Epidemiology of Coronary Artery Disease



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KEYWORDS

- Coronary disease Cardiovascular diseases Myocardial infarction
- Coronary artery bypass Percutaneous coronary intervention

KEY POINTS

- Although the mortality of coronary artery disease (CAD) has declined over recent decades, CAD remains the leading cause of death in the United States (US) and presents a significant economic burden.
- Epidemiologic studies have identified numerous strong risk factors for CAD. Some risk factors for the development of CAD are decreasing within the US population, including smoking, hypertension, dyslipidemia, and physical inactivity. Other risk factors, such as advanced age, diabetes, and obesity are increasing in prevalence.
- Therapies for CAD have evolved over time—the most significant historic advances were the development and refinement of coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), and lipid-lowering medications.
- The contemporary optimal treatment of CAD relies on a multi-modality and multidisciplinary approach, individualizing therapy for each patient based on the best available evidence.
- Despite the increasing prevalence of CAD nationwide, there has been a steady decline in the number of CABGs and PCIs performed in the US for the past decade. Patients with CABG are becoming increasingly older and with more comorbid conditions, although mortality associated with CABG has remained steady.

INTRODUCTION

Coronary artery disease (CAD) is presently the leading cause of death in the United States (US), as it has been since 1990 (Fig. 1).¹ The quantity of years of life lost due

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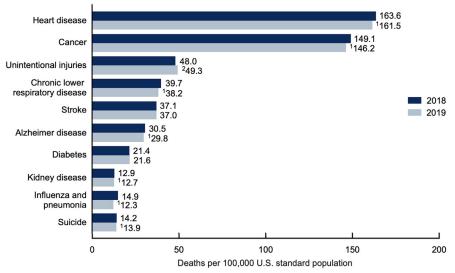


Fig. 1. Age-adjusted death rates for the 10 leading causes of death in the United States in 2018 and 2019. (*Reprinted from* Kochanek et al.¹).

to premature mortality from CAD is greater than the sum of lung cancer, colon cancer, breast cancer, and prostate cancer (**Fig. 2**).² 10.9% of adults aged 45 or older and 17.0% of adults aged 65 or older are estimated to have CAD, and approximately 800,000 Americans suffer a myocardial infarction (MI) each year.² CAD is a major source of health care costs, estimated at \$126.2 billion in 2010 and expected to increase to more than \$177 billion by 2040.³ Vast improvements in care have led to a steady decline in CAD deaths over the past several decades.⁴

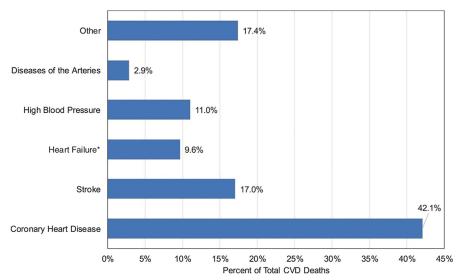


Fig. 2. Percentage breakdown of deaths attributable to cardiovascular disease (CVD) in the US in 2018. (*Reprinted from* Virani et al.²).

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Our current understanding of the natural history and risk factors of CAD was largely informed by the investigators of the Framingham Heart Study. The Framingham Heart Study began in 1948 to identify characteristics that contribute to the development of cardiovascular disease (CVD). At the time CAD was responsible for more than 50% of deaths in the US and there was only a limited understanding of the natural history of CAD.⁵ The investigators sought to enroll subjects with no known or apparent heart disease and follow this cohort over time to identify and determine risk factors for heart disease. The study initially enrolled 5209 residents of Framingham, Massachusetts, chosen because it was representative of the US population at the time and because of its proximity to Boston and Harvard Medical School.⁵ To date, thousands of articles have been published based on Framingham data, and factors such as high blood pressure, cholesterol, diabetes, smoking, and obesity had been identified as risk factors for CAD.^{5,6} The study currently includes the second and third generations of initial subjects and continues to produce relevant epidemiologic information about CVD.

EFFECT OF AGE

Age is a major risk factor for the development of atherosclerotic CVD and CAD,⁷ partially because longer life allows for greater duration of exposure to other risk factors (Fig. 3).⁸ In one study using Framingham data, age was more strongly associated with risk of a CVD event than any other factor among men, and second only to hypertension among women.⁷

US census data indicate that the overall US population is aging. The number of Americans older than 65 is projected to increase from 40 million to more than 80 million by 2040, driven largely by the prolonged life expectancy of "baby boomers." As age is a major risk factor for CAD, it is not surprising that the prevalence of CAD is expected to increase dramatically over this same time period, from 11.7 million to 17.3 million by 2040.³

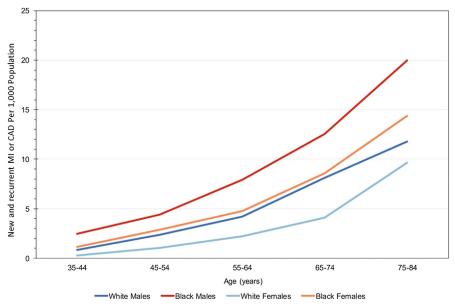


Fig. 3. Incidence of fatal CAD, by age in the US 2005 to 2014. (Reprinted from Virani et al.²).

