The Returns to Preventing Chronic Disease in Europe and the United States

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Since the 1950s, life expectancy in Europe and the United States has improved at a steady pace, driven mostly by gains at older ages. However, these lives are punctuated by more chronic disease than ever before, contributing to substantial morbidity and disability. Using the Future Elderly Model, we simulate longevity and disability over the remaining lifetime for cohorts of older Europeans and Americans. We see that investment in both treatment and prevention for cancer, diabetes, and heart disease show tremendous promise for breaking Europe and the United States out of the expensive equilibrium we now find ourselves in as a result of demographic gains.

I. Introduction

Since the 1950s, life expectancy in Europe and the United States has risen at a steady pace, driven mostly by improvements in mortality at older ages (Goldman et al. 2013; Crimmins 2015). Functional status at older ages

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has also improved, albeit with some attenuation recently (Freedman et al. 2004; Lakdawalla, Bhattacharya, and Goldman 2004; Crimmins and Beltrán-Sánchez 2011) that is more pronounced in the United States than in Europe. These health gains have been driven by advances in public health and a targeted "disease model," which independently delayed or forestalled mortality from major fatal diseases—especially infectious and cardiovascular diseases (CDC 1999; Beltrán-Sánchez, Soneji, and Crimmins 2015). This combination of efforts has extended the quality and quantity of life worldwide. Taken together, the social value of these health improvements has been formidable—up to 50% of gross domestic product in the United States and more elsewhere (Becker, Philipson, and Soares 2005; Murphy and Topel 2006).

Unfortunately, developed nations have become victims of their own success (Gruenberg 1977). Our longer lives are punctuated by more chronic disease than ever before, and this contributes to substantial morbidity (Crimmins 2015). Increases in life expectancy are now associated with increased disability, which can leave healthy-life expectancy—defined as length of life without disability—unaltered or worse (Bhattacharya et al. 2004; Lakdawalla, Bhattacharya, and Goldman 2004; Crimmins and Beltrán-Sánchez 2011; Hulsegge et al. 2013).

The question arises, then, whether a renewed focus on preventing chronic disease—rather than just treating it more effectively—might drive further population health improvement. Innovations in prevention, or effective treatments for chronic illness, may provide a means to reverse declines in quality of life at older ages in Europe and the United States. There is no clear theoretical prediction on the effect of the increase in life expectancy on morbidity and quality of life. On the one hand, the "compression of morbidity" hypothesis foresaw an improvement in health status that would condense the duration and degree of disability, giving rise to the idea that over time individuals would live longer and healthier (Fries 1980, 1989, 2002; Hubert et al. 2002). On the other hand, the "expansion of morbidity" hypothesis foresees an overall worsening of health status, given that individuals would live longer but that the years gained would be spent in worse health (Gruenberg 1977; Kramer 1980; Olshansky et al. 1991). A third hypothesis, labeled "dynamic equilibrium," predicts a sort of maintenance of the status quo (Manton 1982), where despite increases in morbidity, mortality would fall as a result of a lower severity of morbidities. Finally, the "double expansion of morbidity" (Atella et al. 2017b) foresees a longer coexistence with morbidity due to both prolonged longevity and occurrence of chronic conditions earlier in life. Evidence accumulated since the 1980s seem to favor the "compression of morbidity" hypothesis, although more recent analyses suggest that the "double expansion of morbidity" may have been at work in the most recent years.

In the health economics literature there has been debate on prevention, in regard to benefits, value, and methods. In obesity and metabolic disorders, various prevention studies advocate for healthy diets, physical

activity, and statin usage (Chou et al. 2016; LeBlanc et al. 2018). While these studies suggest a benefit to preventive interventions, some studies find that preventive efforts, such as workplace wellness programs and management and coordination initiatives, may not actually benefit patients (McWilliams, Chernew, and Landon 2017; Reif et al. 2020). In terms of cost-effectiveness, a literature synthesis centered on prevention found discordance on the value of preventive care in a number of conditions (Goodell, Cohen, and Neumann 2009). The mixed evidence on prevention may be due to the interventions themselves or to the methods used in assessment. In this particular synthesis, the authors found that many preventive studies did not address competing risks. They also found that a number of studies did not consider quality in terms of life-years, which could offer a more meaningful interpretation of benefits. A separate review of preventive models identified a range of study horizons employed, which can lead to differing results (Miller et al. 2013). Selection of shorter time horizons in preventive studies, rather than lifetime horizons, may omit the additional costs and health benefits associated with longer living. In estimates of the benefits of prevention in this study, all of these factors were considered.

To estimate the potential benefits of a renewed focus on chronic disease at older ages without incurring these methodological issues, we employed the Future Elderly Model (FEM) to project future outcomes in Europe and the United States, using a prevention framework.[1] The FEM is a dynamic microsimulation of European and US health and health dynamics at older ages. While other burden-of-illness studies have employed cause-deleted approaches, which do not account for the presence of competing risks (Manuel, Schultz, and Kopec 2002; Beltrán-Sánchez, Preston, and Canudas-Romo 2008), the FEM accounts for competing risks over a full life horizon (Atella et al. 2021).

In this particular analysis, we focus on cancers, diabetes, and diseases of the heart, which are the three leading causes of death in the United States (Advisory Board 2017) and accounted for 65% of the deaths in Europe in 2020 (OECD/EU 2020). The model simulates total longevity and disability over the course of a lifetime for representative cohorts of older Europeans and Americans. To do this, we consider two counterfactual scenarios. In the first, we reduce the presence of the chronic illness at age 50, if present (i.e., the impact of removing stock). In the second, we reduce the incidence of chronic disease after age 50, among those developing disease after this age (i.e., the impact of removing flow). We then assess the impact on the treated and the average effect on the overall cohort, in terms of life-years (LYs) and disability-free LYs (DFLYs). We study Europe and the United States to understand how differences in older-age prevalence and incidence between the two regions influence the burden of disease, as well as the trade-offs between treatment and prevention by disease (Solé-Auró et al. 2015). In the next section, we describe the model in more detail.

[1] Concerning Europe, because of data availability, the analyses are limited to the following countries: Austria, Belgium, Denmark, France, Germany, Italy, Spain, Sweden, and Switzerland.

II. Methods

We sought to estimate the lifetime benefits of treating and preventing cancer, diabetes, and heart disease at older ages. To do so, we employed the FEM to simulate the lifetime risks of disease, disability, and mortality, which allowed us to project scenarios in which disease prevalence or incidence was reduced. The defining characteristic of the FEM is the modeling of real rather than synthetic cohorts, all of which are followed at the individual level. This allows more heterogeneity in behavior than would be allowed by a cell-based approach. In this analysis, cancer refers to a broad set of cancers (excluding skin cancer), diabetes refers to type 1 and type 2 diabetes mellitus, and heart disease refers to various diseases of the heart, including congestive heart failure, arrhythmia, and other cardiovascular diseases.

The FEM has been used to explore a variety of policy questions related to this study: the benefits of preventing disease (Goldman et al. 2006, 2009, 2013; Goldman and Olshansky 2013; Goldman 2016), the fiscal consequences of worsening population health (Goldman et al. 2010; Gaudette et al. 2015; Zissimopoulos, Crimmins, and St.Clair 2015), the financial risk from new medical technologies (Goldman et al. 2005), the costs of obesity (Lakdawalla, Goldman, and Shang 2005), trends in disability (Chernew et al. 2005), the costs of cancer (Bhattacharya et al. 2005), the returns to early-childhood investments (García et al. 2016), and disparities in life expectancy and their policy implications (Goldman and Orszag 2014; NASEM 2015; Auerbach et al. 2017). A global effort, led by the Organization for Economic Cooperation and Development, the University of Rome Tor Vergata, and the University of Southern California, helped expand the FEM internationally (Atella et al. 2017a). This study reports on research conducted as part of that effort, with findings from the European Union and United States. More recently, a special issue published in *Health Economics* has collected several contributions addressing the role that education can have in determining health status and its dynamics (Atella, Goldman, and McFadden 2021).

The FEM projects health and health-related outcomes for Americans aged 51 and over, using data from the HRS (Health and Retirement Study), which is a representative, longitudinal panel survey of Americans aged 51 and over. Additionally, other countries and institutions have adapted the FEM and feed their own data. The European Union FEM projects outcomes using data from the SHARE (Survey of Health, Ageing and Retirement in Europe) data set of individuals aged 50 and over.

A recent validation study of the FEM indicates robust prediction of quantity and quality of life (Leaf et al. 2020). This was done by comparing FEM mortality and longevity projections to the actual mortality and longevity experience observed over the same period. The study also compared FEM results to actuarial forecasts of mortality and longevity during the same period and found FEM projections to be generally in line with observed

mortality rates with closely matched longevity. Quality of life was evaluated cross-sectionally and longitudinally, and the FEM was found to perform reasonably well at predicting quality of life. Additional FEM cross validation, external validation, and external corroboration are summarized in the technical appendix (technical appendix and supplemental tables and figures are available online).

The model consists of three core components. The initial cohort module sets the health and socioeconomic characteristics of the entering cohorts on the basis of characteristics in the SHARE and HRS data. The transition module estimates the probabilities of entering and exiting various health states, using longitudinal data from the SHARE and HRS data. In this transition module, we use a probit to model binary outcomes for incident cancer, incident diabetes, incident heart disease, nursing home status, and mortality. We use an ordered probit to model two ordered outcomes: smoking status and functional status. And we use ordinary least squares to model BMI (body mass index). These probabilities are then used to simulate the clinical paths of individuals. The summary module aggregates projections on individual-level outcomes into policy outcomes such as life expectancy and disability-free life expectancy.

