

# Protecting the gains: what changes are needed to prevent a reversal of the downward CVD mortality trend?

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## BACKGROUND

- The decline in cardiovascular disease (CVD) mortality over the past 50 years is a public health success story.
- However, this trend may be reversing given risk factor prevalence, changes in risk factors, and insufficient innovations.
- Focus has been on increases in healthcare spending, but there still exists a need for highly effective therapies.
- Model-based analyses can provide insights beyond what is possible from randomized controlled trials.

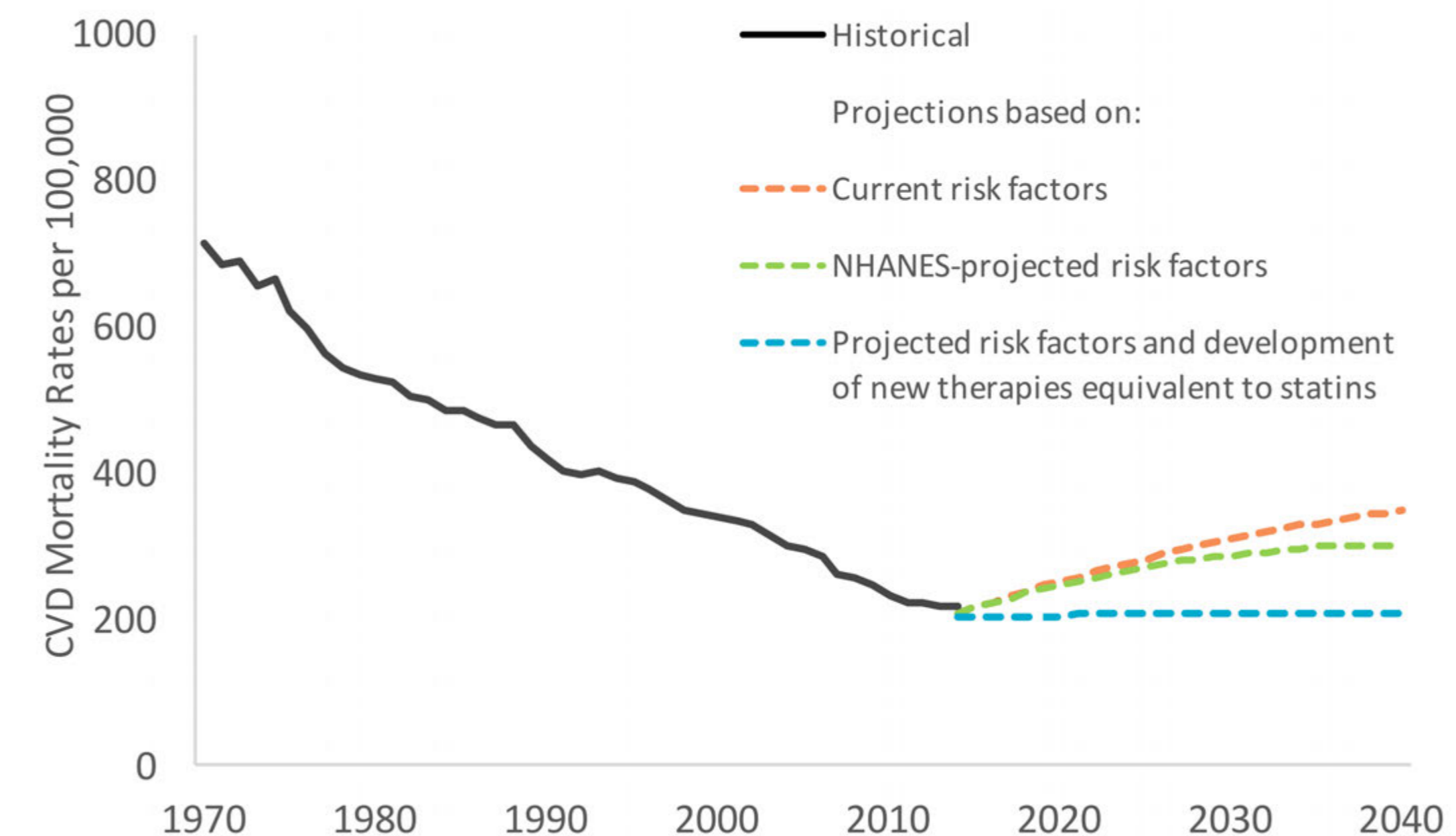
## METHODS

- Analyzed NHANES data to estimate historical CVD risk factors and project future levels.
- Developed a model that incorporated patient-level characteristics from NHANES projections.
- Calculated Framingham Risk Scores; used scores to estimate CVD incidence.
- Combined incident and prevalent cases to predict annual CVD deaths.
- Assessed various scenarios to compare projected annual CVD mortality given uncertainty.