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EFFECT OF BLOOD PRESSURE

High blood pressure was identified as a risk factor for mortality by life insurance companies in the early 20th century shortly after the development of the sphygmomanometer. However, medical professionals at the time largely believed that elevated blood pressures were not harmful, instead arguing that elevated blood pressure was a necessary compensatory condition to permit perfusion in the setting of atherosclerosis.⁹ This concept was challenged in 1961 when elevated blood pressure was identified as a risk factor for CVD in the early outcomes of the Framingham Heart Study.⁶ This was followed by many additional randomized controlled trials, and by 1990 there was strong evidence supporting antihypertensive use.⁹

Presently, hypertension is known to be a major independent risk factor for CAD.¹⁰ There is a strong progressive association between blood pressure and age-specific mortality from CAD, with one large meta-analysis noting a 20 mm Hg increase in systolic BP or 10 mm Hg increase in diastolic BP is associated with roughly twice the risk of death from CAD for patients aged 40 to 69.¹¹ In one study using Framingham data, blood pressure had the strongest association with CVD events in women and was second only to age as a risk factor for men.⁷

Blood pressure is a key feature of the American College of Cardiology (ACC)/American Heart Association (AHA) Heart Risk Calculator,¹² and blood pressure control is a core component of current AHA guidelines on the primary prevention of CVD.¹³ The prevalence of hypertension in US adults is estimated at 32.4% or about 82 million adults. Among adults who self-report hypertension, about 76% use antihypertensive medications.¹⁴ Expenditures related to hypertension were \$79 billion in 2016.

EFFECT OF CHOLESTEROL

Elevated total cholesterol and elevated low-density lipoproteins (LDL) are strongly associated with increased risk of atherosclerotic CVD, while elevated high-density lipoprotein (HDL) cholesterol has been associated with a decreased risk of atherosclerotic CVD. These associations are quite strong, and both serum cholesterol and HDL are incorporated into the ACC/AHA Heart Risk Calculator.¹⁰ Additionally, lipid control and statin treatment are key components of AHA guidelines on the primary prevention of CVD.¹³

The relationship between cholesterol and atherosclerosis was known several decades before the availability of large-scale epidemiologic data. Physicians in the early 20th century were aware of the increased incidence of MI in families with familial hypercholesterolemia, and the relationship between cholesterol and atherosclerosis had been convincingly demonstrated in histologic and animal studies. The Framingham Heart Study provided strong epidemiologic evidence supporting the connection, even in those with mildly elevated cholesterol,⁶ and by 1960 the AHA was recommending dietary changes to reduce cholesterol intake.^{15,16}

Evidence supporting medication used to lower cholesterol and lipid levels emerged in 1985 with the publication of the Coronary Primary Prevention Trial. In this study, middle-age men without known CAD who received cholestyramine achieved lower serum cholesterol and had a 20% to 25% lower incidence of CAD death, nonfatal MI, angina, new positive stress test, or coronary artery bypass grafting (CABG).¹⁷

Statin medications for hypercholesterolemia were first introduced by a Japanese scientist in the 1970s and were made widely commercially available in 1987.^{18,19} Contemporary studies, including many randomized controlled trials, have demonstrated the efficacy of statin therapy in reducing dyslipidemia and the risk of CVD,

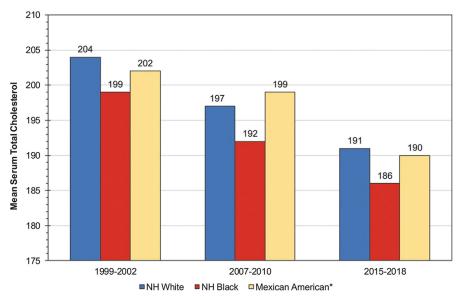


Fig. 4. Age-adjusted trends in mean serum total cholesterol among US adults by race and year. (*Reprinted from* Virani et al.²).

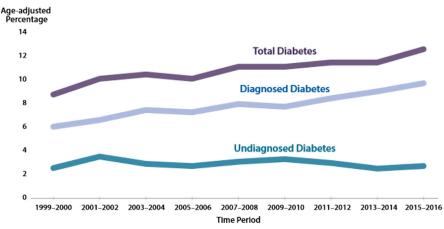
including CAD, and in reducing mortality from CAD.^{20–23} Statin therapy has become a mainstay in the primary and secondary prevention of CAD.

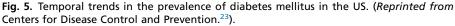
Among US adults, mean serum total cholesterol, LDL, and triglycerides have declined over the past 20 years (**Fig. 4**).² The use of lipid-modifying agents has remained steady in the past decade in the US at around 40 million individuals,¹⁸ though there have been increases in statin use among adults older than age 40.¹⁹ Statin use and high-intensity statin use have been increasing among patients who have had an atherosclerotic CVD event, particular patients with CAD.²² The development of generic statins have led to lower total cost, down from \$17.2 billion in 2003 to \$16.9 billion in 2013, and lower out-of-pocket cost, only \$2 per 30-day period as of 2016 according to one estimate.²²

While the propagation of statins and widespread reduction in dyslipidemia has been an encouraging trend over the past 2 decades, inequities in statin use among specific demographic groups have been a recent subject of interest. Multiple studies have shown lower use among younger adults, women, and some racial and ethnic minorities. These disparities are not fully explained by access to care or health insurance characteristics and remain the subject of research and policy efforts to ensure equitable care for all patients.¹⁹

