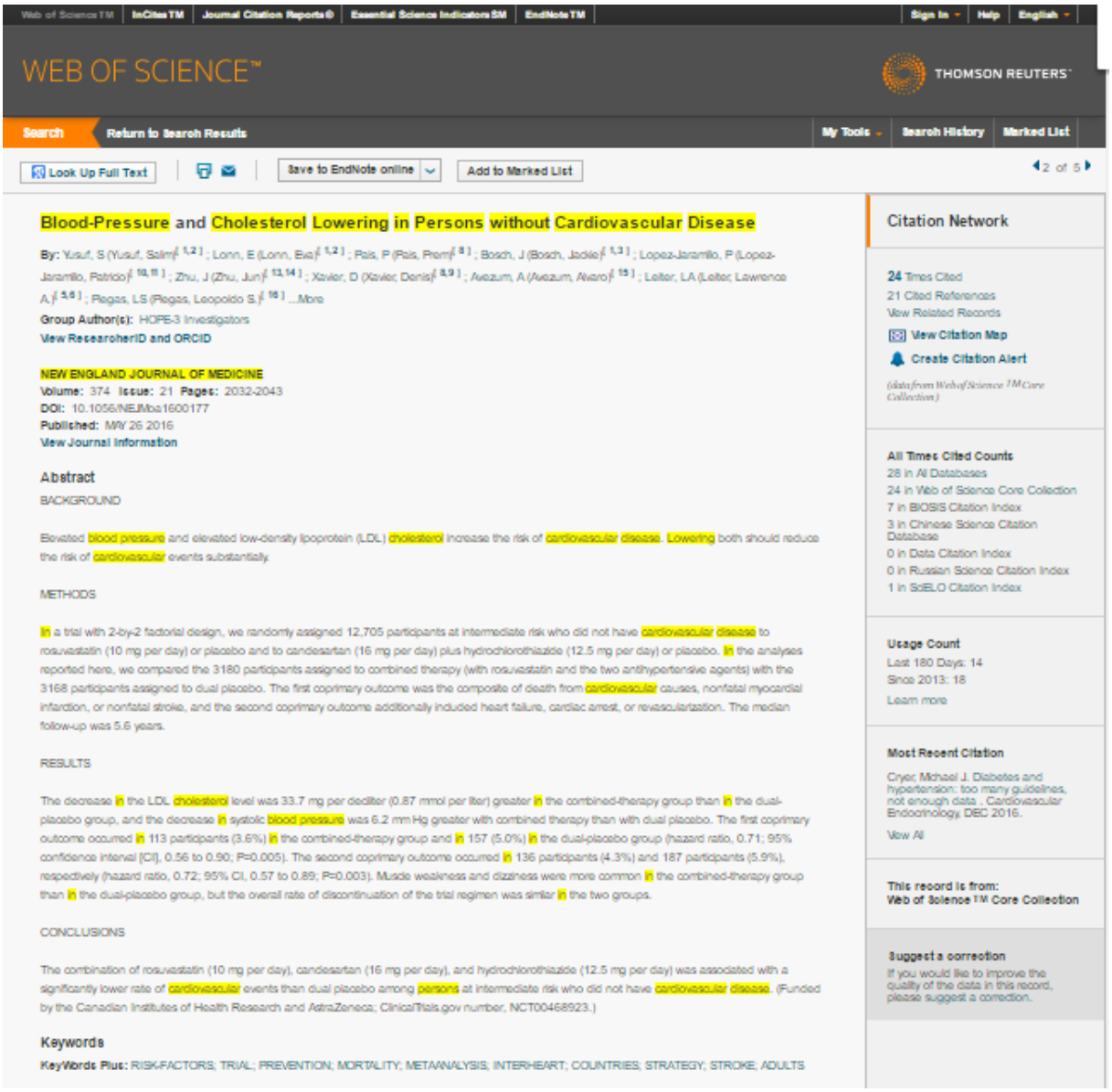

Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

By: Yusuf, S (Yusuf, Salim)[1,2]; Lonn, E (Lonn, Eva)[1,2]; Pais, P (Pais, Prem)[3]; Bosch, J (Bosch, Jackie)[1,3]; Lopez-Jaramillo, P (Lopez-Jaramillo, Patricio)[10,11]; Zhu, J (Zhu, Jun)[12,14]; Xavier, D (Xavier, Denis)[8,9]; Avezum, A (Avezum, Alvaro)[15]; Leiter, LA (Leiter, Lawrence A.)[5,6]; Piegas, LS (Piegas, Leopoldo S.)[16] ...More