## RESULTS

### CVD Mortality Rates per 100,000 Under Three Scenarios

- Impact of an aging US population only, assuming current risk factor levels
- Incorporating NHANES-projected changes in risk factors
- Risk factor changes and development of therapies with efficacy similar to that of statins



## CONCLUSIONS

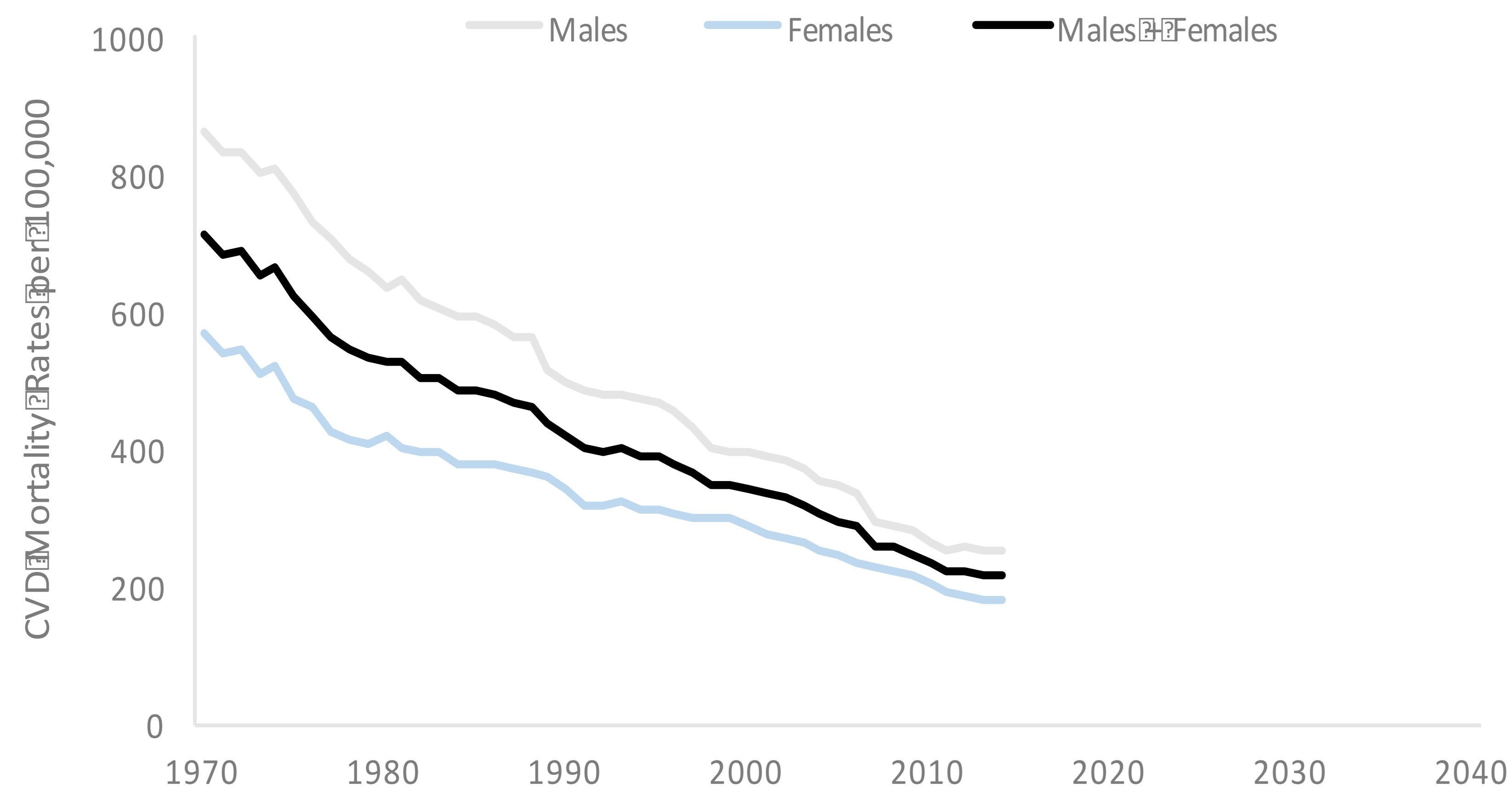
- While increasing access and adherence to currently available treatment options could slow the expected increase in mortality, changes in risk factors and development of new therapies are necessary to improve the outlook for CVD associated morbidity and mortality.
- CVD is the leading area of healthcare spending, with current direct medical costs of \$230 billion and indirect costs of >\$400 billion. However, given the significant disease burden and expected shifts in risk factors, further CVD-related innovations are necessary.



