Preventing, Treating, and Reversing Cardiovascular Disease

The Most Important Topic in Healthcare

Robert Todd Hurst, MD, FACC, FASE

BUMC Resident Conference

August 16, 2022

Disclosure

Relevant Financial Relationship(s)

- None

Off Label Usage

- None

Cardiometabolic Disease

The 21st Century Epidemic

High blood pressure
118 million

Unhealthy cholesterol
100 million

Diabetes/Pre-diabetes
129 million

Unhealthy Weight
183 million

Cardiometabolic disease
(Almost) Everyone has it

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Trends and Disparities in Cardiometabolic Health Among U.S. Adults, 1999-2018

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ABSTRACT

BACKGROUND Few studies have assessed U.S. cardiometabolic health trends—optimal levels of multiple risk factors and absence of clinical cardiovascular disease (CVD)—or its impact on health disparities.

OBJECTIVES The purpose of this study was to investigate U.S. trends in optimal cardiometabolic health from 1999 to 2018.

METHODS We assessed proportions of adults with optimal cardiometabolic health, based on adiposity, blood glucose, blood lipids, blood pressure, and clinical CVD; and optimal, intermediate, and poor levels of each component among 55,081 U.S. adults in the National Health and Nutrition Examination Survey.

RESULTS In 2017-2018, only 6.8% (95% CI: 5.4%-8.1%) of U.S. adults had optimal cardiometabolic health, declining from 1999-2000 (*P* trend = 0.02). Among components of cardiometabolic health, the largest declines were for adiposity (optimal levels: from 33.8% to 24.0%; poor levels: 47.7% to 61.9%) and glucose (optimal levels: 59.4% to 36.9%; poor levels: 8.6% to 13.7%) (*P* trend <0.001 for each). Optimal levels of blood lipids increased from 29.9% to 37.0%, whereas poor decreased from 28.3% to 14.7% (*P* trend <0.001). Trends over time for blood pressure and CVD were smaller. Disparities by age, sex, education, and race/ethnicity were evident in all years, and generally worsened over time. By 2017-2018, prevalence of optimal cardiometabolic health was lower among Americans with lower (5.0% [95% CI: 2.8%-7.2%]) vs higher education (10.3% [95% CI: 7.6%-13.0%]); and among Mexican American (3.2% [95% CI: 1.4%-4.9%]) vs non-Hispanic White (8.4% [95% CI: 6.3%-10.4%]) adults.

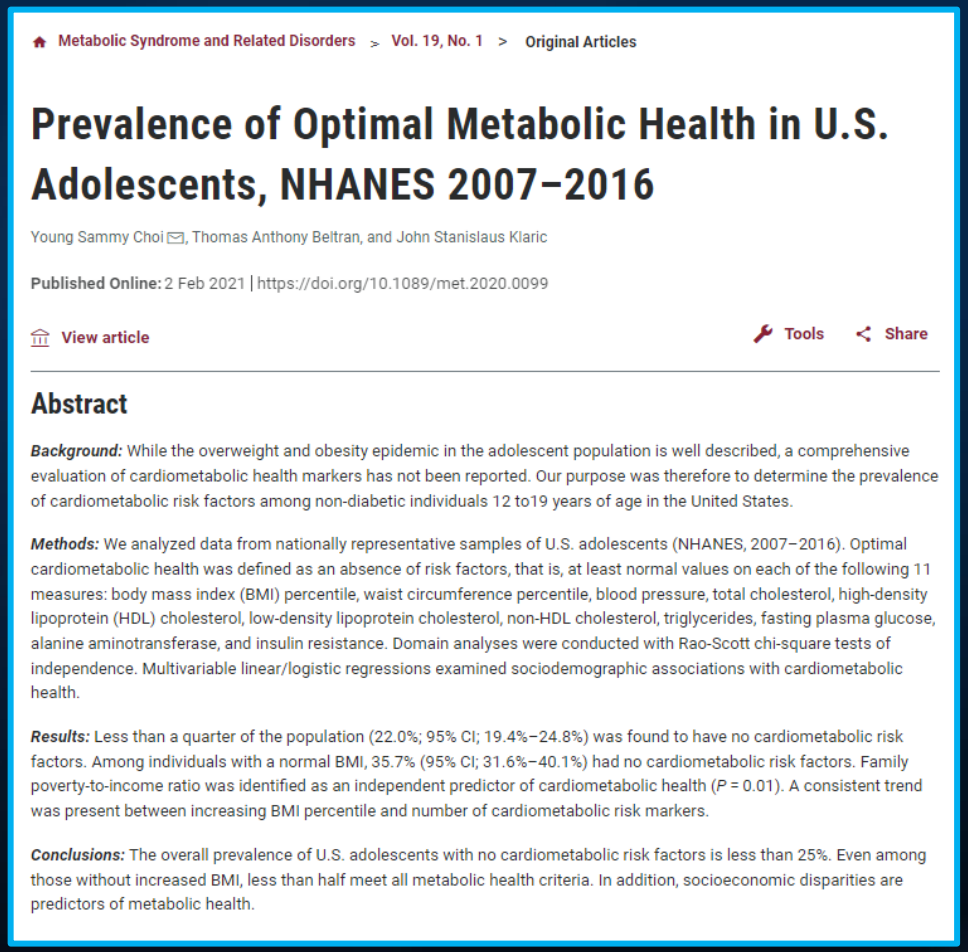
CONCLUSIONS Between 1999 and 2000 and 2017 and 2018, U.S. cardiometabolic health has been poor and worsening, with only 6.8% of adults having optimal cardiometabolic health, and disparities by age, sex, education, and race/ethnicity. These novel findings inform the need for nationwide clinical and public health interventions to improve cardiometabolic health and health equity. (J Am Coll Cardiol 2022;80:138-151) © 2022 by the American College of Cardiology Foundation.

93.2% of adults in the US have at least one cardiometabolic risk factor

J Am Coll Cardiol 2022;80:138–15.

Cardiometabolic disease

A storm is coming



Metabolic Syndrome and Related Disorders > Vol. 19, No. 1 > Original Articles

Prevalence of Optimal Metabolic Health in U.S. Adolescents, NHANES 2007–2016

Young Sammy Choi, Thomas Anthony Beltran, and John Stanislaus Klaric

Published Online: 2 Feb 2021 | https://doi.org/10.1089/met.2020.0099

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Abstract

Background: While the overweight and obesity epidemic in the adolescent population is well described, a comprehensive evaluation of cardiometabolic health markers has not been reported. Our purpose was therefore to determine the prevalence of cardiometabolic risk factors among non-diabetic individuals 12 to19 years of age in the United States.

Methods: We analyzed data from nationally representative samples of U.S. adolescents (NHANES, 2007–2016). Optimal cardiometabolic health was defined as an absence of risk factors, that is, at least normal values on each of the following 11 measures: body mass index (BMI) percentile, waist circumference percentile, blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein cholesterol, non-HDL cholesterol, triglycerides, fasting plasma glucose, alanine aminotransferase, and insulin resistance. Domain analyses were conducted with Rao-Scott chi-square tests of independence. Multivariable linear/logistic regressions examined sociodemographic associations with cardiometabolic health.

Results: Less than a quarter of the population (22.0%; 95% CI; 19.4%–24.8%) was found to have no cardiometabolic risk factors. Among individuals with a normal BMI, 35.7% (95% CI; 31.6%–40.1%) had no cardiometabolic risk factors. Family poverty-to-income ratio was identified as an independent predictor of cardiometabolic health ($P = 0.01$). A consistent trend was present between increasing BMI percentile and number of cardiometabolic risk markers.

Conclusions: The overall prevalence of U.S. adolescents with no cardiometabolic risk factors is less than 25%. Even among those without increased BMI, less than half meet all metabolic health criteria. In addition, socioeconomic disparities are predictors of metabolic health.

78% of adolescents in the US have at least one cardiometabolic risk factor

Metabolic Syndrome and Related Disorders 2020:19(1).

Cardiometabolic disease

A storm is coming

RESEARCH LETTER

Trends in Obesity Prevalence Among Adults Aged 18 Through 25 Years, 1976-2018

Emerging adulthood, from ages 18 through 25 years, is a distinct developmental period characterized by exploration and frequent change (eg, from school to work), ultimately leading to the formation of lifelong habits and adult identity.[1,2] Few studies describe obesity in emerging adults; analyses often group these individuals with adolescents (aged 12-19 years) or young adults (aged 20-39 years), limiting opportunities for developmentally informed intervention and treatment.[3,4] We examined the changes in obesity prevalence nationally among emerging adults in the US over the last 4 decades.

Methods | We used nationally representative data from the National Health and Nutrition Examination Survey (NHANES), a series of cross-sectional surveys including interviews and physical examinations with a stratified, multistage sampling design. We drew from NHANES II (1976-1980), NHANES III (1988-1994), and the continuous NHANES cycles from 1999 through 2018 (response rate range, 48.8%-80%). We limited our study population to nonpregnant emerging adults (aged 18-25 years) of non-Hispanic Black or non-Hispanic White race with complete data for variables of interest (89.8% of defined population had complete data). Given the changes in how the NHANES assessed race and ethnicity over time, we were limited to the aforementioned groups.

Our outcome of interest was body mass index (BMI; calculated as weight in kilograms divided by height in meters squared). We categorized BMI into standard groups of underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obesity (≥30).[5] Covariates included sex (male or female), race and ethnicity (non-Hispanic Black or non-Hispanic White), and household poverty (yes or no). We identified household poverty if the NHANES poverty index (the ratio of family income to the US poverty threshold in NHANES II/III and the ratio of family income to the US

Table. Covariate-Adjusted Mean Body Mass Index (BMI) and Prevalence of BMI Groups Among Non-Hispanic Black and Non-Hispanic White Emerging Adults (Aged 18-25 Years), 1976-2018[a]

	BMI[b]		BMI groups[b]							
			Underweight (<18.5)		Normal weight (18.5-24.9)		Overweight (25.0-29.9)		Obesity (≥30.0)	
Survey year	No.[c]	Mean (95% CI)	No.[c]	Weighted proportion, % (95% CI)[d]	No.[c]	Weighted proportion, % (95% CI)[d]	No.[c]	Weighted proportion, % (95% CI)[d]	No.[c]	Weighted proportion, % (95% CI)[d]
1976-1980	1974	23.1 (22.9-23.4)	127	5.5 (4.4-6.8)	1361	68.7 (66.3-70.9)	351	17.7 (15.9-19.8)	135	6.2 (4.9-7.9)
1988-1994	1396	24.6 (24.2-24.9)	74	4.8 (3.5-6.5)	811	59.5 (56.5-62.5)	281	19.3 (17.0-21.9)	230	14.8 (13.1-16.7)
1999-2000	359	26.5 (25.3-27.8)	14	3.4 (1.3-8.9)	183	47.7 (41.8-53.6)	83	23.9 (17.5-31.9)	79	23.1 (15.6-32.6)
2001-2002	550	26.0 (25.2-26.7)	33	4.6 (2.3-8.9)	293	49.5 (44.3-54.7)	118	24.0 (19.2-29.4)	106	21.3 (17.2-26.1)
2003-2004	608	26.5 (25.7-27.3)	31	4.5 (3.0-6.5)	304	47.2 (42.0-52.4)	130	22.1 (18.1-26.6)	143	24.9 (20.0-30.5)
2005-2006	616	27.1 (26.2-28.0)	23	3.0 (1.9-4.6)	296	45.1 (40.1-50.1)	135	22.8 (18.0-28.4)	162	27.5 (20.6-35.7)
2007-2008	415	26.8 (25.8-27.8)	18	3.8 (2.1-6.8)	200	46.5 (40.7-52.5)	100	22.9 (18.0-28.7)	97	23.3 (17.7-29.9)
2009-2010	484	26.7 (25.7-27.7)	20	2.9 (1.7-4.8)	242	48.7 (39.3-58.2)	98	21.6 (16.6-27.6)	124	24.7 (18.3-32.4)
2011-2012	481	26.9 (25.9-28.0)	25	5.9 (4.0-8.5)	213	44.5 (36.9-52.3)	111	22.3 (17.9-27.5)	132	26.0 (19.9-33.2)
2013-2014	477	27.0 (25.7-28.2)	22	4.3 (2.3-8.1)	223	46.0 (41.4-50.6)	112	23.1 (19.0-27.8)	120	25.8 (20.1-32.4)
2015-2016	337	26.8 (26.1-27.6)	14	4.4 (2.5-7.7)	153	44.3 (39.3-49.5)	85	25.7 (21.9-30.0)	85	25.0 (21.3-29.2)
2017-2018	318	27.7 (26.2-29.1)	22	4.7 (2.3-9.3)	127	37.5 (29.5-46.4)	64	23.6 (18.8-29.4)	105	32.7 (24.7-41.8)
P value[e]		.006		.32		.005		.06		.007
P value for sensitivity analysis[f]		.04		.58		.02		.72		.03

[a] Data are from the National Health and Nutrition Examination Survey (NHANES). All estimates were adjusted for sex, race/ethnicity (non-Hispanic Black vs non-Hispanic White), and poverty index. Race and ethnicity options in NHANES III and the continuous NHANES cycles were defined by the NHANES survey developers and chosen by participants. For NHANES II, the race options were defined by the NHANES survey developers and individuals were classified by observation except in cases when the interviewer was unable to do so, in which case the participant was asked. Ethnicity was not directly assessed. A Hispanic ethnicity variable was constructed based on participant-reported natural origin or ancestry.

[b] Calculated as weight in kilograms divided by height in meters squared.

[c] Counts are unweighted.

[d] Examination weights were used to calculate weighted prevalence estimates and 95% CIs. The rare strata with single sampling units in the data were treated as certainty units to perform variance estimation.

[e] Estimated using a nonparametric, Wilcoxon-type test for trend.

[f] Estimated using survey-weighted, adjusted regressions for pooled data from continuous NHANES, 1999-2018.

