National Institute for Health and Care Excellence

Consultation

Hypertension in adults: diagnosis and management

H. Evidence review for relaxation review

NICE guideline

Intervention evidence review

March 2019

Draft for Consultation

This evidence review was developed by the National Guideline Centre

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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1 Relaxation therapies

1.1 Review question: What is the clinical and cost-effectiveness of relaxation therapies for the management of primary hypertension in adults?

1.2 Introduction

Blood pressure is affected by many physiological parameters including the actions of the kidneys, blood vessels and level of arousal. It is known that blood pressure increases at times of stress, and this forms the basis of the recommendation that individuals should sit quietly for a short period of time before blood pressure measurement. Participation in relaxation therapies (for example, biofeedback, meditation or yoga) may therefore have a sustained blood pressure lowering effect thus leading to a reduction in cardiovascular events. Relaxation therapies for hypertension are not part of current practice in the treatment of hypertension. This chapter assesses the evidence as to whether relaxation therapies are clinically and cost effective for the management of hypertension.

1.3 PICO table

For full details, see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Adults (aged over 18 years) with primary hypertension who do or do not also have type 2 diabetes.
Interventions	Intervention designed to promote relaxation (relaxation therapies). Mind-body and relaxation techniques: • Biofeedback • Breathing • Meditation • Mindfulness • Muscle relaxation • Relaxation imagery • Yoga
Comparisons	Control* including: • No active treatment (usual care or blood pressure [BP] monitoring) • Sham or placebo therapy *Note that studies combining a control intervention with additional interventions will be allowed where all participants (including the intervention arm[s]) received the same additional interventions.
Outcomes	Assessed at 12 or more months (using final endpoint) **Critical** • All-cause mortality • Health-related quality of life • Stroke (ischaemic or haemorrhagic) • Myocardial infarction (MI)

	Important • Heart failure needing hospitalisation • Vascular procedures (including both coronary and carotid artery procedures) • Angina needing hospitalisation • Cessation or reduction of medication • [Combined cardiovascular disease outcomes in the absence of MI and stroke data] • [Coronary heart disease outcome in the absence of MI data]
Study design	Randomised control trials (RCT) and systematic reviews (SR)

1.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[48] Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2018 conflicts of interest policy.

1.5 Clinical evidence

1.5.1 Included studies

One study was included in the review;[55] which is summarised in Table 2 below. Evidence from this study is summarised in the clinical evidence summary below.

This RCT compared relaxation therapy to no treatment with outcomes reported at 1 year.

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix F.

1.5.2 Excluded studies

One Cochrane review[23] relevant to this review question was identified. This was excluded due to having a less than a minimum duration follow up; a median duration of treatment was 8 weeks (range: 5 to 26 weeks).

See the excluded studies list in appendix I.

1.5.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes
Patel, 1988[55]	Relaxation therapy (breathing exercises, deep muscle relaxation and simple meditation), n=49 versus no treatment, n=54	Adults (n=103) Aged 35 to 64 years Prescence of population with diabetes not given.	At 12 months: • Myocardial infarction (MI) • Stroke • Angina

See appendix D for full evidence tables.

1.5.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: Relaxation therapy versus no treatment

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No treatment	Risk difference with Relaxation therapy (95% CI)
Stroke at 12 months	103 (1 study) 12 months	VERY LOW[1,2] due to risk of bias, imprecision	Peto OR 8.18 (0.16 to 414.3)	0 per 1,000	20 more per 1,000 (from 30 fewer to 70 more)
Myocardial infarction at 12 months	103 (1 study) 12 months	VERY LOW[1,2] due to risk of bias, imprecision	Peto OR 0.15 (0 to 7.52)	19 per 1,000	20 fewer per 1,000 (from 70 fewer to 30 more)
Angina at 12 months	103 (1 study) 12 months	VERY LOW[1,2] due to risk of bias, imprecision	Peto OR 0.15 (0 to 7.52)	19 per 1,000	20 fewer per 1,000 (from 70 fewer to 30 more)

[1]Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2]Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

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2 See appendix F for full GRADE tables.

1.6 Economic evidence

1.6.1 Included studies

No relevant health economic studies were identified.

1.6.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.6.3 Resource costs

The resource use involved in providing the relaxation intervention from the clinical evidence included has been costed below for illustration.

The unit costs of the staff involved are shown in Table 4, with the resource use and total costs demonstrated in Table 5.

Table 4: Staff costs

Resource	Detail	Unit cost
GP time	Cost per minute of patient contact (including qualifications and direct care staff costs)	£4
Nurse (GP practice) time	Cost per hour including qualifications	£42

Source: PSSRU 2017 [21]

Table 5: Intervention cost

Resource use	Cost of resource use	Total cost
GP time of 30 minutes per session	£120	
Nurse time of 30 minutes per session	£21	
Total staff cost per 1 hour session	£141	
Total group cost for 8 sessions		**£1,128**
Total per person cost for 8 sessions		**£113**

Note: Each session was 1 hour over 8 weeks. 10 people per group.

This illustrated cost does not include preparation time for staff and can vary depending on the grade of staff involved.

Similar interventions from the PSSRU[21] include mindfulness based cognitive behavioural therapy, costing £88 per hour of direct contact.

1.7 Evidence statements

1.7.1 Clinical evidence statements

Very low quality evidence from 1 study with 103 participants showed a clinically important benefit of relaxation therapy compared to no treatment for occurrence of myocardial infarction and angina at 12 months..

However there was a clinically important harm of relaxation therapy compared to no treatment for the occurrence of stroke at 12 months.

1.7.2 Health economic evidence statements

No relevant economic evaluations were identified.

1.8 Recommendations

No recommendations were made for this review question.

1.8.1 Research recommendations

RR1. What is the clinical and cost-effectiveness of relaxation therapies for the management of primary hypertension in adults in terms of reducing cardiovascular events and improving quality of life?

See also the rationale in appendix J.

1.9 The committee's discussion of the evidence

1.9.1 Interpreting the evidence

1.9.1.1 The outcomes that matter most

The committee considered all-cause mortality, quality of life, stroke and myocardial infarction to be critical outcomes for decision-making. Heart failure, vascular procedures, angina and reduction in medication were also considered important for decision-making. There was no evidence addressing all-cause mortality, quality of life, heart failure and vascular events. There was also no evidence to determine whether or not relaxation therapies could result in a cessation or reduction of medication.

1.9.1.2 The quality of the evidence

Only 1 study was identified to include in the review. The evidence was rated as very low quality due to imprecision and risk of bias. Due to the small sample size, the committee considered that in isolation this evidence was underpowered to detect differences in cardiovascular event rates. The committee also considered the age of the included study and noted that clinical diagnoses in 1988 differ to those in the present day. In particular, the committee highlighted that myocardial infarction outcomes may have previously included conditions such as angina and therefore this may overestimate the effect of reduction in this outcome when compared to the current definition. In addition, the device used for blood pressure measurement was a random 0 sphygmomanometer, which is no longer a validated measurement. Furthermore, it was noted that there was a significant imbalance between the 2 groups in their baseline systolic blood pressure. The improvement in blood pressure for the group receiving relaxation therapy may therefore be the result of regression towards the mean, and must be interpreted with caution. When considering all of these factors, the committee agreed that the available evidence was insufficient to inform recommendations.

1.9.1.3 Benefits and harms

There was a clinically important benefit of relaxation therapy for hypertension with the outcomes of angina and myocardial infarction at 1 year, and conversely there was a clinically important harm for the outcome of stroke at 1 year. However, there were only a small number of participants included within the evidence, which was considered insufficient to

determine differences in cardiovascular events. The very low quality of the evidence and low numbers of events occurring led to considerable uncertainty in the effect size. The committee agreed this was insufficient to determine the effectiveness of relaxation therapies.

Based on the available evidence, the committee agreed it could not justify retaining the recommendation that had been made in the previous guideline for relaxation therapies. The committee was aware of some RCTs that had suggested benefits of relaxation therapies in reducing blood pressure; however, these did not meet the protocol inclusion criteria to be included in this review where the surrogate measure of blood pressure reduction was not considered critical to decision-making. A previous iteration of the guideline in 2004 (CG18) identified some evidence to suggest that relaxation therapies could reduce blood pressure at a short follow-up, however, this was a small reduction and the long term effectiveness of relaxation therapies was not determined. This evidence was not sufficient to determine whether or not relaxation therapies could also reduce cardiovascular events, and the additional evidence reviewed in this update was also not sufficient to determine this. Given the lack of evidence for hard outcomes, the committee considered whether there would be some merit in recommending further research in this area. The committee discussed the study designs that could be utilised for further research and agreed that a well-designed RCT would require extensive resources in order to answer the question of whether relaxation therapies are a clinically effective treatment for hypertension. This would need to be significantly larger than those in the current literature. Due to the small changes in blood pressure that are associated with the interventions, a large number of participants would be required in order to detect any differences between interventions. The committee agreed a research recommendation may be useful.