# Background



**FIGURE 1: HISTORICAL TRENDS IN CVD MORTALITY**



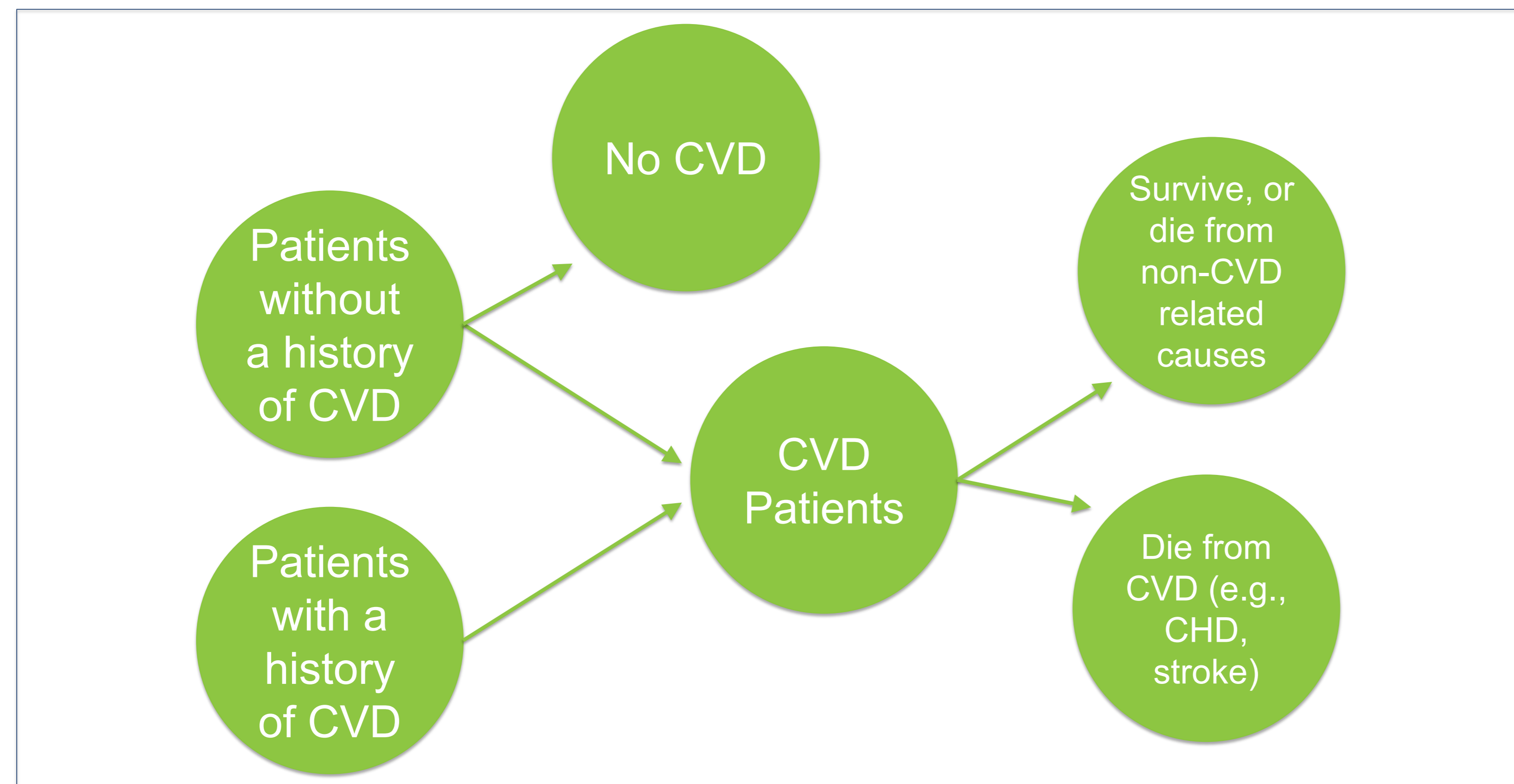
The figure above shows the changes in CVD mortality rates by sex over the past 45 years. While a steep decline had been observed prior to 2010, a previously published joinpoint analysis showed that there was a statistically significant shift in the trend between the periods of 2000-2010 and 2010-onward. In fact, given uncertainty in estimates, it is unclear whether trends since 2010 have been increasing or decreasing.