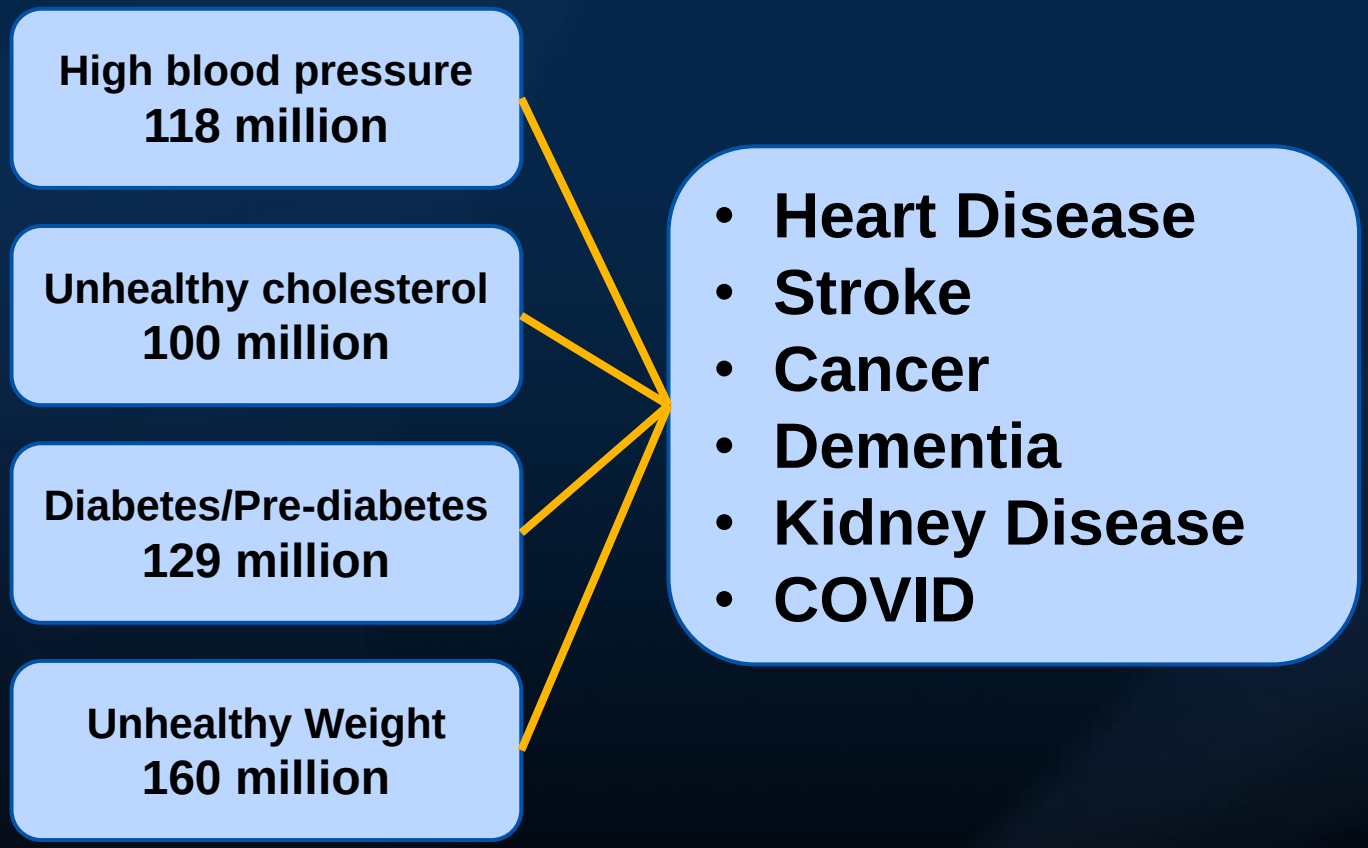
From 1976 to 2018, obesity in those 18-25 years of age increased from 6.2% to 32.7%

That's a 527% increase

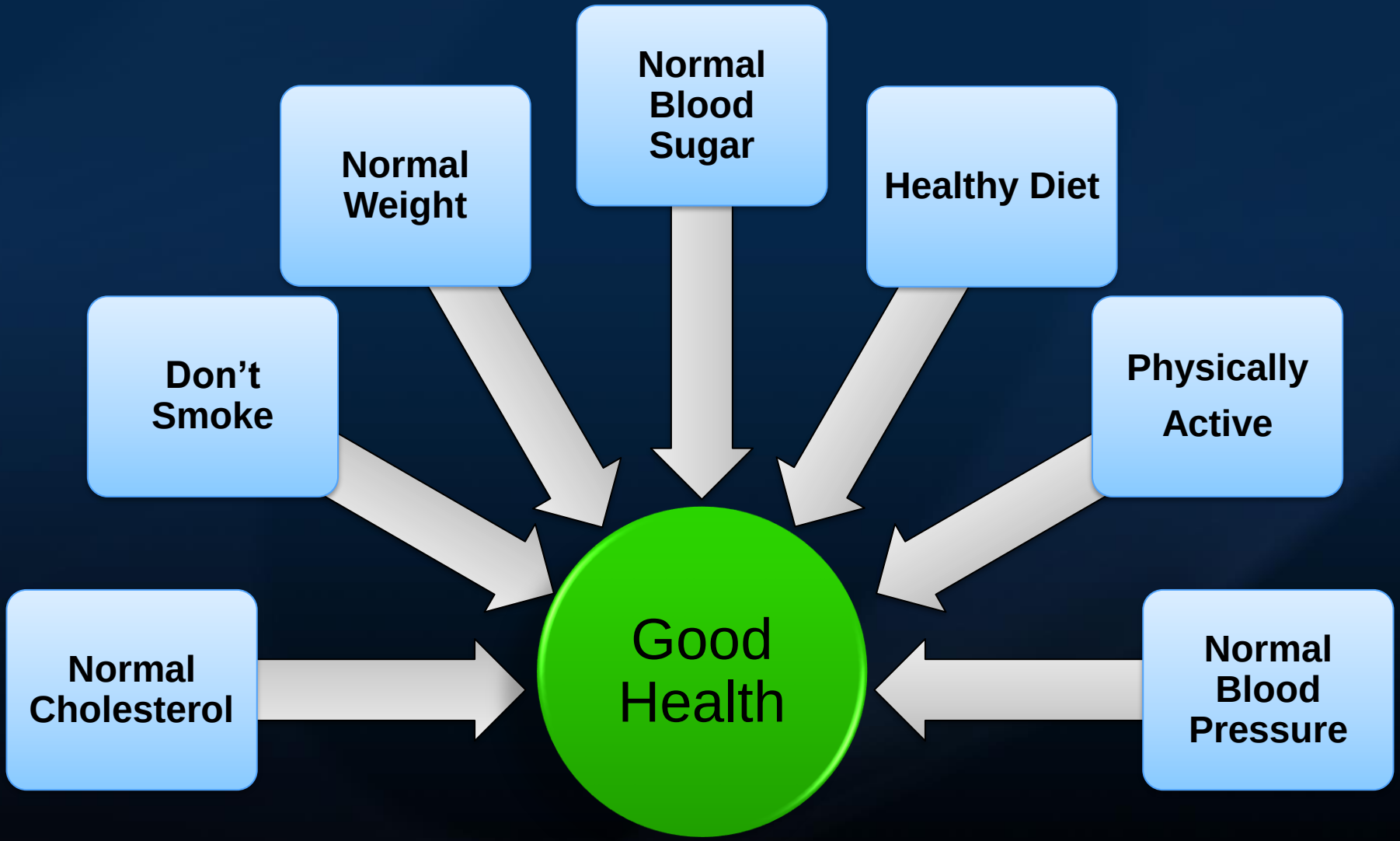
JAMA. 2021;326(20):2073-2074.

Cardiometabolic Disease

Most common cause of death?



Life's Simple 7



Cardiometabolic disease

Prevention

Epidemiology

Prediction of Lifetime Risk for Cardiovascular Disease by Risk Factor Burden at 50 Years of Age

Donald M. Lloyd-Jones, MD, ScM; Eric P. Leip, PhD; Martin G. Larson, ScD; Ralph B. D'Agostino, PhD; Alexa Beiser, PhD; Peter W.F. Wilson, MD; Philip A. Wolf, MD; Daniel Levy, MD

Background—Lifetime risk for atherosclerotic cardiovascular disease (CVD) has not previously been estimated, and the effect of risk factor burden on lifetime risk is unknown.

Methods and Results—We included all Framingham Heart Study participants who were free of CVD (myocardial infarction, coronary insufficiency, angina, stroke, claudication) at 50 years of age. Lifetime risks to 95 years of age were estimated for men and women, with death free of CVD as a competing event. We followed up 3564 men and 4362 women for 111 777 person-years; 1757 had CVD events and 1641 died free of CVD. At 50 years of age, lifetime risks were 51.7% (95% CI, 49.3 to 54.2) for men and 39.2% (95% CI, 37.0 to 41.4) for women, with median survivals of 30 and 36 years, respectively. With more adverse levels of single risk factors, lifetime risks increased and median survivals decreased. Compared with participants with ≥2 major risk factors, those with optimal levels had substantially lower lifetime risks (5.2% versus 68.9% in men, 8.2% versus 50.2% in women) and markedly longer median survivals (>39 versus 28 years in men, >39 versus 31 years in women).

Conclusions—The absence of established risk factors at 50 years of age is associated with very low lifetime risk for CVD and markedly longer survival. These results should promote efforts aimed at preventing development of risk factors in young individuals. Given the high lifetime risks and lower survival in those with intermediate or high risk factor burden at 50 years of age, these data may be useful in communicating risks and supporting intensive preventive therapy. (***Circulation***. **2006;113:791-798.**)

Key Words: cardiovascular disease ■ epidemiology ■ risk factors ■ survival

Despite 4 decades of declining mortality from cardiovascular disease (CVD) in the United States, CVD remains by far the leading cause of morbidity and mortality,[1] and it is soon to be the leading cause of morbidity and mortality in the developing world.[2] Recent data suggest disturbing increases in the prevalence of CVD risk factors such as diabetes, obesity, and the metabolic syndrome,[1,3,4] which may reverse downward trends in CVD mortality. In the face of the enormous public health burden imposed by CVD, renewed efforts are needed to promote prevention.

Clinical Perspective p 798

One tool that may be useful in public health education is an understanding of the lifetime risk for CVD, which has not been estimated in any population to date. Given that lifetime risk estimates provide an absolute risk assessment, they may be more easily understood by clinicians and patients than relative risks, and they may help to motivate beneficial changes in lifestyle or health behaviors. The best example of lifetime risk data being used effectively to change behavior is the wide dissemination of data on lifetime risk for breast cancer (1 in 8 for women at 40 years of age),[5] which appears to have contributed to markedly increased rates of screening for breast cancer in the early 1990s.[6,7]

The Framingham Heart Study, with its well-defined cohorts, long-term follow-up, and careful documentation of risk factors and events, provides a unique opportunity to examine factors that may modify remaining lifetime risk for CVD in the context of overall survival. Factors that increase short-term risk for CVD are well known. However, the effect of risk factors on long-term and lifetime risk may be unpredictable because some risk factors also increase risk for non-CVD death, resulting in competing risks. We sought to estimate the lifetime risk for CVD and to examine overall survival in the presence and absence of established risk factors.

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Guest Editor for this article was Donna K. Arnett, PhD.

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DOI: 10.1161/CIRCULATIONAHA.105.548206

CVD in those with 2 or more risk factors

68.9%

CVD in those with no risk factors

5.2%

RRR = 92.5%

Cardiometabolic disease

Prevention

- CVD by 92%
- Fatty Liver by 81%
- Heart Failure by 78%
- Kidney Disease by 62%
- Atrial Fibrillation by 57%
- Cancer by 50%
- Dementia by 41%

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Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

The ARREST-AF Cohort Study

Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Dennis H. Lau, MBBS, PhD,* Abhinav B. Mehta, MAcrSr,†
Rajiv Mahajan, MD,* Darragh Twomey, MBBS,* Muayad Alasady, MBBS,*† Lorraine Hanley, BSc,*
Nicholas A. Antic, MBBS, PhD,‡ R. Doug McEvoy, MBBS, MD,‡ Jonathan M. Kalman, MBBS, PhD,§
Walter P. Abhayaratna, MBBS, PhD,‖ Prashanthan Sanders, MBBS, PhD*

ABSTRACT

BACKGROUND The long-term outcome of atrial fibrillation (AF) ablation demonstrates attrition. This outcome may be due to failure to attenuate the progressive substrate promoted by cardiovascular risk factors.

OBJECTIVES The goal of this study was to evaluate the impact of risk factor and weight management on AF ablation outcomes.

METHODS Of 281 consecutive patients undergoing AF ablation, 149 with a body mass index ≥27 kg/m^2 and ≥1 cardiac risk factor were offered risk factor management (RFM) according to American Heart Association/American College of Cardiology guidelines. After AF ablation, all 61 patients who opted for RFM and 88 control subjects were assessed every 3 to 6 months by clinic review and 7-day Holter monitoring. Changes in the Atrial Fibrillation Severity Scale scores were determined.

RESULTS There were no differences in baseline characteristics, number of procedures, or follow-up duration between the groups (p = NS). RFM resulted in greater reductions in weight ($p = 0.002$) and blood pressure ($p = 0.006$), and better glycemic control ($p = 0.001$) and lipid profiles ($p = 0.01$). At follow-up, AF frequency, duration, symptoms, and symptom severity decreased more in the RFM group compared with the control group (all $p < 0.001$). Single-procedure drug-unassisted arrhythmia-free survival was greater in RFM patients compared with control subjects ($p < 0.001$). Multiple-procedure arrhythmia-free survival was markedly better in RFM patients compared with control subjects ($p < 0.001$), with 16% and 42.4%, respectively, using antiarrhythmic drugs ($p = 0.004$). On multivariate analysis, type of AF ($p < 0.001$) and RFM (hazard ratio 4.8 [95% confidence interval: 2.04 to 11.4]; $p < 0.001$) were independent predictors of arrhythmia-free survival.

CONCLUSIONS Aggressive RFM improved the long-term success of AF ablation. This study underscores the importance of therapy directed at the primary promoters of the AF substrate to facilitate rhythm control strategies. (J Am Coll Cardiol 2014;64:2222-31) © 2014 by the American College of Cardiology Foundation.

Expert medical care

17.8% Afib free

Expert medical care PLUS treat cardiometabolic risk factors

87% Afib free

RRR- 80%

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ORIGINAL INVESTIGATIONS

Impact of CARDIOrespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation

The CARDIO-FIT Study

Rajeev K. Pathak, MBBS,* Adrian Elliott, PhD,* Melissa E. Middeldorp,* Megan Meredith,* Abhinav B. Mehta, M Act Sr,† Rajiv Mahajan, MD, PhD,* Jeroen M.L. Hendriks, PhD,* Darragh Twomey, MBBS,* Jonathan M. Kalman, MBBS, PhD,‡ Walter P. Abhayaratna, MBBS, PhD,§ Dennis H. Lau, MBBS, PhD,* Prashanthan Sanders, MBBS, PhD*

ABSTRACT

BACKGROUND Obesity begets atrial fibrillation (AF). Although cardiorespiratory fitness is protective against incident AF in obese individuals, its effect on AF recurrence or the benefit of cardiorespiratory fitness gain is unknown.

OBJECTIVES This study sought to evaluate the role of cardiorespiratory fitness and the incremental benefit of cardiorespiratory fitness improvement on rhythm control in obese individuals with AF.

METHODS Of 1,415 consecutive patients with AF, 825 had a body mass index ≥27 kg/m^2 and were offered risk factor management and participation in a tailored exercise program. After exclusions, 308 patients were included in the analysis. Patients underwent exercise stress testing to determine peak metabolic equivalents (METs). To determine a dose response, cardiorespiratory fitness was categorized as: low (<85%), adequate (86% to 100%), and high (>100%). Impact of cardiorespiratory fitness gain was ascertained by the objective gain in fitness at final follow-up (≥2 METs vs. <2 METs). AF rhythm control was determined using 7-day Holter monitoring and AF severity scale questionnaire.

RESULTS There were no differences in baseline characteristics or follow-up duration between the groups defined by cardiorespiratory fitness. Arrhythmia-free survival with and without rhythm control strategies was greatest in patients with high cardiorespiratory fitness compared to adequate or low cardiorespiratory fitness ($p < 0.001$ for both). AF burden and symptom severity decreased significantly in the group with cardiorespiratory fitness gain ≥2 METs as compared to <2 METs group ($p < 0.001$ for all). Arrhythmia-free survival with and without rhythm control strategies was greatest in those with METs gain ≥2 compared to those with METs gain <2 in cardiorespiratory fitness ($p < 0.001$ for both).

CONCLUSIONS Cardiorespiratory fitness predicts arrhythmia recurrence in obese individuals with symptomatic AF. Improvement in cardiorespiratory fitness augments the beneficial effects of weight loss. (Evaluating the Impact of a Weight Loss on the Burden of Atrial Fibrillation [AF] in Obese Patients; ACTRN12614001123639) (J Am Coll Cardiol 2015;66:985–96) © 2015 by the American College of Cardiology Foundation.