1.9.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

The clinical study identified had a relaxation intervention conducted by GPs and nurses. Relaxation therapies involve a lot of staff time to provide the exact cost varying depending on the length of the sessions, the length of the course, the number of people attending, and the grade of staff involved. To estimate, costing up the course from the clinical trial led to over £1,000 for a course of treatment for a group and over £100 per person if there are 10 people per group.

The committee agreed there was no benefit demonstrated from the intervention, as there was only 1 event in 1 arm and no events in the other arm for each outcome. There were also serious methodological flaws with the evidence.

2 References

1. Achmon J, Granek M, Golomb M, Hart J. Behavioral treatment of essential hypertension: A comparison between cognitive therapy and biofeedback of heart rate. Psychosomatic Medicine. 1989; 51(2):152-64

2. Adsett CA, Bellissimo A, Mitchell A, Wilczynski N, Haynes RB. Behavioral and physiological effects of a beta blocker and relaxation therapy on mild hypertensives. Psychosomatic Medicine. 1989; 51(5):523-536

3. Agras WS, Schneider JA, Taylor CB. Relaxation training in essential hypertension: A failure of retraining in relaxation procedures. Behavior Therapy. 1984; 15(2):191-6

4. Agras WS, Taylor CB, Kraemer HC, Southam MA, Schneider JA. Relaxation training for essential hypertension at the worksite: II. The poorly controlled hypertensive. Psychosomatic Medicine. 1987; 49(3):264-73

5. Ahmadpanah M, Paghale SJ, Bakhtyari A, Kaikhavani S, Aghaei E, Nazaribadie M et al. Effects of psychotherapy in combination with pharmacotherapy, when compared to pharmacotherapy only on blood pressure, depression, and anxiety in female patients with hypertension. Journal of Health Psychology. 2016; 21(7):1216-27

6. Aivazyan TA, Zaitsev VP, Salenko BB, Yurenev AP, Patrusheva IF. Efficacy of relaxation techniques in hypertensive patients. Health Psychology. 1988; 7(Suppl):193-200

7. Alageel S, Gulliford MC, McDermott L, Wright AJ. Multiple health behaviour change interventions for primary prevention of cardiovascular disease in primary care: systematic review and meta-analysis. BMJ Open. 2017; 7(6):e015375

8. Alexander CN, Langer EJ, Newman RI, Chandler HM, Davies JL. Transcendental meditation, mindfulness, and longevity: An experimental study with the elderly. Journal of Personality and Social Psychology. 1989; 57(6):950-64

9. Alparslan GB, Akdemir N. Effects of walking and relaxation exercises on controlling hypertension. Journal of the Australian Traditional-Medicine Society. 2010; 16(1):9-14

10. Amigo Vazquez I, Fernandez Rodriguez A, Gonzalez Menendez A. Muscular relaxation and arterial hypertension: A controlled study with medicated and unmedicated patients. Psicologia conductual. 2001; 9(1):131-40

11. Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: A meta-analysis. American Journal of Hypertension. 2008; 21(3):310-6

12. Anonymous. Five-year findings of the hypertension detection and follow-up program. I. Reduction in mortality of persons with high blood pressure, including mild hypertension. JAMA. 1979; 242(23):2562-71

13. Bai Z, Chang J, Chen C, Li P, Yang K, Chi I. Investigating the effect of transcendental meditation on blood pressure: A systematic review and meta-analysis. Journal of Human Hypertension. 2015; 29(11):653-62

14. Bradley RW. Blood pressure biofeedback and relaxation training: The effects of home practice on reduction of blood pressure in persons with essential hypertension. Denton, TE. North Texas State University. 1980. Ph.D.

15. Brandani JZ, Mizuno J, Ciolac EG, Monteiro HL. The hypotensive effect of Yoga's breathing exercises: A systematic review. Complementary Therapies in Clinical Practice. 2017; 28:38-46

16. Bush MF. Combined relaxation and cognitive restructuring skills in the control of borderline essential hypertension. Urbana, IL. University of Illinois. 1988. Ph.D.

17. Canter PH, Ernst E. Insufficient evidence to conclude whether or not transcendental meditation decreases blood pressure: Results of a systematic review of randomized clinical trials. Journal of Hypertension. 2004; 22(11):2049-54

18. Chu P, Gotink RA, Yeh GY, Goldie SJ, Hunink MG. The effectiveness of yoga in modifying risk factors for cardiovascular disease and metabolic syndrome: A systematic review and meta-analysis of randomized controlled trials. European Journal of Preventive Cardiology. 2016; 23(3):291-307

19. Corey SM, Epel E, Schembri M, Pawlowsky SB, Cole RJ, Araneta MRG et al. Effect of restorative yoga vs. stretching on diurnal cortisol dynamics and psychosocial outcomes in individuals with the metabolic syndrome: The PRYSMS randomized controlled trial. Psychoneuroendocrinology. 2014; 49(1):260-271

20. Cramer H, Langhorst J, Dobos G, Lauche R. Yoga for metabolic syndrome: A systematic review and meta-analysis. European Journal of Preventive Cardiology. 2016; 23(18):1982-1993

21. Curtis L, Burns A. Unit costs of health and social care 2017. Canterbury. Personal Social Services Research Unit University of Kent, 2017. Available from: https://www.pssru.ac.uk/project-pages/unit-costs/unit-costs-2017/

22. Dhungana RR, Khanal MK, Joshi S, Kalauni OP, Shakya A, Bhrutel V et al. Impact of a structured yoga program on blood pressure reduction among hypertensive patients: Study protocol for a pragmatic randomized multicenter trial in primary health care settings in Nepal. BMC Complementary and Alternative Medicine. 2018; 18(1):207

23. Dickinson HO, Campbell F, Beyer FR, Nicolson DJ, Cook JV, Ford GA et al. Relaxation therapies for the management of primary hypertension in adults. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004935. DOI: 10.1002/14651858.CD004935.pub2.

24. Glasgow MS, Engel BT, D'Lugoff BC. A controlled study of a standardized behavioral stepped treatment for hypertension. Psychosomatic Medicine. 1989; 51(1):10-26

25. Goebel M, Viol GW, Lorenz GJ, Clemente J. Relaxation and biofeedback in essential hypertension: A preliminary report of a six-year project. American Journal of Clinical Biofeedback. 1980; 3(1):20-29

26. Gotink RA, Younge JO, Wery MF, Utens EMWJ, Michels M, Rizopoulos D et al. Online mindfulness as a promising method to improve exercise capacity in heart disease: 12-month follow-up of a randomized controlled trial. PloS One. 2017; 12(5):e0175923

27. Greenhalgh J, Dickson R, Dundar Y. The effects of biofeedback for the treatment of essential hypertension: A systematic review. Health Technology Assessment. 2009; 13(46):1-104

28. Guohua Z, Maomao H, Feiwen L, Shuzhen L, Jing T, Lidian C. Tai Chi Chuan for the primary prevention of stroke in middle-aged and elderly adults: A systematic review. Evidence-Based Complementary and Alternative Medicine. 2015; 2015:742152

29. Hafer DG. Self-directed relaxation as a treatment for essential hypertension (imagery, autogenic, progressive relaxation). Denton, TE. North Texas State University. 1984. Ph.D.

30. Hafner RJ. Psychological treatment of essential hypertension: A controlled comparison of meditation and meditation plus biofeedback. Biofeedback and Self Regulation. 1982; 7(3):305-316

31. Hartley L, Dyakova M, Holmes J, Clarke A, Lee MS, Ernst E et al. Yoga for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD010072. DOI: http://dx.doi.org/10.1002/14651858.CD010072.pub2.

32. Hartley L, Flowers N, Lee MS, Ernst E, Rees K. Tai chi for primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD010366. DOI: https://dx.doi.org/10.1002/14651858.CD010366.pub2.

33. Hartley L, Lee MS, Kwong JS, Flowers N, Todkill D, Ernst E et al. Qigong for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD010390. DOI: https://dx.doi.org/10.1002/14651858.CD010390.pub2.

34. Hartley L, Mavrodaris A, Flowers N, Ernst E, Rees K. Transcendental meditation for the primary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD010359. DOI: http://dx.doi.org/10.1002/14651858.CD010359.pub2.

