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Should treatment of 'elevated' blood pressure, especially in older people, be based on global risk estimation?

ESC hypertension guidelines, 'elevated' BP, and global risk estimation

The European Society of Cardiology (ESC) has recently issued its own hypertension guidelines entitled 2024 ESC Guidelines for the management of elevated blood pressure and hypertension (ESC-GL) [1] and introduced a new blood pressure (BP) category called 'elevated BP'. 'Elevated BP' is defined as an office BP of 120–139/70–89 mmHg, at variance from the European Society of Hypertension (ESH) definition [2] of these BP values as normal (120–129/70–79 mmHg) and high normal (130–139/80–89 mmHg). The ESC-GL recommend [1] that treatment of people with 'elevated BP' should be guided by the estimated *global* risk of cardiovascular (CV) disease based on a rationale previously discussed [3,4]. To estimate *global* CV risk, ESC-GL recommend [1] considering traditional high-risk conditions such as hypertension-mediated organ damage, chronic kidney disease and type-2 diabetes mellitus, or to use newer risk-prediction models such as Systematic Coronary Risk Evaluation-2 (SCORE2) and SCORE2-Old People (OP) [5,6], when high-risk states are absent. In all people with an 'elevated BP' in whom the 10-year CV risk is $\geq 10\%$, BP lowering treatment is recommended by the ESC-GL [1].

For individuals with high 'elevated BP' (130–139/80–89 mmHg) and 10-year CV risk of 5– $<10\%$, the ESC-GL recommend [1] considering additional risk modifiers associated with an increased CV risk, and if they are present, drug treatment may be considered [1]. If absent, BP-lowering lifestyle measures are recommended for three months [1], followed by pharmacological therapy if BP remains $\geq 130/80$ mmHg [1], or if lifestyle changes have not worked or have not been implemented [1].

The above treatment recommendations by ESC-GL [1] apply to all individuals with an 'elevated BP' irrespective of age. However, recognising the lack of conclusive evidence as well as the added risk of side effects of drug treatment among certain subgroups, the ESC-GL Task Force also recommends [1] that, among patients with 'elevated BP', BP-lowering treatment should always be started based on individual clinical judgement and shared decision-making. To a certain degree this reservation protects against the criticism of indulging into excessive treatment recommendations.

According to the ESC-GL [1], very old and frail patients with hypertension should not be denied the potential benefits of BP-lowering treatment down to a BP target of 120–129/70–79 mmHg. However, in these patients personalised decision-making should be a priority [1]. In this respect, a major consideration [1] should also be whether reversible causes of frailty can be addressed e.g. underlying comorbidities can be identified and treated or patients can undergo supervised muscle-strengthening physiotherapy or supervised exercise and co-ordination and balance training. ESC-GL recommend [1] that all patients must be fully informed about the benefits and risks of starting BP-lowering treatment, so that their preference is considered.

The ESC-GL [1] refer to a systematic review of hypertension guidelines [7], reporting that among 34 hypertension guidelines, 18 recommended a systolic BP of 150 mmHg as the systolic goal in frail and/or older patients, and 4 guidelines endorsed systolic BP targets <130 mmHg or even <120 mmHg in older and/or frail people [8–11]. However, of these 4 guidelines, the Australian ones [8] do not directly support the target systolic BP <120 mmHg to older people. Those of the University of Michigan [10] suggest a systolic BP goal of 150 mmHg in older patients while the Canadian guidelines [11] support aggressive treatment of older patients based on 'elevated' automated office BP measurements. Thus, the ESC-GL [1] more clearly and directly opens for drug treatment of many people with advanced age, high normal ('elevated') BP and mild to moderate frailty, mainly based on the global risk assessment of SCORE2-OP [6].

