

Supplemental Information

Supplementary Table S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Checklist and PRISMA 2020 for Abstracts Checklist

Supplementary Table S2. Time to Benefit for the Primary Prevention of Stroke for Older Adults Treated with More Intensive Hypertension Treatment

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Table S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Checklist and PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1 of the manuscript
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See table below
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 5 of manuscript
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6 of manuscript
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6-7 of manuscript
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6 of manuscript (more details provided in the individual systematic reviews)
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 6 and 7 of manuscript (more details provided in the individual systematic reviews)
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7 of manuscript (one reviewer)
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 7 of manuscript (one reviewer)
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 7 of manuscript
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any	Page 7 of manuscript (studies with missing survival curves were

Section and Topic	Item #	Checklist item	Location where item is reported
		assumptions made about any missing or unclear information.	excluded)
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Risk of bias was already assessed in the systematic reviews included in this study
Effect measures	12	Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	Page 7 and 8 of manuscript (TTB analysis)
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 7 of manuscript and Table 1 with list of excluded studies
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 8 and 9 of manuscript (Digitizelt, Stata module)
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 8 of manuscript (Stata module)
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 8 of manuscript (Stata module)
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	Page 8 of manuscript (I^2 value)
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 8 and 9 of manuscript; Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1; Table 1

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Page 9 of manuscript; Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	N/A
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Figure 3; Supplementary Table S1
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2; Supplementary Table S1
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 10 of manuscript; Figure 3; Supplementary Table S1
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 10 and 11 of manuscript; Table 2; Figure 3; Supplementary Table S1
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11-16 of manuscript
	23b	Discuss any limitations of the evidence included in the review.	Page 16-18 of manuscript
	23c	Discuss any limitations of the review processes used.	Page 17 of manuscript
	23d	Discuss implications of the results for practice, policy, and future research.	Page 11-18 of manuscript
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	N/A
	24b	Indicate where the review protocol can be	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
		accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Acknowledgments section
Competing interests	26	Declare any competing interests of review authors.	Acknowledgments section
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes, Background section
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes, Methods section
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes, Methods section
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	N/A as we only included systematic reviews that have already assessed for risk of bias
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes, Methods section
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g., study risk of bias, inconsistency and imprecision).	Yes, included in confidence intervals of TTb
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes, Acknowledgments section
Registration	12	Provide the register name and registration number.	N/A

Supplementary Table S2. Time to Benefit for the Primary Prevention of Stroke for Older Adults Treated with More Intensive Hypertension Treatment

Study	Time to benefit (95%CI), y		
	ARR=0.002	ARR=0.005	ARR=0.01
Coope ³⁹ 1986	2.6 (0.5-8.4)	3.0 (0.9-7.6)	3.5 (1.4-7.6)
SHEP ⁴⁰ 1991	0.9 (0.2-2.5)	1.5 (0.6-3.1)	2.4 (1.2-4.1)
STOP ⁴¹ 1991	0.4 (0.1-1.4)	0.7 (0.2-1.8)	1.0 (0.3-2.4)
MRC-O ⁴² 1992	3.0 (0.9-7.7)	3.9 (1.7-7.9)	5.3 (2.8-9.2)
Syst-Eur ⁴³ 1997	0.4 (0.1-0.9)	0.9 (0.4-1.8)	2.0 (0.7-4.3)
HYVET ⁴⁴ 2008	1.0 (0.2-3.3)	1.6 (0.4-4.1)	2.5 (0.9-5.6)
Wei ⁴⁵ 2013	0.5 (0.0-1.6)	0.8 (0.1-2.7)	1.5 (0.2-4.6)
SPRINT ²⁴ 2015	4.0 (0.8-12.0)	5.9 (2.2-13.0)	7.8 (4.3-13.3)
STEP ²⁵ 2021	1.1 (0.1-3.9)	4.5 (0.6-17.1)	8.4 (3.8-16.5)
Summary time to benefit, y	0.9 (0.5-1.7)	1.7 (1.0-2.9)	3.0 (1.8-4.9)
Test of heterogeneity			
<i>I</i> ² , %	52.0	60.1	72.2
<i>P</i> value	0.034	0.01	<0.001

Abbreviations:

CI, Confidence interval
y, years

Study Abbreviations:

ARR, Absolute Risk Reduction

SHEP, Systolic Hypertension in the Elderly Program

STOP, Swedish Trial in Old Patients with hypertension

MRC-O, Medical Research Council Trial of Treatment of Hypertension in Older Adults

Syst-Eur, Systolic Hypertension in Europe

HYVET, Hypertension in the Very Elderly Trial

SPRINT, Systolic Blood Pressure Intervention Trial
STEP, Strategy of blood pressure intervention in Elderly hypertensive Patients

The time to benefit (TTB) for $ARR=0.002$ is the time to prevent one stroke per 500 older persons that received antihypertensive treatment. Similarly, the TTB for $ARR=0.005$ is the time to prevent one stroke per 200 older persons treated and the TTB for $ARR=0.01$ is the time to prevent one stroke per 100 older persons treated.