35. Hoelscher TJ, Lichstein KL, Fischer S, Hegarty TB. Relaxation treatment of hypertension: Do home relaxation tapes enhance treatment outcome? Behavior Therapy. 1987; 18(1):33-37

36. Jenaabadi H. Efficacy of anger management training on anger decrease of and blood pressure reactivity among patients with hypertension in Zahedan. Acta Medica Mediterranea. 2018; 34(Special 2):607-612

37. Johnston DW, Gold A, Kentish J, Smith D, Vallance P, Shah D et al. Effect of stress management on blood pressure in mild primary hypertension. BMJ. 1993; 306(6883):963-966

38. Khramelashvili VV, TA Av, Salenko BB. Psychological nondrug treatment of hypertension and the criteria of its effectiveness. Kardiologiia. 1986; 26(1):66-69

39. Kopf S, Oikonomou D, Hartmann M, Feier F, Faude-Lang V, Morcos M et al. Effects of stress reduction on cardiovascular risk factors in type 2 diabetes patients with early kidney disease - results of a randomized controlled trial (HEIDIS). Experimental and Clinical Endocrinology and Diabetes. 2014; 122(6):341-9

40. Kruerke D, Simoes-Wust AP, Kaufmann C, Frank M, Faldey A, Heusser P et al. Can speech-guided breathing influence cardiovascular regulation and mood perception in hypertensive patients? Journal of Alternative and Complementary Medicine. 2018; 24(3):254-261

41. Landman GW, van Hateren KJ, van Dijk PR, Logtenberg SJ, Houweling ST, Groenier KH et al. Efficacy of device-guided breathing for hypertension in blinded, randomized, active-controlled trials: A meta-analysis of individual patient data. JAMA Internal Medicine. 2014; 174(11):1815-21

42. Larson MJ, Steffen PR, Primosch M. The impact of a brief mindfulness meditation intervention on cognitive control and error-related performance monitoring. Frontiers in Human Neuroscience. 2013; 7:308

43. Lee MS, Lee EN, Kim JI, Ernst E. Tai chi for lowering resting blood pressure in the elderly: A systematic review. Journal of Evaluation in Clinical Practice. 2010; 16(4):818-24

44. Levenson JC, Rollman BL, Ritterband LM, Strollo PJ, Smith KJ, Yabes JG et al. Hypertension with unsatisfactory sleep health (HUSH): study protocol for a randomized controlled trial. Trials [Electronic Resource]. 2017; 18(1):256

45. Mikolasek M, Berg J, Witt CM, Barth J. Effectiveness of mindfulness- and relaxation-based ehealth interventions for patients with medical conditions: A systematic review and synthesis. International Journal of Behavioral Medicine. 2018; 25(1):1-16

46. Momeni J, Omidi A, Raygan F, Akbari H. The effects of mindfulness-based stress reduction on cardiac patients' blood pressure, perceived stress, and anger: A single-blind randomized controlled trial. Journal of the American Society of Hypertension. 2016; 10(10):763-771

47. Nagele E, Jeitler K, Horvath K, Semlitsch T, Posch N, Herrmann KH et al. Clinical effectiveness of stress-reduction techniques in patients with hypertension: Systematic review and meta-analysis. Journal of Hypertension. 2014; 32(10):1936-44

48. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

49. Nowlis, David P, Borzone, Ximena C. Long-term psychosomatic effects of biofeedback vs. relaxation training. 1980:6

50. Ooi SL, Giovino M, Pak SC. Transcendental meditation for lowering blood pressure: An overview of systematic reviews and meta-analyses. Complementary Therapies in Medicine. 2017; 34:26-34

51. Pandic S, Ekman I, Nord L, Kjellgren KI. Device-guided breathing exercises in the treatment of hypertension - perceptions and effects. CVD prevention and control. 2008; 3(3):163-169

52. Park SH, Han KS. Blood pressure response to meditation and yoga: A systematic review and meta-analysis. Journal of Alternative and Complementary Medicine. 2017; 23(9):685-695

53. Patel C. 12-month follow-up of yoga and bio-feedback in the management of hypertension. The Lancet. 1975; 306(7898):62-64

54. Patel C. Yoga and biofeedback in the management of hypertension. Journal of Psychosomatic Research. 1975; 19(5-6):355-360

55. Patel C, Marmot M. Can general practitioners use training in relaxation and management of stress to reduce mild hypertension? BMJ. 1988; 296(6614):21-24

56. Patel C, Marmot MG, Terry DJ. Controlled trial of biofeedback-aided behavioural methods in reducing mild hypertension. BMJ. 1981; 282(6281):2005-2008

57. Patel C, Marmot MG, Terry DJ, Carruthers M, Hunt B, Patel M. Trial of relaxation in reducing coronary risk: Four year follow up. BMJ. 1985; 290(6475):1103-1106

58. Patel C, North WR. Randomised controlled trial of yoga and bio-feedback in management of hypertension. The Lancet. 1975; 2(7925):93-95

59. Pender NJ. Effects of progressive muscle relaxation training on anxiety and health locus of control among hypertensive adults. Research in Nursing and Health. 1985; 8(1):67-72

60. Perry RT. The effects of systematic relaxation training and circadian rhythm on systolic and diastolic blood pressure in borderline/essential hypertensive subjects. Texas, TE. East Texas Estate Univeristy. 1984. Ph.D.

61. Petersen I, Bhana A, Folb N, Thornicroft G, Zani B, Selohilwe O et al. Collaborative care for the detection and management of depression among adults with hypertension in South Africa: study protocol for the PRIME-SA randomised controlled trial. Trials [Electronic Resource]. 2018; 19(1):192

62. Posadzki P, Cramer H, Kuzdzal A, Lee MS, Ernst E. Yoga for hypertension: A systematic review of randomized clinical trials. Complementary Therapies in Medicine. 2014; 22(3):511-22

63. Rosas Marchiori MF, Kozasa EH, Miranda RD, Monezi Andrade AL, Perrotti TC, Leite JR. Decrease in blood pressure and improved psychological aspects through meditation training in hypertensive older adults: A randomized control study. Geriatrics & Gerontology International. 2015; 15(10):1158-1164

64. Seer P, Raeburn JM. Meditation training and essential hypertension: A methodological study. Journal of Behavioral Medicine. 1980; 3(1):59-71

65. Siu PM, Yu AP, Benzie IF, Woo J. Effects of 1-year yoga on cardiovascular risk factors in middle-aged and older adults with metabolic syndrome: A randomized trial. Diabetology & Metabolic Syndrome. 2015; 7:40

66. Southam MA. Generalized effects of relaxation training in essential hypertension. Stanford, CA. Stanford University. 1981. Ph.D.

67. Southam MA, Agras WS, Taylor CB, Kraemer HC. Relaxation training. Blood pressure lowering during the working day. Archives of General Psychiatry. 1982; 39(6):715-717

68. Sriloy M, Nair PMK, Pranav K, Sathyanath D. Immediate effect of manual acupuncture stimulation of four points versus slow breathing in declination of blood pressure in primary hypertension: A parallel randomized control trial. Acupuncture and Related Therapies. 2015; 3(2-3):15-18

69. Sun J, Buys N. Community-based mind-body meditative tai chi program and its effects on improvement of blood pressure, weight, renal function, serum lipoprotein, and quality of life in chinese adults with hypertension. American Journal of Cardiology. 2015; 116(7):1076-1081

70. Supa'at I, Zakaria Z, Maskon O, Aminuddin A, Nordin NA. Effects of Swedish massage therapy on blood pressure, heart rate, and inflammatory markers in hypertensive women. Evidence-Based Complementary and Alternative Medicine. 2013; 2013:171852

71. Tulloh RMR, Garratt V, Tagney J, Turner-Cobb J, Marques E, Greenwood R et al. A pilot randomised controlled trial investigating a mindfulness-based stress reduction (MBSR) intervention in individuals with pulmonary arterial hypertension (PAH): the PATHWAYS study. Pilot & Feasibility Studies. 2018; 4:78

72. Ursua RA, Aguilar DE, Wyatt LC, Trinh-Shevrin C, Gamboa L, Valdellon P et al. A community health worker intervention to improve blood pressure among Filipino Americans with hypertension: a randomized controlled trial. Preventive medicine reports. 2018; 11:42-48

73. Vaccarino V, Kondwani KA, Kelley ME, Murrah NV, Boyd L, Ahmed Y et al. Effect of meditation on endothelial function in black Americans with metabolic syndrome: A randomized trial. Psychosomatic Medicine. 2013; 75(6):591-599

74. van Montfrans GA, Karemaker JM, Wieling W, Dunning AJ. Relaxation therapy and continuous ambulatory blood pressure in mild hypertension: A controlled study. BMJ. 1990; 300(6736):1368-72

75. Venturelli M, Cè E, Limonta E, Schena F, Caimi B, Carugo S et al. Effects of endurance, circuit, and relaxing training on cardiovascular risk factors in hypertensive elderly patients. Age (dordrecht, netherlands). 2015; 37(5):101

76. Wolff M, Sundquist K, Larsson Lönn S, Midlöv P. Impact of yoga on blood pressure and quality of life in patients with hypertension - a controlled trial in primary care, matched for systolic blood pressure. BMC Cardiovascular Disorders. 2013; 13:111

77. Wood CJ. Evaluation of meditation and relaxation on physiological response during the performance of fine motor and gross motor tasks. Perceptual and Motor Skills. 1986; 62(1):91-98