Evidence-based drug treatment of hypertension and assessment of CV risk

Drug treatment of hypertension to prevent CV morbidity and mortality is evidence-based in the sense that numerous randomised controlled trials (RCTs) in various populations with low, intermediate, and high CV risks have shown protective benefit of the five major BP lowering drug classes, i.e. angiotensin converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics and, as extensively detailed, also beta-blockers [12,13]. Modern treatment [2] favours

combination drugs with two or three of these medication classes, typically starting with low doses which, if needed, are increased to full doses to reach the established BP target.

Despite such apparently simple and straight forward treatment principles, the diagnostic and therapeutic approaches to hypertension remain complex and challenging in about one third of the adult population. This is why guidelines for handling hypertension – the most prominent ones being those of the ESH [2], the International Society of Hypertension [14], and the American College of Cardiology/American Heart Association (ACC/AHA) [9], are regularly updated. Considering the multiplicity of hypertension phenotypes and the clinical complexity of different antihypertensive drugs, the timing of the drug treatment initiation, the type and speed of treatment titration, and the values to choose as BP targets for treatment, are all difficult decisions to make. In this context, easily available tools to support the decision-making process have been developed and are recommended by the guidelines. In this context, risk stratification tools can increase the clinical information from the RCTs and their evidence on drug benefits, helping to adopt the best treatment decisions in patients with various risk levels in whom treatment of different intensities may be needed.

SCORE and SCORE2: the basis of cardiovascular risk assessments

The Systematic Coronary Risk Evaluation (SCORE) [15] was developed from Northern and Southern European populations to predict the 10-year risk of CV disease and was applied in the previous joint European Hypertension Guidelines, including those published in 2018 [16]. However, a limitation of SCORE was that it only estimated Athero-Sclerotic Cardio-Vascular-Disease (ASCVD) mortality, not taking morbidity into consideration [15]. This was addressed in the updated SCORE2 tool [5], derived from, and extensively validated in, numerous European cohort studies of several hundred thousand people, and included in the ESH 2023 HT-GL [2]. With the use of SCORE2 to assess ASCVD risk for ages 40–69 years, the risk assessment of European people is now more aligned with the pooled cohort equations [17,18,19] to estimate the 10-year risk of fatal and non-fatal ASCVD events in North American adults as recommended in the European [2] and American [9] hypertension guidelines.

Another tool for older patients: SCORE2-older persons

ESH guidelines [2] recommend a separate risk assessment tool, SCORE2-OP for adults above 70 years [6]. The SCORE2-OP study design [6] was similar to the

SCORE2 model [5], with model coefficients derived from the Cohort of Norway (CONOR) study [20]. This study population [20] was selected because it was considered by the SCORE2-OP Working Group [6] to be a large, representative population-based cohort, and it had previously been used for model derivation [21–23]. The model was then recalibrated to four geographical risk regions across Europe and beyond, using contemporary age- and sex-specific incidences and risk factor distributions. External validation was performed in prospective cohorts from different risk regions, and the model was applied to estimate individualised treatment benefit from BP and serum cholesterol lowering to illustrate how SCORE2-OP [6] can be used for treatment decision-making in clinical practice.

To estimate the effect of BP lowering on CV diseases, average relative treatment effects from large meta-analyses were added to SCORE2-OP [6]. The SCORE2-OP Working Group [6] estimated the absolute treatment effect from BP lowering to the target of <140 mmHg in older persons with hypertension from Hypertension in the Very Elderly Trial (HYVET) [24] and the Systolic Blood Pressure Intervention Trial (SPRINT) [25,26], using a hazard ratio (HR) of 0.80 per 10 mmHg systolic BP reduction from a Blood Pressure Lowering Treatment Trialists Cooperation (BPLTTC) meta-analysis [27]. As for SCORE2 [5], the novelty of SCORE2-OP [6] was the inclusion of ASCVD morbidity since previous risk models in older persons had only focused on ASCVD mortality.