EFFECT OF DIABETES MELLITUS

Diabetes mellitus was one of the first risk factors for CAD identified in the Framingham study⁶ and continues to be a major contributor to the burden of CAD in the US and worldwide.² The Centers for Disease Control and Prevention (CDC) estimates 34.2 million Americans have diabetes, about 10% of the population, including 21.4% of those more than age 65. The number of youth and adolescents with diabetes is also at an all-time high – nearly one-quarter of a million Americans under age 20– and has doubled since 2003. An additional 88 million Americans are prediabetic (Fig. 5).²³





CVD is the leading cause of morbidity and mortality in patients with diabetes.²⁴ Diabetics are almost twice as likely to die from CVD compared with patients without diabetes; much of this risk is related to CAD and MI.^{24,25} In 2016, there were an estimated 1.7 million hospitalizations for CVD in diabetics, including 438,000 for CAD.²³ Diabetes is associated with many other CAD risk factors, including obesity, physical inactivity, tobacco use, hypertension, and hyperlipidemia.^{23,26} Pathophysiologically, diabetes is associated with accelerated atherosclerosis leading to complex CAD^{26–28} and greater atherosclerotic disease of the aorta,²⁹ diastolic dysfunction, and heart failure.²⁴ The association between diabetes and CAD is so profound that some studies suggest that patients with diabetes with no history of MI have the same risk of cardiovascular death as nondiabetic patients with prior MI.³⁰

EFFECT OF TOBACCO USE Smoking

Cigarette smoking became the most prevalent form of tobacco use during the early 20th century, peaking in 1964 at which time 40% of US adults regularly smoked cigarettes, including the majority (53%) of adult men. Even though much was known about the deleterious health effects of cigarette smoking, including its association with lung cancer, cigarette smoking was considered a perfectly acceptable practice in homes and public spaces.³¹

In the early 1960s, a presidentially directed comprehensive review of 7000 scientific articles by 150 experts convincingly demonstrated the increased risks of lung cancer, chronic bronchitis, emphysema, CAD, and mortality associated with smoking cigarettes. Importantly, this report gained widespread attention from the US public and media. Cigarette smoking was thus identified as a major public health concern, marking a major shift in American culture. Cigarette smoking began to decline after the publication of this report in 1964, a trend that has continued for over 5 decades (**Fig. 6**).^{31,32}

With ongoing efforts by physicians and public health officials to educate the public and advocate for appropriate public policy, rates of cigarette smoking are at an alltime low among US adults. Despite these improvements, smoking has remained the leading cause of preventable disease, disability, and death in the US. As of 2018%,

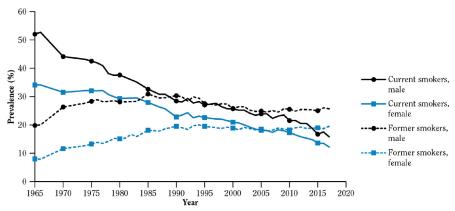


Fig. 6. Temporal trends in the prevalence of current and former smokers in the US. (*Reprinted from* U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.³²).

19.7% of US adults used any type of tobacco product, and 13.7% of US adults reported cigarette use every day or some days.^{2,33}

While smoking has been linked to serious diseases of multiple organ systems, the most significant mechanism by which smoking causes death and disability is CAD. Exposure to tobacco smoke is associated with a relative risk of developing CAD between 1.4 and 6.3, depending on age and the tobacco dose.^{34,35} Smokers have an increased relative risk of death from CAD of 2.50 in men and 2.86 in women.³⁶ Even exposure to second-hand smoke confers an increased risk of CAD.³⁵ Death from MI and CAD is lower among former smokers than current smokers, though quitting does not completely eliminate future risk.³² While the pathophysiology is known to be multifactorial, the direct effects of nicotine–release of catecholamines stimulating increased heart rate and myocardial demand, endothelial dysfunction, lipid abnormalities, and insulin resistance are thought to be principally responsible.³⁴

EFFECT OF SMOKELESS TOBACCO AND ELECTRONIC NICOTINE DELIVERY SYSTEMS

Smokeless tobacco products also contain high doses of nicotine and have been extensively studied. These products carry a significant risk of CAD (RR: 2.23); the effects of smoking plus use of smokeless tobacco have been shown to be multiplicative (smoking alone RR: 2.95, smoking plus smokeless RR 4.09).³⁷

While smoking has steadily declined since 1964, the usage of electronic nicotine delivery systems, also known e-cigarettes or vaping, has increased dramatically in recent years and has become a \$2 billion industry.³⁸ Presently e-cigarettes are the most common nicotine product among youth – 10.5% of middle school students and 27.5% of high school students reporting use within 30 days.³⁹ By comparison, cigarette use in the preceding 30 days among middle and high school students in the US was 2.3% and 5.8%, respectively, in 2019.^{2,33}

As vaporized nicotine products are relatively new, there are scant epidemiologic data available to assess associated risks. The heterogeneity of chemicals contained within them is vast and difficult to study.³⁸ The strongest similarity between e-cigarettes and combustible cigarettes is nicotine, which is known to acutely cause cate-cholamine release, increased myocardial demand, and induce endothelial

dysfunction, and is known to be addictive.^{34,38} Given the staggeringly high proportion of youth and adolescents using e-cigarettes, and the known increased risk of future cigarette use, e-cigarettes may reverse the trend of decreased morbidity and mortality due to tobacco and nicotine use in the US that has been sustained since the Surgeon General's report in 1964.