- Cardiovascular disease (CVD) mortality has decreased by more than 60% over the past 50 years, due to behavioral modifications, development of preventive therapeutics (e.g., statins, antihypertensive agents), and acute interventions (e.g., angioplasty, surgery).
- However, emerging data indicate that progress has slowed and the incidence of CVD may be on the rise.
- With an aging US population, an increase in adolescent smoking rates, an expected continued rise in obesity and diabetes prevalence, and competing needs for limited resources, future patterns of CVD are uncertain.
- While many studies have explored the causes of the previous decline in CVD mortality, there is a gap in the literature regarding projections of future mortality and the impact of forthcoming pharmacological innovations.

**References:** Jiemin Ma, Elizabeth M. Ward, Rebecca L. Siegel, et al. Temporal Trends in Mortality in the United States, 1969-2013. *JAMA*. 2015;314(16):1731-1739.



## MODEL SCHEMATIC



## GENERAL METHODS

- A Microsoft Excel based model was developed to project future trends in CVD mortality.
- The model considered both patients without a history of CVD and those who had experienced a CVD event prior to entry into the model.
- Patients with CVD, either incident cases after entering the model or with prevalent cases upon entering the model, faced risks of CVD mortality, non-CVD mortality, or could survive.
- Annual CVD deaths from 2015 to 2040 were estimated, and extrapolated to the entire US population (accounting for demographic shifts) and adjusted as rates per 100,000.
- A series of scenarios were conducted, differing by trends in risk factors and technological innovations, to assess the impact of varying assumptions.

## ESTIMATING INCIDENT CASES

- An analysis of NHANES data was conducted to assess current levels of risk factors (i.e., total cholesterol, HDL-C, systolic blood pressure), stratified by sex, smoking status, diabetes status, and patients receiving treatment for hypertension.
- Using the most recent 12 years of NHANES data, risk factors were projected annually.
- Hypothetical cohorts of 1 million patients were created, assigned an age and risk factor profile, and the 10-year risk of CVD was estimated using the Framingham Risk Score.
- Based on estimated risk scores, patients could experience a CVD event.

## INCORPORATING PREVALENT CASES

- As the Framingham Risk Equation only applies to those without a history of CVD, we separately included those who had experienced previous events.
- Prevalent cases, estimated using data from the 2017 AHA Statistical Update, were included in the model and susceptible to CVD mortality.

## PROJECTING MORTALITY OVER TIME

- Those with CVD, either an incident case or a history of CVD prior to entering the model, were at risk of dying from CVD each year based on real-world case fatality rates.
- Those who survived a given year continued to the following year, where they were again at risk of dying.
- Those who died of CVD, or of non-CVD causes, were removed from the pool of susceptible people.