The misuse of SCORE2-OP by the 2024 hypertension guidelines of the European Society of Cardiology

Many persons within the ‘elevated BP’ range will have an estimated 10-year global risk for CV events of $\geq 10\%$, which, according to the ESC-GL [1], merits BP-lowering drug treatment. This CV risk threshold will include almost the entire older population due to the association of high risk with age because the ESC recommendations [1] apply to all individuals with ‘elevated BP’, irrespective of age, including people above 85 years. In middle- and high-CV risk countries, literally every person above 70 years with a BP >130/80 mmHg will be a candidate to receive antihypertensive drug treatment (Figure 1). This strategy [1], will further apply to all men above 70 years, and all women above 75 years, even in low-CV risk countries in Europe.

Such a therapeutic strategy of older hypertensive persons is not, as we see it, sound but rather appears as a point of major clinical concerns. In fact, the SCORE2-OP Working Group [6] has never recommended applying its risk chart assessment to CV risk factors, including BP, that are not clearly elevated. On the contrary, for older persons, the SCORE2-OP Working Group [6]

points out that there is currently no CV disease risk threshold for initiating risk factor lowering treatment in international guidelines. Should such thresholds be considered [6], their value should differ according to age as both the potential harms and the gains in CV disease free life expectancy from preventive therapy heavily depend on age.

National and international guidelines need to consider different treatment thresholds for young, middle-aged, old, and very old persons. In this context, the Norwegian guidelines [28] for the primary prevention of CV disease (highly relevant to this issue since SCORE2-OP [6] is based on CONOR [20]) has recommended a graded risk score approach to pharmacological management, i.e. 10-year CV risk over 5% in ages 45–54 years, > 10% risk in ages 55–64 years, and >15% in ages 65–74 years [20]. In addition, no specific 10-year risk level at which to initiate drug treatment of specific risk factors such as high BP or high serum cholesterol has been recommended for older people based on SCORE2-OP, although

a ‘global’ 10-year risk level higher than the 15% for ages 65–74 years has been mentioned [20]. By linear extrapolations, the risk level should then be 20% for ages 75–84 years and even higher for ages 85 years and above. Applying such a simple principle [20], the colour codes for the SCORE2-OP [6] risk chart (Figure) would be very different.

Within the BP range renamed as ‘elevated BP’ by the ESC-GL [1], the efficacy of BP-lowering therapy has apparently been shown in an individual participant meta-analysis of RCTs [29]. However, this makes the misuse of SCORE2-OP [6] by the ESC-GL [1] even more problematic because the results from this meta-analysis [29] have been extensively criticised [30–32] for including large numbers of people from non-hypertension comparative RCTs (in which the purpose is to see the non-BP dependent protective effect of different antihypertensive drugs in absence or with minimal BP reductions) and for several additional methodological problems. No dedicated RCT has ever been carried out in persons without