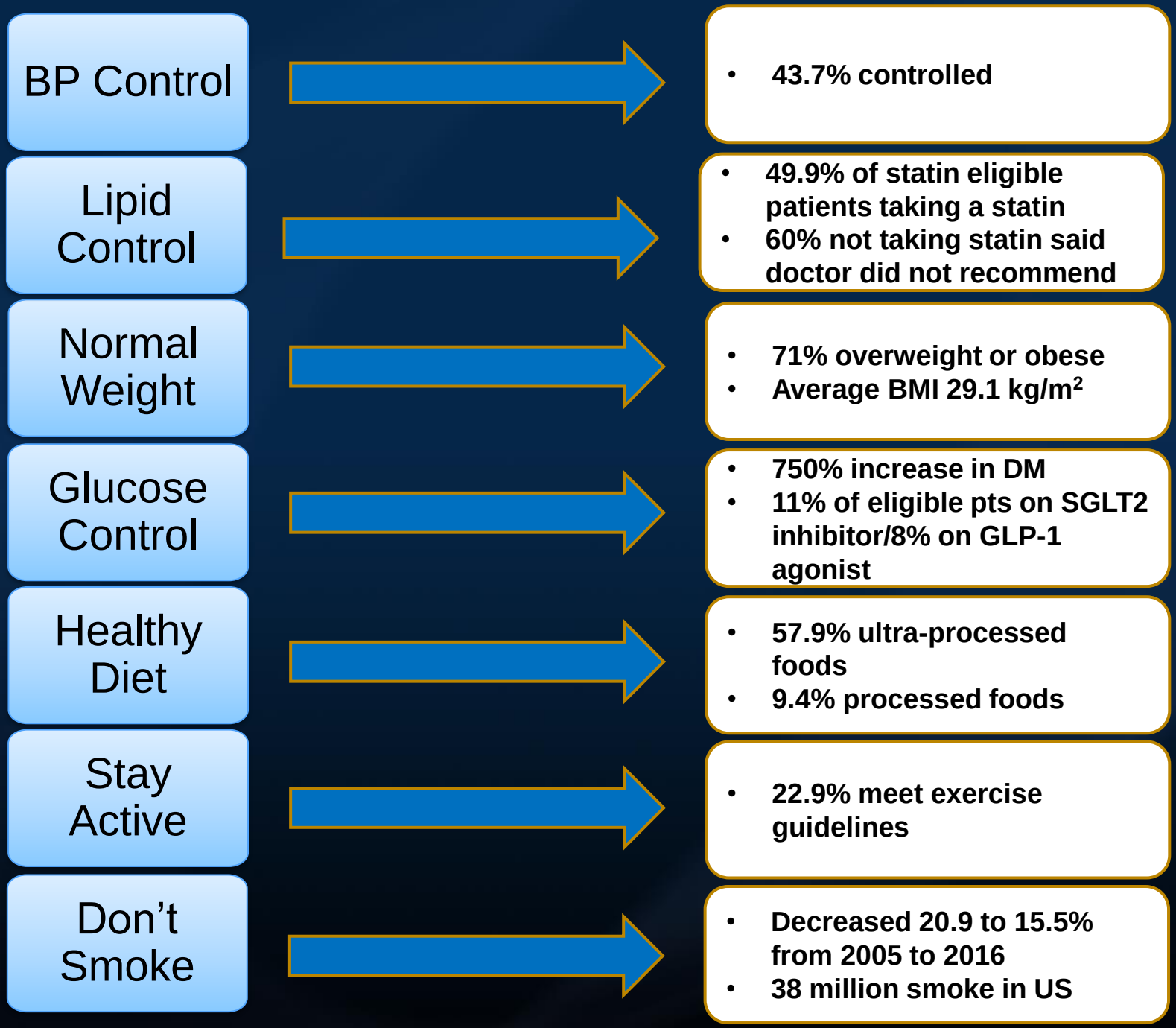
Expert medical care

66% Recurrent Afib

Expert medical care PLUS treat cardiometabolic risk factors, 10% weight loss, and 2 MET improvement in fitness

6% Recurrent Afib

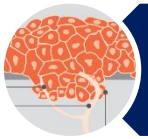
RRR- 91%


BP Control
• 43.7% controlled
Lipid Control
• 49.9% of statin eligible patients taking a statin
• 60% not taking statin said doctor did not recommend
Normal Weight
• 71% overweight or obese
• Average BMI 29.1 kg/m2
Glucose Control
• 750% increase in DM
• 11% of eligible pts on SGLT2 inhibitor/8% on GLP-1 agonist
Healthy Diet
• 57.9% ultra-processed foods
• 9.4% processed foods
Stay Active
• 22.9% meet exercise guidelines
Don't Smoke
• Decreased 20.9 to 15.5% from 2005 to 2016
• 38 million smoke in US

We know how to prevent these diseases, yet…

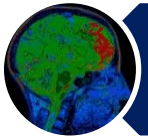
Heart disease

Up 50%



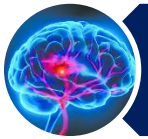
Cancer

Up 26%



Dementia

Up 88%



Stroke

Up 70%

Fatty liver disease

Up 225%

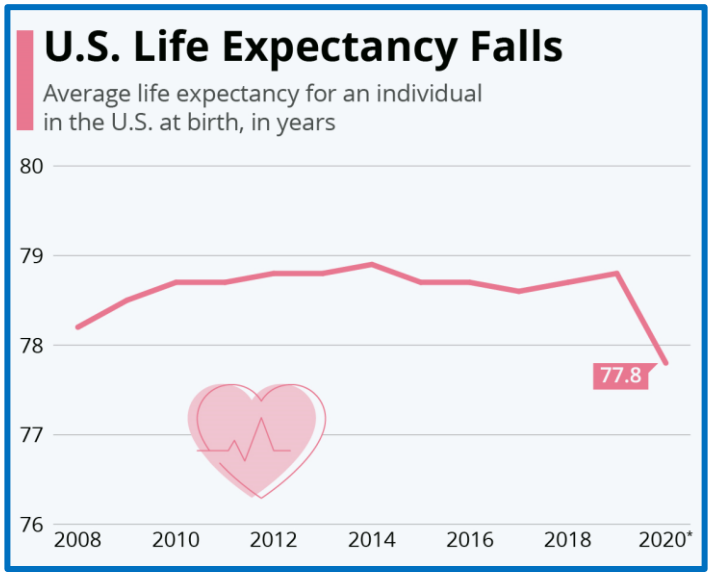
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

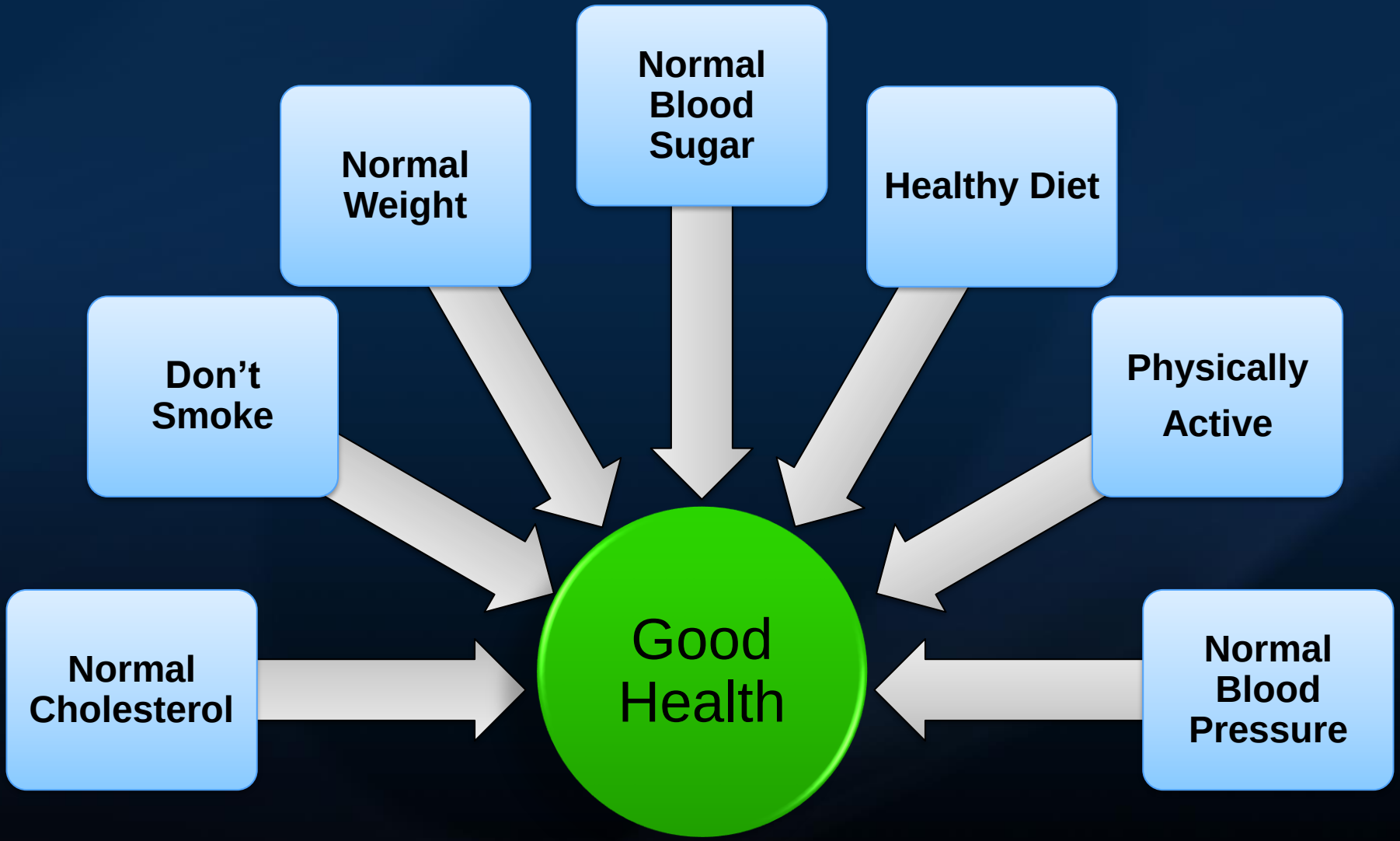
March 17, 2005

A Potential Decline in Life Expectancy in the United States in the 21st Century

S. Jay Olshansky, Ph.D., Douglas J. Passaro, M.D., Ronald C. Hershow, M.D., Jennifer Layden, M.P.H., Bruce A. Carnes, Ph.D., Jacob Brody, M.D., Leonard Hayflick, Ph.D., Robert N. Butler, M.D., David B. Allison, Ph.D., and David S. Ludwig, M.D., Ph.D.



Treating Cardiometabolic Disease



Hypertension

Leading cause of death/disability world-wide

Leading cause of cardiovascular death in US

2nd most common cause of preventable death

1,100 deaths PER DAY

Call to Action to Control Hypertension

Surgeon General

Opinion

VIEWPOINT

A National Commitment to Improve the Care of Patients With Hypertension in the US

Jerome M. Adams, MD, MPH
Office of the Surgeon General, Department of Health and Human Services, Washington, DC.

Janet S. Wright, MD
Office of the Surgeon General, Department of Health and Human Services, Washington, DC.

Author Audio Interview

Video and Supplemental content

Hypertension is common, costly, and controllable. Almost 1 in 2 US adults has hypertension, and among those, the estimated rate of controlled blood pressure was only 43.7% in 2017-2018 a decline from 53.8% in 2013-2014.[1] Uncontrolled blood pressure can lead to largely preventable events such as myocardial infarction, stroke, and maternal mortality, as well as debilitating and expensive conditions such as kidney disease, heart failure, and cognitive decline. Hypertensive disorders of pregnancy, which have increased in the US, contribute to adverse maternal and child health outcomes and can increase a woman's lifetime risk of cardiovascular disease. Disparities in blood pressure control and, consequently, in these health outcomes, persist by race and ethnicity, age, and geography. Yet broad and equitable hypertension control is possible, and some health care practices and systems have achieved rates of 80% or higher across a wide spectrum of sites and populations served.[2-5]

These facts about hypertension—a highly prevalent, poorly managed, inequitably experienced, and highly controllable condition—are more than sufficient to merit the *Surgeon General's Call to Action to Control Hypertension*.[6] Some may question the release of this report now, when the challenge of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become the most pressing health priority in the US. However, it is precisely the effects of the pandemic, and the painful lessons that are being learned, that add even greater urgency to improving hypertension control rates for all US adults.[7] The coronavirus disease 2019 (COVID-19) pandemic has revealed substantial differences in exposure to the SARS-CoV-2 virus and severe outcomes from COVID-19. The higher rates of infection, severe complications, and death among people of color, in particular, are at least in part due to social determinants of health: housing, transportation, education, access to health care, availability of healthy food options, a secure income, and freedom from structural and institutional barriers related to race and bias. These same determinants either support or impede success in controlling high blood pressure.

> Implementing the goals and strategies in the *Call to Action*...could help patients, clinicians, and communities achieve the health, wealth, and equity benefits that national hypertension control can bring.

When coupled with widespread implementation of best practices in clinical settings and empowering individuals to actively manage their blood pressure, acknowledging and addressing a community's social conditions may generate sustained improvements in control of both hypertension and COVID-19.

Now is the time to draw attention and drive action to proven strategies that improve blood pressure control. Controlling hypertension requires sustained and specific actions by individuals with and at risk for high blood pressure; health care and public health professionals and the systems in which they operate; and communities. Smart, substantive, and ongoing investments by each of these sectors are needed to achieve better health outcomes in the near term, but also a more resilient, equitable, and prosperous nation in the future.

The goals and strategies presented in the Surgeon General's *Call to Action* provide a national roadmap to drive change (eFigure in the Supplement). The 3 goals are: (1) make hypertension control a national priority; (2) ensure that communities support hypertension control; and (3) optimize patient care for hypertension control. The goals and strategies are grounded in the evidence, informed by experiences of high-performing systems and communities, and adaptable to match the resources available and the populations served.

The first major goal is to declare hypertension control a national priority; this is justified by the costs in lives, health, and dollars lost to a largely controllable condition. Generating widespread awareness of the effect of uncontrolled blood pressure on health and the economy is the first step in galvanizing action by the diverse set of sectors outlined in the document. Among the partners essential to achieving a national aim of hypertension control are payers and employers, who, by prioritizing blood pressure control in value-based contracting and incentive programs, could enable practices to invest in the teams and processes proven to achieve high performance over time. Payers and employers also could help individuals manage their hypertension by eliminating cost-sharing for blood pressure monitors and medications. Setting blood pressure control as a population health priority also draws attention to the profound disparities associated with hypertension, with racial and ethnic minority groups experiencing higher rates of hypertension, lower levels of blood pressure control, and greater risk of direct or indirect (eg, COVID-19–related) complications. The reason to establish this goal is not merely to

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- **Highly prevalent**
- **Poorly managed**
- **Inequitably experienced**
- **Highly controllable**

JAMA. 2020;324(18):1825-1826.

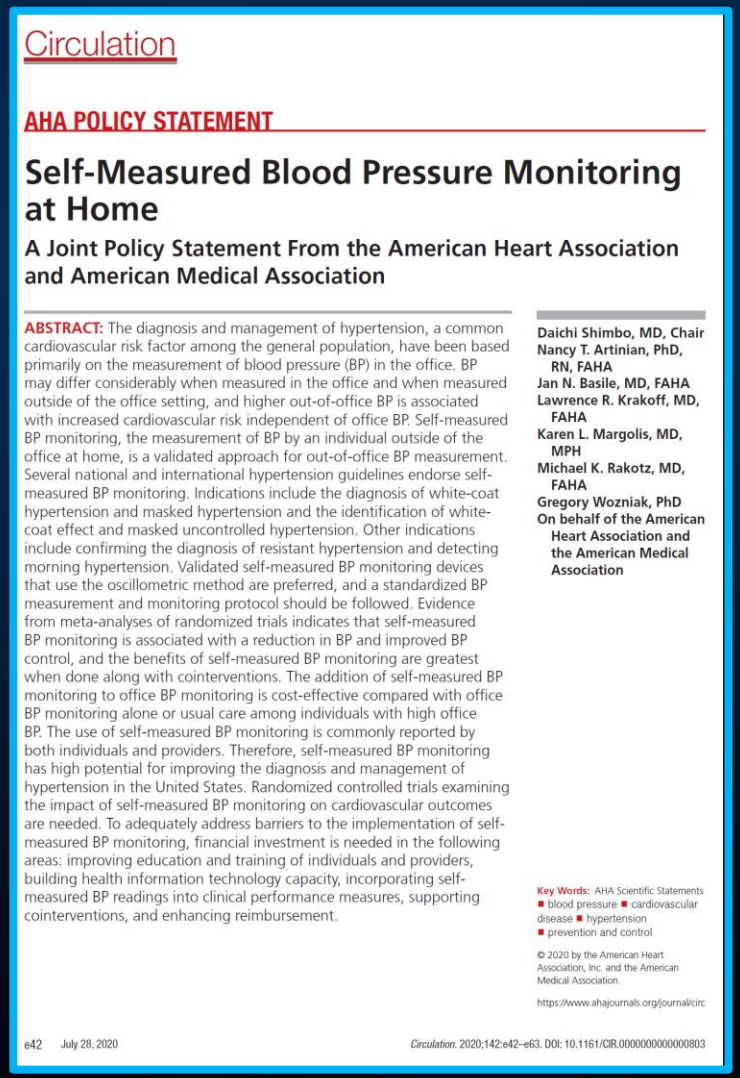
Hypertension

50-75% due to lifestyle choices

Physical activity, weight loss, sleep, stress

EtOH, NSAIDS, OSA, Salt

Optimize Patient Care
Home Blood Pressure



Circulation

AHA POLICY STATEMENT

Self-Measured Blood Pressure Monitoring at Home

A Joint Policy Statement From the American Heart Association and American Medical Association

ABSTRACT: The diagnosis and management of hypertension, a common cardiovascular risk factor among the general population, have been based primarily on the measurement of blood pressure (BP) in the office. BP may differ considerably when measured in the office and when measured outside of the office setting, and higher out-of-office BP is associated with increased cardiovascular risk independent of office BP. Self-measured BP monitoring, the measurement of BP by an individual outside of the office at home, is a validated approach for out-of-office BP measurement. Several national and international hypertension guidelines endorse self-measured BP monitoring. Indications include the diagnosis of white-coat hypertension and masked hypertension and the identification of white-coat effect and masked uncontrolled hypertension. Other indications include confirming the diagnosis of resistant hypertension and detecting morning hypertension. Validated self-measured BP monitoring devices that use the oscillometric method are preferred, and a standardized BP measurement and monitoring protocol should be followed. Evidence from meta-analyses of randomized trials indicates that self-measured BP monitoring is associated with a reduction in BP and improved BP control, and the benefits of self-measured BP monitoring are greatest when done along with cointerventions. The addition of self-measured BP monitoring to office BP monitoring is cost-effective compared with office BP monitoring alone or usual care among individuals with high office BP. The use of self-measured BP monitoring is commonly reported by both individuals and providers. Therefore, self-measured BP monitoring has high potential for improving the diagnosis and management of hypertension in the United States. Randomized controlled trials examining the impact of self-measured BP monitoring on cardiovascular outcomes are needed. To adequately address barriers to the implementation of self-measured BP monitoring, financial investment is needed in the following areas: improving education and training of individuals and providers, building health information technology capacity, incorporating self-measured BP readings into clinical performance measures, supporting cointerventions, and enhancing reimbursement.