78. Yang H, Wu X, Wang M. The effect of three different meditation exercises on hypertension: A network meta-analysis. Evidence-Based Complementary and Alternative Medicine. 2017; 2017:9784271

79. Yeh GY, Wang C, Wayne PM, Phillips RS. The effect of tai chi exercise on blood pressure: A systematic review. Preventive Cardiology. 2008; 11(2):82-9

1 Appendices

2 Appendix A: Review protocols

3 **Table 6: Review protocol: Relaxation therapy**

Field	Content
Review question	What is the clinical and cost-effectiveness of relaxation therapies for the management of primary hypertension in adults?
Type of review question	Intervention review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details, see the health economic review protocol for this NICE guideline.
Objective of the review	To establish the clinical and cost effectiveness of relaxation therapies for the management of primary hypertension.
Eligibility criteria – population / disease / condition / issue / domain	Adults (aged 18 years or older) with primary hypertension who do or do not also have type 2 diabetes.
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Intervention designed to promote relaxation (relaxation therapies). Mind-body and relaxation techniques: • Biofeedback • Breathing • Meditation • Mindfulness • Muscle relaxation • Relaxation imagery • Yoga
Eligibility criteria – comparator(s) / control or reference (gold) standard	Control* including: • No active treatment (usual care or BP monitoring) • Sham or placebo therapy *Note that studies combining a control intervention with additional interventions will be allowed where all participants (including the intervention arm[s]) received the same additional interventions.
Outcomes and prioritisation	Assessed at 12 or more months (using final endpoint) **Critical** • All-cause mortality • Health-related quality of life • Stroke (ischaemic or haemorrhagic) • MI **Important** • Heart failure needing hospitalisation • Vascular procedures (including both coronary and carotid artery procedures) • Angina needing hospitalisation • Cessation or reduction of medication

	• [Combined cardiovascular disease outcomes in the absence of MI and stroke data] • [Coronary heart disease outcome in the absence of MI data]
Eligibility criteria – study design	RCTs and SRs
Other inclusion exclusion criteria	Minimum follow up time: 1 year Exclusions: • Papers that evaluate relaxation therapies combined with other interventions such as diet or exercise or stable drug therapy. Unless all participants (including control) received the same additional interventions. This includes studies allowing participants to adjust antihypertensive medication. • Studies including participants with type 1 diabetes or chronic kidney disease (A3 or above [heavy proteinuria]). For the Type 2 diabetes strata studies including participants with chronic kidney disease (A2 or above [heavy proteinuria]). • Indirect populations with secondary causes of hypertension such as tumours or structural vascular defects (Conn's adenoma, phaeochromocytoma, renovascular hypertension) • Pregnant women • Crossover trials • Children (aged under 18 years)
Proposed sensitivity / subgroup analysis, or meta-regression	Subgroups analysis for heterogeneity • Age (75 as a cut off)* • Family origin (African and Caribbean, White, South Asian) • Concomitant pharmacological therapy for hypertension (Y/N) • Severity of hypertension *To note that we will also extract evidence in those >80 years old if this evidence is reported separately.
Selection process – duplicate screening / selection / analysis	A senior research fellow will undertake quality assurance prior to completion.
Data management (software)	Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). GRADEpro will be used to assess the quality of evidence for each outcome. Endnote will be used for bibliography, citations, sifting and reference management.
Information sources – databases and dates	Medline, Embase, the Cochrane Library, CINAHL and AMED Language: Restrict to English only Key papers: Cochrane review (2008): http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004935.pub2/epdf
Identify if an update	Yes, it is an update
Author contacts	https://www.nice.org.uk/guidance/cg127
Highlight if amendment to previous protocol	For details, please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details, please see appendix B

Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details, please see evidence tables in appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to appraise individual studies critically. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details, please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details, please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details, please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details, please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details, please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Anthony Wierzbicki in line with section 3 of Developing NICE guidelines: the manual. Staff from the NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details, please see Developing NICE guidelines: the manual.
Sources of funding / support	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	The NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds the NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

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2 **Table 7: Health economic review protocol**

Review question	**All questions – health economic evidence**
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis).

	• Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. No date cut-off from the previous guideline was used.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the US will also be excluded. Studies published after 2002 that were included in the previous guideline(s) will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[48] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations', then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations', then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both, then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to exclude selectively the remaining studies. All studies excluded based on applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the US will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable).

	• Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2002 or later (including any such studies included in the previous guideline[s]) but that depend on unit costs and resource data entirely or predominantly before 2002 will be rated as 'Not applicable'. • Studies published before 2002 (including any such studies included in the previous guideline[s]) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review, the more useful the analysis will be for decision-making in the guideline. • Generally, economic evaluations based on excludes from the clinical review will be excluded.

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Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017.

For more detailed information, please see the Methodology Review.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 02 October 2018	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 02 October 2018	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to Issue 8 of 12, August 2018 CENTRAL to Issue 7 of 12, July 2018 DARE and NHSEED to Issue 2 of 4, April 2015 HTA to Issue 4 of 4, October 2016	None
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 02 October 2018	Exclusions
AMED, Allied and Complementary Medicine (OVID)	Inception – 02 October 2018	Exclusions Randomised controlled trials Systematic review studies

Table 9: Medline (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	exp pregnancy/
9.	exp Hypertension, Pregnancy-Induced/ not exp Hypertension/
10.	(pre eclampsia or pre-eclampsia or preeclampsia).ti,ab.
11.	exp Hypertension, Portal/ not exp Hypertension/
12.	exp Hypertension, Pulmonary/ not exp Hypertension/

13.	exp Intracranial Hypertension/ not exp Hypertension/
14.	exp Ocular Hypertension/ not exp Hypertension/
15.	exp Diabetes Mellitus, Type 1/ not exp Diabetes Mellitus, Type 2/
16.	or/8-15
17.	7 not 16
18.	letter/
19.	editorial/
20.	news/
21.	exp historical article/
22.	Anecdotes as Topic/
23.	comment/
24.	case report/
25.	(letter or comment*).ti.
26.	or/18-25
27.	randomized controlled trial/ or random*.ti,ab.
28.	26 not 27
29.	animals/ not humans/
30.	exp Animals, Laboratory/
31.	exp Animal Experimentation/
32.	exp Models, Animal/
33.	exp Rodentia/
34.	(rat or rats or mouse or mice).ti.
35.	or/28-34
36.	17 not 35
37.	(exp child/ or exp pediatrics/ or exp infant/) not (exp a dolescent/ or exp adult/ or exp middle age/ or exp aged/)
38.	36 not 37
39.	limit 38 to English language
40.	exp Mind-Body Therapies/
41.	(mind body or mindbody).ti,ab.
42.	((relax* or breath*) adj3 (behavior* or behaviour* or therap* or technic*or technique* or practic* or exerc* or educat* or manag* or train* or method*)).ti,ab.
43.	((stress* or cognitive or talk* or assertiveness or anger) adj3 (treatment* or therap* or train* or educat* or manag* or technique*)).ti,ab.
44.	((behaviour* or behavior*) adj3 (intervention* or therap* or train* or educat* or manag*)).ti,ab.
45.	Feedback, Psychological/
46.	(biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback).ti,ab.
47.	((physiologic* or psychophysiologic*) adj2 (feedback or feed back)).ti,ab.
48.	exp Meditation/
49.	(meditat* or meditation* or mindful*).ti,ab.
50.	autogenic*.ti,ab.
51.	((hypnosis or hypnot* or reverie or trance) adj2 (therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*)).ti,ab.
52.	((imagery or imagination or imagining) adj3 (relax* or guide* or led or lead*)).ti,ab.
53.	(yoga* or yogic or pilates).ti,ab.
54.	Muscle Relaxation/

55.	((muscle* or muscular*) adj3 (relax* or stretch* or flex* or exercise*)).ti,ab.
56.	or/40-55
57.	39 and 56
58.	randomized controlled trial.pt.
59.	controlled clinical trial.pt.
60.	randomi#ed.ti,ab.
61.	placebo.ab.
62.	randomly.ti,ab.
63.	Clinical Trials as topic.sh.
64.	trial.ti.
65.	or/58-64
66.	Meta-Analysis/
67.	exp Meta-Analysis as Topic/
68.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
69.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
70.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
71.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
72.	(search* adj4 literature).ab.
73.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
74.	cochrane.jw.
75.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
76.	or/66-75
77.	65 or 76
78.	57 and 77

Table 10: Embase (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	exp pregnancy/
9.	exp Maternal Hypertension/
10.	(pre eclampsia or pre-eclampsia or preeclampsia).ti,ab.
11.	exp Hypertension, Portal/ not exp Hypertension/
12.	exp Hypertension, Pulmonary/ not exp Hypertension/
13.	exp Intracranial Hypertension/
14.	exp Ocular Hypertension/ not exp Hypertension/
15.	exp Diabetes Mellitus, Type 1/ not exp Diabetes Mellitus, Type 2/
16.	or/8-15
17.	7 not 16
18.	letter.pt. or letter/
19.	note.pt.