Simulation begins in 2009 in the European Union FEM and in 2010 in the US FEM, with initial populations aged 50/51 and 51/52 taken from the SHARE and HRS data sets, respectively. The size of the entering Europe cohort is adjusted to reflect European national populations, gender, and age on the basis of United Nations World Population Prospects data (United Nations 2017). The size of the entering US cohort is adjusted to reflect the population in the US Census by gender, race, and ethnicity. The FEM cycles biannually, and simulants that survive each 2-year period continue cycling forward until the end of their lifetime.

To estimate our effect sizes in the analysis, we first consider a base case in which we project the remaining life expectancy (and healthy-life expectancy) for those aged 50/51 in the European Union FEM and aged 51/52 in the US FEM. This base case will be used to understand the impact of counterfactual scenarios that we invoke. Some simulants will already have chronic disease at the time of model entry, while others will develop these diseases in the future.

A. Transitions in Health, Economic Status, Mortality, and Functional Status

The transition models dictate movement across health states as a function of risk and demographic factors. We used first-order Markovian limited-dependent variable models (probits, ordered probits, multinomial logits, censored regressions, etc.).[2]

The technical appendix provides details on the parametric structure, estimation, and validation of the model, including all the key inputs and

[2] We find that the data requirements for estimating higher-order Markov models bias the sample toward healthier individuals, as explained in the technical appendix.

outputs of the model and how they were measured. We summarize our approach for modeling chronic disease and mortality through a matrix in table 1. This particular table shows how chronic diseases in the model are used to predict future chronic disease states, as well as downstream disability and mortality. For example, diabetes status in the current period will directly affect mortality, functional limitations, and chronic disease incidence in the following period. Additionally, diabetes status in the current period will also have indirect effects on mortality through the functional limitation and disease pathways in the subsequent periods. This table also illustrates how our model allows for competing risks, such that if one disease is precluded, simulants face other competing risks for disability and mortality. We also present the transition models for cancer, diabetes, and heart disease in table 2, which uses a probit regression and involves predictors such as age, sex, race and ethnicity, education, smoking status, chronic disease, and BMI, as well as interaction terms. These are presented in terms of marginal effects at the means.

The data for our transition models come from the 2007–15 biennial waves of SHARE and the 1998–2016 biennial waves of the HRS survey. Assumptions about future all-cause mortality reduction for Europe come from the United Nations World Population Prospects data (United Nations 2017), and all-cause mortality forecasts for the United States come from the intermediate projections of the Social Security Administration (OASDI Trustees 2011).

B. Outcomes

The microsimulation is stochastic, meaning that transitions are randomly drawn from the independent distributions of state variables, which is estimated from the SHARE and HRS data. Each of the transition probabilities are predicted for a simulant on the basis of their time-invariant and prior time-varying characteristics. This probability is then converted into a state by comparing the predicted probability against a random number. This is done in a Monte Carlo fashion, so that each simulant faces many simulated life courses to ensure independence from any particular sequence of random numbers. There are 25 replications per simulant, which are then averaged for each simulant to calculate outcomes such as disease prevalence (cancer, diabetes, heart disease), remaining life expectancy, and remaining healthy-life expectancy (defined as having no limitations in Activities of Daily Living, no limitations in Instrumental Activities of Daily Living, and no nursing home use). This generates the baseline outcomes of interest.

C. Counterfactual Scenarios

We simulated scenarios to model the benefits of treating or preventing the three chronic diseases at older ages. The first scenario eliminates

TABLE 1

Transition Matrix Illustrating the Relationship between Chronic Diseases and Their Downstream Impact on Disability and Mortality

Explanatory Variable at Year $t-2$	Outcome Variable at Year t									
	Died	Cancer	Diabetes	Heart Disease	Stroke	Hypertension	Lung Disease	Congestive Heart Failure	ADL	IADL
Cancer	X				X				X	X
Diabetes	X			X	X	X		X	X	X
Heart disease	X				X			X	X	X
Stroke	X								X	X
Hypertension	X			X	X			X	X	X
Lung disease	X								X	X
Congestive heart failure	*[a]									
ADL	X								X	X
IADL	X								X	X

Note.—ADL = Activities of Daily Living; IADL = Instrumental ADL. Year t refers to any year in the microsimulation.

[a] Congestive heart failure is a predictor of mortality when modeling the United States but not when modeling Europe.

TABLE 2
TRANSITION MODELS FOR THE INCIDENCE OF CHRONIC DISEASE:
MARGINAL EFFECTS AT MEANS

Predictors	Chronic Disease Model (Probit Regression)		
	Cancer	Diabetes	Heart Disease
	A. United States		
Black	−.0056***	.0092***	−.0061***
Hispanic	−.0080***	.0256***	−.0073***
Less than high school education	−.0010	.0058***	.0028
College education	.0032**	−.0015	−.0027
Male	.0073***	.0063***	.0131***
Male × less than high school	.0023	−.0040	−.0036
Male × Black	.0079***	.0030	−.0099***
Male × Hispanic	.0007	−.0060**	−.0068*
Male × college	−.0017	.0009	.0024
Age < 65 (2-year lag)	.0014***	.0011***	.0016***
Age 65–74 (2-year lag)	.0009***	.0000	.0018***
Age ≥ 75 (2-year lag)	−.0001	−.0004**	.0014***
Never smoked (2-year lag)	.0033**	−.0013	.0084***
Widowed (2-year lag)	−.0005	.0028*	.0020
Stroke (at age 50)	.0068	−.0001	.0195
Hypertension (at age 50)	.0032	.0137***	.0039
Lung disease (at age 50)	.0162**	−.0006	.0478***
Ever smoked (at age 50)	.0026**	−.0013	.0029**
Never smoked (at age 50)	.0034**	.0057***	.0067***
ln(BMI ≤ 30) (2-year lag)	−.0018	.0664***	−.0018
ln(BMI > 30) (2-year lag)	−.0130*	.0714***	.0197**
ln(BMI ≤ 30) (at age 50)	.0060	.0396***	.0118*
ln(BMI > 30) (at age 50)	.0161**	−.0116	.0185*
lnΔage	.0161***	.0240***	.0185***
Cancer (at age 50)		.0011	.0146***
Diabetes (at age 50)	−.0005		.0121***
Heart disease (at age 50)	.0049	.0122***	
Hypertension (2-year lag)			.0166***
Diabetes (2-year lag)			.0080***
Hypertension (2-year lag) × less than high school			−.0011
Hypertension (2-year lag) × college			−.0038
Diabetes (2-year lag) × less than high school			.0037
Diabetes (2-year lag) × college			.0014
	B. Europe		
Male	.0043***	.0064***	.0124***
Lag of age spline < 65	.0011***	.0010***	.0020***
Lag of age spline 65–74	.0014***	.0006***	.0024***
Lag of age spline ≥ 75	−.0002	.0006***	.0018***
Less than high school	−.0027*	−.0003	.0009
Some college or more	−.0006	−.0063***	.0008
Lag of BMI spline ≤ 30	.0002	.0729***	.0290***
Lag of BMI spline > 30	.0085	.0552***	.0416***
Lag of current smoking	.0047*	−.0043**	.0025
Diabetes at age 50	−.0028		.0060
Cancer at age 50		.0076	.0150**
Heart problem at age 50	.0073	.0103**	
Lung disease at age 50	.0022	−.0003	.0176***
Stroke at age 50	−.0088	.0011	.0259*
High blood pressure at age 50	.0035*	.0101***	.0058**
BMI at age 50 spline ≤ 30	−.0062	−.0001	−.0068

TABLE 2 (*Continued*)

Predictors	Chronic Disease Model (Probit Regression)		
	Cancer	Diabetes	Heart Disease
BMI at age 50 spline > 30	.0039	.0229*	−.0154
Smoking at age 50	.0046**	.0038*	.0073***
Ever smoked at age 50	.0075***	−.0020	.0032
Lag of widowed	.0022	.0066*	.0038
lnΔage	.0121**	.0100**	.0011
Widowed at age 50	−.0068**	−.0044*	.0009
Single at age 50	.0011	.0016	−.0024
Lag of diabetes			.0068**
Lag of hypertension			.0105***
Spain	.0017	.0168***	−.0003
Germany	.0106***	−.0053**	−.0058*
Austria	.0061*	−.0003	.0014
Belgium	.0041	−.0070***	−.0035
France	.0021	−.0088***	.0014
Switzerland	.0087**	−.0121***	−.0108***
Sweden	.0095**	−.0102***	−.0081***
Denmark	.0043***	.0064***	.0124***

Source.—These transition models were estimated using seven waves of the HRS data (panel A) and six waves of the SHARE data (panel B).
Note.—BMI = body mass index. Italy serves as the base-case country in the transition models in panel B.
* $p < .10$.
** $p < .05$.
*** $p < .01$.

chronic disease at the simulation start; the second scenario eliminates the incidence of chronic disease as the simulation progresses. Below, we describe each type briefly.

1. Eliminating Initially Prevalent Chronic Disease Scenarios

This scenario allows us to adjust the prevalence of disease for people who had disease when entering the model at ages 50/51. Colloquially, it modifies the stock. To do so, we modify the base case by reducing the initial prevalence of either cancer, diabetes, or heart disease by 10%, 20%, and so forth by 10 percentage point increments all the way to 100%. The difference between the base case and a 100% reduction estimates the burden of prevalent disease at age 50/51. These disease analyses are conducted independently from one another.