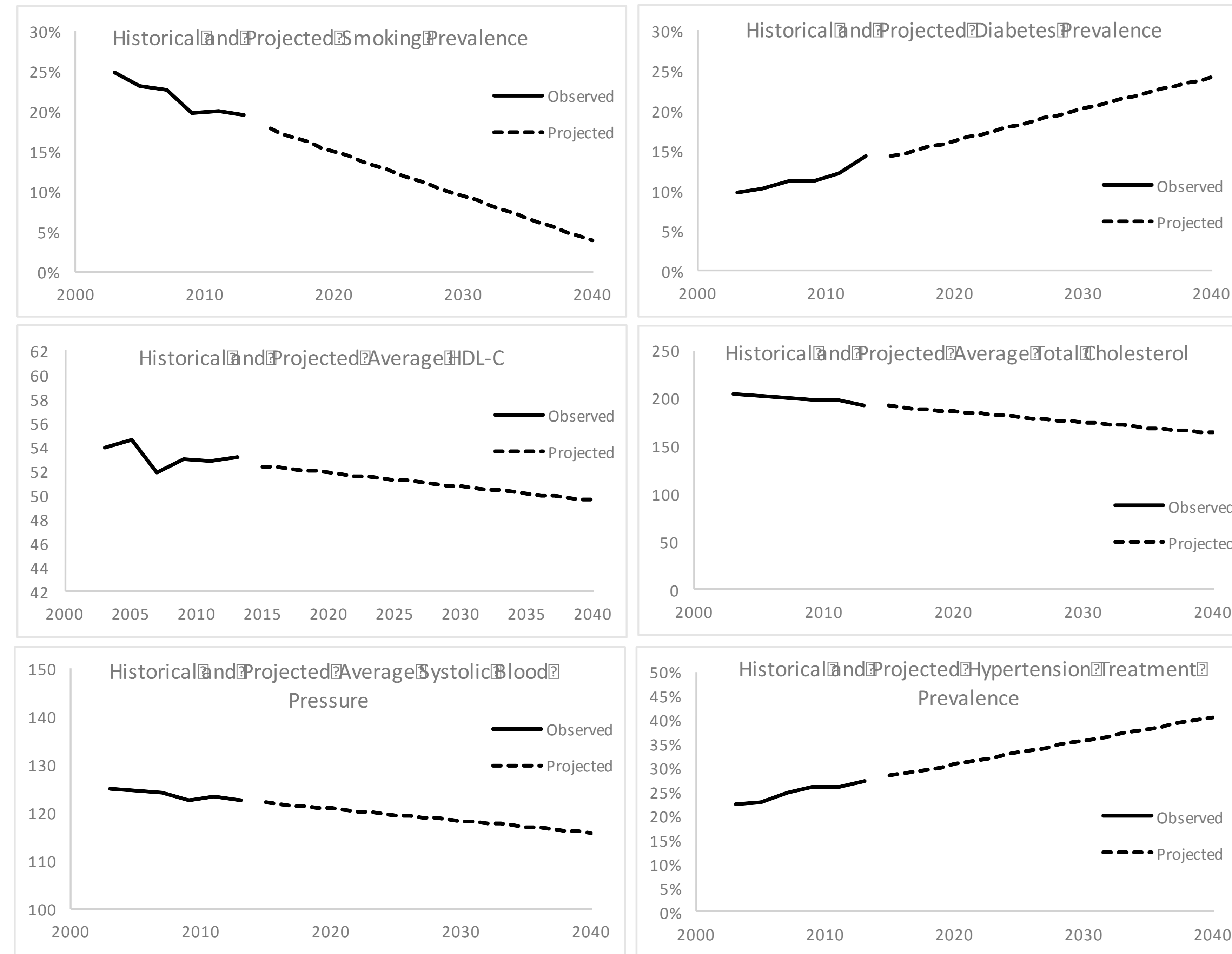
### References:

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# Results



**FIGURES 2A-F. LEVELS OF CVD RISK FACTORS FROM 2000 - 2040**



Figures 2A-F show trends in risk factors from 2003 to 2040. Historical values (2003-2013) are based on observed NHANES data, and projections (2015-2040) are based on linear regression of NHANES data. In the model, risk factors are incorporated separately by sex, smoking status, diabetes status, and treatment for hypertension. The model also incorporated a growing and aging US population.