EFFECT OF OBESITY

Obesity is defined as a body mass index (BMI) greater than 30. Body weight was identified as a risk factor for CVD early in the Framingham study and has been extensively studied since then.³³ The relationship between BMI and risk of death from CVD is not linear; studies have instead demonstrated a J-shaped curve with differences in risk starting to emerge around BMI 26.5 in men and 25 in women, with a steep inflection point and exponentially increasing risk beyond BMI 40.⁴⁰ In one study involving only women, obesity (BMI > 30) conferred a relative risk of 2.48 for the development of CAD, while severe obesity (BMI > 40) conferred a relative risk of more than 5. Weight gain during adulthood, even as little as 4 to 10 kg, was associated with increased risk. Increased levels of physical activity attenuated the negative effects of obesity but did not eliminate CAD risk.^{41,42}

Despite a common misperception of adipose tissue as simply a storage repository for biologic fuel, adipose tissue is quite metabolically active and is known to secrete many cytokines and bioactive mediators that may lead to the progression of CAD. These have been noted to increase the risk of thrombotic disease including MI, cause dysregulation of lipid levels, induce insulin resistance, contribute to endothelial dysfunction, and accelerate atherosclerosis.⁴²

Independent of BMI or the measured amount of subcutaneous fat, visceral fat mass has been shown to be a significant risk factor for CAD, hyperglycemia, hyperlipidemia, and hypertension,⁴⁰ and has been associated with severity of CAD measured angiographically.⁴³ This may be because visceral fat is more metabolically active than subcutaneous fat, secreting higher volumes of cytokines and bioactive mediators.⁴⁴

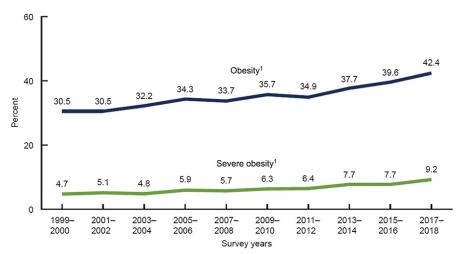


Fig. 7. Temporal trends in the prevalence of obesity (BMI > 30) and severe obesity (BMI > 40). (*Reprinted from* Virani et al.²).

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The proportion of US adults who are at a healthy bodyweight has been declining for several decades, presently down to 27.7% of the population from 41.7% in 1988 to 1994. Over the same period of time, the proportion of US adults who are obese has nearly doubled from 22.8% to 38.6% (Fig. 7). The proportion of children aged 6 to 11 who are obese has increased from 11.3% to 17.9%, and the proportion of children aged 12 to 19 who are obese has increased from 10.5% to 20.6%.⁴

EFFECTS OF PHYSICAL INACTIVITY

Physical inactivity is often thought of as one component, along with nutrition, that contributes to the development of obesity. However, lack of exercise is a significant risk factor for the development of CAD independent of bodyweight. While it is true physical inactivity contributes to the development of obesity, and that the combination of the 2 confers a greater risk of CAD than either in isolation, the risk of developing CAD is elevated in patients with healthy bodyweight who are physically inactive, and the risk of CAD is lower in obese patient who exercise in comparison with those who do not.⁴¹

Physical activity and exercise can attenuate but not eliminate the deleterious effects of obesity.⁴² Exercise is associated with lower incidence of CVD, lower mortality, and lower incidence of CVD risk factors including hypertension, obesity, and impaired blood glucose.⁴⁵ Enhanced activity of nitric oxide synthase and circulating progenitor cells at the endothelial level along with coronary angiogenesis have been postulated as the mechanisms by which regular physical activity and exercise may prevent or attenuate the development of CAD.⁴⁶

Recent findings related to the levels of physical activity of average Americans are a mix of encouraging and discouraging trends. It has been encouraging to note that among adults, there has been a steadily increasing percentage of the population that is meeting US Health and Human Services (HHS) recommendations for exercise, a trend that has been ongoing since 2008 (Fig. 8). As of 2018, more than half of

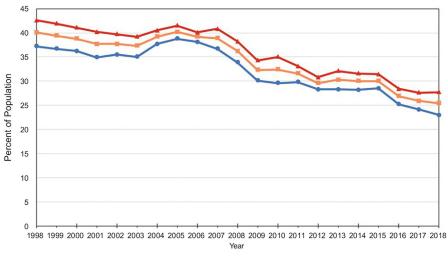




Fig. 8. Temporal trends in physical inactivity in US adults. (Reprinted from Virani et al.²).

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey es por Elsevier en junio 15, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados. American adults engaged in greater than 150 minutes per week of moderate physical activity or 75 minutes per week of vigorous physical activity, meeting the recommended activity recommendations. This measure has steadily increased from just more than 40% in 2008. Nearly one-quarter of US adults engage in no leisure-time physical activity, which was 36.3% in 2008 and has decreased steadily.^{4,45}

However, over the same time-period inactivity among American youth has gotten much worse, with the number of children and adolescents meeting activity recommendations slowly dropping year over year since 2011. Less than one-quarter of US children and adolescents engage in 60 minutes of moderate physical activity per day as recommended by HHS with higher rates among males (30.9%) in comparison to females (15.4%).⁴⁷ These trends are likely contributing to the burdens of childhood obesity and diabetes among America's youth and may lead to more widespread CVD in the future.