20.	editorial.pt.
21.	case report/ or case study/
22.	(letter or comment*).ti.
23.	or/18-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animal/ not human/
27.	nonhuman/
28.	exp Animal Experiment/
29.	exp Experimental Animal/
30.	animal model/
31.	exp Rodent/
32.	(rat or rats or mouse or mice).ti.
33.	or/25-32
34.	17 not 33
35.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
36.	34 not 35
37.	limit 36 to English language
38.	*Alternative medicine/
39.	(mind body or mindbody).ti,ab.
40.	((relax* or breath*) adj3 (behavior* or behaviour* or therap* or technic*or technique* or practic* or exerc* or educat* or manag* or train* or method*)).ti,ab.
41.	((stress* or cognitive or talk* or assertiveness or anger) adj3 (treatment* or therap* or train* or educat* or manag* or technique*)).ti,ab.
42.	((behaviour* or behavior*) adj3 (intervention* or therap* or train* or educat* or manag*)).ti,ab.
43.	*feedback system/
44.	(biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback).ti,ab.
45.	((physiologic* or psychophysiologic*) adj2 (feedback or feed back)).ti,ab.
46.	exp *Meditation/
47.	Transcendental, meditation/
48.	(meditat* or meditation* or mindful*).ti,ab.
49.	autogenic*.ti,ab.
50.	((hypnosis or hypnot* or reverie or trance) adj2 (therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*)).ti,ab.
51.	((imagery or imagination or imagining) adj3 (relax* or guide* or led or lead*)).ti,ab.
52.	(yoga* or yogic or pilates).ti,ab.
53.	*Muscle Relaxation/
54.	((muscle* or muscular*) adj3 (relax* or stretch* or flex* or exercise*)).ti,ab.
55.	or/38-54
56.	37 and 55
57.	random*.ti,ab.
58.	factorial*.ti,ab.
59.	(crossover* or cross over*).ti,ab.
60.	((doubl* or singl*) adj blind*).ti,ab.
61.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
62.	crossover procedure/

63.	single blind procedure/
64.	randomized controlled trial/
65.	double blind procedure/
66.	or/57-65
67.	systematic review/
68.	meta-analysis/
69.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
70.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
71.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
72.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
73.	(search* adj4 literature).ab.
74.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
75.	cochrane.jw.
76.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
77.	or/67-76
78.	66 or 77
79.	56 and 78

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2 **Table 11: Cochrane Library (Wiley) search terms**

#1.	MeSH descriptor: [Hypertension] explode all trees
#2.	hypertens*:ti,ab
#3.	(elevat* near/2 blood next pressur*):ti,ab
#4.	(high near/1 blood near/1 pressur*):ti,ab
#5.	(increase* near/2 blood pressur*):ti,ab
#6.	((systolic or diastolic or arterial) near/2 pressur*):ti,ab
#7.	(or #1-#6)
#8.	MeSH descriptor: [Mind-Body Therapies] explode all trees
#9.	(mind body or mindbody):ti,ab
#10.	((relax* or breath*) near/3 (behavior* or behaviour* or therap* or technic* or technique* or practic* or exerc* or educat* or manag* or train* or method*)):ti,ab
#11.	((stress* or cognitive or talk* or assertiveness or anger) near/3 (treatment* or therap* or train* or educat* or manag* or technique*)):ti,ab
#12.	((behaviour* or behavior*) near/3 (intervention* or therap* or train* or educat* or manag*)):ti,ab
#13.	MeSH descriptor: [Feedback, Psychological] explode all trees
#14.	(biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback):ti,ab
#15.	((physiologic* or psychophysiologic*) near/2 (feedback or feed back)):ti,ab
#16.	MeSH descriptor: [Meditation] explode all trees
#17.	(meditat* or meditation* or mindful*):ti,ab
#18.	autogenic*:ti,ab
#19.	((hypnosis or hypnot* or reverie or trance) near/2 (therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*)):ti,ab
#20.	((imagery or imagination or imagining) near/3 (relax* or guide* or led or lead*)):ti,ab
#21.	(yoga* or yogic or pilates):ti,ab

#22.	MeSH descriptor: [Muscle Relaxation] explode all trees
#23.	((muscle* or muscular*) near/3 (relax* or stretch* or flex* or exercise*)):ti,ab
#24.	(or #8-#23)
#25.	#7 and #24

Table 12: CINAHL (EBSCO) search terms

S1.	MH hypertension
S2.	TI hypertens* OR AB hypertens*
S3.	TI blood pressure* OR AB blood pressure*
S4.	TI ((high or elevat* or increas*)) OR AB ((high or elevat* or increas*))
S5.	TI (systolic or diastolic or arterial) AND AB (systolic or diastolic or arterial)
S6.	S4 OR S5
S7.	S3 AND S6
S8.	S1 OR S2 OR S7
S9.	(MH "Mind Body Techniques+") OR (MH "Hypnosis+") OR (MM "Meditation") OR (MH "Relaxation Techniques+") OR (MH "Yoga+") OR (MM "Buteyko Method")
S10.	TI (mind body or mindbody) OR AB (mind body or mindbody)
S11.	TI (relax* or breath*) OR AB (relax* or breath*)
S12.	TI (behavior* or behaviour* or therap* or technic*or technique* or practic* or exerc* or educat* or manag* or train* or method*) OR AB (behavior* or behaviour* or therap* or technic*or technique* or practic* or exerc* or educat* or manag* or train* or method*)
S13.	S11 AND S12
S14.	TI (stress* or cognitive or talk* or assertiveness or anger) OR AB (stress* or cognitive or talk* or assertiveness or anger)
S15.	TI (treatment* or therap* or train* or educat* or manag* or technique*) OR AB (treatment* or therap* or train* or educat* or manag* or technique*)
S16.	S14 AND S15
S17.	TI (behaviour* or behavior*) OR AB (behaviour* or behavior*)
S18.	TI (intervention* or therap* or train* or educat* or manag*) OR AB (intervention* or therap* or train* or educat* or manag*)
S19.	S17 AND S18
S20.	TI ((biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback)) OR AB ((biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback))
S21.	TI (physiologic* or psychophysiologic*) OR AB (physiologic* or psychophysiologic*)
S22.	TI (feedback or feed back) OR AB (feedback or feed back)
S23.	S21 AND S22
S24.	MH Meditation
S25.	TI ((meditat* or meditation* or mindful*)) OR AB ((meditat* or meditation* or mindful*))
S26.	TI autogenic* AND AB autogenic*
S27.	TI ((hypnosis or hypnot* or reverie or trance)) OR AB ((hypnosis or hypnot* or reverie or trance))
S28.	(therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*) OR AB (therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*)
S29.	S27 AND S28
S30.	TI (imagery or imagination or imagining) OR AB (imagery or imagination or imagining)
S31.	TI (relax* or guide* or led or lead*) OR AB (relax* or guide* or led or lead*)
S32.	S30 AND S31
S33.	TI ((yoga* or yogic or pilates)) OR AB ((yoga* or yogic or pilates))

S34.	MH Muscle Relaxation
S35.	TI (muscle* or muscular*) OR AB (muscle* or muscular*)
S36.	TI (relax* or stretch* or flex* or exercise*) OR AB (relax* or stretch* or flex* or exercise*)
S37.	S35 AND S36
S38.	S9 OR S10 OR S13 OR S16 OR S19 OR S20 OR S23 OR S24 OR S25 OR S26 OR S29 OR S32 OR S34 OR S37
S39.	S8 AND S38 Limiters - English Language; Exclude MEDLINE records; Human; Publication Type: Clinical Trial, Journal Article, Meta Analysis, Randomized Controlled Trial, Review, Systematic Review; Age Groups: All Adult; Language: English

Table 13: AMED (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	case report/
9.	(letter or comment*).ti.
10.	animals/ not humans/
11.	or/8-10
12.	7 not 11
13.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp Middle Aged/ or exp aged/)
14.	12 not 13
15.	limit 14 to English
16.	(mind body or mindbody).ti,ab.
17.	((relax* or breath*) adj3 (behavior* or behaviour* or therap* or technic*or technique* or practic* or exerc* or educat* or manag* or train* or method*)).ti,ab.
18.	((stress* or cognitive or talk* or assertiveness or anger) adj3 (treatment* or therap* or train* or educat* or manag* or technique*)).ti,ab.
19.	((behaviour* or behavior*) adj3 (intervention* or therap* or train* or educat* or manag*)).ti,ab.
20.	(biofeedback or bio feedback or neurofeedback or neuro feedback or myofeedback or myo feedback).ti,ab.
21.	((physiologic* or psychophysiologic*) adj2 (feedback or feed back)).ti,ab.
22.	(meditat* or meditation* or mindful*).ti,ab.
23.	autogenic*.ti,ab.
24.	((hypnosis or hypnot* or reverie or trance) adj2 (therap* or train* or technique* or relax* or guide* or led or lead* or treatment* or intervention*)).ti,ab.
25.	((imagery or imagination or imagining) adj3 (relax* or guide* or led or lead*)).ti,ab.
26.	(yoga* or yogic or pilates).ti,ab.
27.	((muscle* or muscular*) adj3 (relax* or stretch* or flex* or exercise*)).ti,ab.
28.	breathing therapies/ or mind body medicine/ or yoga/
29.	behavior therapy/ or exp hypnosis/ or imagery/
30.	Complementary therapies/