In exhibiting results for the prevalence-reduction scenarios, we present estimates among the prevalent.

2. Preventing Older Incident Chronic Disease Scenarios

We adjust the incidence of each chronic disease separately to reflect better prevention at older ages. To generate these counterfactual cohorts, we modify the base case by reducing the probability of contracting either cancer,

diabetes, or heart disease by 10%, 20%, and so forth by 10 percentage point decrements all the way to 100%. The difference between the base case and a 100% reduction estimates the burden of incident disease after age 50/51. These disease analyses are conducted independently from one another.

In exhibiting results for the incidence-reduction scenarios, we present estimates among the incident.

D. Production Curves

Rather than pitting investments in chronic disease prevention (e.g., obesity management) against investments in the treatment of chronic disease complications (e.g., improved heart attack care), we look at interventions that involve a combination of both treatment and prevention, for example, an intervention that offers *X*% of treatment among the prevalent and *Y*% of prevention among the incident. We construct production curves to visualize the combinations of, for example, diabetes treatment and diabetes prevention to achieve various population-level extensions in life expectancy or healthy-life expectancy. These curves are estimated on the basis of our findings from the prevalence- and incidence-reduction scenarios.

III. Results

Our key research objectives are (1) to understand the potential impact of treating and preventing cancer, diabetes, or heart disease among the prevalent and the incident and (2) to compare interventions between cancer, diabetes, and heart disease from the perspective of the full cohort.

A. Baseline Characteristics

The cohort examined in the United States is characterized by a higher level of education than the corresponding cohort in Europe (table 3). While approximately 22% of Europeans had attained some college education or more, 60% of Americans had achieved this academic level. Similar percentages of Americans and Europeans had less than high school education (10% and 12%, respectively). Compared to Europeans, Americans also had a higher mean BMI (29.3 vs. 26.1) and were more likely to have a BMI of 30 or higher (40% vs. 16%). The Europe cohort was approximately 1 year younger than the US cohort. This difference in initial cohort age is due to differences in eligibility criteria: the starting age for the European SHARE panel survey is 50/51, while for the US HRS panel survey it is 51/52. The Europe and US cohorts also had similar percentage female and percentage currently smoking.

B. Remaining Life Expectancy and Lifetime Chronic Disease Risk

In both the Europe and the United States, persons with some college education or more experience greater remaining longevity and healthy

TABLE 3
BASELINE CHARACTERISTICS OF THE OLDER EUROPE AND US COHORTS

Characteristic	Europe	United States
Age, mean (SD)	51.1 (.5)	52.0 (.6)
Female, %	50	51
Body mass index, mean (SD)	26.1 (4.4)	29.3 (6.1)
Body mass index category (%):		
<25	43	21
≥25 and <30	40	39
≥30	16	40
Smoking status (%):		
Former smoker	27	32
Ever smoked	53	56
Currently smoke	26	24
Education level (%):		
Less than high school	12	10
High school graduate	66	30
Some college or more	22	60
Initial disease prevalence (%):		
Cancer ever	2	6
Diabetes ever	5	12
Heart disease ever	5	9

Note.—Characteristics for the Europe cohort pertain to the age 50/51 cohort in the 2009 SHARE data, while characteristics for the US cohort pertain to the age 51/52 cohort in the 2010 HRS data.

longevity than those with less than high school education. In particular, between the most and least educated groups evaluated, there exists a difference of 2.2 and 6.2 remaining LYs and a difference of 3.7 and 9.6 remaining DFLYs in Europe and the United States, respectively (suppl. table 1).

Compared to Europe, the initial prevalences of cancer, diabetes, and heart disease are all higher in the United States (fig. 1). The initial prevalence of diabetes reaches upward of 12% in the United States, whereas in Europe it is 5%. However, the lifetime incidence of heart disease after age 50 is 62% in Europe, whereas in the United States it is lower at 53%. And while the lifetime risk of cancer and diabetes becomes similar over time between the Europe and US cohorts, the lifetime risk of heart disease is higher in Europe (67%) than in the United States (62%).

In the United States, there is also an educational gradient for diabetes. Simulants with lower levels of education are more likely to have diabetes (fig. 1). Approximately 9% of Americans with at least some college education have diabetes at age 51, while in the case of those with less than high school education the figure is 27%. Similarly, the risk of diabetes in the United States after age 51 is greater in those less educated.

In both Europe and the United States, there is also an educational gradient for cancer (fig. 1). In contrast to the narrative for diabetes, the more educated have a higher initial prevalence of cancer than the less educated. The more educated also have a higher risk of cancer after ages 50 and 51 in Europe and the United States, respectively. This may be driven

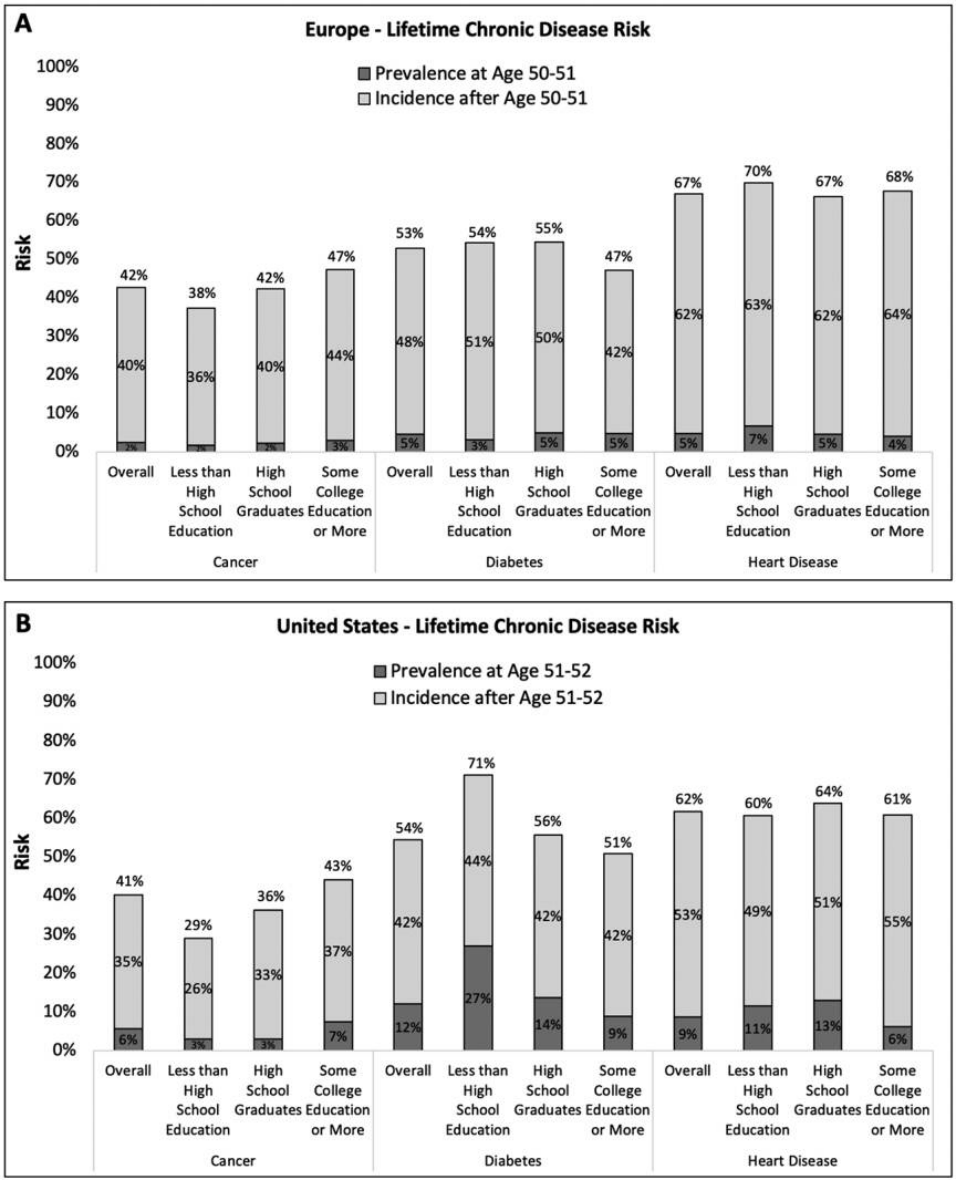

Figure 1.—Lifetime risk of chronic disease in the cohorts of older Europeans (*A*) and Americans (*B*), overall and by education.

by greater longevity in the more educated in both populations, which leads to higher lifetime risk (suppl. table 1).