Daichi Shimbo, MD, Chair
Nancy T. Artinian, PhD, RN, FAHA
Jan N. Basile, MD, FAHA
Lawrence R. Krakoff, MD, FAHA
Karen L. Margolis, MD, MPH
Michael K. Rakotz, MD, FAHA
Gregory Wozniak, PhD
On behalf of the American Heart Association and the American Medical Association

Key Words: AHA Scientific Statements ■ blood pressure ■ cardiovascular disease ■ hypertension ■ prevention and control

https://www.ahajournals.org/journal/circ

Circulation. 2020;142:e42–e63. DOI: 10.1161/CIR.0000000000000803

- **Simple start**
  - **Outside office BP**
    - **Associated with lower BP and improved control**
    - **Cost effective**
    - **Payment barriers still exist**

***Circulation.* 2020;142:e42–e63.**

Optimize Patient Care
Use the Right Meds

Opinion

VIEWPOINT

A National Commitment to Improve the Care of Patients With Hypertension in the US

Jerome M. Adams, MD, MPH
Office of the Surgeon General, Department of Health and Human Services, Washington, DC.

Janet S. Wright, MD
Office of the Surgeon General, Department of Health and Human Services, Washington, DC.

Author Audio Interview

Video and Supplemental content

Hypertension is common, costly, and controllable. Almost 1 in 2 US adults has hypertension, and among those, the estimated rate of controlled blood pressure was only 43.7% in 2017-2018 a decline from 53.8% in 2013-2014.[1] Uncontrolled blood pressure can lead to largely preventable events such as myocardial infarction, stroke, and maternal mortality, as well as debilitating and expensive conditions such as kidney disease, heart failure, and cognitive decline. Hypertensive disorders of pregnancy, which have increased in the US, contribute to adverse maternal and child health outcomes and can increase a woman's lifetime risk of cardiovascular disease. Disparities in blood pressure control and, consequently, in these health outcomes, persist by race and ethnicity, age, and geography. Yet broad and equitable hypertension control is possible, and some health care practices and systems have achieved rates of 80% or higher across a wide spectrum of sites and populations served.[2-5]

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The first major goal is to declare hypertension control a national priority; this is justified by the costs in lives, health, and dollars lost to a largely controllable condition. Generating widespread awareness of the effect of uncontrolled blood pressure on health and the economy is the first step in galvanizing action by the diverse set of sectors outlined in the document. Among the partners essential to achieving a national aim of hypertension control are payers and employers, who, by prioritizing blood pressure control in value-based contracting and incentive programs, could enable practices to invest in the teams and processes proven to achieve high performance over time. Payers and employers also could help individuals manage their hypertension by eliminating cost-sharing for blood pressure monitors and medications. Setting blood pressure control as a population health priority also draws attention to the profound disparities associated with hypertension, with racial and ethnic minority groups experiencing higher rates of hypertension, lower levels of blood pressure control, and greater risk of direct or indirect (eg, COVID-19–related) complications. The reason to establish this goal is not merely to

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- **Simple start**
- **Use first line generic meds**
  - **Chlorthalidone or indapamide > HCTZ**
  - **ACEi OR ARB**
  - **Amlodipine**
- **Screen for sleep apnea**

***JAMA*. 2020;324(18):1825-1826.**

•. 2020 Jul 7;173(1):10-20.
•. 2020 Jul 7;173(1):10-20.

Primary Aldosteronism
Underrecognized?

The Unrecognized Prevalence of Primary Aldosteronism:
A Cross-sectional Study

Jenifer M. Brown, MD, Mohammed Siddiqui, MD, David A. Calhoun, MD, Robert M. Carey, MD, Paul N. Hopkins, MD, MSPH, Gordon H. Williams, MD, Anand Vaidya, MD, MMSc
Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (J.M.B., G.H.W., A.V.); University of Alabama at Birmingham, Birmingham, Alabama (M.S., D.A.C.); University of Virginia Health System, Charlottesville, Virginia (R.M.C.); and University of Utah School of Medicine, Salt Lake City, Utah (P.N.H.).

Abstract

Background: Primary aldosteronism is a nonsuppressible renin-independent aldosterone production that causes hypertension and cardiovascular disease.

Objective: To characterize the prevalence of nonsuppressible renin-independent aldosterone production, as well as biochemically overt primary aldosteronism, in relation to blood pressure.

Design: Cross-sectional study.

Setting: 4 U.S. academic medical centers.

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Analysis and interpretation of the data: J.M. Brown, M. Siddiqui, D.A. Calhoun, R.M. Carey, A. Vaidya.
Drafting of the article: J.M. Brown, M. Siddiqui, A. Vaidya. Critical revision of the article for important intellectual content: J.M. Brown, M. Siddiqui, R.M. Carey, P.N. Hopkins, G.H. Williams, A. Vaidya.
Final approval of the article: J.M. Brown, M. Siddiqui, D.A. Calhoun, R.M. Carey, P.N. Hopkins, G.H. Williams, A. Vaidya. Provision of study materials or patients: M. Siddiqui, R.M. Carey, G.H. Williams, A. Vaidya.
Statistical expertise: P.N. Hopkins, A. Vaidya.
Obtaining of funding: D.A. Calhoun, R.M. Carey, A. Vaidya. Administrative, technical, or logistic support: P.N. Hopkins, G.H. Williams, A. Vaidya.
Collection and assembly of data: J.M. Brown, M. Siddiqui, D.A. Calhoun, R.M. Carey, P.N. Hopkins, A. Vaidya.

Disclosures: Dr. Brown reports grants from the National Heart, Lung, and Blood Institute. Dr. Williams reports grants from the National Institutes of Health. Dr. Vaidya reports consultancy for Catalys Pacific, Corcept Therapeutics, HRA Pharma, Orphagen, and Selenity Therapeutics and grants from the National Institutes of Health and Ventus Charitable Foundation. Authors not named here have disclosed no conflicts of interest. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M20-0065.

Reproducible Research Statement: *Study protocol:* See the Supplement (available at Annals.org). *Statistical code:* Available from Dr. Vaidya (e-mail, anandvaidya@bwh.harvard.edu). *Data set:* Not available.

Current author addresses and author contributions are available at Annals.org.

- **Simple start**
  - **Consider primary aldosteronism?**
    - **May be up to 20% of resistant hypertensives (1 in 1000 are screened)**
    - **Strongly consider with hypokalemia, OSA or adrenal mass**
    - **Secret weapon in resistant HTN**
      - **Aldactone**

***Ann Intern Med* 2020;173:10-20.**

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Underrecognized?

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A Cross-sectional Study

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- **Simple start**
  - **Consider primary aldosteronism?**
    - **Screen with 8 AM paired aldosterone and plasma renin**
    - **Consider salt restriction and mineralocorticoid antagonists**

***Ann Intern Med* 2020;173:10-20.**

Hygia Chronotherapy

Nighttime meds

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 4565–4576
doi:10.1093/eurheartj/ehz754

CLINICAL RESEARCH
Hypertension

Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial

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See page 4577 for the editorial comment on this article (doi: 10.1093/eurheartj/ehz836)

Aims The Hygia Chronotherapy Trial, conducted within the clinical primary care setting, was designed to test whether bedtime in comparison to usual upon awakening hypertension therapy exerts better cardiovascular disease (CVD) risk reduction.

Methods and results In this multicentre, controlled, prospective endpoint trial, 19 084 hypertensive patients (10 614 men/8470 women, 60.5 ± 13.7 years of age) were assigned (1:1) to ingest the entire daily dose of ≥1 hypertension medications at bedtime ($n = 9552$) or all of them upon awakening ($n = 9532$). At inclusion and at every scheduled clinic visit (at least annually) throughout follow-up, ambulatory blood pressure (ABP) monitoring was performed for 48 h. During the 6.3-year median patient follow-up, 1752 participants experienced the primary CVD outcome (CVD death, myocardial infarction, coronary revascularization, heart failure, or stroke). Patients of the bedtime, compared with the upon-waking, treatment-time regimen showed significantly lower hazard ratio—adjusted for significant influential characteristics of age, sex, type 2 diabetes, chronic kidney disease, smoking, HDL cholesterol, asleep systolic blood pressure (BP) mean, sleep-time relative systolic BP decline, and previous CVD event—of the primary CVD outcome [0.55 (95% CI 0.50–0.61), $P < 0.001$] and each of its single components ($P < 0.001$ in all cases), i.e. CVD death [0.44 (0.34–0.56)], myocardial infarction [0.66 (0.52–0.84)], coronary revascularization [0.60 (0.47–0.75)], heart failure [0.58 (0.49–0.70)], and stroke [0.51 (0.41–0.63)].

Conclusion Routine ingestion by hypertensive patients of ≥1 prescribed BP-lowering medications at bedtime, as opposed to upon waking, results in improved ABP control (significantly enhanced decrease in asleep BP and increased sleep-time relative BP decline, i.e. BP dipping) and, most importantly, markedly diminished occurrence of major CVD events.

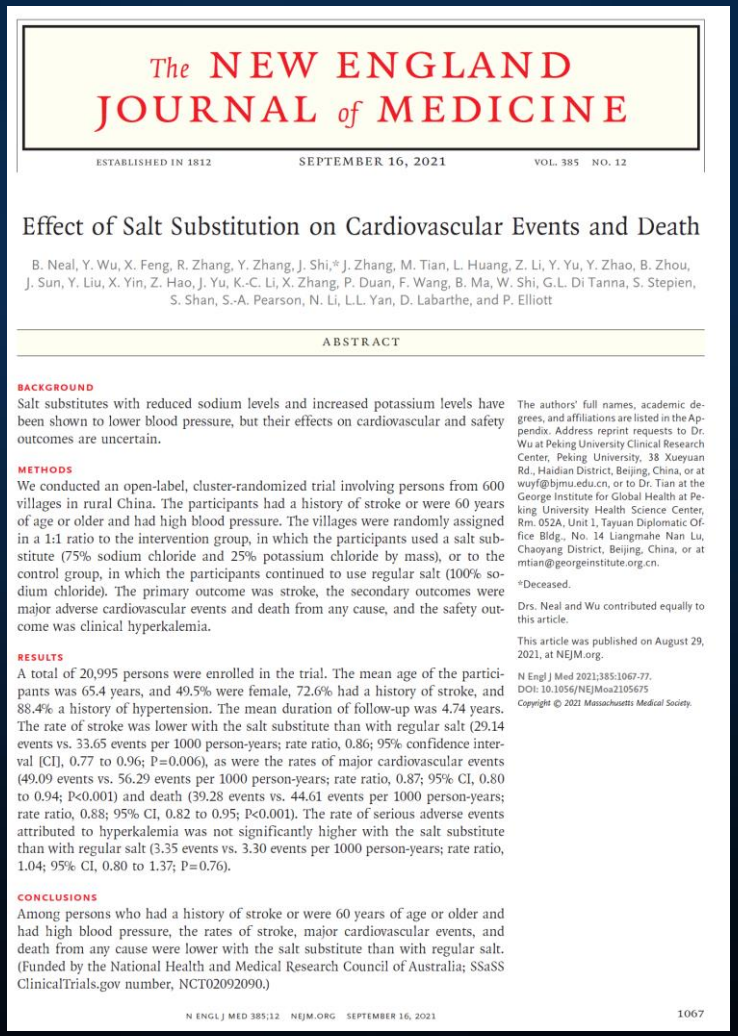
Trial registration ClinicalTrials.gov, number NCT00741585.

- n = 19,084, randomized to taking meds at bedtime or on awakening
- 6.3 year follow-up
- Improved BP control
- Lower combined primary endpoint, HR 0.55
  - CVD death 0.44
  - MI 0.66
  - CHF 0.58
  - Stroke 0.51

European Heart Journal 2020;21:3925-3932.

Salt-substitute

25% KCL



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Effect of Salt Substitution on Cardiovascular Events and Death

B. Neal, Y. Wu, X. Feng, R. Zhang, Y. Zhang, J. Shi,* J. Zhang, M. Tian, L. Huang, Z. Li, Y. Yu, Y. Zhao, B. Zhou, J. Sun, Y. Liu, X. Yin, Z. Hao, J. Yu, K.-C. Li, X. Zhang, P. Duan, F. Wang, B. Ma, W. Shi, G.L. Di Tanna, S. Stepien, S. Shan, S.-A. Pearson, N. Li, L.L. Yan, D. Labarthe, and P. Elliott

ABSTRACT

BACKGROUND

Salt substitutes with reduced sodium levels and increased potassium levels have been shown to lower blood pressure, but their effects on cardiovascular and safety outcomes are uncertain.

METHODS

We conducted an open-label, cluster-randomized trial involving persons from 600 villages in rural China. The participants had a history of stroke or were 60 years of age or older and had high blood pressure. The villages were randomly assigned in a 1:1 ratio to the intervention group, in which the participants used a salt substitute (75% sodium chloride and 25% potassium chloride by mass), or to the control group, in which the participants continued to use regular salt (100% sodium chloride). The primary outcome was stroke, the secondary outcomes were major adverse cardiovascular events and death from any cause, and the safety outcome was clinical hyperkalemia.

RESULTS

A total of 20,995 persons were enrolled in the trial. The mean age of the participants was 65.4 years, and 49.5% were female, 72.6% had a history of stroke, and 88.4% a history of hypertension. The mean duration of follow-up was 4.74 years. The rate of stroke was lower with the salt substitute than with regular salt (29.14 events vs. 33.65 events per 1000 person-years; rate ratio, 0.86; 95% confidence interval [CI], 0.77 to 0.96; P=0.006), as were the rates of major cardiovascular events (49.09 events vs. 56.29 events per 1000 person-years; rate ratio, 0.87; 95% CI, 0.80 to 0.94; P<0.001) and death (39.28 events vs. 44.61 events per 1000 person-years; rate ratio, 0.88; 95% CI, 0.82 to 0.95; P<0.001). The rate of serious adverse events attributed to hyperkalemia was not significantly higher with the salt substitute than with regular salt (3.35 events vs. 3.30 events per 1000 person-years; rate ratio, 1.04; 95% CI, 0.80 to 1.37; P=0.76).