31.	exp Exercise therapy/
32.	exp Meditation/ or Muscle Relaxation/
33.	or/16-32
34.	15 and 33
35.	Meta-Analysis/
36.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
37.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
38.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
39.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
40.	(search* adj4 literature).ab.
41.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
42.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
43.	or/35-42
44.	randomized controlled trials/
45.	randomized controlled trial.pt.
46.	controlled clinical trial.pt.
47.	placebo.ab.
48.	random*.ti,ab.
49.	trial.ti,ab.
50.	groups.ab.
51.	or/44-50
52.	43 or 51
53.	34 and 52

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to hypertension in adults population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics, economic modelling and quality of life studies.

Table 14: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014–28 August 2018	Exclusions Health economics studies
Embase	2014–28 August 2018	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception–28 August 2018 NHS EED - Inception to March 2015	None

Table 15: Medline (Ovid) search terms

1.	exp Hypertension/
2.	hypertens*.ti,ab.

3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	letter/
9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	Economics/
29.	Value of life/
30.	exp "Costs and Cost Analysis"/
31.	exp Economics, Hospital/
32.	exp Economics, Medical/
33.	Economics, Nursing/
34.	Economics, Pharmaceutical/
35.	exp "Fees and Charges"/
36.	exp Budgets/
37.	budget*.ti,ab.
38.	cost*.ti.
39.	(economic* or pharmaco?economic*).ti.
40.	(price* or pricing*).ti,ab.
41.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
42.	(financ* or fee or fees).ti,ab.
43.	(value adj2 (money or monetary)).ti,ab.
44.	or/28-43
45.	27 and 44

Table 16: Embase (Ovid) search terms

1.	exp Hypertension/

2.	hypertens*.ti,ab.
3.	(elevat* adj2 blood adj pressur*).ti,ab.
4.	(high adj blood adj pressur*).ti,ab.
5.	(increase* adj2 blood pressur*).ti,ab.
6.	((systolic or diastolic or arterial) adj2 pressur*).ti,ab.
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	limit 24 to English language
26.	health economics/
27.	exp economic evaluation/
28.	exp health care cost/
29.	exp fee/
30.	budget/
31.	funding/
32.	budget*.ti,ab.
33.	cost*.ti.
34.	(economic* or pharmaco?economic*).ti.
35.	(price* or pricing*).ti,ab.
36.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
37.	(financ* or fee or fees).ti,ab.
38.	(value adj2 (money or monetary)).ti,ab.
39.	or/26-38
40.	25 and 39

Table 17: NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Hypertension EXPLODE ALL TREES IN NHSEED,HTA
#2.	(Hypertens*) IN NHSEED, HTA

#3.	(elevat* adj2 blood adj pressur*) IN NHSEED, HTA
#4.	(high adj blood adj pressur*) IN NHSEED, HTA
#5.	(increase* adj2 blood pressur*) IN NHSEED, HTA
#6.	((systolic or diastolic or arterial) adj2 pressur*) IN NHSEED, HTA
#7.	#1 OR #2 OR #3 OR #4 OR #5 OR #6

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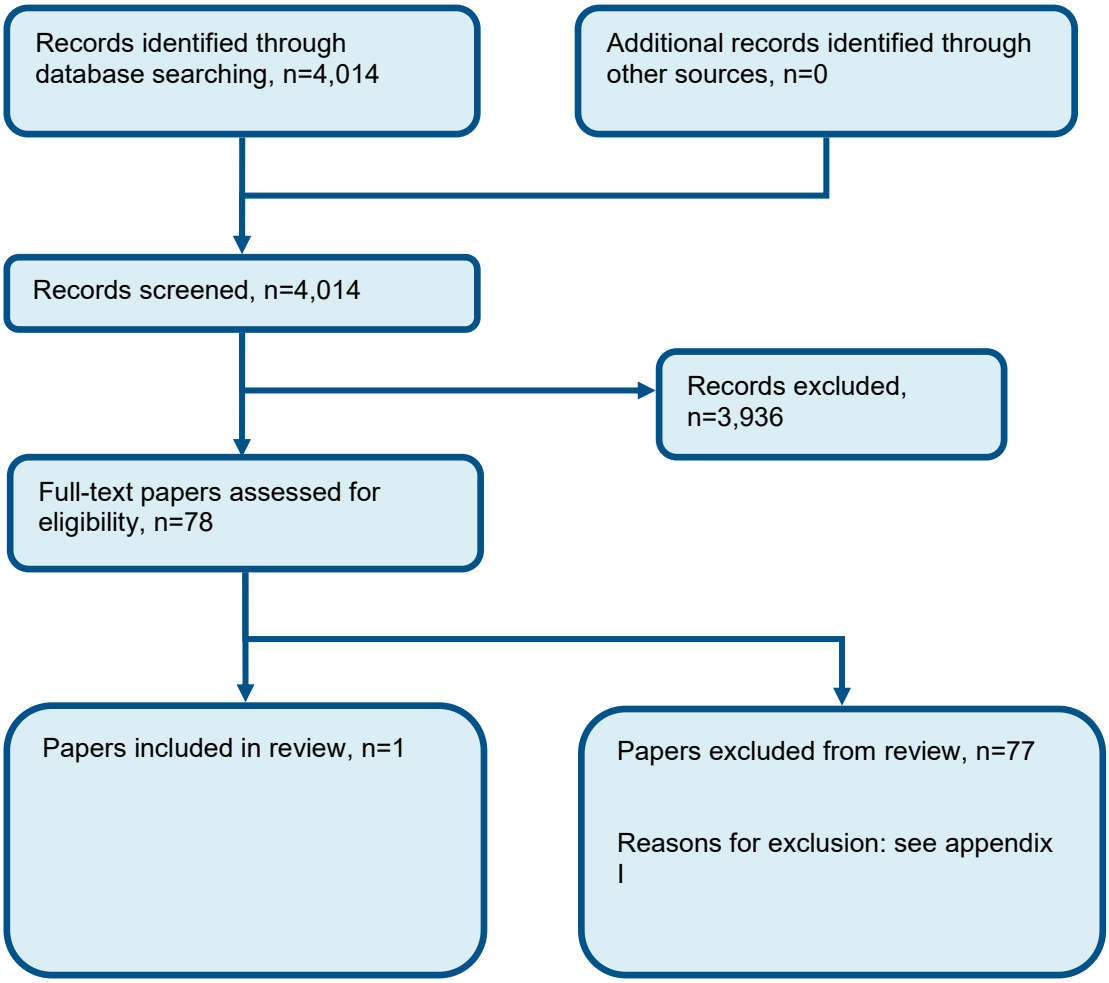
Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of relaxation therapy



Appendix D: Clinical evidence tables

Study	Patel 1988[55]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=104)
Countries and setting	Conducted in the UK; Setting: General practices
Line of therapy	First line
Duration of study	Intervention plus follow up: 8 weeks plus 1 year follow up (FU)
Method of assessment of guideline condition	Adequate method of assessment or diagnosis
Stratum	Overall
Subgroup analysis within study	Stratified then randomised
Inclusion criteria	All participants had previously taken part in the Medical Research Council's treatment of mild hypertension trial, which was carried out in 192 general practices in Britain and included 17,354 people aged 35–64 years at entry, with phase V diastolic blood pressure in the range of 90–109 mmHg. They were treated with active drugs or placebos. In the second phase, 2,756 early entrants who had competed 6 years of the trial were randomised to continue or discontinue treatment with active drugs or placebos. The last 134 recruits to the second phase, who consented to enter both the second phase and the relaxation trial, were further randomised to receive or not receive relaxation therapy.
Exclusion criteria	Not reported
Age, sex and family origin	Age - Range: 35-64. Sex (M: F): 52 male, 51 female. Family origin: N/A
Further population details	1. Age 2. Concomitant pharmacological treatment 3. Family origin 4. Hypertension severity
Indirectness of population	No indirectness
Interventions	(n=49) Intervention 1: Meditation. Relaxation therapy - Conducted by GPs. People attended once a week for 1 hour for 8 weeks in groups of 10. During the first 30 minutes, the GP discussed the topics involved and in the last 30 minutes, the nurse carried out training in breathing exercises, deep muscle relaxation and simple meditation using the instruction cassette tape. Each person was also given a relaxation and meditation instruction cassette tape for daily practice at home. Emphasis was placed on the gradual integration of relaxation into everyday life. Duration 8 weeks. Concurrent medication/care: N/A. Indirectness: No indirectness