C. Benefits of Prevalence Reduction for Those Treated

In both Europe and the United States, we estimate that the burden on life expectancy at age 50/51 is highest from cancer (fig. 2; suppl. table 2). In Europe, this prevalence burden is 5.8 LYs, and in the United States it is 4.4 LYs. In Europe, diabetes (2.4 LYs) and heart disease (2.1 LYs) have the next-highest burdens on life expectancy. In the United States, heart

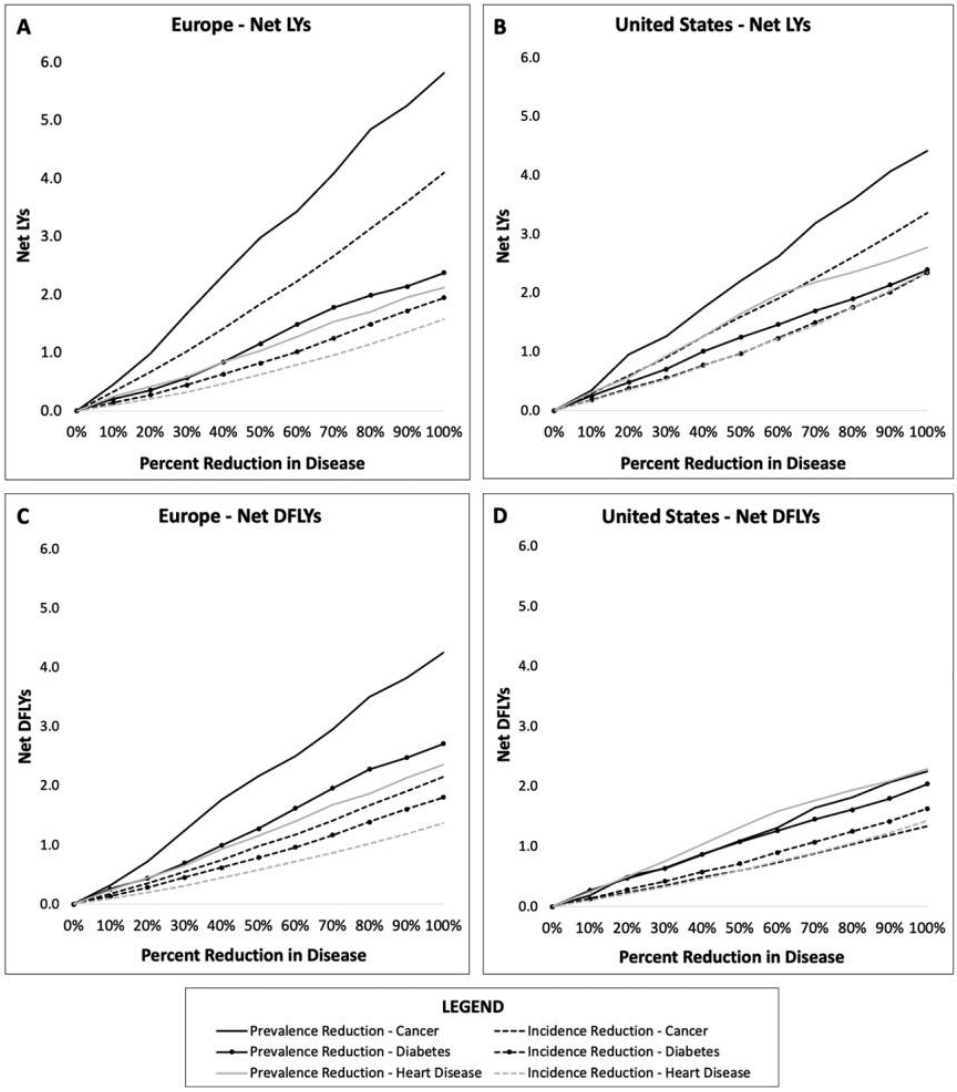

Figure 2.—Gains in mean life-years (LYs; *A*, *B*) and disability-free LYs (DFLYs; *C*, *D*) from older-age prevalence reduction among the prevalent and incidence reduction among the incident.

disease (2.8 LYs) and diabetes (2.4 LYs) have the next-highest burdens on life expectancy.

In Europe, the burden on healthy-life expectancy from chronic disease at age 50/51 is highest from cancer (4.3 DFLYs), followed by diabetes (2.7 DFLYs) and heart disease (2.4 DFLYs; fig. 2). In the United States, this prevalence burden on healthy-life expectancy is highest from heart disease and cancer (2.3 DFLYs), followed by diabetes (2.0 DFLYs).

For each year of prevalence burden on life expectancy in Europe due to diabetes, we estimate that there is a 1.1-year burden on healthy-life expectancy (suppl. table 3). For heart disease and cancer, this value is 1.1 and 0.7, respectively. This indicates that from intervention on diabetes and heart disease there is a relative compression of morbidity and that

from intervention on cancer there is a relative expansion of morbidity. In the United States, for each year of this prevalence burden on life expectancy due to diabetes, we estimate that there is a 0.9-year burden on healthy-life expectancy. For heart disease and cancer, this value is 0.8 and 0.5, respectively. These findings differ from those in Europe, as they suggest that all three interventions in the United States lead to a relative expansion of morbidity.

In Europe, chronic disease may exacerbate health disparities by education. As a consequence of heart disease, those with less than high school education experience greater losses in life expectancy (2.0 vs. 1.6 LYs) and healthy-life expectancy (2.4 vs. 1.8 DFLYs; suppl. table 4), compared to those with some college education or more. The greater losses in the less educated can be partially explained by the gradient of initial heart disease prevalence in Europeans with less education (fig. 1). In the case of the United States, as a consequence of cancer, those with less than high school education experience greater losses in life expectancy (5.3 vs. 4.6 LYs), compared to those with some college education or more (suppl. table 4).

As such, in both Europe and the United States, intervention on these chronic diseases can offer reductions in health disparities between educational groups (suppl. figs. 1–3; suppl. table 4). In terms of prevalence reduction, heart disease presents an opportunity to narrow health disparities between educational groups in Europe, whereas in the United States the candidate would be cancer instead.

D. Benefits of Incidence Reduction for Those Treated

We find that in both Europe and the United States, the burden on life expectancy after age 50/51 is highest from cancer (fig. 2; suppl. table 2). In Europe, this incidence burden is 4.1 LYs, and in the United States it is 3.4 LYs. In Europe, diabetes (2.0 LYs) and heart disease (1.6 LYs) have the next-highest burdens on life expectancy. In the United States, diabetes (2.4 LYs) and heart disease (2.4 LYs) tie as having the second-highest burden on life expectancy.

In Europe, the burden on healthy-life expectancy after age 50/51 is highest from cancer (2.2 DFLYs), followed by diabetes (1.8 DFLYs) and heart disease (1.4 DFLYs; suppl. table 2). However, in the United States, this incidence burden on healthy-life expectancy is highest from diabetes (1.6 DFLYs), followed by heart disease (1.4 DFLYs) and cancer (1.3 DFLYs).

For each year of incidence burden on life expectancy in Europe due to diabetes, we estimate that there is a 0.9-year burden on healthy-life expectancy (suppl. table 3). For heart disease and cancer, this value is 0.9 and 0.5, respectively. In the United States, for each year of this incidence burden on life expectancy due to diabetes, we estimate that there is a 0.7-year burden on healthy-life expectancy. For heart disease and cancer, this value is 0.6 and 0.4, respectively. All of these interventions lead to a relative expansion of morbidity.

In terms of reducing health disparities between educational groups, in Europe we find that incidence reduction for heart disease and also cancer would help narrow these health disparities. In the United States, incidence reduction offers minimal opportunities to reduce them (suppl. figs. 1–3; suppl. table 5).

E. Contrasting Prevalence and Incidence Reduction for the Average Cohort Member

We also explore interventions that involve a combination of treatment and prevention and assess their effects on the average cohort member. In figures 3 and 4, production curves show the range of treatment and prevention options within each disease needed to achieve different levels of cohort-wide gains in life expectancy and healthy-life expectancy.

There is a greater trade-off between prevalence and incidence reduction (holding all costs equal) in Europe than in the United States, as indicated by the production curves for Europe, which are all less steep than their counterparts in the United States (figs. 3, 4). This is in part a reflection of the lower prevalence of chronic disease (relative to incidence of chronic disease) in Europe (fig. 1). While Europe starts from a low prevalence at age 50, it catches up with the United States through greater incidence.

If we compare by chronic disease, cancer has a flatter production curve in both regions than diabetes or heart disease—with this being more striking for Europe (figs. 3, 4). This implies that prevention is more productive than treatment for cancer, holding all costs equal, than it is for diabetes or heart disease.

When we compare how well interventions extend healthy-life expectancy (relative to life expectancy), we find that cancer requires much more intervention than diabetes or heart disease to achieve the same healthy-life expectancy gains as life expectancy gains (figs. 3, 4). This is the case in both regions. If we were to compare Europe and the United States, this finding is starker in the United States because of how poorly gains in healthy-life expectancy track gains in life expectancy there (suppl. table 3).

In terms of the actual magnitude of intervention needed, cancer generally requires less intervention (on a percentage basis) to achieve the same gains as diabetes or heart disease (figs. 3, 4). This driven in part by how prevalent cancer and incident cancer are much more debilitating than diabetes or heart disease (fig. 2). This finding is more striking in Europe than in the United States and may indicate greater trade-offs to consider in Europe.