CONCLUSIONS

Among persons who had a history of stroke or were 60 years of age or older and had high blood pressure, the rates of stroke, major cardiovascular events, and death from any cause were lower with the salt substitute than with regular salt. (Funded by the National Health and Medical Research Council of Australia; SSaSS ClinicalTrials.gov number, NCT02092090.)

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*Deceased.

Drs. Neal and Wu contributed equally to this article.

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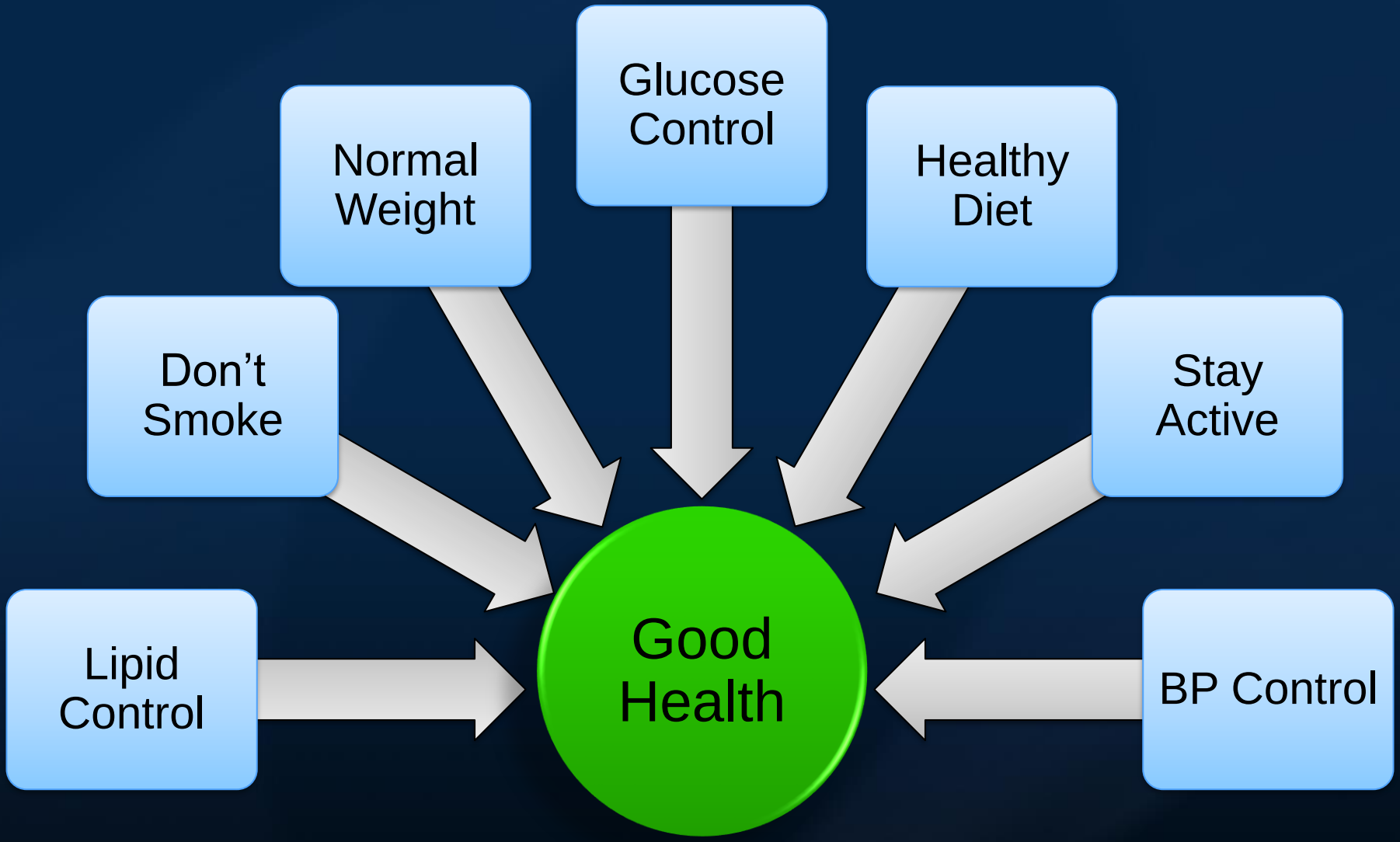
DOI: 10.1056/NEJMoa2105675

- n = 20,995 with stroke or 60+ with HTN
- 4.74 year follow-up
- Stroke reduced HR = 0.86
- CVD reduced HR = 0.87

N Engl J Med 2021;385:1067-77.


Glucose Control
Normal Weight
Healthy Diet
Don't Smoke
Stay Active
Lipid Control
Good Health
BP Control

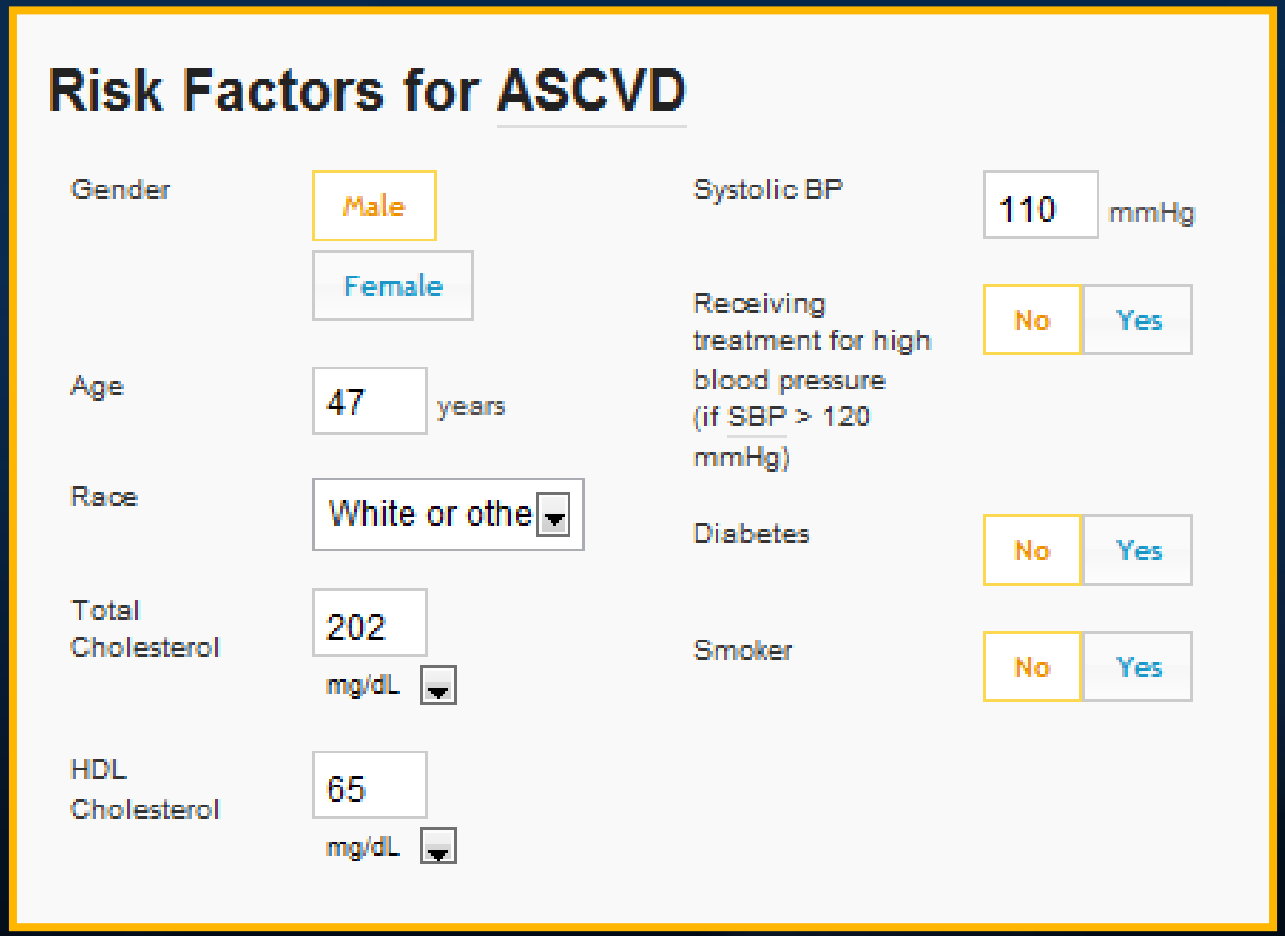
Statin Therapy

- **Age 40-75 “routinely” assess lipids and ASCVD risk**
- **Age 20-39 q 4-6 years**

Clinical CVD	Diabetes Age 40-75, LDL 70-189	No Diabetes Age 40-75, LDL 70-189	LDL ≥190
High intensity statin Add ezetimibe and/or PCSK9 if LDL > 70	Moderate Intensity Statin in all High Intensity Statin with Multiple Risk Factors	Calculate 10-year risk	High intensity statin

Risk < 5% Emphasize lifestyle	**Risk 5-7.5%** If risk enhancers, consider Moderate Intensity Statin	**Risk 7.5 - < 20%** Moderate Intensity Statin	**Risk ≥20%** High Intensity Statin

ASCVD Risk Score



So Many Risk Scores

That aren't used

- **Framingham**
  - **MI and CVD death**
- **Reynold's Risk Score**
  - **Includes CRP and Family history**
  - **MI, CVA, CVD death, revascularization**
- **ASCVD/pooled cohort equation**
  - **Includes race**
  - **MI, CVD death, and CVA**

57-year-old Physician

Concerned About Heart Risk

- **No history or symptoms of CVD**
- **Personal history of high cholesterol (greater than 300 mg/dL during residency)**
- **Family history of CVD**
  - **Father had MI at 76 years**

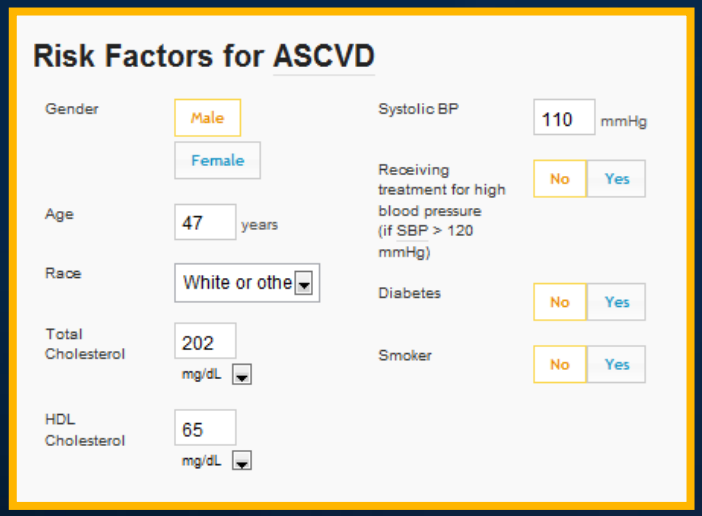
57-year-old Physician

Concerned About Heart Risk

- **Smoked 2 packs for 8 years, quit 30 years ago**
- **No diabetes**
- **BP 116/58 mm Hg**
- **BMI 27 Kg/m2**
- **Exercises regularly**
- **Primarily plant-based diet**

57-year-old Physician

- Outside stress test 2 years ago negative by report
- Currently
  - T Chol 224 mg/dl
  - TG 47 mg/dl
  - HDL 67 mg/dl
  - LDL 128 mg/dl
  - Glucose 106 mg/dl



ASCVD Risk Score

5%

What Would You Do For This Patient?

A) Reassure and congratulate him

B) Start a statin

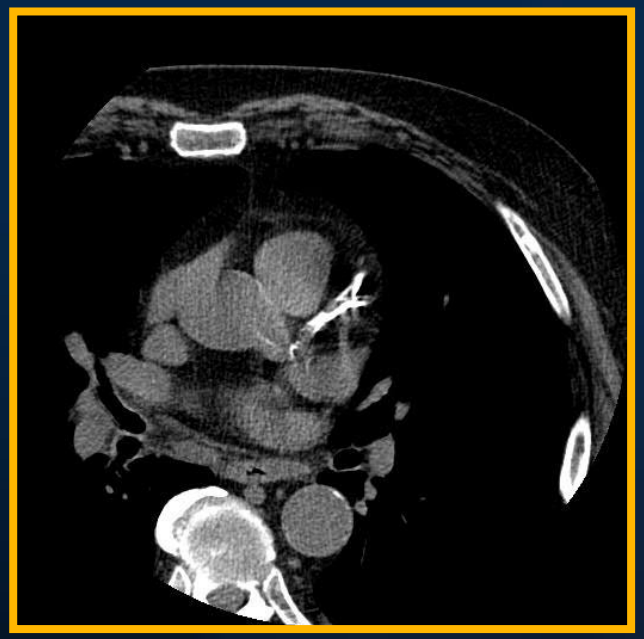
C) Carotid ultrasound

D) Stress test

E) Coronary artery calcium score

CT Coronary Calcium Score

- Total calcium score
  4,444 AU
- 99th percentile compared to gender and age matched controls

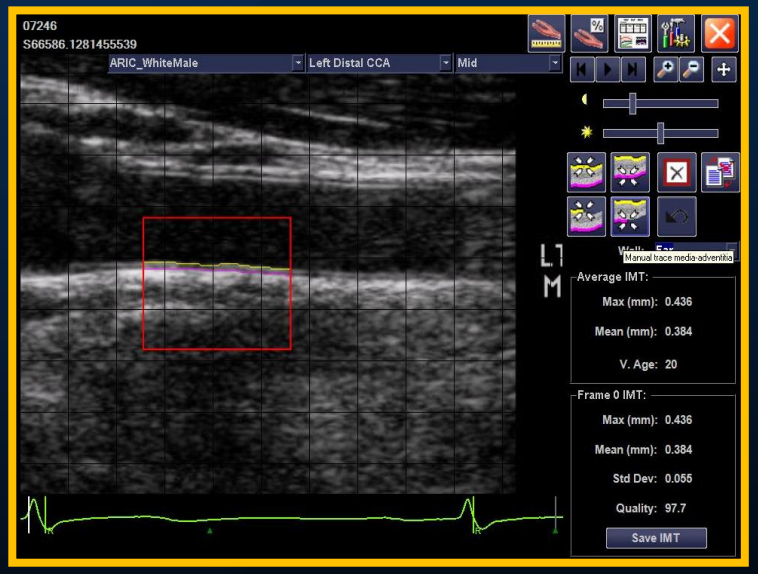


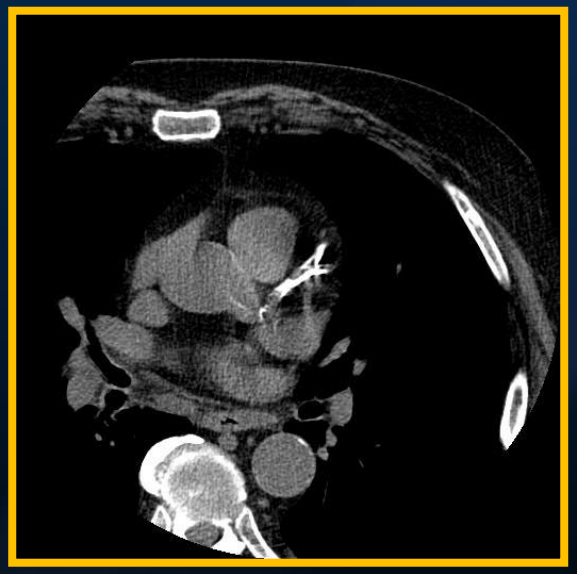
What Would You Do For This Patient?

A) Reassure and congratulate him

B) Start a statin

When do we need additional information to assess CV risk?