HISTORY OF CORONARY ARTERY BYPASS GRAFTING

Attempts to surgically treat CAD during the early 20th century were largely unsuccessful. However, the 1960s saw many critical advancements in the care of CAD, including the development of coronary angiography⁴⁸ and the proliferation of safe and effective technology and techniques for cardiopulmonary bypass.⁴⁹ There were also many breakthroughs in surgical technique, including left internal mammary artery (LIMA) grafting to the left anterior descending artery (LAD)⁵⁰ as well as aortocoronary grafting using reversed saphenous vein. Initially used as a technique for revisions or as a "bail out" during coronary endarterectomy,⁵¹ the use of saphenous vein as coronary grafting conduit was later broadly applied to revascularize other coronary vessels for patients whose anterior wall was revascularized with internal mammary arterial grafting.⁵²

Once CABG was established as a safe and reproducible treatment option for patients with CAD, several randomized controlled trials were undertaken to determine which patients might benefit from surgical revascularization. These studies broadly demonstrated a survival advantage of CABG over medical therapy alone in many patient populations and ushered in an era of profound growth of surgical procedural volumes. These studies also laid the foundation for modern indications for CABG including left main disease and 3-vessel disease.

THERAPIES FOR CORONARY ARTERY DISEASE

The mainstay of treatment of CAD is medical therapy aimed at risk reduction, alleviation of symptoms, and improved quality of life. Elective revascularization is appropriate for patients for whom medical therapy does not adequately meet these objectives; urgent or emergent revascularization is indicated in the setting of an acute coronary syndrome.

Coronary angioplasty was first performed in a human in 1977 and was quickly followed by the development of bare-metal stents in the mid-1980s and drug-eluting stents in the late 1990s and early 2000s.⁵³ Many randomized controlled trials were undertaken to evaluate bare-metal stents versus CABG in patients in multi-vessel disease. These studies tended to demonstrate a long-term survival advantage or fewer major adverse cardiac and cerebrovascular events in patients with CABG.54·55 This trend was expected to reverse with the comparison of CABG to drug-eluting stents in more recent randomized controlled trials, such as SYNTAX,⁵⁶ FREEDOM,⁵⁷ and BEST.⁵⁸ However, these studies continued to demonstrate the superiority of CABG in specific patients–in particular those with clinically or angiographically worse CAD. The feasibility of treating left main disease with percutaneous coronary intervention (PCI) has recently been evaluated in 2 large randomized controlled trials, with somewhat mixed results. 59,60

When patients with complex CAD require revascularization, leading cardiology and cardiothoracic surgery societies recommend balanced, multidisciplinary decision-making with a "Heart Team" to determine whether CABG or PCI represents optimal therapy for an individual patient. At a minimum, the Heart Team consists of an interventional cardiologist and a cardiac surgeon. Utilization of the Heart Team promotes patient autonomy via better informed consent, helps ensure the best evidence-based approach for each individual patient, reduces variability among providers and institutions, and may have a mortality benefit.^{61,62}

RECENT TRENDS IN INVASIVE THERAPIES

According to the data from the Nationwide Inpatient Sample (NIS) database, 201,000 CABGs were performed in 2016, down from 337,000 in 2003. Data from the Society of Thoracic Surgeons (STS) database showed a similar decline throughout the early 2000s.^{63,64} The NIS database reported that 440,000 PCIs were performed in 2016, down from 777,000 in 2003. Decreasing national CABG procedural volume has been the trend since the 1990s with the emergence of PCI as a less invasive alternative. However, the decrease in PCI volume is a more recent development (Fig. 9). It has been suggested that the downtrend in all revascularization procedures has been due to a combination of improvements in medical therapy and the dissemination of data questioning the benefit of revascularization in stable CAD.⁶³

CABG continues to be the most commonly performed procedure in cardiac surgery; approximately 85% of all cardiac surgeries are isolated CABG. The large majority of CABGs are performed with cardiopulmonary bypass; off-pump procedures declined steadily through the last decade and hit a nadir around 10% in 2013 to 2014, though there was a slight uptrend to around 13% in 2016.

SHIFTING DEMOGRAPHICS FOR PATIENTS WITH CORONARY ARTERY BYPASS GRAFTING

The indications for CABG, as well as the increasing age of the population and increasing prevalence of diabetes, obesity, and other comorbidities, have led to a

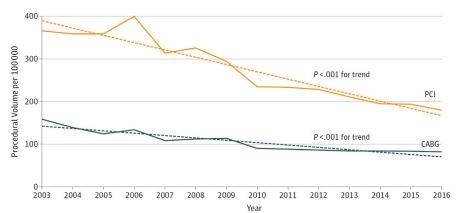
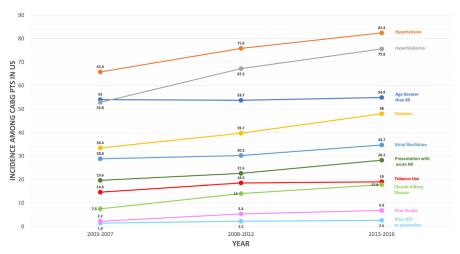


Fig. 9. Temporal Trend in the Annual Rate of Percutaneous and Surgical Coronary Revascularization per 100,000 US Adults. Dashed line indicates the mean trend and the solid line the year-to-year trend. (*Reprinted from* Alkhouli et al.⁶³).