IV. Discussion

In both Europe and the United States, breakthroughs in prevention would provide more efficient tools in increasing cohort-level life expectancy than breakthroughs in treatment, holding all costs equal. This is clearly seen

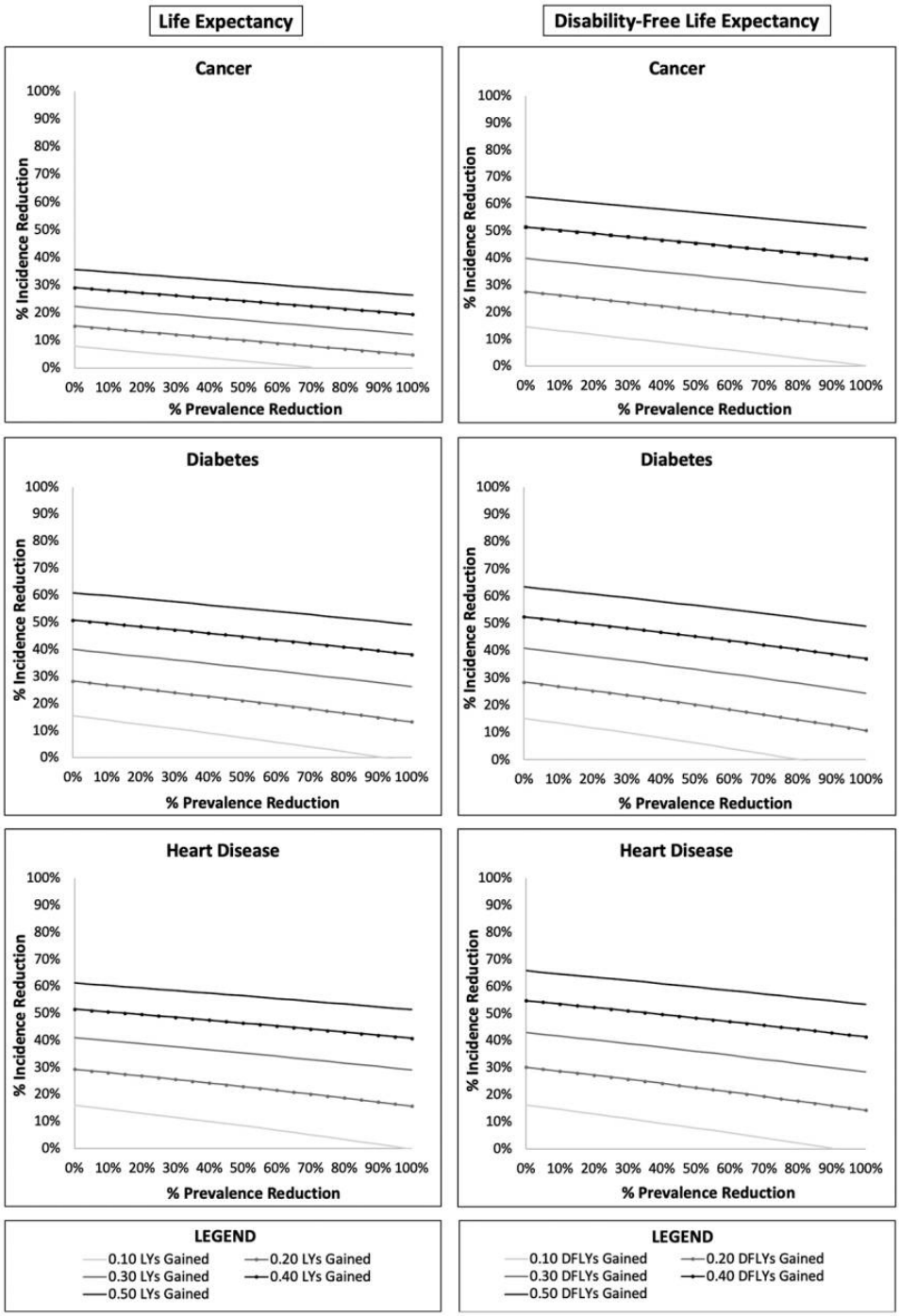

Figure 3.—Europe: production curves that reflect the different combinations of prevalence and incidence reduction required to achieve various cohort-level gains in life expectancy and healthy-life expectancy. LY = life-years. DFLYs = disability-free LYs.

in the production curves, all of which have slopes less than −1—driven by the greater incidence after age 50/51 relative to initial prevalence. In Europe, this is especially the case, as onset of chronic disease occurs later in life there than in the United States. Europe starts from a lower initial prevalence than

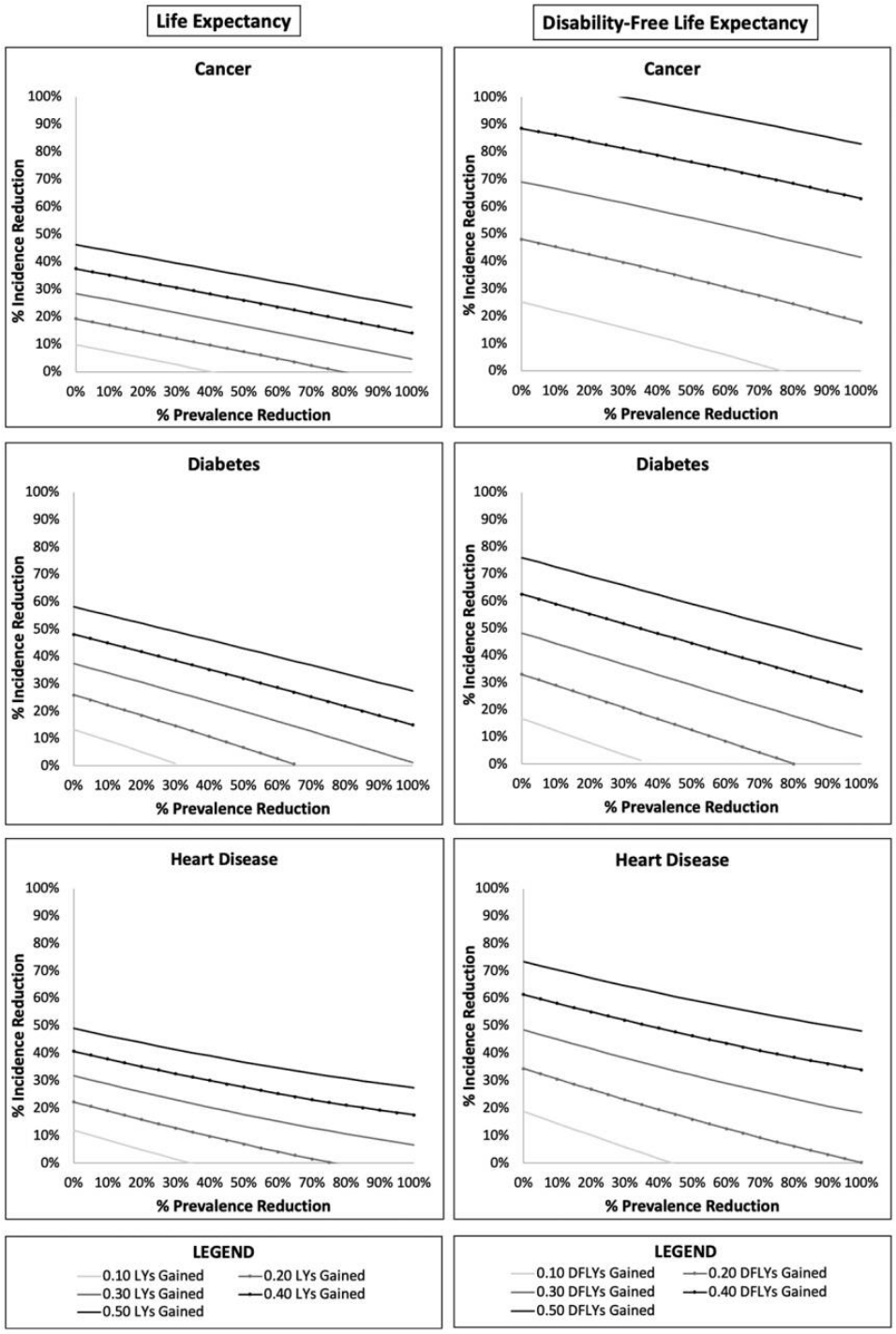

Figure 4.—United States: production curves that reflect the different combinations of prevalence and incidence reduction required to achieve various cohort-level gains in life expectancy and healthy-life expectancy. LY = life-years. DFLYs = disability-free LYs.

the United States but catches up through higher incidence and longer life. As a result, treatments hold stronger value in the United States than they would in Europe. Trends recently identified in Europe suggest that there may be an emerging shift toward earlier onset of chronic disease

(Atella et al. 2017b)—if these trends hold, then production curves in Europe may become more like the production curves in the United States over time and emphasize greater productivity from treatment than they currently do.

The findings we have discussed can provide policy makers and stakeholders an understanding of the trade-offs between investments in treatment and investments in prevention, across the three chronic diseases. Another key component of such decision-making would surely involve the likelihood of such breakthroughs, as well as the investment needed for such breakthroughs. Below, we provide reference points for effectiveness from our production curves and discuss these sets of interventions within the context of historical effect sizes and cost. We choose these reference points on the basis of their ability to increase cohort-level life expectancy by 0.10 LYs, which is similar to the annual gain in e_{45} and e_{51} (life expectancy of individuals aged 45 and 51, respectively) in Europe and the United States. In the European Union, e_{45} increased by 2.75 LYs from 2000 to 2015 (WHO 2018). In the United States, e_{51} increased by 1.9 LYs from 1997 to 2015, according to the Centers for Disease Control and Prevention life tables (CDC 1997–; Beltrán-Sánchez, Soneji, and Crimmins 2015). Through these reference points, we give examples of more extreme interventions (i.e., corner points) as well as more moderate interventions.