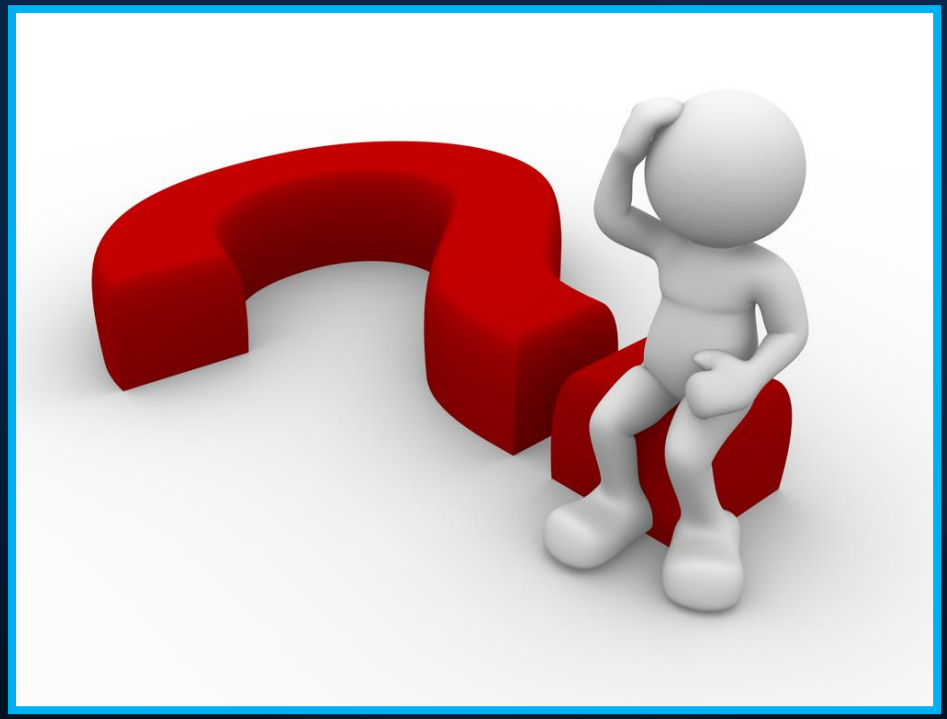




When to do Additional Testing?

Statin or No Statin?

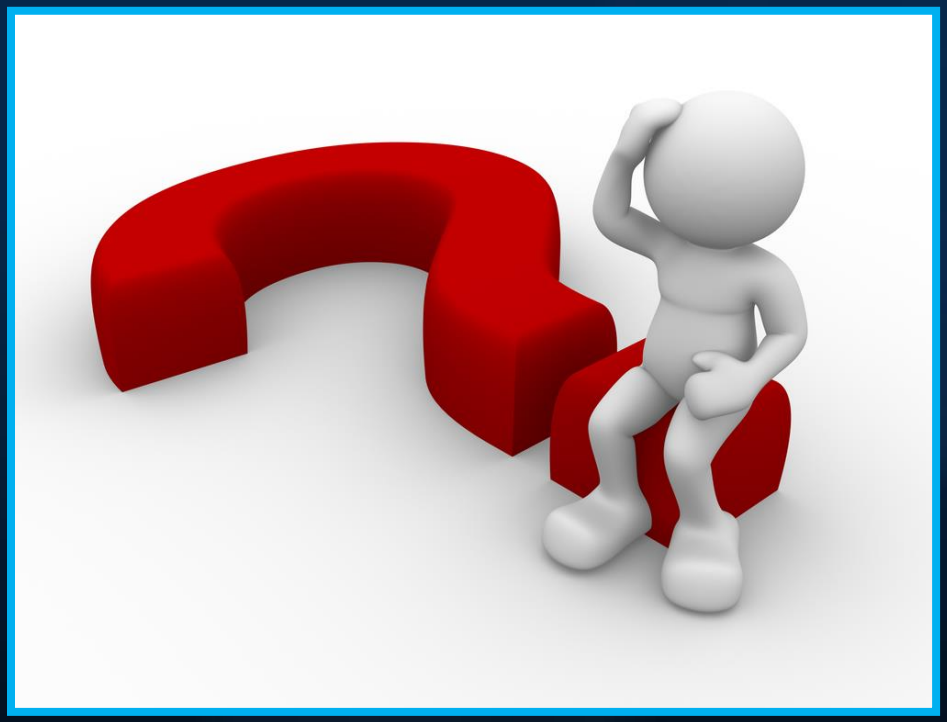
- **Family history of CVD**
- **Striking risk factor in a young person**
- **“Grey zone” ASCVD risk score (5-7.5%)**



When NOT to do Additional Testing?

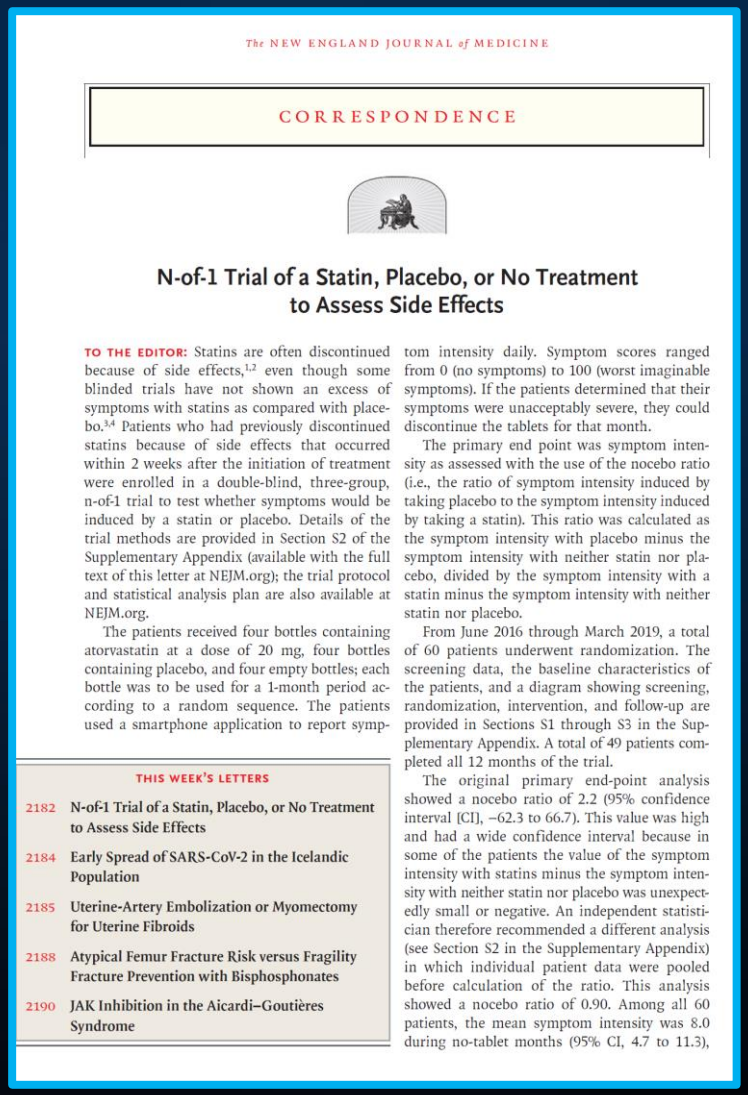
CV Risk Stratification

- **Established CVD**
- **Already on a statin**
- **Patient and provider agree**
- **To assess effectiveness of treatment**



Statins

Are Side Effects Real?



The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

N-of-1 Trial of a Statin, Placebo, or No Treatment to Assess Side Effects

TO THE EDITOR: Statins are often discontinued because of side effects,[1,2] even though some blinded trials have not shown an excess of symptoms with statins as compared with placebo.[3,4] Patients who had previously discontinued statins because of side effects that occurred within 2 weeks after the initiation of treatment were enrolled in a double-blind, three-group, n-of-1 trial to test whether symptoms would be induced by a statin or placebo. Details of the trial methods are provided in Section S2 of the Supplementary Appendix (available with the full text of this letter at NEJM.org); the trial protocol and statistical analysis plan are also available at NEJM.org.

The patients received four bottles containing atorvastatin at a dose of 20 mg, four bottles containing placebo, and four empty bottles; each bottle was to be used for a 1-month period according to a random sequence. The patients used a smartphone application to report symptom intensity daily. Symptom scores ranged from 0 (no symptoms) to 100 (worst imaginable symptoms). If the patients determined that their symptoms were unacceptably severe, they could discontinue the tablets for that month.

The primary end point was symptom intensity as assessed with the use of the nocebo ratio (i.e., the ratio of symptom intensity induced by taking placebo to the symptom intensity induced by taking a statin). This ratio was calculated as the symptom intensity with placebo minus the symptom intensity with neither statin nor placebo, divided by the symptom intensity with a statin minus the symptom intensity with neither statin nor placebo.

From June 2016 through March 2019, a total of 60 patients underwent randomization. The screening data, the baseline characteristics of the patients, and a diagram showing screening, randomization, intervention, and follow-up are provided in Sections S1 through S3 in the Supplementary Appendix. A total of 49 patients completed all 12 months of the trial.

The original primary end-point analysis showed a nocebo ratio of 2.2 (95% confidence interval [CI], −62.3 to 66.7). This value was high and had a wide confidence interval because in some of the patients the value of the symptom intensity with statins minus the symptom intensity with neither statin nor placebo was unexpectedly small or negative. An independent statistician therefore recommended a different analysis (see Section S2 in the Supplementary Appendix) in which individual patient data were pooled before calculation of the ratio. This analysis showed a nocebo ratio of 0.90. Among all 60 patients, the mean symptom intensity was 8.0 during no-tablet months (95% CI, 4.7 to 11.3),

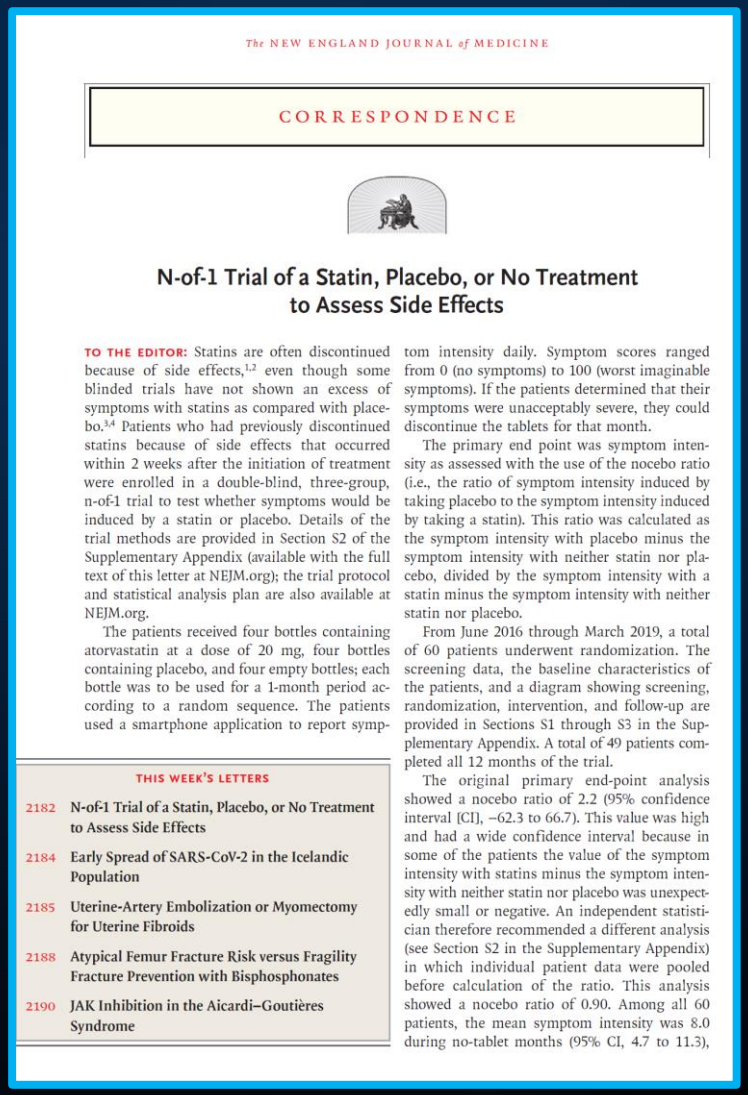
THIS WEEK'S LETTERS

- N-of-1 study design, 60 subjects with statin intolerance
- 4 bottles of atorva 20 mg, placebo, or empty
- Alternate bottles for a month over 1 year
- Symptoms tracked with smart phone app

N Engl J Med 2020;383:epub, Nov 15.

Statins

Are Side Effects Real?



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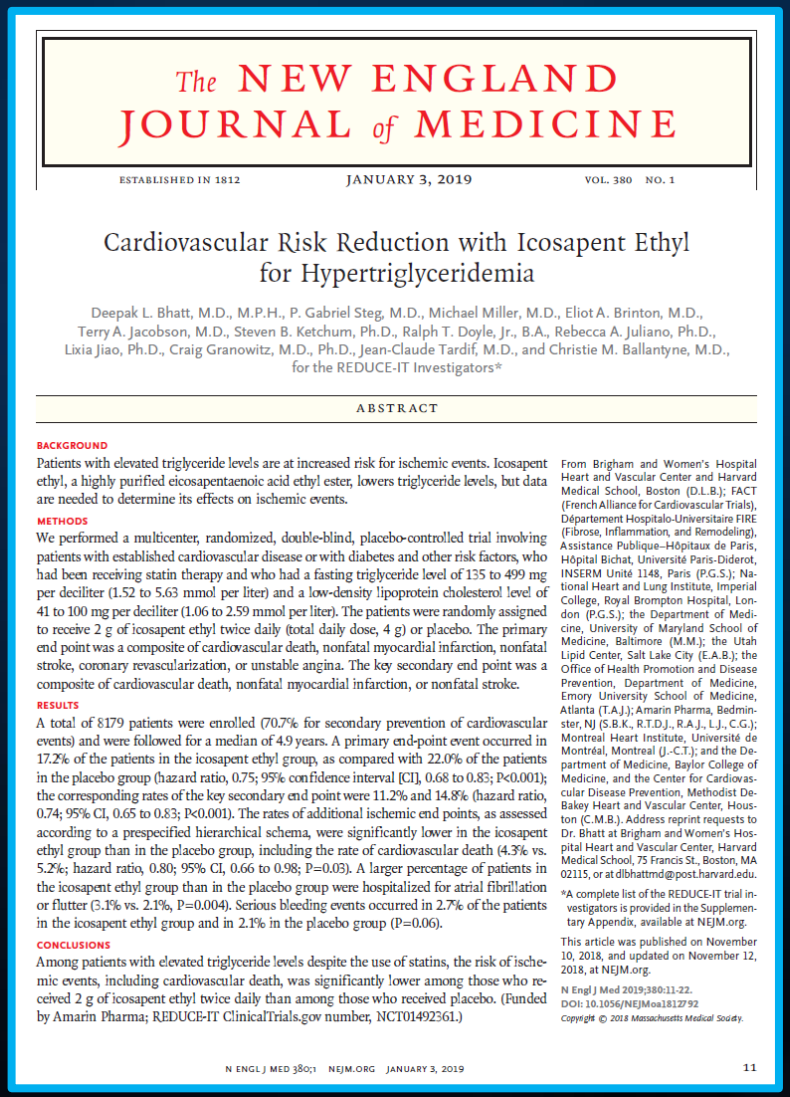
THIS WEEK'S LETTERS

- 90% of symptoms while taking atorva also reported in placebo
- No pill bottles ~ half the symptoms
- All subjects shown results at end of trial – 50% restarted statins

N Engl J Med 2020;383:epub, Nov 15.

REDUCE-IT

Icosapent ethyl (Vascepa®)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 3, 2019 VOL. 380 NO. 1

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*

ABSTRACT

BACKGROUND

Patients with elevated triglyceride levels are at increased risk for ischemic events. Icosapent ethyl, a highly purified eicosapentaenoic acid ethyl ester, lowers triglyceride levels, but data are needed to determine its effects on ischemic events.

