98]
Kono 2013	72.9	9.5	34	80.7	10.7	34	7.1%	−7.80 [−12.61, −2.99]
McManus 2009	74	10.3	49	74	12.2	53	8.1%	0.00 [−4.37, 4.37]
Total (95% CI)			**844**			**867**	**100.0%**	**−1.60 [−3.09, −0.11]**

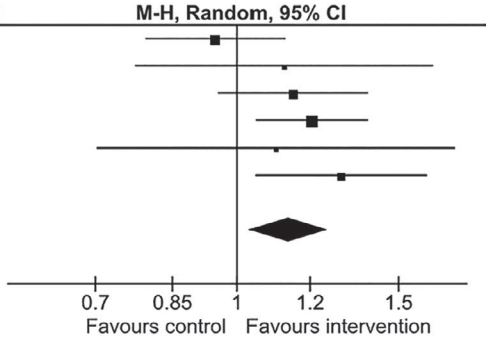
Heterogeneity: $\tau^2 = 2.18$; $\chi^2 = 16.53$, df = 10 ($P = 0.09$); $I^2 = 40\%$
Test for overall effect: $Z = 2.10$ ($P = 0.04$)



(C) Probability of reaching recommended systolic blood pressure (<140 mmHg)

Study or Subgroup	Intervention Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Allen 2009	106	190	112	190	22.4%	0.95 [0.80, 1.13]
Boss 2014	9	10	8	10	6.4%	1.13 [0.78, 1.63]
Cheng 2018	115	204	98	200	20.3%	1.15 [0.96, 1.39]
Irewall 2015	165	241	138	243	29.8%	1.21 [1.05, 1.39]
Joubert 2006	18	35	21	45	4.5%	1.10 [0.70, 1.73]
Joubert 2009	66	88	52	90	16.5%	1.30 [1.05, 1.61]
Total (95% CI)		**768**		**778**	**100.0%**	**1.14 [1.03, 1.25]**
Total events	479		429			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 6.51$, df = 5 ($P = 0.26$); $I^2 = 23\%$
Test for overall effect: $Z = 2.52$ ($P = 0.01$)



(D) Blood LDL

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Boss 2014	82	0	10	98.6	0	10		Not estimable
Cheng 2018	86.8	38.9	204	92.3	41.1	200	39.8%	−0.14 [−0.33, 0.06]
Holzemer 2011	81	21.8	12	100.9	55.8	15	5.2%	−0.44 [−1.21, 0.33]
Irewall 2015	88.8	27	241	100.39	34.7	243	42.8%	−0.37 [−0.55, −0.19]
Kono 2013	103.4	24.8	34	102.6	20.8	34	12.2%	0.03 [−0.44, 0.51]
Total (95% CI)			**501**			**502**	**100.0%**	**−0.23 [−0.41, −0.05]**

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 4.65$, df = 3 ($P = 0.20$); $I^2 = 36\%$
Test for overall effect: $Z = 2.51$ ($P = 0.01$)

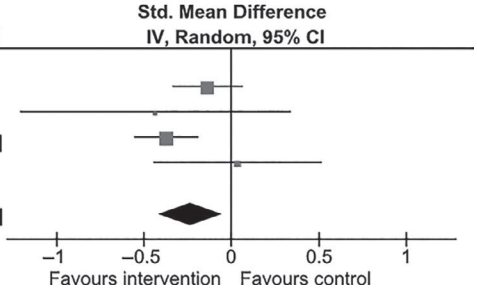


FIGURE 3 Forest plots (Only statistically significant analyses are shown)

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interests.

AUTHORS CONTRIBUTIONS

All contributors eligible for authorship are listed as authors according to the Danish Code of Conduct for Research Integrity.[35] JL designed the study and wrote the protocol in collaboration with TM, TC, SM, DO; JL performed the literature search; Study selection was performed by JL, TM, MML; Analysis was performed by JL; All authors participated in the assessment of quality and risk of bias, data extraction, and writing the report.