Temporal Changes in Baseline Characteristics of Patients Undergoing CABG (2003-2016)

Fig. 10. Temporal changes in baseline characteristics of patients undergoing CABG (2003–2016). (*Data derived* from Alkhouli et al.⁶³).

shifting demographic of patients undergoing CABG, with a trend toward patients with CABG being older and with more comorbidities than in the past. Data from the NIS database have demonstrated a 2-fold increase in the proportion of patients with CABG with chronic kidney disease between 2003 and 2016 and a 3-fold increase in patients with prior stroke. It is also becoming more common for CABG to be performed nonelectively, often for acute MI (Fig. 10). Despite these findings, the STS and NIS databases both demonstrate decreased absolute mortality for patients with CABG over time.⁶³⁻⁶⁵ Similar recent trends have been noted within the Veterans Affairs health care system; patients have become more medically complex–older, higher average BMI, more diabetes, and more heart failure – and more angiographically complex (more left main disease, higher prevalence of previous PCI). Despite these changes, perioperative mortality has decreased over time.⁶⁶

UNIQUE POPULATIONS-DIABETICS

The FREEDOM trial specifically investigated CABG versus PCI with drug-eluting stents in diabetics with multivessel disease and demonstrated reduced all-cause mortality, fewer major adverse cardiac and cerebrovascular events, and fewer MIs among patients undergoing CABG.⁵⁷ As data have accumulated regarding the efficacy of CABG for diabetics, and as the incidence of diabetes has risen in the general population, the proportion of patients with CABG who are diabetic has grown to an all-time high, up to about 50% according to one estimate, up from less than 40% in 2006.⁶⁴ Given projections for the continued growth of the prevalence of diabetes in the US and world populations,⁶⁷ surgeons should expect to see high numbers of patients with diabetes referred for CABG in the coming decades.

Unfortunately, patients with diabetes fare worse after CABG in comparison to nondiabetics, a disparity that has decreased with improvements in surgical technique, cardiac anesthesia, and cardiac critical care. Indeed, patients with diabetes have greater risks of perioperative complications such as stroke, renal failure, deep sternal

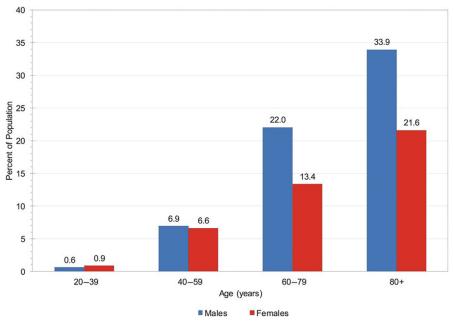


Fig. 11. Prevalence of CAD by age and sex in the US, 2015 to 2018. (*Reprinted from* Virani et al.²).

wound infection, and death within 30 days,⁶⁸ as well as worse all-cause mortality at 5 years.⁶⁹

UNIQUE POPULATIONS-WOMEN

CAD and associated mortality are more common in men than in women (Fig. 11), and women who have CAD are more likely to have a nonobstructive pattern.⁷⁰ However, data from the STS database noted proportionately more women undergoing CABG over time throughout the 1990s (25.7% of all patients with CABG in 1990 vs 28.7% in 1999).⁶⁵ Women undergoing CABG tend to be older than their male counterparts and have more comorbid conditions at the time of operation, including obesity, diabetes, hypertension, chronic kidney disease, chronic lung disease, and concomitant valvular disease. Women are also more likely to present with ACS or cardiogenic shock,⁶² although some data have indicated that women with ACS are less likely to undergo angiography and revascularization.⁷¹ While long-term outcomes seem to be similar between men and women, periprocedural outcomes are worse for women, including mortality, prolonged ICU stay, and wound complications.⁶²

SUMMARY

Although the mortality of CAD has declined over recent decades, CAD remains the leading cause of death in the US and presents a highly significant economic burden. Epidemiologic studies have identified numerous strong risk factors for CAD. Some risk factors for the development of CAD are decreasing within the US population, including smoking, hypertension, dyslipidemia, and physical inactivity. Other risk factors, such as advanced age, diabetes, and obesity are increasing in prevalence. Therapies for CAD have evolved over time-the most significant historic advances were the

development and refinement of CABG, PCI, and lipid-lowering medications. The contemporary optimal treatment of CAD relies on a multi-modality and multidisciplinary approach, individualizing therapy for each patient based on the best available evidence. There has been a steady decline in the number of CABGs and PCIs performed in the US for the past decade. Patients with CABG are becoming older and with more comorbid conditions, although mortality associated with CABG has remained steady.

CLINICS CARE POINTS

- Epidemiologic studies have demonstrated the increasing prevalence of CAD and increasing prevalence of many CAD risk factors. However, the number of CABGs and PCIs has decreased in recent years.
- For patients who may require revascularization, utilization of a "Heart Team" approach is an essential best practice to optimize patient outcomes.
- Patients referred for CABG will likely continue to be older, have more significant comorbid conditions, and have more angiographically complex lesions. It is imperative to ensure elective patients with CABG are medically optimized before surgery.
- CABG is becoming more common among women and diabetics, both of whom have worse perioperative outcomes.

DISCLOSURE

The authors have nothing to disclose.