In terms of diabetes, we could extend cohort-level life expectancy in Europe by 0.10 LYs by reducing prevalence and incidence, respectively, by 0% and 15.4%, 35.0% and 9.9%, or 95% and 0.0%. In the United States, this might involve reducing prevalence and incidence by 0.0% and 13.4%, 15% and 7.2%, or 30% and 0.0%—which all require less interventional effort when compared to Europe. In diabetes, intensive lifestyle intervention (ILI) and metformin can reduce diabetes incidence by 58% and 31%, respectively, in people at risk for type 2 diabetes (Aroda and Ratner 2018). Metformin's annual cost in the Diabetes Prevention Program (DPP) trial, before patent loss, was approximately $671 per subject (in 2000 dollars; Hernan et al. 2003). In the DPP trial, the cost for ILI was $1,399 per subject in year 1 and $679 per subject in year 2 (in 2000 dollars; Hernan et al. 2003). If similar breakthroughs in diabetes prevention come to fruition in the future, these breakthroughs would exceed the incidence reductions required from our reference points. Treatments for diabetes can include metformin, ILIs, and caloric restriction programs, as well as bariatric surgery. The LookAHEAD (Action for Health in Diabetes) trial found that 11.5% of ILI patients experienced any diabetes remission, compared to just 2% of the control group at the end of year 1, with costs for ILI equating to $2,865 in year 1 and $1,120 in years 5–9 (Gregg et al. 2012; Rushing et al. 2017). The caloric restriction program of the Diabetes Remission Clinical Trial (DiRECT) led to diabetes remission at 2 years in 36% of the treated (vs. 3% in controls) and cost £1,913 in year 1 (Lean et al. 2019; Xin et al. 2019). Bariatric surgery can lead to remission of type 2 diabetes in over

56.7% of procedures in obese patients and can cost from $15,000 to $25,000 or more in the United States (Salem, Jensen, and Flum 2005; Kashyap et al. 2010). Such weight-control interventions, while treating diabetes, may also offer treatment benefits to heart disease and cancer. Breakthroughs like these historical diabetes treatment options may or may not achieve prevalence reduction required from our reference points, but in combination with prevention could achieve a 0.10-LY extension in cohort-level life expectancy.

In terms of heart disease, we could extend cohort-level life expectancy by 0.10 LYs by reducing prevalence and incidence, respectively, by 0% and 15.9%, 35.0% and 10.8%, or 99.0% and 0.0%. In the United States, this might involve reducing prevalence and incidence by 0.0% and 11.9%, 15% and 6.6%, or 34.0% and 0.0%—which all require less interventional effort when compared to Europe as well. In terms of prevention, statins have been shown to reduce the risk of major vascular events by 22% for each 1.0 mmol/L reduction in LDL-C (low-density lipoprotein cholesterol) and cost between $600 and $1,000 per year before patent loss (in 2002 dollars) in subjects with an LDL level of 100–129 mg/dL (Brandle et al. 2003; Baigent et al. 2010). A preventive breakthrough like statins would exceed the incidence reductions required for our reference points. Treatments such as beta blockers have been shown to reduce the combined risk of death or hospitalization because of heart failure by 37% in patients with chronic heart failure (Lechat et al. 1998). The price of branded beta blockers was estimated to be around $600 per year before patent loss (in 1998 dollars) in one costing study (Phillips et al. 2000). Coronary artery bypass grafting in heart failure patients with ischemic cardiomyopathy aged 47–53 can lead to greater reduction in 10-year all-cause mortality than medical therapy alone (hazard ratio: 0.55; 95% confidence interval: 0.43–0.71), and the average price for bypass surgery is estimated to be $151,785 (Giacomino et al. 2016; Petrie et al. 2016). While a breakthrough similar to a statin is highly productive alone, we can offset the need for such an efficacious preventive breakthrough by pursuing treatment as well. Additionally, our analysis of interventional effect by education suggests that innovation in heart disease prevention and treatment could narrow health disparities by education in Europe.

In terms of cancer, we could extend life expectancy by 0.10 LYs by reducing prevalence and incidence, respectively, by 0% and 7.8%, 30.0% and 4.6%, or 70.0% and 0.0%. In the United States, this might involve reducing prevalence and incidence by 0.0% and 10.0%, 15% and 6.3%, or 40.0% and 0.0%. Prevention programs for more prevalent cancers, such as lung cancers, can help reduce cancer incidence. Heavy smokers who quit, which can be seen as a form of lung cancer prevention, had a 39.1% lower risk of lung cancer within 5 years than current smokers, and smoking cessation services can cost approximately $189/18 months (Barnett et al. 2015; Tindle et al. 2018). While smoking prevention reduces lung cancer,

it may offer preventive benefits for diabetes and heart disease, too. An alternative to such programs is implementation of policy-level measures, which could tax and regulate tobacco products. Effective preventive programs for other common cancers, such as breast cancer or colorectal cancer, may be more challenging because of a wider array of causal factors. Treatments for cancer include chemoradiation, checkpoint inhibitors, and cell therapies. Chemoradiation for breast cancer can achieve histologically proven complete remission in 42% of chemoradiation patients and has been estimated to cost $15,877 in the first year (Gerlach et al. 2003; Blumen, Fitch, and Polkus 2016). In non–small-cell lung cancer, 5-year overall survival in patients receiving PD-L1 (programmed death–ligand 1) checkpoint inhibitors has been shown to be 31.9%, while it is 16.3% in chemotherapy patients, with the price of checkpoint inhibitors upward of $100,000–$200,000 a year in the United States (Pietrangelo 2016; Reck et al. 2021). New treatments, such as chimeric antigen receptor T-cell therapies, may offer curative or near-curative options; however, these are very expensive therapies that cost upward of $454,000 (Lyman et al. 2020). Innovations similar to such historical treatments could achieve the prevalence reduction required in our reference points, especially those at the forefront in cures. Additionally, our analysis of interventional effects by education suggests that innovation in cancer prevention could narrow health disparities by education in Europe, while innovation in cancer treatment could narrow health disparities by education in the United States.

We find that in diabetes and heart disease, historical preventive therapies such as metformin and statins have offered effective options in reducing incident disease. Future breakthroughs like these could help break Europe and the United States out of the expensive equilibrium in which we now find ourselves as a result of demographic gains. However, prevention is likely to require broad investments in large populations, with many people requiring preventive investments to prevent a single chronic disease. If older Europeans and Americans at risk for these chronic diseases could be targeted with risk modeling ex ante with perfect prediction and treated with such breakthroughs, this would help negate the societal budget impact and make such a preventive option highly valuable—especially since preventions often can affect more than one condition at the same time. For example, smoking prevention can affect both cancer and chronic obstructive pulmonary disease, and dietary/exercise interventions can affect diabetes, obesity, and heart diseases.

We find that historical treatments for cancer have been shown to be more expensive than those for diabetes and heart disease. This is due in part to the debilitating nature of cancer as well as the challenging nature of the research. Although investments in treatment are more expensive per patient, as they are targeted, they may be cheaper than wider-scale prevention campaigns. Compared to cancer, we see there have been much cheaper historical treatment options in diabetes and heart disease, such as caloric restriction programs and beta blockers, which have offered meaningful

gains in reducing prevalence and for a larger number of individuals. If a new wave of such breakthroughs came to fruition in diabetes and heart disease, they would allow much more targeted effort than prevention, and possibly at a cost that can be more easily shouldered.

Limitations.—There are several limitations in our analysis. This is a simulation model, and typical limitations for simulations apply, such as our assumption of no changes in the underlying parameters that govern health-related behavior, should breakthrough medical therapies come to fruition.

In our population-level analyses, we reduce incidence of chronic disease among those developing disease after age 50/51, and we reduce prevalence of chronic disease at age 50/51. However, in the latter we do not eliminate future incidence, as we provide only a one-time shock. We also treat chronic disease intervention independently in this study, rather than evaluating an array of combined interventions.

Additionally, extending life expectancy in older adults would appreciably increase entitlement expenses for governments, such as health and pension expenditure in both Europe and the United States. However, past research has suggested that changes in regulatory policies, such as raising the age of Medicare eligibility in the United States and the typical retirement age for Social Security, could help neutralize these costs, which is corroborated by several pension reforms adopted in Europe in the past 2 decades. Additionally, by extending life expectancy and healthy-life expectancy, these longer-living older adults can contribute longer economically to society to help fund these expenses. A previous study has estimated the economic value of delayed aging in the United States to be $7.1 trillion over 50 years, which sits at the bottom end of the spectrum for our analyses, since we explore perfect prevention, rather than a delay in aging, and evaluate the more encompassing burden of disease (Goldman et al. 2013).

V. Conclusions

Biomedical breakthroughs in treating or preventing these chronic diseases may provide an opportunity to extend both life expectancy and quality of life at older ages. We find that while cancer generally requires less treatment and prevention than diabetes or heart disease to achieve the same gains in life expectancy, it offers proportionately less extension in healthy-life expectancy. Diabetes can offer gains in longevity that track well with gains in healthy-life expectancy, which in Europe, in particular, can also offer a compression of morbidity. A look at historical treatment effectiveness and costs may shine light on which treatment and prevention investments offer the best value for society. Regardless of prioritization, we see that investments in both treatments (or even possible cures) and preventions for these three illnesses show tremendous promise for breaking Europe and the United States out of the expensive equilibrium in which we now find ourselves as a result of demographic gains.

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Supplemental Table 1. Remaining Life Expectancy and Healthy Life Expectancy in the Overall Europe and United States Populations, in the Base Case

	Mean Remaining LYs				Mean Remaining DFLYs			
Population	All	Less than High School Education	High School Graduates	Some College Education or More	All	Less than High School Education	High School Graduates	Some College Education or More
Europe	35.0	34.8	34.3	37.0	28.9	28.3	28.1	32.0
United States	31.1	26.4	29.6	32.6	23.3	15.7	22.0	25.3

Note. – LYs = life-year; DFLYs = disability-free life-years. Estimates for the Europe cohort pertain to subjects entering at age 50-51 in the 2009 SHARE data, and estimates for the United States cohort pertain to subjects entering at age 51-52 in the 2010 HRS data.