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REFERENCES

1. Olsen TS. Chapter 21 Stroke recurrence and prognosis after stroke. In: Fisher M., eds. *Handbook of clinical neurology*. Edinburgh; New York: Elsevier, pp. 407-421.
2. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Long-term disability after first-ever stroke and related prognostic factors in the Perth Community Stroke Study, 1989–1990. *Stroke*. 2002;33:1034-1040.
3. O'Donnell MJ, Xavier D, Liu L, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet (London, England)*. 2010;376:112-123.
4. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol*. 2016;15:913-924.
5. Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014;45:2160-2236.
6. Bridgwood B, Lager KE, Mistri AK, et al. Interventions for improving modifiable risk factor control in the secondary prevention of stroke. *Cochrane Database Syst Rev*. 2018;5:CD009103.
7. Lawrence M, Pringle J, Kerr S, et al. Multimodal secondary prevention behavioral interventions for TIA and stroke: a systematic review and meta-analysis. *PLoS One*. 2015;10:e0120902.
8. Deijle IA, Van Schaik SM, Van Wegen EEH, et al. Lifestyle interventions to prevent cardiovascular events after stroke and transient ischemic attack: systematic review and meta-analysis. *Stroke*. 2017;48:174-179.
9. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
10. Higgins JP, Altman DG, Sterne JA. Chapter 8: Assessing risk of bias in included studies. In: Green S, Higgins J, eds. *Cochrane Handbook for Systematic Reviews of Interventions*, ver 5.1.0. The Cochrane Collaboration, 2011. www.training.cochrane.org/handbook.
11. The Nordic Cochrane Centre. Review Manager (RevMan). https://community.cochrane.org/help/tools-and-software/revman-5
12. Borenstein M, Hedges LV, Higgins JPT, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1:97-111.
13. Lager KE, Mistri AK, Khunti K, et al. Interventions for improving modifiable risk factor control in the secondary prevention of stroke. *Cochrane Database System Rev*. 2014;CD0091(5):CD009103.
14. Lawrence M, Pringle J, Kerr S, et al. Stroke survivors' and family members' perspectives of multimodal lifestyle interventions for secondary prevention of stroke and transient ischemic attack: a qualitative review and meta-aggregation. *Disabil Rehabil*. 2016;38:11-21.
15. Fens M, van Heugten CM, Beusmans GHMI, et al. Not as transient: patients with transient ischaemic attack or minor stroke experience cognitive and communication problems; an exploratory study. *Eur J Gen Pract*. 2013;19:11-16.
16. Nordin Å, Sunnerhagen KS, Axelsson ÅB. Patients' expectations of coming home with Very Early Supported Discharge and home rehabilitation after stroke - an interview study. *BMC Neurol*. 2015;15:235.
17. Fishbein M, Ajzen I. *Predicting and changing behavior: the reasoned action approach*. New York: Psychology Press; 2009.
18. Rigotti NA, Clair C, Munafò MR, et al. Interventions for smoking cessation in hospitalised patients. *Cochrane Database Syst Rev*. 2012(5):CD001837.
19. Sterne JA, Egger M, Moher D. Chapter 10: Addressing reporting biases. In: Higgins J, Green S, eds. *Cochrane handbook for systematic reviews of interventions, ver 5.1.0*. The Cochrane Collaboration, 2011.
20. Allen KR, Hazelett S, Jarjoura D, et al. Effectiveness of a postdischarge care management model for stroke and transient ischemic attack: a randomized trial. *J Stroke Cerebrovasc Dis*. 2002;11:88-98.
21. Barker-Collo S, Krishnamurthi R, Witt E, et al. Improving adherence to secondary stroke prevention strategies through motivational interviewing: randomized controlled trial. *Stroke*. 2015;46:3451-3458.
22. Cheng EM, Cunningham WE, Towfighi A, et al. Efficacy of a chronic care-based intervention on secondary stroke prevention among vulnerable stroke survivors: a randomized controlled trial. *Circ Cardiovasc Qual Outcomes*. 2018;11:e003228.
23. Damush TM, Ofner S, Yu Z, et al. Implementation of a stroke self-management program: a randomized controlled pilot study of veterans with stroke. *Transl Behav Med*. 2011;1:561-572.
24. Faulkner J, Lambrick D, Woolley B, et al. The long-term effect of exercise on vascular risk factors and aerobic fitness in those with transient ischaemic attack: a randomized controlled trial. *J Hypertens*. 2014;32:2064-2070.
25. Gillham S, Endacott R. Impact of enhanced secondary prevention on health behaviour in patients following minor stroke and transient ischaemic attack: a randomized controlled trial. *Clin Rehabil*. 2010;24:822-830.
26. Hornnes N, Larsen K, Boysen G. Blood pressure 1 year after stroke: the need to optimize secondary prevention. *J Stroke Cerebrovasc Dis*. 2009;20:16-23.
27. Irewall A-L, Ögren J, Bergström L, et al. Nurse-led, telephone-based, secondary preventive follow-up after stroke or transient ischemic attack improves blood pressure and LDL cholesterol: results from the first 12 months of the randomized, controlled NAILED stroke risk factor trial. *PLoS One*. 2015;10:e0139997.
28. Joubert J, Reid C, Joubert L, et al. Risk factor management and depression post-stroke: the value of an integrated model of care. *J Clin Neurosci*. 2006;13:84-90.
29. Kim J-I, Lee S, Kim J-H. Effects of a web-based stroke education program on recurrence prevention behaviors among stroke patients: a pilot study. *Health Educ Res*. 2013;28:488-501.
30. Kirk H, Kersten P, Crawford P, et al. The cardiac model of rehabilitation for reducing cardiovascular risk factors post transient