METHODS

We performed a multicenter, randomized, double-blind, placebo-controlled trial involving patients with established cardiovascular disease or with diabetes and other risk factors, who had been receiving statin therapy and who had a fasting triglyceride level of 135 to 499 mg per deciliter (1.52 to 5.63 mmol per liter) and a low-density lipoprotein cholesterol level of 41 to 100 mg per deciliter (1.06 to 2.59 mmol per liter). The patients were randomly assigned to receive 2 g of icosapent ethyl twice daily (total daily dose, 4 g) or placebo. The primary end point was a composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina. The key secondary end point was a composite of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

RESULTS

A total of 8179 patients were enrolled (70.7% for secondary prevention of cardiovascular events) and were followed for a median of 4.9 years. A primary end-point event occurred in 17.2% of the patients in the icosapent ethyl group, as compared with 22.0% of the patients in the placebo group (hazard ratio, 0.75; 95% confidence interval [CI], 0.68 to 0.83; P<0.001); the corresponding rates of the key secondary end point were 11.2% and 14.8% (hazard ratio, 0.74; 95% CI, 0.65 to 0.83; P<0.001). The rates of additional ischemic end points, as assessed according to a prespecified hierarchical schema, were significantly lower in the icosapent ethyl group than in the placebo group, including the rate of cardiovascular death (4.3% vs. 5.2%; hazard ratio, 0.80; 95% CI, 0.66 to 0.98; P=0.03). A larger percentage of patients in the icosapent ethyl group than in the placebo group were hospitalized for atrial fibrillation or flutter (3.1% vs. 2.1%, P=0.004). Serious bleeding events occurred in 2.7% of the patients in the icosapent ethyl group and in 2.1% in the placebo group (P=0.06).

CONCLUSIONS

Among patients with elevated triglyceride levels despite the use of statins, the risk of ischemic events, including cardiovascular death, was significantly lower among those who received 2 g of icosapent ethyl twice daily than among those who received placebo. (Funded by Amarin Pharma; REDUCE-IT ClinicalTrials.gov number, NCT01492361.)

From Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston (D.L.B.); FACT (French Alliance for Cardiovascular Trials), Département Hospitalo-Universitaire FIRE (Fibrose, Inflammation, and Remodeling), Assistance Publique–Hôpitaux de Paris, Hôpital Bichat, Université Paris-Diderot, INSERM Unité 1148, Paris (P.G.S.); National Heart and Lung Institute, Imperial College, Royal Brompton Hospital, London (P.G.S.); the Department of Medicine, University of Maryland School of Medicine, Baltimore (M.M.); the Utah Lipid Center, Salt Lake City (E.A.B.); the Office of Health Promotion and Disease Prevention, Department of Medicine, Emory University School of Medicine, Atlanta (T.A.J.); Amarin Pharma, Bedminster, NJ (S.B.K., R.T.D.J., R.A.J., L.J., C.G.); Montreal Heart Institute, Université de Montréal, Montreal (J.-C.T.); and the Department of Medicine, Baylor College of Medicine, and the Center for Cardiovascular Disease Prevention, Methodist DeBakey Heart and Vascular Center, Houston (C.M.B.). Address reprint requests to Dr. Bhatt at Brigham and Women's Hospital Heart and Vascular Center, Harvard Medical School, 75 Francis St., Boston, MA 02115, or at dlbhattmd@post.harvard.edu.

*A complete list of the REDUCE-IT trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 10, 2018, and updated on November 12, 2018, at NEJM.org.

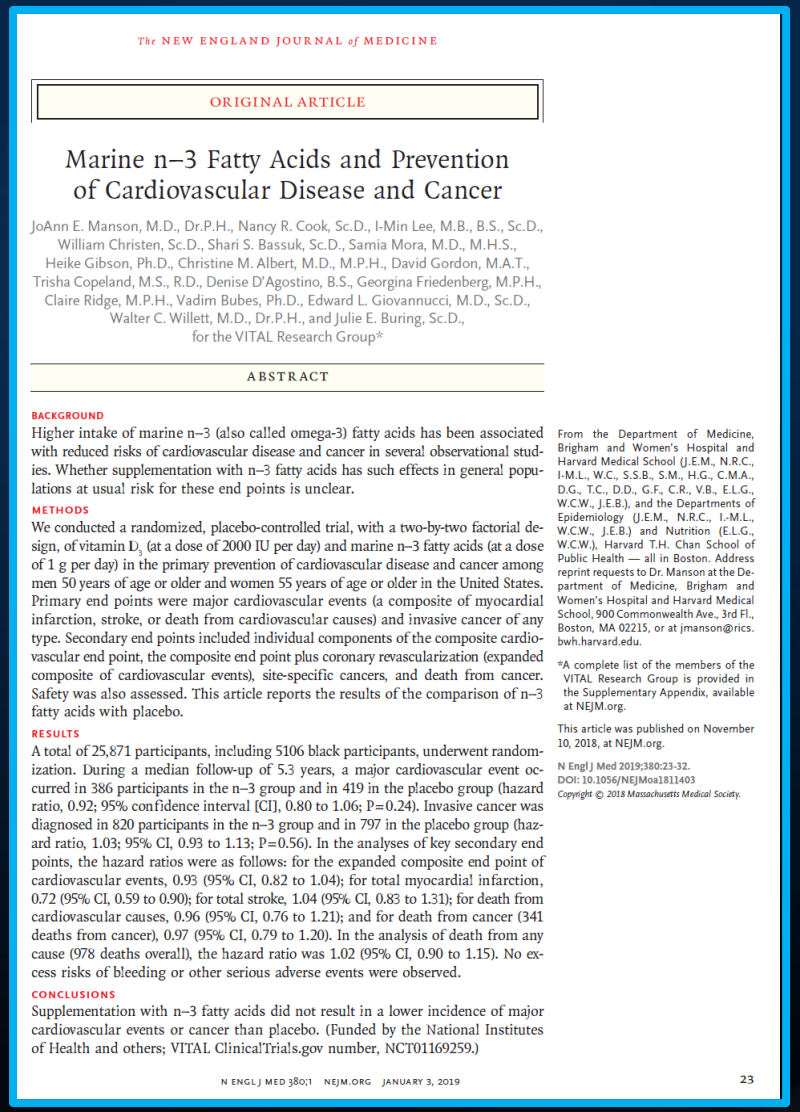
N Engl J Med 2019;380:11-22.
DOI: 10.1056/NEJMoa1812792

- **n = 8179 with CVD or DM and other risk factors on a statin**
- **TG 135-499 mg/dL, LDL 40-100 mg/dL on a statin**
- **CV death reduced 20%**
- **Primary endpoint reduced 25%**

N Engl J Med 2019; 380:11-22

VITAL

Vitamin D and Fish Oil



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Marine n–3 Fatty Acids and Prevention of Cardiovascular Disease and Cancer

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., Christine M. Albert, M.D., M.P.H., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., Vadim Bubes, Ph.D., Edward L. Giovannucci, M.D., Sc.D., Walter C. Willett, M.D., Dr.P.H., and Julie E. Buring, Sc.D., for the VITAL Research Group*

ABSTRACT

BACKGROUND

Higher intake of marine n–3 (also called omega-3) fatty acids has been associated with reduced risks of cardiovascular disease and cancer in several observational studies. Whether supplementation with n–3 fatty acids has such effects in general populations at usual risk for these end points is unclear.

METHODS

We conducted a randomized, placebo-controlled trial, with a two-by-two factorial design, of vitamin D_3 (at a dose of 2000 IU per day) and marine n–3 fatty acids (at a dose of 1 g per day) in the primary prevention of cardiovascular disease and cancer among men 50 years of age or older and women 55 years of age or older in the United States. Primary end points were major cardiovascular events (a composite of myocardial infarction, stroke, or death from cardiovascular causes) and invasive cancer of any type. Secondary end points included individual components of the composite cardiovascular end point, the composite end point plus coronary revascularization (expanded composite of cardiovascular events), site-specific cancers, and death from cancer. Safety was also assessed. This article reports the results of the comparison of n–3 fatty acids with placebo.

RESULTS

A total of 25,871 participants, including 5106 black participants, underwent randomization. During a median follow-up of 5.3 years, a major cardiovascular event occurred in 386 participants in the n–3 group and in 419 in the placebo group (hazard ratio, 0.92; 95% confidence interval [CI], 0.80 to 1.06; P=0.24). Invasive cancer was diagnosed in 820 participants in the n–3 group and in 797 in the placebo group (hazard ratio, 1.03; 95% CI, 0.93 to 1.13; P=0.56). In the analyses of key secondary end points, the hazard ratios were as follows: for the expanded composite end point of cardiovascular events, 0.93 (95% CI, 0.82 to 1.04); for total myocardial infarction, 0.72 (95% CI, 0.59 to 0.90); for total stroke, 1.04 (95% CI, 0.83 to 1.31); for death from cardiovascular causes, 0.96 (95% CI, 0.76 to 1.21); and for death from cancer (341 deaths from cancer), 0.97 (95% CI, 0.79 to 1.20). In the analysis of death from any cause (978 deaths overall), the hazard ratio was 1.02 (95% CI, 0.90 to 1.15). No excess risks of bleeding or other serious adverse events were observed.

CONCLUSIONS

Supplementation with n–3 fatty acids did not result in a lower incidence of major cardiovascular events or cancer than placebo. (Funded by the National Institutes of Health and others; VITAL ClinicalTrials.gov number, NCT01169259.)

From the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School (J.E.M., N.R.C., I-M.L., W.C., S.S.B., S.M., H.G., C.M.A., D.G., T.C., D.D., G.F., C.R., V.B., E.L.G., W.C.W., J.E.B.), and the Departments of Epidemiology (J.E.M., N.R.C., I.-M.L., W.C.W., J.E.B.) and Nutrition (E.L.G., W.C.W.), Harvard T.H. Chan School of Public Health — all in Boston. Address reprint requests to Dr. Manson at the Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, 900 Commonwealth Ave., 3rd Fl., Boston, MA 02215, or at jmanson@rics.bwh.harvard.edu.

*A complete list of the members of the VITAL Research Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 10, 2018, at NEJM.org.

N Engl J Med 2019;380:23-32.
DOI: 10.1056/NEJMoa1811403

- **n = 25,871, primary prevention of CVD and cancer in men >50 and women > 55**
- **Randomized to 2,000 IU Vit D and 1 gm fish oil, FU 5.3 years**
- **NO difference in outcomes**

N Engl J Med 2019; 380:23-32
N Engl J Med 2019; 380:33-44

REDUCE-IT

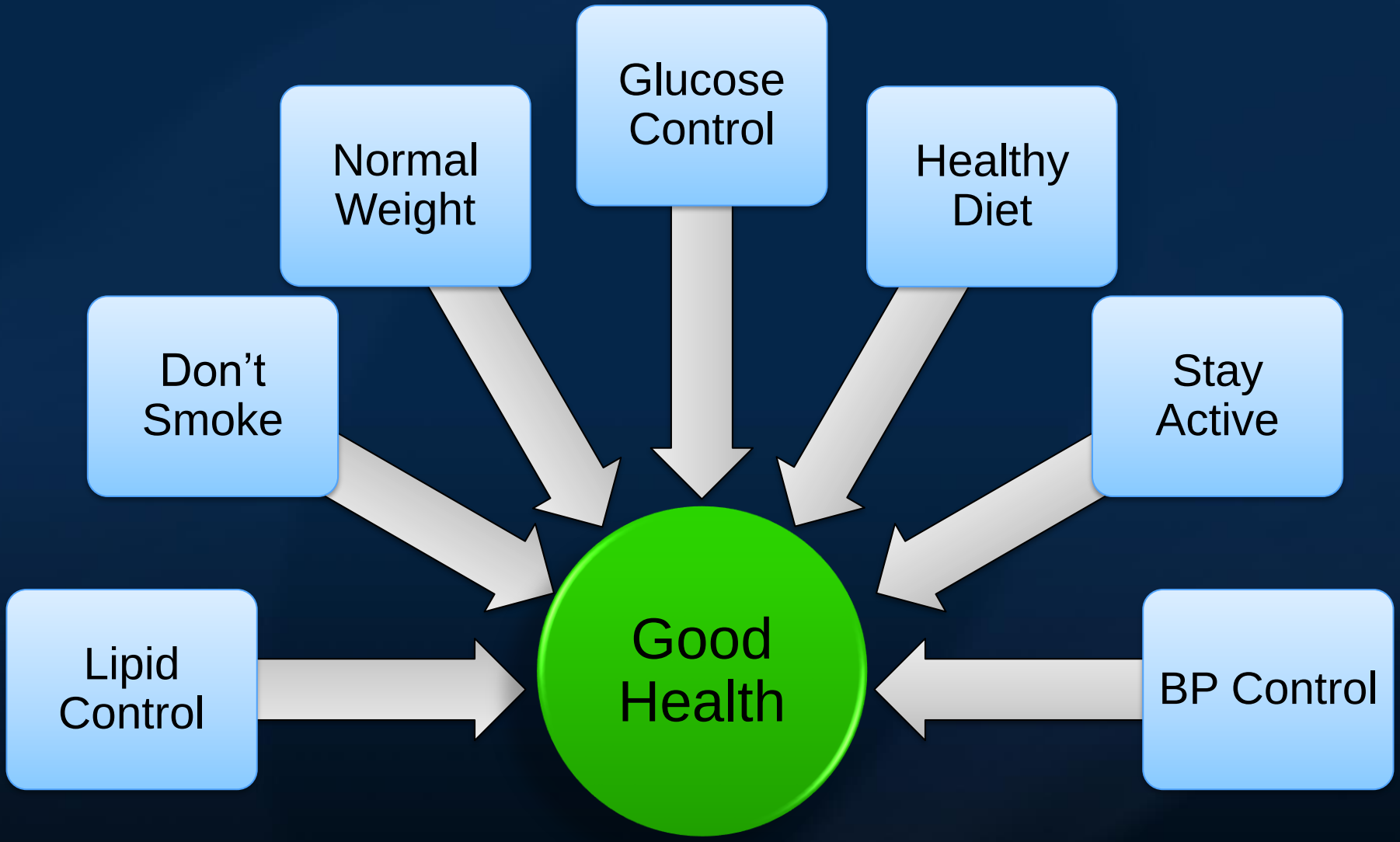
Other Things of Interest

- **Amazing outcome! (Too amazing?)**
- **Outlier result or is it the pure EPA that is important?**
- **Questionable effect of mineral oil placebo**
- **ADA, ALA and ESC have all given strong recommendation to add icosapent ethyl to statin therapy in high-risk pts with TG > 135 mg/dL**

Omega 3 FA

What do we recommend now?