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Supplemental Table 2. Gains in Mean LYs and DFLYs from Older Age Prevalence Reduction among the Prevalent and Incidence Reduction among the Incident

Europe	Intervention	LYs Gained			DFLYs Gained		
		Cancer	Diabetes	Heart Disease	Cancer	Diabetes	Heart Disease
Prevalence Reduction (among those with disease at model entry)	0%	0.0	0.0	0.0	0.0	0.0	0.0
	10%	0.5	0.2	0.2	0.3	0.3	0.2
	20%	1.0	0.4	0.4	0.7	0.4	0.5
	30%	1.7	0.6	0.6	1.3	0.7	0.7
	40%	2.3	0.8	0.8	1.8	1.0	0.9
	50%	3.0	1.2	1.0	2.2	1.3	1.2
	60%	3.4	1.5	1.3	2.5	1.6	1.4
	70%	4.1	1.8	1.5	3.0	2.0	1.7
	80%	4.8	2.0	1.7	3.5	2.3	1.9
	90%	5.3	2.1	2.0	3.8	2.5	2.1
	100%	5.8	2.4	2.1	4.3	2.7	2.4
Incidence Reduction (among those developing disease after model entry)	0%	0.0	0.0	0.0	0.0	0.0	0.0
	10%	0.3	0.1	0.1	0.2	0.1	0.1
	20%	0.7	0.3	0.2	0.4	0.3	0.2
	30%	1.0	0.4	0.3	0.6	0.5	0.3
	40%	1.4	0.6	0.5	0.7	0.6	0.5
	50%	1.8	0.8	0.6	1.0	0.8	0.6
	60%	2.2	1.0	0.8	1.2	1.0	0.7
	70%	2.7	1.3	1.0	1.4	1.2	0.9
	80%	3.1	1.5	1.2	1.7	1.4	1.0
	90%	3.6	1.7	1.4	1.9	1.6	1.2
	100%	4.1	2.0	1.6	2.2	1.8	1.4

United States	Intervention	LYs Gained			DFLYs Gained		
		Cancer	Diabetes	Heart Disease	Cancer	Diabetes	Heart Disease
Prevalence Reduction (among those with disease at model entry)	0%	0.0	0.0	0.0	0.0	0.0	0.0
	10%	0.3	0.3	0.3	0.2	0.3	0.2
	20%	1.0	0.5	0.6	0.5	0.5	0.5
	30%	1.3	0.7	0.9	0.6	0.6	0.8
	40%	1.8	1.0	1.3	0.9	0.9	1.0
	50%	2.2	1.3	1.6	1.1	1.1	1.3
	60%	2.6	1.5	2.0	1.3	1.3	1.6
	70%	3.2	1.7	2.2	1.6	1.5	1.8
	80%	3.6	1.9	2.4	1.8	1.6	1.9
	90%	4.1	2.1	2.6	2.1	1.8	2.1
	100%	4.4	2.4	2.8	2.3	2.0	2.3
Incidence Reduction (among those developing disease after model entry)	0%	0.0	0.0	0.0	0.0	0.0	0.0
	10%	0.3	0.2	0.2	0.1	0.1	0.1
	20%	0.6	0.4	0.4	0.2	0.3	0.2
	30%	0.9	0.6	0.5	0.3	0.4	0.3
	40%	1.3	0.8	0.8	0.5	0.6	0.5
	50%	1.6	1.0	1.0	0.6	0.7	0.6
	60%	1.9	1.2	1.2	0.7	0.9	0.8
	70%	2.3	1.5	1.5	0.9	1.1	0.9
	80%	2.6	1.8	1.8	1.0	1.3	1.1
	90%	3.0	2.0	2.0	1.2	1.4	1.2
	100%	3.4	2.4	2.4	1.3	1.6	1.4

Note: LYs = life-years. DFLYs = disability-free life-years.

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Supplemental Table 3. Ratio of the Burden in Disability-Free Life-Years to the Burden in Life-Years, from Disease at Age 50/51 and from Disease After Age 50/51

	Europe		United States	
	Burden from Disease at Age 50/51	Burden from Disease after Age 50/51	Burden from Disease at Age 50/51	Burden from Disease after Age 50/51
Cancer	0.73	0.53	0.51	0.40
Diabetes	1.14	0.93	0.85	0.70
Heart Disease	1.11	0.87	0.83	0.61

Supplemental Table 4. Gain in Mean LY and DFLYs from Older Age 100% Prevalence Reduction for the Treatment-on-the-Treated Populations, by Education

Europe								
	Mean Net LYs				Mean Net DFLYs			
Chronic Disease Intervened on	All	Less than High School Education	High School Graduates	Some College Education or More	All	Less than High School Education	High School Graduates	Some College Education or More
Cancer	5.8	5.5	5.8	6.0	4.3	3.8	4.2	4.6
Diabetes	2.4	2.3	2.4	2.2	2.7	2.9	2.7	2.6
Heart Disease	2.1	2.0	2.3	1.6	2.4	2.4	2.5	1.8
United States								
	Mean Net LYs				Mean Net DFLYs			
Chronic Disease Intervened on	All	Less than High School Education	High School Graduates	Some College Education or More	All	Less than High School Education	High School Graduates	Some College Education or More
Cancer	4.4	5.3	3.5	4.6	2.2	2.2	1.6	2.4
Diabetes	2.4	1.9	2.5	2.6	2.0	1.7	2.0	2.2
Heart Disease	2.8	2.5	2.9	2.7	2.3	1.7	2.5	2.2

Note. – LYs = life-years; DFLYs = disability-free life-years.

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Supplemental Table 5. Gain in Mean LY and DFLYs from Older Age 100% Incidence Reduction for the Treatment-on-the-Treated Populations, by Education

Europe								
	Mean Net LYs				Mean Net DFLYs			
Chronic Disease Intervened on	All	Less than High School Education	High School Graduates	Some College Education or More	All	Less than High School Education	High School Graduates	Some College Education or More
Cancer	4.1	5.3	4.1	4.2	2.2	2.2	2.1	2.4
Diabetes	1.9	1.9	1.9	1.8	1.8	1.7	1.8	1.8
Heart Disease	1.6	2.5	1.6	1.4	1.4	1.7	1.4	1.3
United States								
	Mean Net LYs				Mean Net DFLYs			
Chronic Disease Intervened on	All	Less than High School Education	High School Graduates	Some College Education or More	All	Less than High School Education	High School Graduates	Some College Education or More
Cancer	3.4	3.0	3.2	3.5	1.3	0.9	1.3	1.4
Diabetes	2.3	1.9	2.4	2.4	1.6	1.5	1.5	1.7
Heart Disease	2.3	2.3	2.3	2.4	1.4	1.1	1.4	1.5

Note. – LYs = life-years; DFLYs = disability-free life-years.

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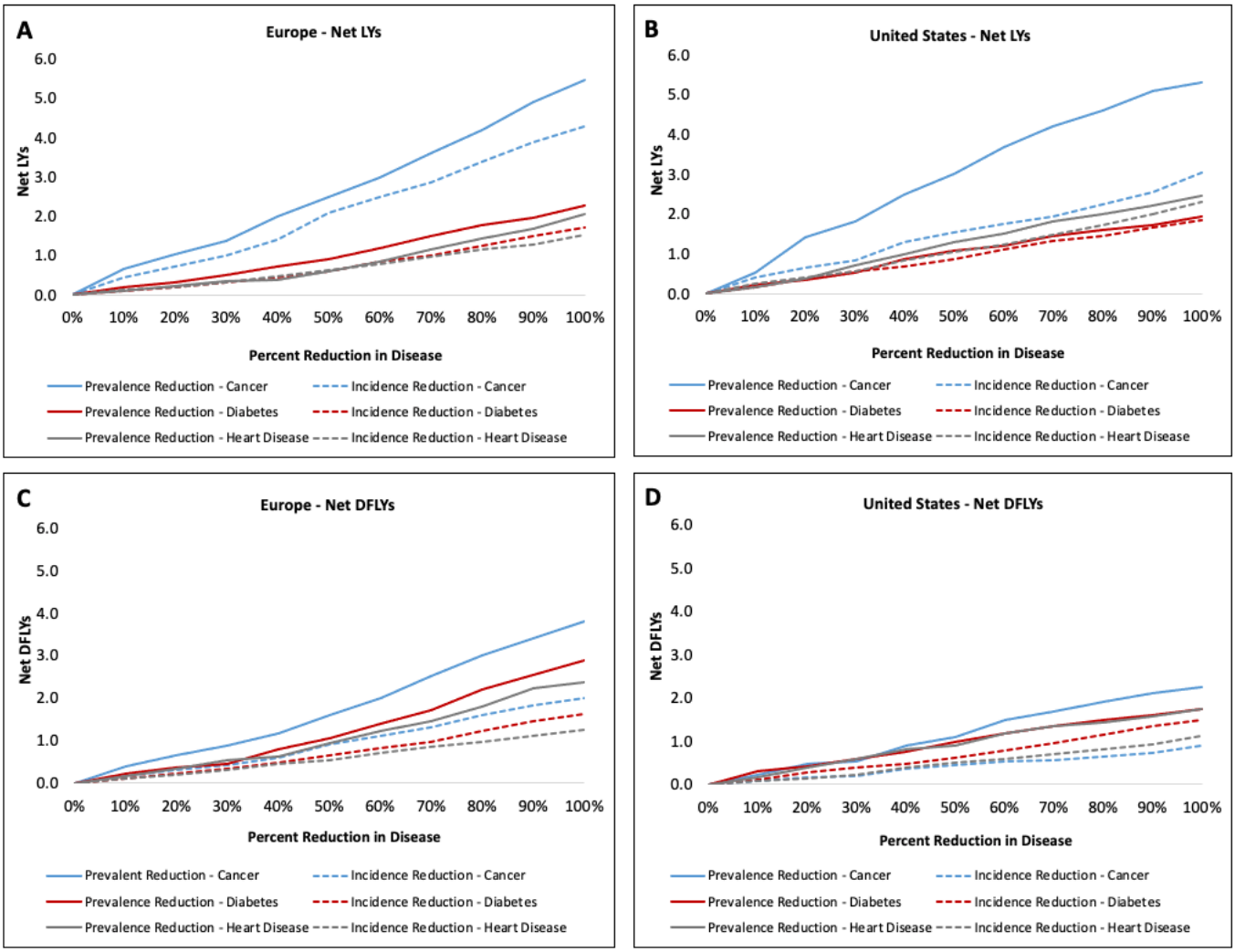
Supplemental Figure 1