ischaemic attack and stroke: a randomized controlled trial. *Clin Rehabil*. 2014;28:339-349.
31. Kono Y, Yamada S, Yamaguchi J, et al. Secondary prevention of new vascular events with lifestyle intervention in patients with noncardioembolic mild ischemic stroke: a single-center randomized controlled trial. *Cerebrovasc Dis*. 2013;36:88-97.
32. Morén C, Welmer A-K, Hagströmer M, et al. The effects of 'physical activity on prescription' in persons with transient ischemic attack: a randomized controlled study. *J Neurol Phys Ther*. 2016;40:176-183.
33. Wan L-H, Zhang X-P, Mo M-M, et al. Effectiveness of goal-setting telephone follow-up on health behaviors of patients with ischemic stroke: a randomized controlled trial. *J Stroke Cerebrovasc Dis*. 2016;25:2259-2270.
34. Wolfe CDA, Redfern J, Rudd AG, et al. Cluster randomized controlled trial of a patient and general practitioner intervention to improve the management of multiple risk factors after stroke: stop stroke. *Stroke*. 2010;41:2470-2476.
35. Ministry of Higher Education and Science. Danish code of conduct for research integrity. Kbh: Ministry of Higher Education and Science; 2014. https://ufm.dk/publikationer/2014/filer-2014/the-danish-code-of-conduct-for-research-integrity.pdf.
36. Adie K, James MA. Does telephone follow-up improve blood pressure after minor stroke or TIA? *Age Ageing*. 2010;39:598-603.
37. Allen K, Hazelett S, Jarjoura D, et al. A randomized trial testing the superiority of a postdischarge care management model for stroke survivors. *J Stroke Cerebrovasc Dis*. 2009;18:443-452.
38. Boss HM, Van Schaik SM, Deijle IA, et al. Safety and feasibility of post-stroke care and exercise after minor ischemic stroke or transient ischemic attack: MotiveS & MoveIT. *NeuroRehabilitation*. 2014;34:401-407.
39. Boysen G, Krarup L-H, Zeng X, et al. ExStroke Pilot Trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: a multinational randomised controlled clinical trial. *BMJ*. 2009;339:b2810.
40. Brunner Frandsen N, Sorensen M, Hyldahl TK, et al. Smoking cessation intervention after ischemic stroke or transient ischemic attack. a randomized controlled pilot trial. *Nicotine Tob Res*. 2012;14:443-447.
41. Chanruengvanich W, Kasemkitwattana S, Charoenyooth C, et al. RCT: self-regulated exercise program in transient ischemic attack and minor stroke patients. *Thai J Nurs Res*. 2006;10:165-179.
42. English C, Healy GN, Olds T, et al. Reducing sitting time after stroke: a phase II safety and feasibility randomized controlled trial. *Arch Phys Med Rehabil*. 2016;97:273-280.
43. Evans-Hudnall GL, Stanley MA, Clark AN, et al. Improving secondary stroke self-care among underserved ethnic minority individuals: a randomized clinical trial of a pilot intervention. *J Behav Med*. 2014;37:196-204.
44. Flemming KD, Allison TG, Covalt JL, et al. Utility of a post-hospitalization stroke prevention program managed by nurses. *Hosp Pract*. 1995;2013(41):70-79.
45. Holzemer EM, Thanavaro J, Malmstrom TK, et al. Modifying risk factors after TIA and stroke: the impact of intensive education. *J Nurse Pract*. 2011;7:372-377.
46. Joubert J, Reid C, Barton D, et al. Integrated care improves risk-factor modification after stroke: initial results of the Integrated Care for the Reduction of Secondary Stroke model. *J Neurol Neurosurg Psychiatry*. 2009;80:279-284.
47. McManus JA, Craig A, McAlpine C, et al. Does behaviour modification affect post-stroke risk factor control? Three-year follow-up of a randomized controlled trial. *Clin Rehabil*. 2009;23:99-105.
48. Nir Z, Zolotogorsky Z, Sugarman H. Structured nursing intervention versus routine rehabilitation after stroke. *Am J Phys Med Rehabil*. 2004;83:522-529.
49. Peng B, Ni J, Anderson CS, et al. Implementation of a structured guideline-based program for the secondary prevention of ischemic stroke in China. *Stroke*. 2014;45:515-519.
50. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE handbook. 2013. http://gdt.guidelinedevelopment.org/central_prod/_design/client/handbook/handbook.html. Accessed 16 June 2020.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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