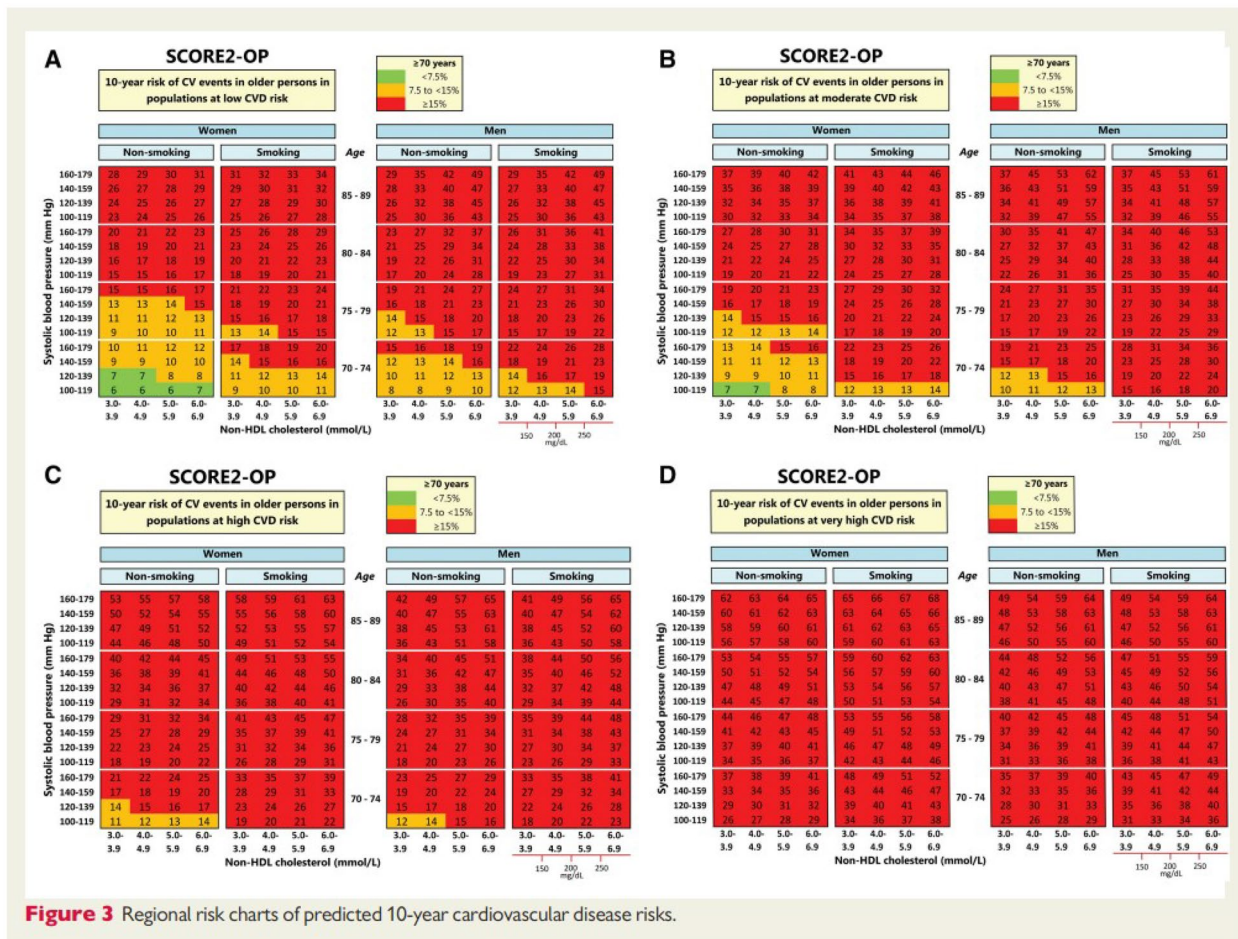


Figure 1. Two-dimensional risk charts of SCORE2-OP [6] for all four cardiovascular (CV) risk regions of Europa (A: low risk, B: moderate risk, C: high risk, D: very high risk) are shown in the Figure 1, and for practical purposes displayed according to non-high-density lipoprotein cholesterol (HDL-c) rather than total cholesterol (TC) and HDL-c. The figure shows that almost all older people (OP) (men and women) have a 10-year global CV risk >7.5–10%. This would according to the 2024 European Society of Cardiology Guidelines for the management of elevated blood pressure and hypertension [1] suggest that most older people with BP in the ranges of 130–139/80–89mmHg should receive antihypertensive medications. The figure is taken from [6] with licence from Oxford University Press.

hypertension, including people with baseline systolic BP <140 mmHg, except perhaps for a RCT of people with so-called 'intermediate-risk' in the placebo-controlled Heart Outcomes Prevention Evaluation-3 (HOPE-3) trial [33]. In HOPE-3 [33] there was clinical benefit of treating hypertensive patients only in patients with a mean baseline systolic BP >143 mmHg but no benefit for study participants with lower systolic BP.