Group Author(s): HOPE-3 Investigators

View ResearcherID and ORCID

NEW ENGLAND JOURNAL OF MEDICINE

Volume: 374 Issue: 21 Pages: 2032-2043

DOI: 10.1056/NEJMoa1600177

Published: MAY 26 2016

View Journal Information

Abstract

BACKGROUND

Elevated blood pressure and elevated low-density lipoprotein (LDL) cholesterol increase the risk of cardiovascular disease. Lowering both should reduce the risk of cardiovascular events substantially.

METHODS

In a trial with 2-by-2 factorial design, we randomly assigned 12,705 participants at intermediate risk who did not have cardiovascular disease to rosuvastatin (10 mg per day) or placebo and to candesartan (16 mg per day) plus hydrochlorothiazide (12.5 mg per day) or placebo. In the analyses reported here, we compared the 3180 participants assigned to combined therapy (with rosuvastatin and the two antihypertensive agents) with the 3168 participants assigned to dual placebo. The first coprimary outcome was the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included heart failure, cardiac arrest, or revascularization. The median follow-up was 5.6 years.

RESULTS

The decrease in the LDL cholesterol level was 33.7 mg per deciliter (0.87 mmol per liter) greater in the combined-therapy group than in the dual-placebo group, and the decrease in systolic blood pressure was 6.2 mm Hg greater with combined therapy than with dual placebo. The first coprimary outcome occurred in 113 participants (3.6%) in the combined-therapy group and in 157 (5.0%) in the dual-placebo group (hazard ratio, 0.71; 95% confidence interval [CI], 0.56 to 0.90; P=0.005). The second coprimary outcome occurred in 136 participants (4.3%) and 187 participants (5.9%), respectively (hazard ratio, 0.72; 95% CI, 0.57 to 0.89; P=0.003). Muscle weakness and dizziness were more common in the combined-therapy group than in the dual-placebo group, but the overall rate of discontinuation of the trial regimen was similar in the two groups.

CONCLUSIONS

The combination of rosuvastatin (10 mg per day), candesartan (16 mg per day), and hydrochlorothiazide (12.5 mg per day) was associated with a significantly lower rate of cardiovascular events than dual placebo among persons at intermediate risk who did not have cardiovascular disease. (Funded by the Canadian Institutes of Health Research and AstraZeneca; ClinicalTrials.gov number, NCT00468923.)

Keywords

KeyWords Plus: RISK-FACTORS; TRIAL; PREVENTION; MORTALITY; METAANALYSIS; INTERHEART; COUNTRIES; STRATEGY; STROKE; ADULTS

Author Information

Reprint Address: Yusuf, S (reprint author)

Populat Hlth Res Inst, 237 Barton St E, Hamilton, ON L8L 2X2, Canada.

Addresses:

- [1] McMaster Univ, Hamilton Hlth Sci, Populat Hlth Res Inst, Hamilton, ON, Canada
- [2] McMaster Univ, Dept Med, Hamilton, ON, Canada
- [3] McMaster Univ, Sch Rehabil Sci, Hamilton, ON, Canada
- [4] McMaster Univ, Dept Clin Epidemiol & Biostat, Hamilton, ON, Canada
- [5] Univ Toronto, St Michaels Hosp, Li Ka Shing Knowledge Inst, Toronto, ON, Canada
- [6] Univ Toronto, St Michaels Hosp, Keenan Res Ctr Biomed Sci, Toronto, ON, Canada
- [7] Univ Laval, Inst Univ Cardiol & Pneumol Quebec, Quebec City, PQ, Canada
- [8] St Johns Res Inst, Bangalore, Karnataka, India
- [9] St Johns Med Coll, Bangalore, Karnataka, India
- [10] Univ Santander, Fdn Oftalmol Santander, Bucaramanga, Colombia
- [11] Univ Santander, Inst Mesira, Sch Med, Bucaramanga, Colombia
- [12] Univ Norte, Barranquilla, Colombia
- [13] Chinese Acad Med Sci, Fu Wai Hosp, Beijing 100730, Peoples R China
- [14] Peking Union Med Coll, Beijing 100021, Peoples R China
- [15] Dante Pazzanese Inst Cardiol, Sao Paulo, Brazil
- [16] HCor Heart Hosp, Sao Paulo, Brazil
- [17] Inst Cardiol, Kiev, Ukraine
- [18] Semmelweis Univ, Hungarian Inst Cardiol, H-1085 Budapest, Hungary
- [19] Univ Cape Town, Hatter Inst Cardiovasc Res Africa, Dept Med, Soweto Cardiovasc Res Grp, ZA-7925 Cape Town, South Africa
- [20] Inst Clin Cardiol, Russian Cardiol Res Complex, Moscow, Russia
- [21] Univ Amsterdam, Acad Med Ctr, Dept Cardiol, Meibergdreef 9, NL-1105 AZ Amsterdam, Netherlands
- [22] Uppsala Univ, Clin Res Ctr, Dept Med Sci, Cardiol, Uppsala, Sweden
- [23] Univ Teknologi Majis Amanah Rakyat, Selayang, Malaysia
- [24] Univ Coll Sedaya Int Univ, Kuala Lumpur, Malaysia
- [25] Technion Israel Inst Technol, Ruth & Bruce Rappaport Sch Med, Lady Davis Carmel Med Ctr, Haifa, Israel
- [26] Univ Hosp Motol, Prague, Czech Republic
- [27] Univ Leicester, Diabet Res Ctr, Leicester, Leics, England
- [28] Univ Leicester, Dept Cardiovasc Sci, Leicester, Leics, England
- [29] Glenfield Hosp, Natl Inst Hlth Res, Leicester Cardiovasc Biomed Res Unit, Leicester, Leics, England
- [30] Monash Ctr Cardiovasc Res & Educ Therapeut, Primary Care Diabet & Vasc Med, Melbourne, Vic, Australia
- [31] Monash Univ, Dept Epidemiol & Prevent Med, Melbourne, Vic 3004, Australia
- [32] Curtin Univ, Sch Publ Hlth, Perth, WA 6845, Australia
- [33] Inst Cardiovasc Rosario, Rosario, Santa Fe, Argentina
- [34] Univ Philippines, Coll Med, Manila, Philippines

E-mail Addresses: yusufs@mcmaster.ca

Funding

Funding Agency	Grant Number
Canadian Institutes of Health Research	
AstraZeneca	

View funding text

Publisher

MASSACHUSETTS MEDICAL SOC, WALTHAM WOODS CENTER, 860 WINTER ST,, WALTHAM, MA 02451-1413 USA

Categories / Classification

Research Areas: General & Internal Medicine

Web of Science Categories: Medicine, General & Internal

Document Information

Document Type: Article

Language: English

Accession Number: WOS:000376443500006

PubMed ID: 27039945

ISSN: 0028-4793

eISSN: 1533-4406

Journal Information

Impact Factor: Journal Citation Reports®

Other Information

IDS Number: DM6BN

Cited References in Web of Science Core Collection: 21

Times Cited in Web of Science Core Collection: 24

Document details

Back to results | < Previous 3 of 91 Next >

Full Text | View at Publisher | Export | Download | Add to List | More...

New England Journal of Medicine

Volume 374, Issue 21, 26 May 2016, Pages 2032-2043

Blood-pressure and cholesterol lowering in persons without cardiovascular disease (Article)

Yusuf, S.[a,b], Lonn, E.[a,b], Pais, P.[g], Bosch, J.[a,c], López-Jaramillo, P.[i], Zhu, J.[k], Xavier, D.[g,h], Avezum, A.[i], Leiter, L.A.[j], Piegas, L.S.[m], Parkhomenko, A.[n], Keltai, M.[o], Keltai, K.[o], Sliwa, K.[p], Chazova, I.[q], Peters, R.J.G.[r], Held, C.[s], Yusoff, K.[tu], Lewis, B.S.[v], Jansky, P.[ao], Khunti, K.[x], Toff, W.D.[yz], Reid, C.M.[aaab], Varigos, J.[ab], Accini, J.L.[ac], McKelvie, R.[ab], Pogue, J.[w], Jung, H.[a], Liu, L.[k], Díaz, R.[ad], Dans, A.[ae], Dagenais, G.[f]

[a] Population Health Research Institute, Hamilton Health Sciences, McMaster University, 237 Barton St. E., Hamilton, ON, Canada

[b] Department of Medicine, McMaster University, Hamilton, ON, Canada

[c] School of Rehabilitation Science, McMaster University, Hamilton, ON, Canada

View additional affiliations

View references (21)