REFERENCES

- 1. Kochanek KDXJ, Arias E. Mortality in the United States, 2019. NCHS data brief, no 395. Hyattsville, MD: National Center for Health Statistics; 2020.
- 2. Virani SS, Alonso A, Aparicio HJ, et al. Heart disease and stroke statistics-2021 update: a report from the american heart association. Circulation 2021;143(8): e254–743.
- Odden MC, Coxson PG, Moran A, et al. The impact of the aging population on coronary heart disease in the United States. Am J Med 2011;124(9):827–33.e825.
- 4. Office of Disease Prevention and Health PromotionHealthy People 2020. Washington, DC: U.S. Department of Health and Human Services; 2021. Available at: https://www.healthypeople.gov/2020/data-search/. Accessed 01 August 2021.
- Mahmood SS, Levy D, Vasan RS, et al. The framingham heart study and the epidemiology of cardiovascular disease: a historical perspective. Lancet 2014; 383(9921):999–1008.
- 6. Kannel WB, Dawber TR, Kagan A, et al. Factors of risk in the development of coronary heart disease–six year follow-up experience. The framingham study. Ann Intern Med 1961;55:33–50.
- D'Agostino RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation 2008;117(6): 743–53.
- Lloyd-Jones DM, Leip EP, Larson MG, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. Circulation 2006; 113(6):791–8.

- **9**. Kotchen TA. Historical trends and milestones in hypertension research: a model of the process of translational research. Hypertension 2011;58(4):522–38.
- Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American college of cardiology/american heart association task force on practice guidelines. J Am Coll Cardiol 2014;63(25 Pt B):2935–59.
- Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360(9349):1903–13.
- Rosendorff C, Black HR, Cannon CP, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the american heart association council for high blood pressure research and the councils on clinical cardiology and epidemiology and prevention. Circulation 2007;115(21):2761–88.
- Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. Circulation 2019;140(11):e596–646.
- Samanic CM, Barbour KE, Liu Y, et al. Prevalence of self-reported hypertension and antihypertensive medication use among adults - United States, 2017. MMWR Morb Mortal Wkly Rep 2020;69(14):393–8.
- 15. Hajar R. Statins: past and present. Heart Views 2011;12(3):121-7.
- Endo A. A historical perspective on the discovery of statins. Proc Jpn Acad Ser B Phys Biol Sci 2010;86(5):484–93.
- 17. The lipid research clinics coronary primary prevention trial results. I. reduction in incidence of coronary heart disease. JAMA 1984;251(3):351–64.
- 18. Blais JE, Wei Y, Yap KKW, et al. Trends in lipid-modifying agent use in 83 countries. Atherosclerosis 2021;328:44–51.
- Salami JA, Warraich H, Valero-Elizondo J, et al. National trends in statin use and expenditures in the US adult population from 2002 to 2013: insights from the medical expenditure panel survey. JAMA Cardiol 2017;2(1):56–65.
- Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study. Lancet 1994;344(8934): 1383–9.
- Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* Jun 25 2019;73(24):e285–350. https://doi.org/10.1016/j.jacc.2018.11.003.
- Yao X, Shah ND, Gersh BJ, et al. Assessment of trends in statin therapy for secondary prevention of atherosclerotic cardiovascular disease in US adults from 2007 to 2016. JAMA Netw Open 2020;3(11):e2025505.
- Centers for Disease Control and Prevention. National diabetes statistics report, 2020. Centers for Disease Control and Prevention. Atlanta, GA: U.S. Dept of Health and Human Services; 2020.
- Leon BM, Maddox TM. Diabetes and cardiovascular disease: epidemiology, biological mechanisms, treatment recommendations and future research. World J Diabetes 2015;6(13):1246–58.
- Lee CD, Folsom AR, Pankow JS, et al. Cardiovascular events in diabetic and nondiabetic adults with or without history of myocardial infarction. Circulation 2004;109(7):855–60.

- 26. Kappetein AP, Head SJ, Morice MC, et al. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. Eur J Cardiothorac Surg 2013;43(5):1006–13.
- 27. Nicholls SJ, Tuzcu EM, Kalidindi S, et al. Effect of diabetes on progression of coronary atherosclerosis and arterial remodeling: a pooled analysis of 5 intravascular ultrasound trials. J Am Coll Cardiol 2008;52(4):255–62.
- Lester WM, Roberts WC. Diabetes mellitus for 25 years or more. Analysis of cardiovascular findings in seven patients studied at necropsy. Am J Med 1986;81(2): 275–9.
- 29. Iwakawa N, Tanaka A, Ishii H, et al. Impact of diabetes mellitus on the aortic wall changes as atherosclerosis progresses: aortic dilatation and calcification. J Atheroscler Thromb 2020;27(6):509–15.
- **30.** Haffner SM, Lehto S, Rönnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339(4):229–34.
- 31. U.S. Department of Health and Human Services. The health consequences of smoking: 50 Years of progress. A report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention,; 2014. National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014. Printed with corrections.
- 32. U.S. Department of Health and Human Services.. Smoking Cessation. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2020.
- **33.** Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67(5):968–77.
- **34.** U.S. Department of Health and Human Services. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2010.
- Law MR, Morris JK, Wald NJ. Environmental tobacco smoke exposure and ischaemic heart disease: an evaluation of the evidence. BMJ 1997;315(7114): 973–80.
- **36.** Thun MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. N Engl J Med 2013;368(4):351–64.
- Teo KK, Ounpuu S, Hawken S, et al. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet 2006; 368(9536):647–58.
- **38.** U.S. Department of Health and Human Services. E-Cigarette use among youth and young adults. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2016.
- **39.** Wang TW, Gentzke AS, Creamer MR, et al. Tobacco product use and associated factors among middle and high school students United States, 2019. MMWR Surveill Summ 2019;68(12):1–22.