Conclusions

The 2024 ESC-Guidelines have introduced a new BP category called 'elevated BP', which is defined as an office systolic BP of 120–139 mmHg or a diastolic BP of 70–89 mmHg. Many people within the 'elevated BP' range will have an estimated 10-year risk for CV events $\geq 10\%$, which, according to the ESC-Guidelines, is sufficient to merit BP-lowering drug treatment. This CV risk threshold will include almost the entire older population due to the close association of high CV risk with age, making the ESC treatment strategy pertinent to a huge number of individuals around the world as well as virtually to the whole older population. This aggressive treatment strategy, extended to people with 'elevated BP' (>130/80 mmHg, previously high normal BP), appears to us without support from the literature – not only for older people as discussed in this editorial paper, but also for the population below 70 years of age.







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References

- [1] McEvoy JW, McCarthy CP, Bruno RM, et al. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J*. 2024;45(38):3912–4018. doi:10.1093/eurheartj/ehae178.
- [2] Mancia G, Kreutz R, Brunström M, et al. 2023 ESH guidelines for the management of arterial hypertension the Task Force for the management of arterial hypertension of the European Society of Hypertension: endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens*. 2023; 41(12):1874–2071. doi:10.1097/HJH.0000000000003480.
- [3] Karmali KN, Lloyd-Jones DM, van der Leeuw J, et al. Blood pressure-lowering treatment strategies based on cardiovascular risk versus blood pressure: a meta-analysis of individual participant data. *PLoS Med*. 2018;15(3):e1002538. doi:10.1371/journal.pmed.1002538.
- [4] Thomopoulos C, Parati G, Zanchetti A. Effects of blood-pressure-lowering treatment on outcome incidence. 12. Effects in individuals with high-normal and normal blood pressure: overview and meta-analyses of randomized trials. *J Hypertens*. 2017;35(11):2150–2160. doi:10.1097/HJH.00000000000015475.
- [5] SCORE2 Working Group and ESC Cardiovascular Risk Collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. *Eur Heart J*. 2021;42(25):2439–2454. doi:10.1093/eurheartj/ehab309.
- [6] SCORE2-OP Working Group and ESC Cardiovascular Risk Collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. *Eur Heart J*. 2021;42(25):2455–2467. doi:10.1093/eurheartj/ehab312.
- [7] Bogaerts JMK, von Ballmoos LM, Achterberg WP, et al. Do we AGREE on the targets of antihypertensive drug treatment in older adults: a systematic review of guidelines on primary prevention of cardiovascular diseases. *Age Ageing*. 2022;51(1):14. doi:10.1093/ageing/afab1928.
- [8] Gabb GM, Mangoni A, Anderson CS, et al. Guideline for the diagnosis and management of hypertension in adults - 2016. *Med J Aust*. 2016;205(2):85–89. doi:10.5694/mja16.00526.
- [9] Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127–e248. doi:10.1016/j.jacc.2017.11.006.