Study	Patel 1988[55]
	(n=54) Intervention 2: Breathing. Control group - no relaxation therapy. Duration 8 weeks. Concurrent medication/care: N/A. Indirectness: No indirectness
Funding	Study funded by industry (Supported by the British Heart Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RELAXATION THERAPY versus NO ACTIVE TREATMENT Protocol outcome 1: Stroke (ischaemic or haemorrhagic) at ≥12 months - Actual outcome: Stroke at 12 months; Group 1: 1/49, Group 2: 0/54 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Difference in blood pressure; Group 1 Number missing: 5, Reason: 1 died, 2 moved away, 2 didn't attend; Group 2 Number missing: 3, Reason: 1 had MI, 1 moved away, 1 didn't attend Protocol outcome 2: Myocardial infarction at ≥12 months - Actual outcome: Myocardial infarction at 12 months; Group 1: 0/49, Group 2: 1/54 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Difference in blood pressure; Group 1 Number missing: 5, Reason: 1 died, 2 moved away, 2 didn't attend; Group 2 Number missing: 3, Reason: 1 had MI, 1 moved away, 1 didn't attend Protocol outcome 3: Angina needing hospitalisation at ≥12 months - Actual outcome: Angina at 12 months; Group 1: 0/49, Group 2: 1/54 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness; Baseline details: Difference in blood pressure; Group 1 Number missing: 5, Reason: 1 died, 2 moved away, 2 didn't attend; Group 2 Number missing: 3, Reason: 1 had MI, 1 moved away, 1 didn't attend	
Protocol outcomes not reported by the study	Health related quality of life at ≥12 months; All-cause mortality at ≥12 months; Heart failure needing hospitalisation at ≥12 months; Vascular procedures (including both coronary and carotid artery procedures) at ≥12 months; Cessation or reduction of medication at ≥12 months

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Appendix E: Forest plots

E.1 Relaxation therapy versus no treatment

Figure 2: Stroke at 12 months

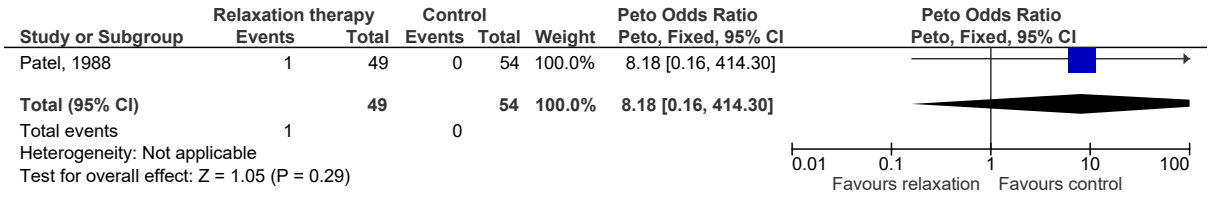


Figure 3: Myocardial Infarction at 12 months

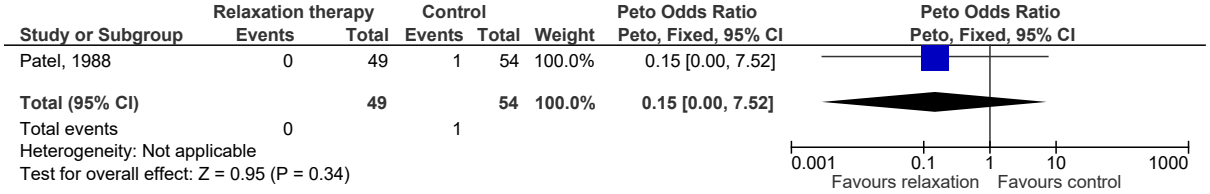
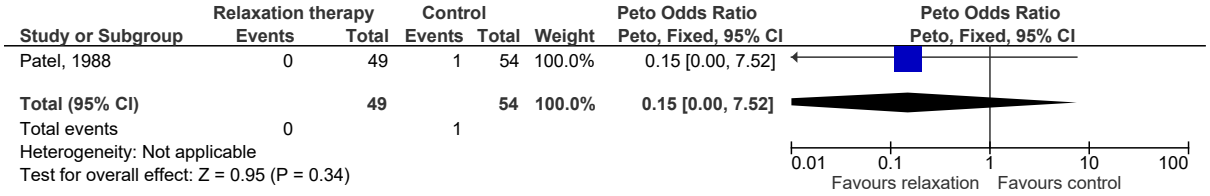


Figure 4: Angina at 12 months



Appendix F: GRADE tables

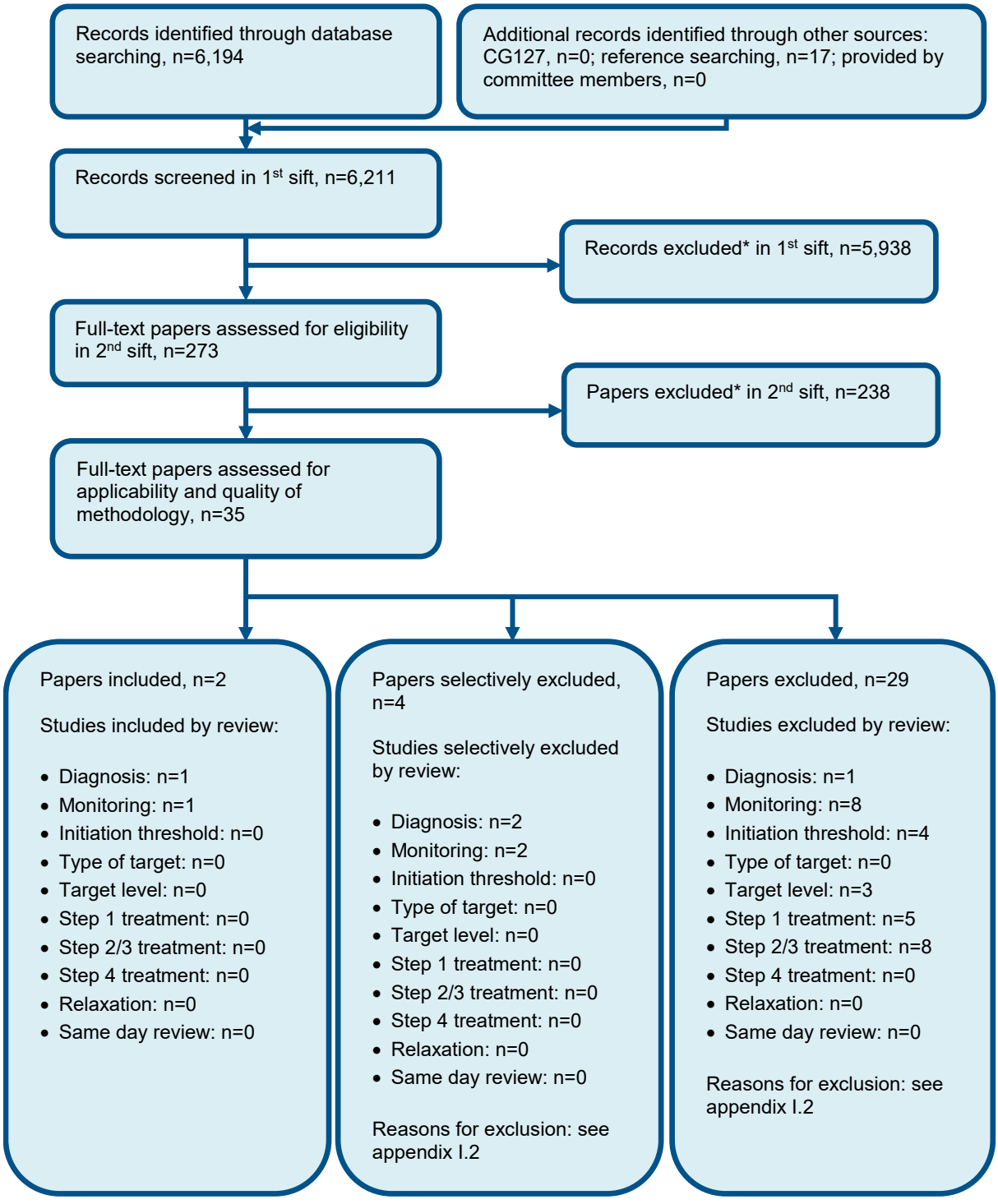
Table 18: Clinical evidence profile: Relaxation therapy versus no treatment