- 40. Calle EE, Thun MJ, Petrelli JM, et al. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341(15):1097–105.
- Li TY, Rana JS, Manson JE, et al. Obesity as compared with physical activity in predicting risk of coronary heart disease in women. Circulation 2006;113(4): 499–506.
- 42. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. Nature 2006;444(7121):875–80.
- **43.** Zamboni M, Armellini F, Sheiban I, et al. Relation of body fat distribution in men and degree of coronary narrowings in coronary artery disease. Am J Cardiol 1992;70(13):1135–8.
- 44. Matsuzawa Y. The metabolic syndrome and adipocytokines. FEBS Lett 2006; 580(12):2917–21.
- 45. Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. JAMA 2018;320(19):2020–8.
- **46.** Winzer EB, Woitek F, Linke A. Physical Activity in the Prevention and Treatment of Coronary Artery Disease. J Am Heart Assoc 2018;7(4).
- Merlo CL, Jones SE, Michael SL, et al. Dietary and Physical activity behaviors among high school students - youth risk behavior survey, United States, 2019. MMWR Suppl 2020;69(1):64–76.
- Sones FM Jr, Shirey EK. Cine coronary arteriography. Mod Concepts Cardiovasc Dis 1962;31:735–8.
- **49.** Stoney WS. Evolution of cardiopulmonary bypass. Circulation 2009;119(21): 2844–53.
- 50. Kolessov VI. Mammary artery-coronary artery anastomosis as method of treatment for angina pectoris. J Thorac Cardiovasc Surg 1967;54(4):535–44.
- 51. Mueller RL, Rosengart TK, Isom OW. The history of surgery for ischemic heart disease. Ann Thorac Surg 1997;63(3):869–78.
- 52. Favaloro RG. Landmarks in the development of coronary artery bypass surgery. Circulation 1998;98(5):466–78.
- 53. Iqbal J, Gunn J, Serruys PW. Coronary stents: historical development, current status and future directions. Br Med Bull 2013;106:193–211.
- 54. Booth J, Clayton T, Pepper J, et al. Randomized, controlled trial of coronary artery bypass surgery versus percutaneous coronary intervention in patients with multi-vessel coronary artery disease: six-year follow-up from the Stent or Surgery Trial (SoS). Circulation 2008;118(4):381–8.
- 55. Daemen J, Boersma E, Flather M, et al. Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. Circulation 2008; 118(11):1146–54.
- Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360(10):961–72.
- 57. Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012;367(25):2375–84.
- 58. Park SJ, Ahn JM, Kim YH, et al. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med 2015;372(13):1204–12.
- 59. Holm NR, Mäkikallio T, Lindsay MM, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. Lancet 2020;395(10219):191–9.

- **60.** Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. N Engl J Med 2016;375(23):2223–35.
- Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J 2019;40(2):87–165.
- Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery: a report of the american college of cardiology foundation/american heart association task force on practice guidelines. Circulation 2011;124(23):e652–735.
- Alkhouli M, Alqahtani F, Kalra A, et al. Trends in characteristics and outcomes of patients undergoing coronary revascularization in the United States, 2003-2016. JAMA Netw Open 2020;3(2):e1921326.
- 64. D'Agostino RS, Jacobs JP, Badhwar V, et al. The society of thoracic surgeons adult cardiac surgery database: 2018 update on outcomes and quality. Ann Thorac Surg 2018;105(1):15–23.
- 65. Ferguson TB Jr, Hammill BG, Peterson ED, et al. A decade of change–risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: a report from the STS national database committee and the duke clinical research institute. society of thoracic surgeons. Ann Thorac Surg 2002;73(2): 480–9 [discussion 489-490].
- 66. Cornwell LD, Omer S, Rosengart T, et al. Changes over time in risk profiles of patients who undergo coronary artery bypass graft surgery: the veterans affairs surgical quality improvement program (VASQIP). JAMA Surg 2015;150(4):308–15.
- 67. Bommer C, Sagalova V, Heesemann E, et al. Global economic burden of diabetes in adults: projections from 2015 to 2030. Diabetes Care 2018;41(5):963–70.
- **68.** Shahian DM, O'Brien SM, Filardo G, et al. The society of thoracic surgeons 2008 cardiac surgery risk models: part 1–coronary artery bypass grafting surgery. Ann Thorac Surg 2009;88(1 Suppl):S2–22.
- **69.** Alserius T, Hammar N, Nordqvist T, et al. Improved survival after coronary artery bypass grafting has not influenced the mortality disadvantage in patients with diabetes mellitus. J Thorac Cardiovasc Surg 2009;138(5):1115–22.
- **70.** Brown JC, Gerhardt TE, Kwon E. Risk factors for coronary artery disease. Stat-Pearls. Treasure Island (FL): StatPearls Publishing; 2021.
- Anand SS, Xie CC, Mehta S, et al. Differences in the management and prognosis of women and men who suffer from acute coronary syndromes. J Am Coll Cardiol 2005;46(10):1845–51.