**FIGURE 3. 2040 MORTALITY BASED ON PREDICTED CHANGES IN INDIVIDUAL RISK FACTORS**

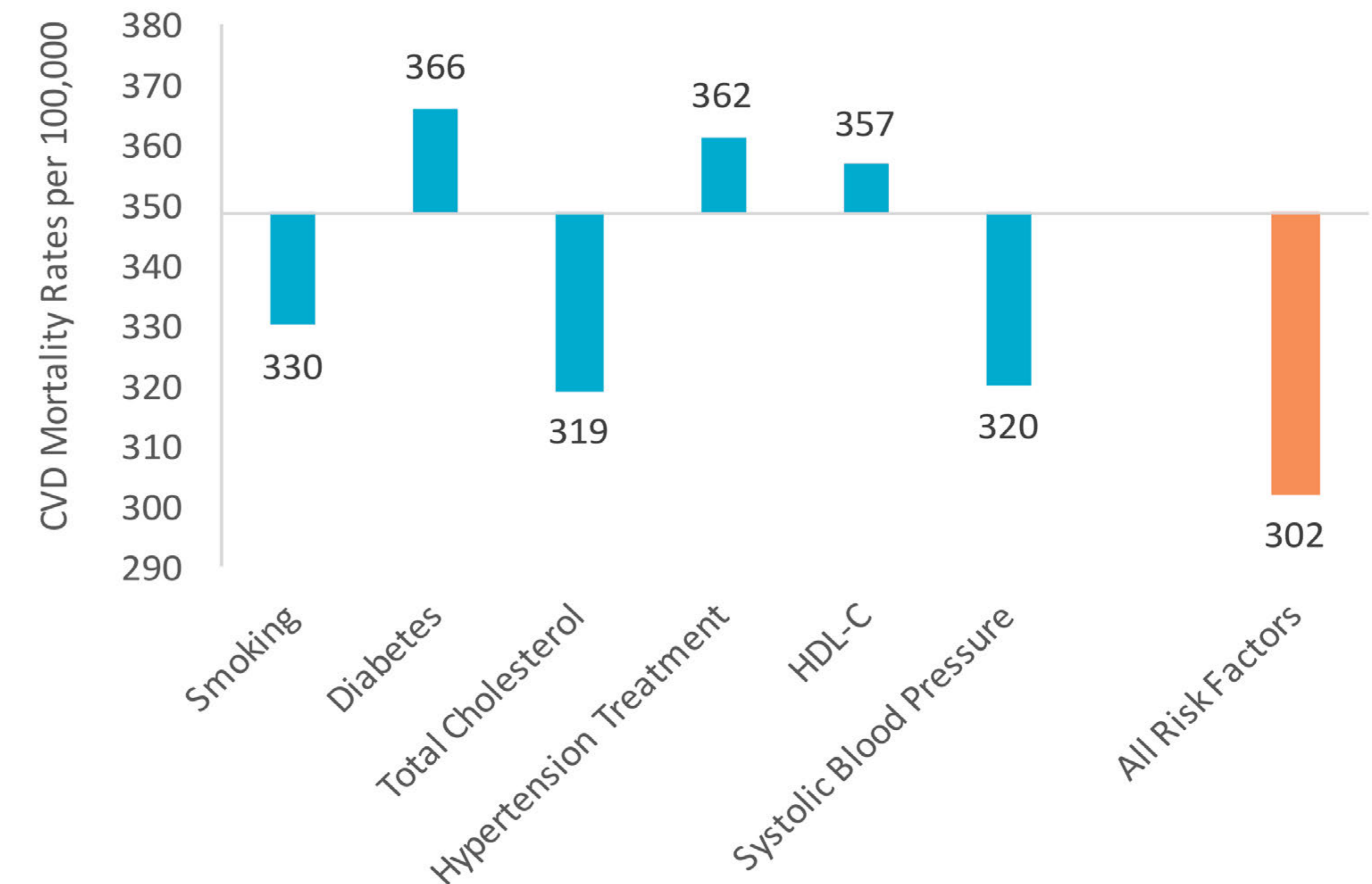


Figure 3 depicts the CVD mortality rates per 100,000 individuals in 2040 when considering changes in individual risk factors. The horizontal line represents the projected mortality if current levels of risk factors remain constant, and is equal to 350 deaths per 100K. The first 6 vertical bars represent the change, compared to the status quo scenario, when allowing that risk factor to vary as projected using previous NHANES observations. From these data, the expected decreases in smoking, total cholesterol, and systolic blood pressure are projected to decrease the overall CVD mortality burden, whereas the increase in diabetes and decrease in HDL-C are expected to increase the CVD mortality burden. The cumulative effect of all risk factor changes is shown in the vertical bar farthest to the right.