- [10] Jimbo MDM, Ealovega MW, Van Harrison R, et al. UMHS hypertension guideline. July 2019. http://www.med.umich.edu/linfo/FHP/practiceguides/ne_whtn/htn.pdf
- [11] Rabi DM, McBrien KA, Sapir-Pichhadze R, et al. Hypertension Canada's 2020 comprehensive guidelines for the prevention, diagnosis, risk assessment, and treatment of hypertension in adults and children. *Can J Cardiol.* 2020;36(5):596–624. doi:10.1016/j.cjca.2020.02.086.
- [12] Mancia G, Kjeldsen SE. Randomized clinical outcome trials in hypertension. *Hypertension.* 2024;81(1):17–23. doi:10.1161/HYPERTENSIONAHA.123.21725.
- [13] Mancia G, Kjeldsen SE, Kreutz R, et al. Individualized beta-blocker treatment for high blood pressure dictated by medical comorbidities: indications beyond the 2018 European Society of Cardiology/European Society of Hypertension guidelines. *Hypertension.* 2022;79(6):1153–1166. doi:10.1161/HYPERTENSIONAHA.122.19020.
- [14] Unger T, Borghi C, Charchar F, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension.* 2020;75(6):1334–1357. doi:10.1161/HYPERTENSIONAHA.120.15026.
- [15] Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J.* 2003;24(11):987–1003. doi:10.1016/s0195-668x(03)00114-3.
- [16] Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: the Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens.* 2018;36(10):1953–2041. doi:10.1097/HJH.0000000000001940.
- [17] Preiss D, Kristensen SL. The new pooled cohort equations risk calculator. *Can J Cardiol.* 2015;31(5):613–619. doi:10.1016/j.cjca.2015.02.001.
- [18] Medina-Inojosa JR, Somers VK, Garcia M, et al. Performance of the ACC/AHA Pooled Cohort Cardiovascular Risk Equations in clinical practice. *J Am Coll Cardiol.* 2023;82(15):1499–1508. doi:10.1016/j.jacc.2023.07.018.
- [19] Vemu PL, Yang E, Ebinger JE. Moving toward a consensus. Comparison of the 2023 ESH and 2017 ACC/AHA hypertension guidelines. *JACC Adv.* 2024;3(10):101230. doi:10.1016/j.jaccadv.2024.101230.
- [20] Naess O, Sogaard AJ, Arnesen E, et al. Cohort profile: cohort of Norway (CONOR). *Int J Epidemiol.* 2008;37(3):481–485. doi:10.1093/ije/dym217.
- [21] Cooney MT, Selmer R, Lindman A, et al. Cardiovascular risk estimation in older persons: SCORE O.P. *Eur J Prev Cardiol.* 2016;23(10):1093–1103. doi:10.1177/2047487315588390.
- [22] Selmer R, Igländ J, Ariansen I, et al. NORRISK 2: a Norwegian risk model for acute cerebral stroke and myocardial infarction. *Eur J Prev Cardiol.* 2017;24(7):773–782. doi:10.1177/2047487317693949.
- [23] Rabanal KS, Igländ J, Tell GS, et al. Validation of the cardiovascular risk model NORRISK 2 in South Asians and people with diabetes. *Scand Cardiovasc J.* 2021;55(1):56–62. doi:10.1080/14017431.2020.1821909.
- [24] Bulpitt C, Fletcher A, Beckett N, et al. Hypertension in the Very Elderly Trial (HYVET): protocol for the main trial. *Drugs Aging.* 2001;18(3):151–164. doi:10.2165/00002512-200118030-00001.
- [25] Wright J, Williamson J, Whelton P, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med.* 2015;373:2103–2116.
- [26] Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥ 75 years: a randomized clinical trial. *JAMA.* 2016;315(24):2673–2682. doi:10.1001/jama.2016.7050.
- [27] Etehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet.* 2016;387(10022):957–967. doi:10.1016/S0140-6736(15)01225-8.
- [28] Klemsdal TO, Gjelsvik B, Elling I, et al. New guidelines for the prevention of cardiovascular disease. *J Norw Med Ass.* 2017;137. doi:10.4045/tidsskr.15.0109.
- [29] Rahimi K, Bidel Z, Nazarzadeh M, et al. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet.* 2021;397(10285):1625–1636. doi:10.1016/S0140-6736(21)00590-0.
- [30] Kreutz R, Brunström M, Thomopoulos C, et al. Do recent meta-analyses truly prove that treatment with blood pressure-lowering drugs is beneficial at any blood pressure value, no matter how low? A critical review. *J Hypertens.* 2022;40(5):839–846. doi:10.1097/HJH.0000000000003056.
- [31] Brunström M, Thomopoulos C, Carlberg B, et al. Methodological aspects of meta-analyses assessing the effect of blood pressure-lowering treatment on clinical outcomes. *Hypertension.* 2022;79(3):491–504. doi:10.1161/HYPERTENSIONAHA.121.18413.
- [32] Kjeldsen SE, Brunström M, Thomopoulos C, et al. Blood pressure reduction and major cardiovascular events in people with and without type 2 diabetes. *Lancet Diabetes Endocrinol.* 2022;10(12):840. doi:10.1016/S2213-8587(22)00312-6.
- [33] Lonn EM, Bosch J, López-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med.* 2016;374(21):2009–2020. doi:10.1056/NEJMoa1600175.

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