- **As best as I can tell:**
  - **Fish oil (EPA/DHA) at any dose does not change CVD or cancer outcomes and MAY increase Afib and bleeding**
  - **If TG are high, fish oil is reasonable, icosapent ethyl preferred if insurance will cover**


Glucose Control
Normal Weight
Healthy Diet
Don't Smoke
Stay Active
Lipid Control
Good Health
BP Control

SGLT2 Inhibitors

Benefits

- **Death rate** **-30%**
- **CHF** **-25-35%**
- **MI** **-10-15%**
- **ESRD** **-40-50%**
- **Albuminuria** **-25-35%**
- **Weight loss** **-2 Kg**
- **BP** **-4/2 mmHg**
- **HgbA1c** **-0.7-1.0%**

SGLT2 Inhibitors

Adverse effects

- **Ketoacidosis**

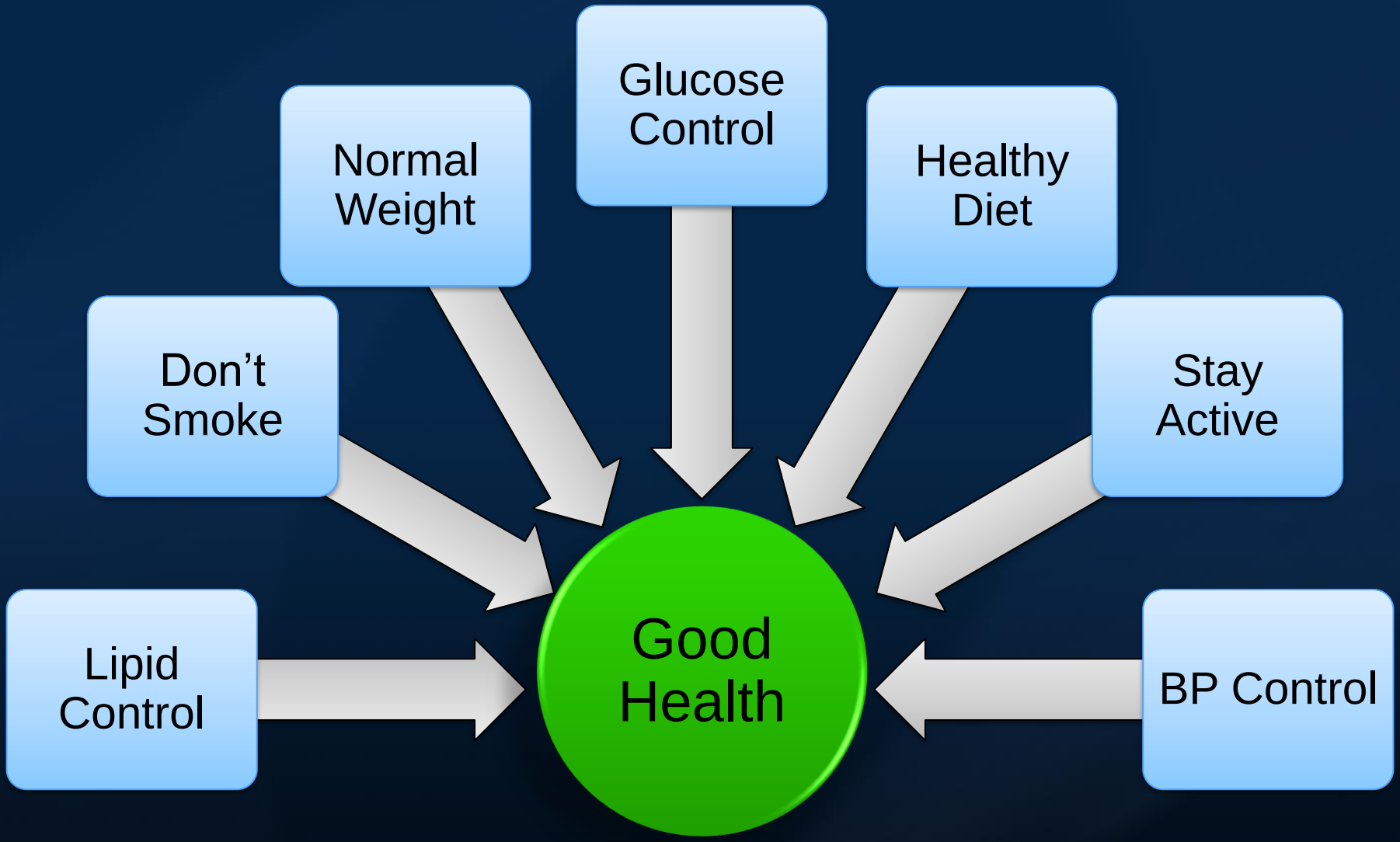
  0.3% to 0.6%

- **Diarrhea**

  6% to 8.5%

- **Genital mycotic infection**

  0.9% to 2.4%


Glucose Control
Normal Weight
Healthy Diet
Don't Smoke
Stay Active
Lipid Control
Good Health
BP Control


life
SMOKING
KILLS

According to a recent Nationwide survey:

MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

Smoking

Your mother was right

480,000 deaths per year from smoking

16 million smoking related illnesses per year

2-4 times more heart disease

23 times more likely to get lung cancer

15 types of cancer are increased in smokers

Most Smokers Want to Quit

But it's not easy

76% of smokers want to quit

59% have tried to quit in the last year

6% were successful

Early and Late Benefits

Lots of reasons to quit

- **1 month - lung function improves**
- **1 year – heart attack risk cut in half**
- **10 years – risk of heart disease is same as never smoking**
- **20 years – risk of lung disease, cancer, heart disease same as never smoking**

How much does pharmocotherapy and counseling increase smoking cessation rates?

A) 2 times

B) 5-6 times

C) 10 times

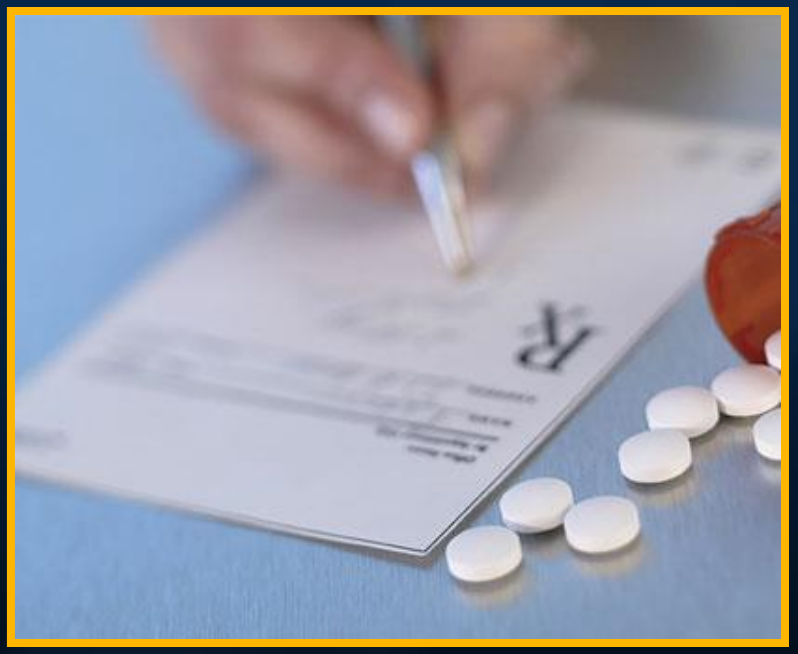
D) It doesn’t

Counseling AND medications are more effective than either alone.

1-800-QUIT-NOW

It's free. It's personalized.
It's up to you.

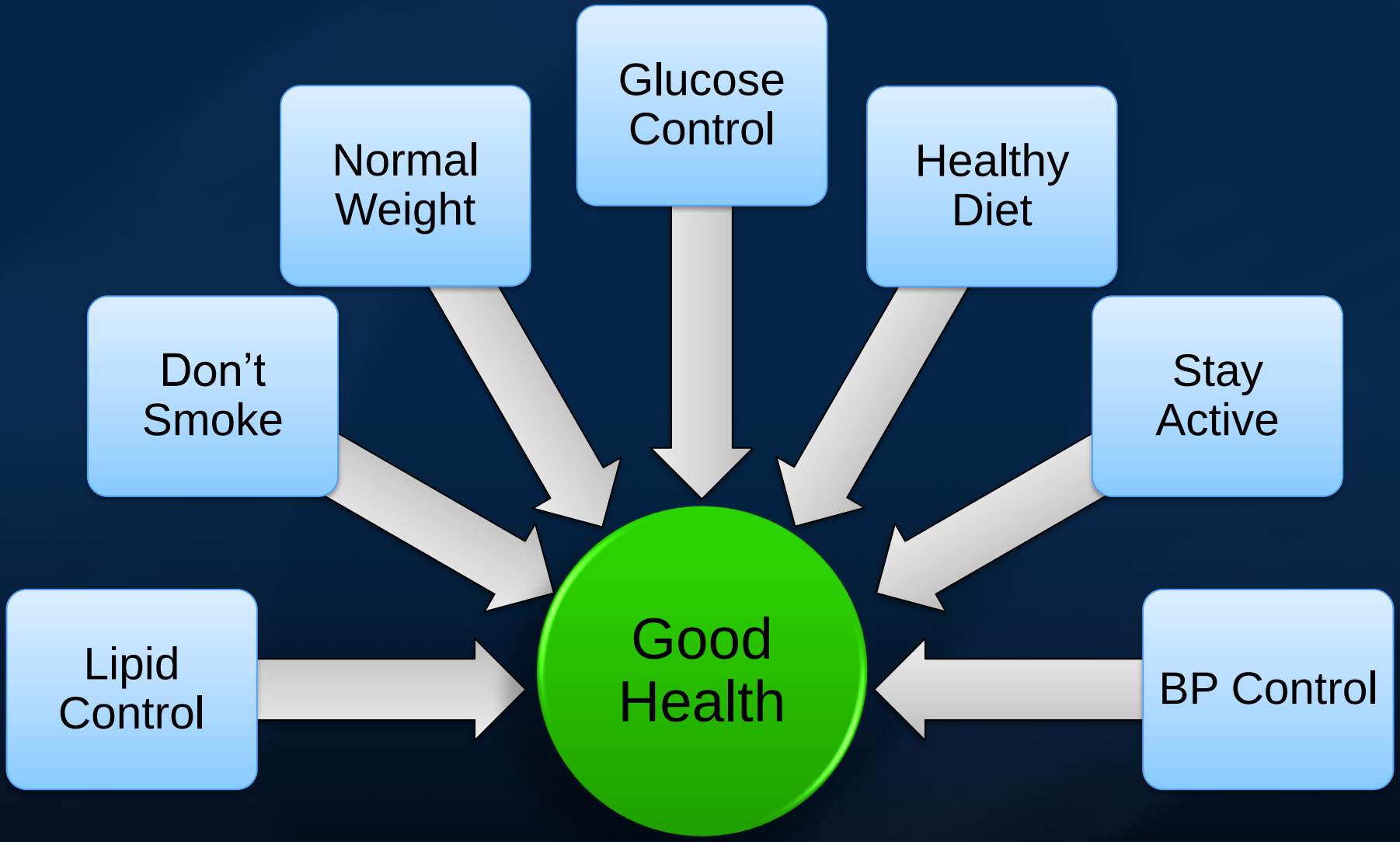
+



Guideline-based Recommendations for the Management of Tobacco Addiction.

- Screen all patients starting at 9 years of age for their use of tobacco products, and counsel children not to smoke or vape.
- All persons who smoke should be advised to stop as soon as possible and should be treated with medications and provided counseling if they smoke five or more cigarettes per day.
- Refer the patient to counseling when counseling is unavailable within the clinical setting.
- Prescribe varenicline or combination nicotine patch plus a short-acting nicotine-replacement formulation as the first choice to smokers regardless of their willingness to set a quit date.
- Consider extending treatment with varenicline for up to 26 weeks or treatment with bupropion for up to 52 weeks in patients who are at high risk for relapse at the end of 12 weeks.
- Vaping products are not approved by the Food and Drug Administration for use in smoking cessation.

N Engl J Med 2022; 387:345-354


Glucose Control
Normal Weight
Healthy Diet
Don't Smoke
Stay Active
Lipid Control
Good Health
BP Control

Weight (Fat) Loss for Physicians

- Eat less, move more advice helps no one.
- The biggest barrier to weight loss is insulin resistance
  - **Lower insulin** (avoid highly processed carbs, lower energy intake)
  - **Improve response to insulin** (exercise, exercise, exercise, sleep, stress, avoid toxins)

STEP 1

SEMAGLUTIDE FOR OBESITY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*

- **n= 1961 subjects**
- **Randomized to semaglutide 2.4 mg q week or placebo**
- **68 weeks follow-up**
- **14.9% Vs. 2.4% body weight loss in intervention group**
  - **86.4% lost 5% body weight**
  - **69.1% lost 10% body weight**

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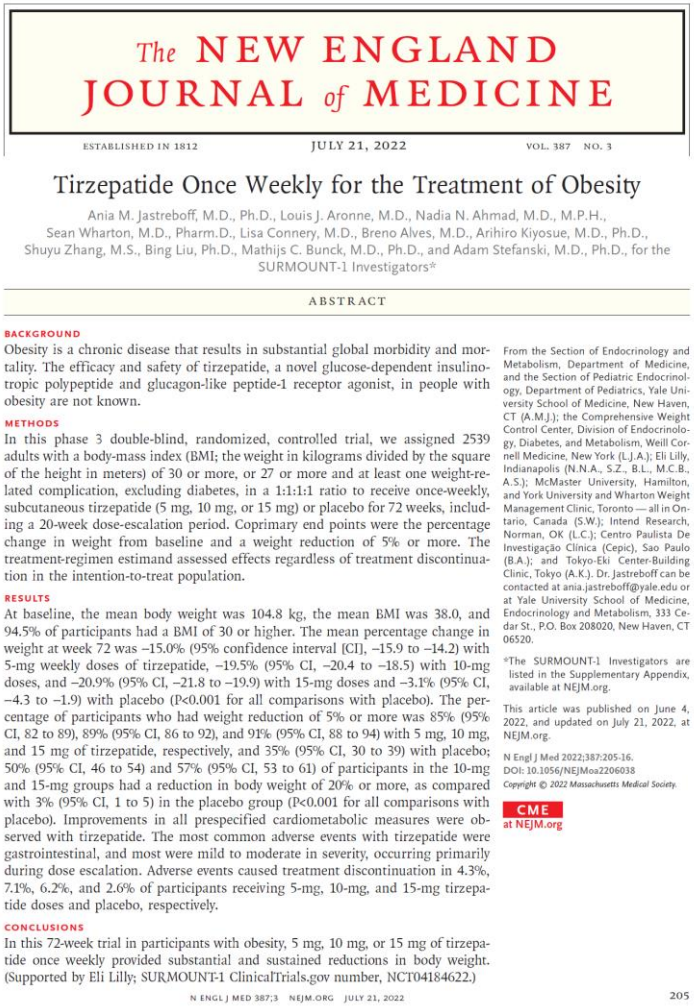
SURMOUNT-1

TIRZEPATIDE FOR OBESITY



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Tirzepatide Once Weekly for the Treatment of Obesity

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ABSTRACT

BACKGROUND

Obesity is a chronic disease that results in substantial global morbidity and mortality. The efficacy and safety of tirzepatide, a novel glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist, in people with obesity are not known.

METHODS

In this phase 3 double-blind, randomized, controlled trial, we assigned 2539 adults with a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 30 or more, or 27 or more and at least one weight-related complication, excluding diabetes, in a 1:1:1:1 ratio to receive once-weekly, subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks, including a 20-week dose-escalation period. Coprimary end points were the percentage change in weight from baseline and a weight reduction of 5% or more. The treatment-regimen estimand assessed effects regardless of treatment discontinuation in the intention-to-treat population.

RESULTS

At baseline, the mean body weight was 104.8 kg, the mean BMI was 38.0, and 94.5% of participants had a BMI of 30 or higher. The mean percentage change in weight at week 72 was −15.0% (95% confidence interval [CI], −15.9 to −14.2) with 5-mg weekly doses of tirzepatide, −19.5% (95% CI, −20.4 to −18.5) with 10-mg doses, and −20.9% (95% CI, −21.8 to −19.9) with 15-mg doses and −3.1% (95% CI, −4.3 to −1.9) with placebo (P<0.001 for all comparisons with placebo). The percentage of participants who had weight reduction of 5% or more was 85% (95% CI, 82 to 89), 89% (95% CI, 86 to 92), and 91% (95% CI, 88 to 94) with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively, and 35% (95% CI, 30 to 39) with placebo; 50% (95% CI, 46 to 54) and 57% (95% CI, 53 to 61) of participants in the 10-mg and 15-mg groups had a reduction in body weight of 20% or more, as compared with 3% (95% CI, 1 to 5) in the placebo group (P<0.001 for all comparisons with placebo). Improvements in all prespecified cardiometabolic measures were observed with tirzepatide. The most common adverse events with tirzepatide were gastrointestinal, and most were mild to moderate in severity, occurring primarily during dose escalation. Adverse events caused treatment discontinuation in 4.3%, 7.1%, 6.2%, and 2.6% of participants receiving 5-mg, 10-mg, and 15-mg tirzepatide doses and placebo, respectively.

CONCLUSIONS

In this 72-week trial in participants with obesity, 5 mg, 10 mg, or 15 mg of tirzepatide once weekly provided substantial and sustained reductions in body weight. (Supported by Eli Lilly; SURMOUNT-1 ClinicalTrials.gov number, NCT04184622.)

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*The SURMOUNT-1 Investigators are listed in the Supplementary Appendix, available at NEJM.org.

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CME at NEJM.org

- **n= 1961 subjects**
- **Randomized to tirzepatide or placebo**
- **72 weeks follow-up**
- **20.9% Vs. 3.1% body weight loss in 15 mg group**
  - **91% lost 5% or more of body weight**
  - **57% lost 20% or more of body weight**

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Preventing, Treating, and Reversing Cardiovascular Disease

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