**FIGURE 4. MORTALITY PROJECTIONS FOR THREE SCENARIOS**

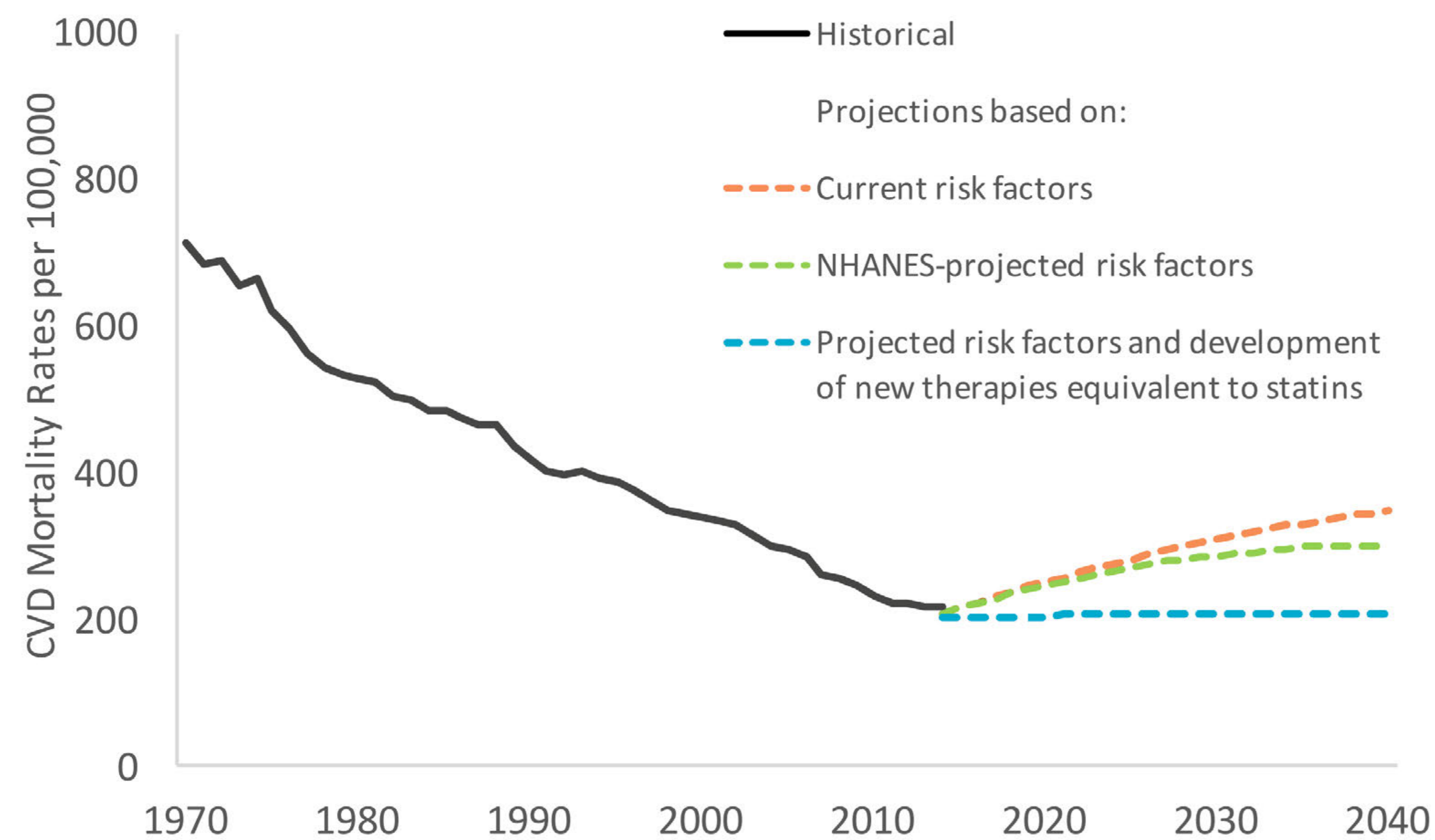


Figure 4 depicts results for three scenarios. The first, displayed in orange, is based on no change in current levels of risk factors. The increase in CVD mortality in this scenario is driven by an aging population. The second scenario, displayed in green, reflects the impact of changes in risk factors as predicted based on NHANES data. The third scenario incorporates an aging population, a change in risk factors, and assumes innovations are introduced and immediately provide the same incremental benefits as the introduction of statins.

