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 (studies with missing survival curves were | Page 7 of manuscript                                                |
| 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; Figure 3; Table 2; 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 | 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 | 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. | N/A                             |
| Support            | 24c    | Describe and explain any amendments to information provided at registration or in the protocol. | N/A                             |
|                    |        | N/A as we only included systematic reviews that have already assessed for risk of bias |                                |
| Competing interests| 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 |
|                    |        | N/A                             |                                |
| Availability of data, code and other materials | 26 | Declare any competing interests of review authors. | Acknowledgments section |
|                    |        | N/A                             |                                |
|                    | 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             |        | Identify the report as a systematic review. | Yes |
| BACKGROUND        |        | Provide an explicit statement of the main objective(s) or question(s) the review addresses. | Yes, Background section |
| METHODS           |        | Specify the inclusion and exclusion criteria for the review. | Yes, Methods section |
| Eligibility criteria | 3 | 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      | 4 | Specify the methods used to assess risk of bias in the included studies. | N/A |
| Synthesis of results | 5 | Specify the methods used to present and synthesise results. | Yes, Methods section |
| RESULTS           |        | Give the total number of included studies and participants and summarise relevant characteristics of studies. | Yes |
| Synthesis of results | 6 | 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 Abbreviations | Time to benefit (95%CI), y | ARR=0.002 | ARR=0.005 | ARR=0.01 |
|---------------------|-----------------------------|-----------|-----------|----------|
| Coope\textsuperscript{39} 1986 | 2.6 (0.5-8.4) | 3.0 (0.9-7.6) | 3.5 (1.4-7.6) |
| SHEP\textsuperscript{40} 1991 | 0.9 (0.2-2.5) | 1.5 (0.6-3.1) | 2.4 (1.2-4.1) |
| STOP\textsuperscript{41} 1991 | 0.4 (0.1-1.4) | 0.7 (0.2-1.8) | 1.0 (0.3-2.4) |
| MRC-O\textsuperscript{42} 1992 | 3.0 (0.9-7.7) | 3.9 (1.7-7.9) | 5.3 (2.8-9.2) |
| Syst-Eur\textsuperscript{43} 1997 | 0.4 (0.1-0.9) | 0.9 (0.4-1.8) | 2.0 (0.7-4.3) |
| HYVET\textsuperscript{44} 2008 | 1.0 (0.2-3.3) | 1.6 (0.4-4.1) | 2.5 (0.9-5.6) |
| Wei\textsuperscript{45} 2013 | 0.5 (0.0-1.6) | 0.8 (0.1-2.7) | 1.5 (0.2-4.6) |
| SPRINT\textsuperscript{24} 2015 | 4.0 (0.8-12.0) | 5.9 (2.2-13.0) | 7.8 (4.3-13.3) |
| STEP\textsuperscript{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

| $I^2$, % | 52.0 | 60.1 | 72.2 |
| $P$ 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.