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relaxation therapy	No treatment	Relative (95% CI)	Absolute		
Stroke at 12 months (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/49 (2%)	0%	Peto OR 8.18 (0.16 to 414.3)	20 more per 1000 (from 30 fewer to 70 more)	⊕OOO VERY LOW	CRITICAL
Myocardial Infarction at 12 months (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/49 (0%)	1.9%	Peto OR 0.15 (0 to 7.52)	20 fewer per 1000 (from 70 fewer to 30 more)	⊕OOO VERY LOW	CRITICAL
Angina at 12 months (follow-up 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/49 (0%)	1.9%	Peto OR 0.15 (0 to 7.52)	12 fewer per 1000 (from 70 fewer to 30 more)	⊕OOO VERY LOW	IMPORTANT

[1]Downgraded by 1 increment if the majority of the evidence was at high risk of bias and downgraded by 2 increments if the majority of the evidence was at very high risk of bias.
[2]Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Appendix G: Health economic evidence selection

Figure 5: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H: Health economic evidence tables

None.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 19: Studies excluded from the clinical review

Study	Exclusion reason
Achmon 1989[1]	Less than minimum duration
Adsett 1989[2]	Inappropriate comparison
Agras 1984[3]	No relevant outcomes
Agras 1987[4]	No relevant outcomes
Ahmadpanah 2016[5]	Less than minimum duration
Aivazyan 1988[6]	No relevant outcomes
Alageel 2017[7]	Not review population
Alexander 1989[8]	Not review population
Alparslan 2010[9]	Less than minimum duration
Amigo Vazquez 2001[10]	Not in English
Anderson 2008[11]	Systematic Review, references checked
Anonymous 1979[12]	Inappropriate comparison
Bai 2015[13]	Systematic Review, references checked
Bradley 1980[14]	Less than minimum duration
Brandani 2017[15]	Systematic Review, references checked
Bush 1988[16]	Unavailable
Canter 2004[17]	Systematic Review, references checked
Chu 2016[18]	Systematic Review, references checked
Corey 2014[19]	Not review population
Cramer 2016[20]	Not review population
Dhungana 2018[22]	Protocol
Dickinson 2008[23]	Cochrane review, less than minimum duration
Glasgow 1989[24]	Inappropriate comparison
Goebel 1980[25]	Less than minimum duration
Gotink 2017[26]	Not review population
Greenhalgh 2009[27]	Systematic Review, references checked
Guohua 2015[28]	Systematic Review, references checked
Hafer 1984[29]	Less than minimum duration
Hafner 1982[30]	Less than minimum duration
Hartley 2014[32]	No relevant outcomes
Hartley 2014[34]	No relevant outcomes
Hartley 2014[31]	No relevant outcomes
Hartley 2015[33]	No relevant outcomes

Study	Exclusion reason
Hoelscher 1987[35]	Less than minimum duration
Jenaabadi 2018[36]	Less than minimum duration
Johnston 1993[37]	No relevant outcomes
Khramelashvili 1986[38]	Not in English
Kopf 2014[39]	Not review population
Kruerke 2018[40]	Incorrect study population
Landman 2014[41]	Less than minimum duration
Larson 2013[42]	Inappropriate comparison. No relevant outcomes
Lee 2010[43]	Systematic Review, references checked
Levenson 2017[44]	Protocol
Mikolasek 2018[45]	Systematic Review, references checked
Momeni 2016[46]	No relevant outcomes
Nagele 2014[47]	Systematic Review, references checked
Nowlis 1980[49]	Unavailable
Ooi 2017[50]	Systematic Review, references checked
Pandic 2008[51]	Less than minimum duration
Park 2017[52]	Systematic Review, references checked
Patel 1975[53]	No relevant outcomes
Patel 1975[58]	No relevant outcomes
Patel 1975[54]	No relevant outcomes
Patel 1981[56]	Less than minimum duration
Patel 1985[57]	Not review population
Pender 1985[59]	Less than minimum duration
Perry 1984[60]	Less than minimum duration
Petersen 2018[61]	Protocol
Posadzki 2014[62]	Systematic Review, references checked
Rosas Marchiori 2015[63]	No relevant outcomes
Seer 1980[64]	Less than minimum duration
Siu 2015[65]	Not review population
Southam 1981[66]	Unavailable
Southam 1982[67]	Less than minimum duration
Sriloy 2015[68]	No relevant outcomes
Sun 2015[69]	Inappropriate comparison
Supa'at 2013[70]	Less than minimum duration
Tulloh 2018[71]	Incorrect study population
Ursua 2018[72]	Less than minimum duration
Vaccarino 2013[73]	No relevant outcomes
van Montfrans 1990[74]	No relevant outcomes
Venturelli 2015[75]	Less than minimum duration
Wolff 2013[76]	Less than minimum duration
Wood 1986[77]	Not review population
Yang 2017[78]	Less than minimum duration
Yeh 2008[79]	Less than minimum duration

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I.2 Excluded health economic studies

None.

Appendix J: Research recommendations

J.1 Relaxation therapies

Research question: What is the clinical and cost-effectiveness of relaxation therapies for the management of primary hypertension in adults in terms of reducing cardiovascular events and improving quality of life?

Why this is important:

It is known that blood pressure is increased at times of stress and conversely is reduced when levels of arousal are low. It is unknown whether participation in relaxation therapies can lead to a reduction in cardiovascular events. Relaxation therapies do not form part of current practice in the management of hypertension, as there is a lack of evidence assessing either their clinical- or cost-effectiveness.

Despite the benefits of antihypertensive medication, many individuals with hypertension do not achieve their target blood pressure. The reasons for poorly controlled hypertension are multifactorial, and within this population are individuals who are unable to, or choose not to, take medication. The identification of relaxation therapies as an alternative or complimentary treatment approach may reduce the proportion of individuals with poorly controlled hypertension with consequent improvement in health outcomes.

This research recommendation has been written to guide the design of studies so that the evidence generated is of sufficient, high quality for inclusion in future guidance.

Criteria for selecting high-priority research recommendations:

PICO question	Population: Adults with primary hypertension. Intervention(s): Intervention designed to promote relaxation (relaxation therapies). Comparison: Usual care, sham or placebo therapy. Outcome(s): All-cause mortality, stroke, myocardial infarction and health-related quality of life to be assessed at 12 months or more.
Importance to patients or the population	The current approach to managing hypertension involves combining lifestyle optimisation with antihypertensive medication. The identification of benefit from relaxation therapies would identify a third treatment modality. It is likely that relaxation therapies would be acceptable to people, especially those that are unable to, or choose not to, take medication.
Relevance to NICE guidance	High quality research in this area would generate new evidence and may enable future updates of this guidance to make recommendations on the use of relaxation therapies for the management of hypertension. If studies investigate different methods of relaxation therapies, then it may be possible to make recommendations regarding method and/or intensity of therapy.
Relevance to the NHS	Relaxation therapies for the management of hypertension are not currently available on the NHS. Any impact on future service delivery or finances are dependent on the clinical- and cost-effectiveness of the intervention.
National priorities	No.
Current evidence base	Only a single study was included in the evidence review. The evidence from this was graded as 'very low' quality due to high risk of bias and imprecision. Several potentially relevant studies were identified in the literature search, but these were excluded due to ineligible populations, short duration or lack of suitable endpoints. Currently, there is no appropriate evidence base on which recommendations for the use of relaxation therapy can make.

Equality	No effect on 'protected characteristics' as defined in the Equality Act.
Study design	• Randomised control trial of a relaxation therapy in addition to usual care, ideally versus sham or placebo. • Study duration 12 months or more. • Outcomes to include all-cause mortality, cardiovascular events and health-related quality of life as a minimum. • Surrogate outcome (for example, blood pressure or user acceptability) may also be included but are unlikely to inform future guidance.
Feasibility	Hard outcome measures are required for 2 reasons. Firstly, these outcome measures are the standard on which the current guidelines are based. Secondly, it is unlikely that a double-blind study can be conducted into relaxation therapies, and so outcome measures must be selected to minimise potential bias. To demonstrate a significant difference in outcomes for relaxation therapies in addition to usual care the study will need to recruit many participants for a prolonged period. It is unlikely that the study could be completed in less than 5 years, but this is consistent with other cardiovascular studies. The costs are dependent on the choice of relaxation therapy. Current guidelines recommend that all hypertensive individuals be offered antihypertensive medication, except those with stage 1 hypertension at low-risk of cardiovascular events. This recommendation is based on evidence of clinical- and cost-effectiveness. It is therefore unlikely to be ethical to randomise people who would normally be offered medication to receive either medication or relaxation therapy. The likely study population would therefore be either low-risk stage 1 hypertensive individuals in whom antihypertensive medication may be considered, or individuals with hypertension who are already taking medication. These limitations will affect the event rate and thus increase the required size or duration of the study.
Other comments	The study may attract commercial funders including companies developing physical or digital adjuncts for relaxation.
Importance	Low: the research is of interest and will fill existing evidence gaps.

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