**FIGURE 5. MORTALITY PROJECTIONS GIVEN INNOVATIONS**

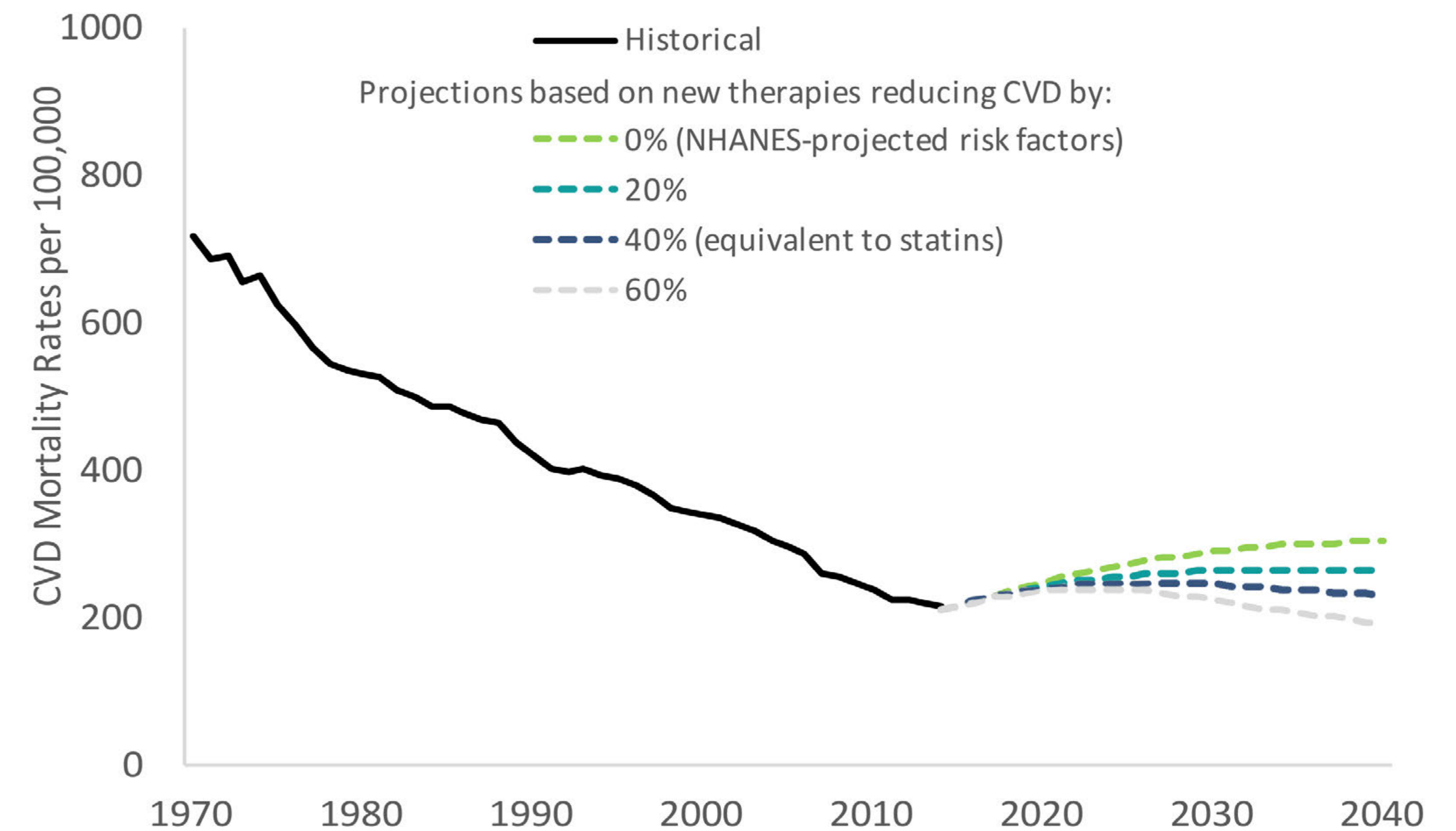


Figure 5 includes results when incorporating projected changes in risk factors and immediate introduction of innovations that decrease CVD incidence. In each scenario with technological improvements, the incidence in 2015 is unchanged, decreases linearly until reaching a maximum decrease in year 2030, and then remains constant until 2040. The maximum decreases in incidence vary between scenarios and range from 20% and 60%.