Abstract

BACKGROUND Elevated **blood pressure** and elevated low-density lipoprotein (LDL) **cholesterol** increase the risk of **cardiovascular disease**. **Lowering** both should reduce the risk of **cardiovascular** events substantially. METHODS **In** a trial with 2-by-2 factorial design, we randomly assigned 12,705 participants at intermediate risk who did not have **cardiovascular disease** to rosuvastatin (10 mg per day) or placebo and to candesartan (16 mg per day) plus hydrochlorothiazide (12.5 mg per day) or placebo. **In** the analyses reported here, we compared the 3180 participants assigned to combined therapy (with rosuvastatin and the two antihypertensive agents) with the 3168 participants assigned to dual placebo. The first coprimary outcome was the composite of death from **cardiovascular** causes, nonfatal myocardial infarction, or nonfatal stroke, and the second coprimary outcome additionally included heart failure, cardiac arrest, or revascularization. The median follow-up was 5.6 years. RESULTS The decrease **in** the LDL **cholesterol** level was 33.7 mg per deciliter (0.87 mmol per liter) greater **in** the combined-therapy group than **in** the dual-placebo group, and the decrease **in** systolic **blood pressure** was 6.2 mm Hg greater with combined therapy than with dual placebo. The first coprimary outcome occurred **in** 113 participants (3.6%) **in** the combined-therapy group and **in** 157 (5.0%) **in** the dual-placebo group (hazard ratio, 0.71; 95% confidence interval [CI], 0.56 to 0.90; P = 0.005). The second coprimary outcome occurred **in** 136 participants (4.3%) and 187 participants (5.9%), respectively (hazard ratio, 0.72; 95% CI, 0.57 to 0.89; P = 0.003). Muscle weakness and dizziness were more common **in** the combined-therapy group than **in** the dual-placebo group, but the overall rate of discontinuation of the trial regimen was similar **in** the two groups. CONCLUSIONS The combination of rosuvastatin (10 mg per day), candesartan (16 mg per day), and hydrochlorothiazide (12.5 mg per day) was associated with a significantly lower rate of **cardiovascular** events than dual placebo among **persons** at intermediate risk who did not have **cardiovascular disease**. Copyright © 2016 Massachusetts Medical Society. All rights reserved.

Indexed keywords

EMTREE drug terms: antihypertensive agent; candesartan; hydrochlorothiazide; low density lipoprotein **cholesterol**; placebo; rosuvastatin; antihypertensive agent; benzimidazole derivative; candesartan; hydrochlorothiazide; hydroxymethylglutaryl coenzyme A reductase inhibitor; low density lipoprotein **cholesterol**; rosuvastatin; tetrazole derivative

EMTREE medical terms: adult; Article; **blood pressure** measurement; **cardiovascular disease**; **cardiovascular** risk; cerebrovascular accident; **cholesterol blood** level; controlled study; dizziness; double blind procedure; factorial design; female; heart arrest; heart failure; heart infarction; human; hypotension; major clinical study; middle aged; multicenter study; muscle weakness; myalgia; priority journal; randomized controlled trial; revascularization; risk factor; risk reduction; aged; **blood**; **Cardiovascular** Diseases; clinical trial; combination drug therapy; comparative study; hypertension; male; medication compliance

MeSH: Aged; Antihypertensive Agents; Benzimidazoles; **Cardiovascular** Diseases; **Cholesterol**, LDL; Double-Blind Method; Drug Therapy, Combination; Female; Humans; Hydrochlorothiazide; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Hypertension; Male; Medication Adherence; Middle Aged; Risk Factors; Rosuvastatin Calcium; Tetrazoles

Medline is the source for the MeSH terms of this document.

Chemicals and CAS Registry Numbers: candesartan, 139481-59-7; hydrochlorothiazide, 58-93-5; rosuvastatin, 147098-18-8, 147098-20-2;Antihypertensive Agents; Benzimidazoles; candesartan; Cholesterol, LDL; Hydrochlorothiazide; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Rosuvastatin Calcium; Tetrazoles

ISSN: 00284793 **CODEN:** NEJMA **Source Type:** Journal **Original language:** English
DOI: 10.1056/NEJMoa1600177 **PubMed ID:** 27039945 **Document Type:** Article
Publisher: Massachussetts Medical Society

Funding details

Funding number	Funding sponsor	Acronym
	AstraZeneca	