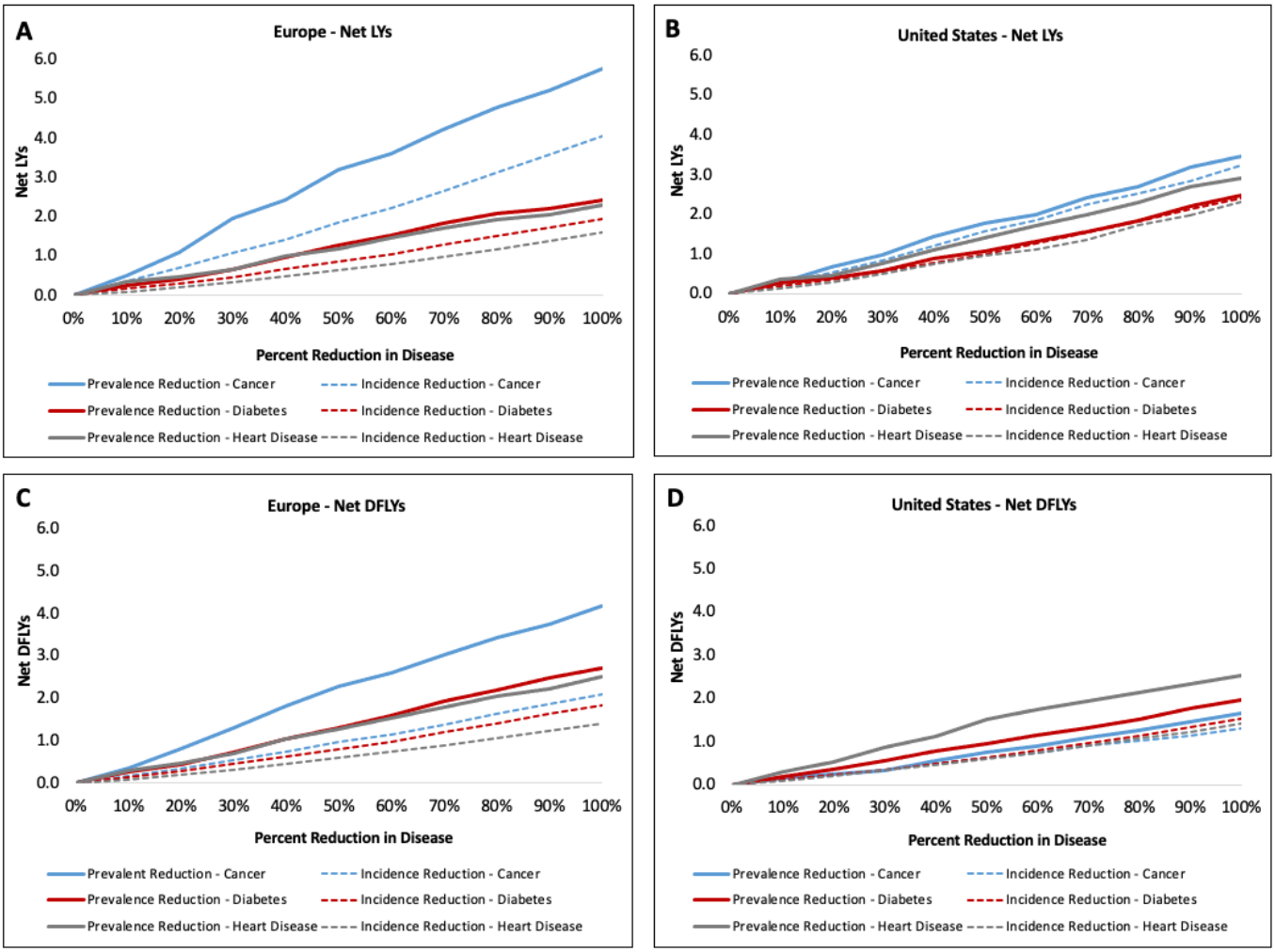
Gains in Mean LYs and DFLYs from Older Age Prevalence Reduction among the Prevalent and Incidence Reduction among the Incident, among those with Less than High School Education



Note. – LY = life-years. DFLYs = disability-free life-years.

Supplemental Figure 2

Gains in Mean LYs and DFLYs from Older Age Prevalence Reduction among the Prevalent and Incidence Reduction among the Incident, among High School Graduates



Note. – LY = life-years. DFLYs = disability-free life-years.

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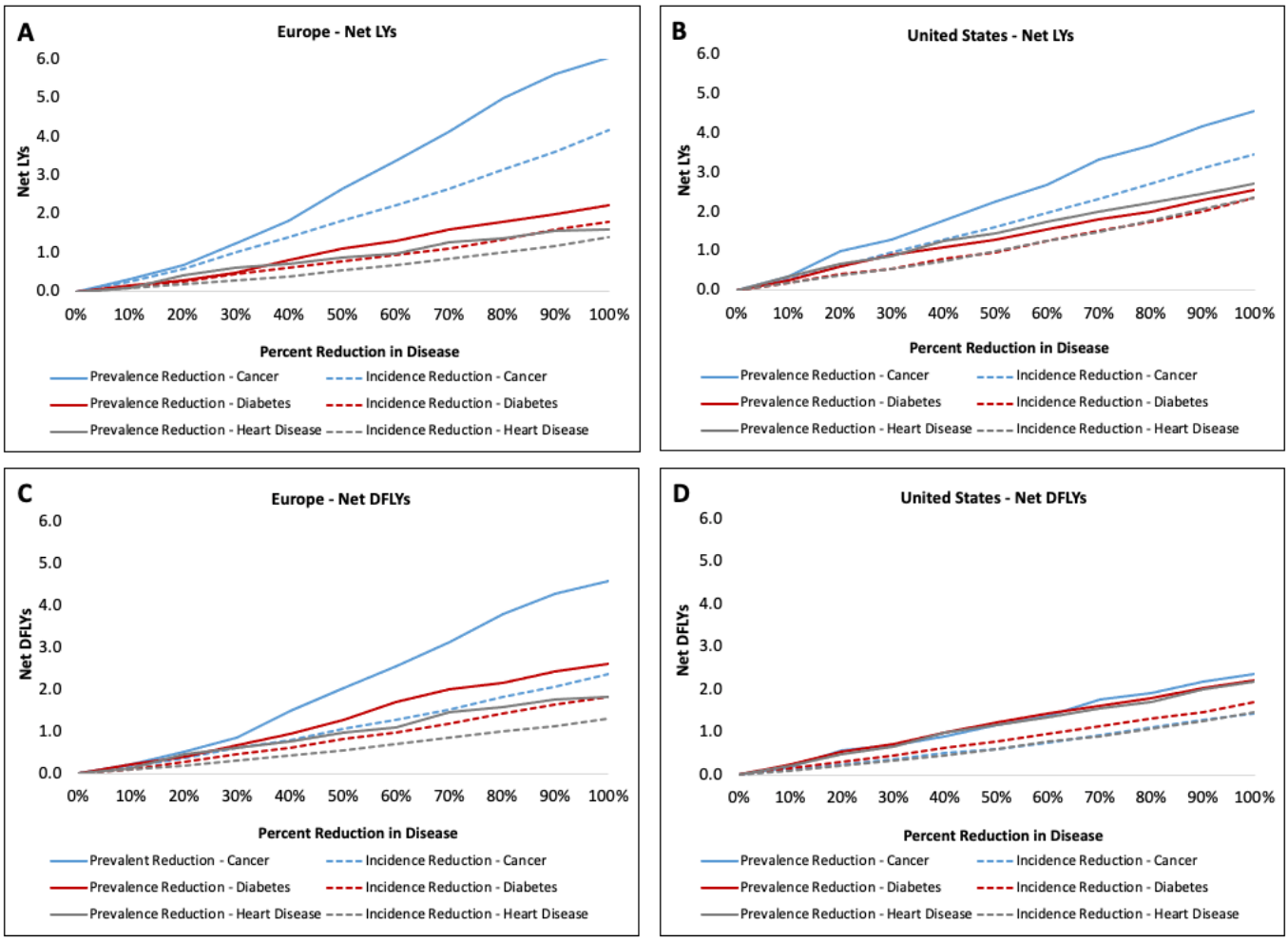
Supplemental Figure 3

Gains in Mean LYs and DFLYs from Older Age Prevalence Reduction among the Prevalent and Incidence Reduction among the Incident, among those with Some College Education or More



Note. – LY = life-years. DFLYs = disability-free life-years.