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ABSTRACT

GLP-1 therapies for obesity promise substantial health improvements, but little is known about how their benefits vary across socioeconomic and demographic groups. Using a nationally representative microsimulation model of US adults and Shapely-value decomposition, we estimate the lifetime health and economic benefits of GLP-1 treatment and examine how those gains vary across individuals. The largest differences emerge across education. Individuals with less than a high school education experience experience roughly 14% higher gains in lifetime net social value, 16-17% larger improvements in discounted generalized risk- and severity-adjusted life-years (GRASA-QALYs), and 20% greater increases in life expectancy relative to the cohort mean, whereas individuals with college degrees experience gains 15-27% below the mean across these outcomes. Black and Hispanic individuals also tend to experience larger improvements in health outcomes and social value than White individuals, including larger gains in GRASA-QALYs and life expectancy and larger reductions in diabetes risk and duration. Females likewise experience larger predicted treatment gains than men. These patterns are consistent with the idea that the largest gains arise among populations facing greater socioeconomic constraints in sustaining behavioral weight control. GLP-1 innovation may therefore mitigate inequality in obesity-related disease and survival, advancing equity in population health.

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Introduction

The recent emergence of glucagon-like peptide-1 (GLP-1) receptor agonists has transformed the treatment landscape for obesity and metabolic disease. Clinical trials, real-world studies, and population modeling analyses consistently show that these therapies can produce substantial and sustained weight loss and reduce risks of major cardiometabolic conditions, including diabetes and cardiovascular disease (1–4). At the population level, obesity remains one of the most pressing public health challenges in the United States, affecting more than 40% of adults and contributing hundreds of billions of dollars in annual medical spending (5). Because excess weight is strongly associated with chronic diseases that drive long-term healthcare costs and mortality, effective pharmacological treatment has the potential to generate large lifetime health and economic gains (6).

Emerging real-world evidence also suggests that the diffusion of GLP-1 therapies is already reshaping treatment patterns in obesity care, while raising important questions about who ultimately receives and benefits from these treatments (7). The societal stakes of this innovation are substantial. GLP-1 therapies have been shown to produce large and sustained reductions in body weight and improve a range of cardiometabolic outcomes, including diabetes and cardiovascular disease. At the population level, these effects can translate into gains of nearly two years of life and more than five fewer years of chronic illness among younger adults, with corresponding improvements in population health and meaningful economic value (5,8–11).

Despite the magnitude of these potential gains, a central question remains largely unanswered: who stands to benefit the most from these therapies if insurers covered them for clinically eligible individuals? Most existing studies focus on average treatment effects, clinical efficacy within selected populations, or short-term weight loss outcomes. Much less is known about how the long-term real-world benefits of GLP-1 therapy vary across clinically eligible individuals with different demographic, socioeconomic, and health characteristics. Understanding this heterogeneity is crucial for evaluating the broader societal impact of these drugs and for informing policy decisions related to coverage, targeting, and value assessment.

To address this question, we combine a nationally representative, empirically calibrated health microsimulation model of the U.S. adult population with a decomposition framework designed to uncover the drivers of individual-level treatment benefits. The simulation generates counterfactual lifetime trajectories of health, disease incidence, survival, and economic outcomes with and without the weight loss that would be generated by GLP-1 treatment. As shorthand, we refer to this for the balance of the paper as “medically induced weight loss.” We then apply a Shapley-value decomposition that quantifies how each individual’s baseline characteristics determine the benefits that accrue from medically induced weight loss. Rather than simply identifying which individuals would benefit the most, this approach quantifies how different characteristics contribute to the realized benefits of treatment, allowing us to identify which factors structure the distribution of gains across outcomes such as life expectancy, quality-adjusted life years, medical spending, disease incidence, and disease-specific person-years. We do not attempt to model the trajectory of weight-loss medication costs, both because substantial price changes over time complicate this enterprise and because we focus on how benefits would vary across the population if these drugs were made available to all eligible individuals via broad insurance access (12).

We find substantial heterogeneity in the distribution of benefits. While baseline metabolic risk remains an important determinant of gains, socioeconomic characteristics also play a central role. In particular, individuals who have attained less education and who belong to historically disadvantaged populations experience larger improvements in health outcomes and social value relative to more advantaged groups, consistent with evidence that disadvantaged populations — including Black, Hispanic, and female individuals—often face greater challenges in achieving and

sustaining weight loss in behavioral interventions (13–15). These patterns are consistent with prior work showing that medical innovations can either increase or decrease disparities depending on their complexity and the extent to which they rely on patient behaviors (16).

One interpretation of these patterns is provided by the economics of health production. In the canonical health-capital framework, individuals generate health through a combination of medical care, time, and behavioral inputs, with education increasing the efficiency with which these inputs are transformed into health (17). A large empirical literature documents that more educated individuals are typically better able to adhere to treatment regimens, process health information, and sustain complex health behaviors, generating persistent socioeconomic gradients in health outcomes (18–22). Because weight management traditionally depends heavily on sustained behavioral self-management, these behavioral inputs can be costly to sustain, particularly in environments characterized by time constraints, stress, and facing greater economic constraints, including limited access to healthy food environments. Individuals with greater human capital may be better positioned to produce health through these behavioral inputs. By directly modifying physiological pathways that regulate appetite and metabolism, GLP-1 therapies reduce reliance on these behavioral mechanisms. In this sense, biomedical innovation may partially substitute for self-management capital, attenuating the role of human capital in the health production process and disproportionately benefiting groups with lower human capital levels (16).

Results

Lifetime Health and Economic Effects of GLP-1 Therapy

We first examine simulated lifetime outcomes for adults aged 40–50 at baseline, the age group with the highest observed uptake of GLP-1 therapy and the point at which individuals become eligible for treatment in our model. In this cohort, medically induced weight loss generates substantial lifetime health and economic gains relative to the status quo. The mean treatment effect on lifetime net social value (monetized discounted risk- and severity-adjusted QALYs (GRASA-QALYs) plus lifetime medical and disability cost savings) is $192,735. Discounted lifetime GRASA-QALYs increase by 1.195. Mean survival rises by 1.38 life-years. Discounted lifetime medical spending falls by $12,120 per person. For diabetes, the mean treatment effect reduces the probability of ever developing the disease by 15 percentage points (pp) and averts 3.53 years of disease per person. For hypertension, incidence declines by 5.4 pp and cumulative disease duration by 1.75 years per person. For heart disease, incidence declines by 3.6 pp with 0.73 years per person averted. Disability incidence, defined as the presence of any limitation in activities of daily living (ADLs) or instrumental activities of daily living (IADLs), declines by 0.8 pp and disabled years per person decline by 0.983. These magnitudes are comparable to prior modeling studies reporting lifetime gains of a similar order across QALYs, survival, and disease risk reductions (8–10).

Distribution of Lifetime Health and Economic Benefits

Although average effects are large, the benefits of medically induced weight loss vary sharply across individuals, with the greatest health gains and cost reductions concentrated in identifiable subgroups—this heterogeneity is the central focus of the study. We focus our presentation on how outcomes vary across the following baseline characteristics: race and ethnicity, sex, educational attainment, baseline BMI, and baseline age. These characteristics account for the largest shifts in predicted benefits relative to the cohort mean and therefore anchor the heterogeneity analysis that follows. Table 1 summarizes the direction of these gradients across outcomes. These distributional patterns are illustrated in Figures 1–6, where for each outcome we present predicted individual-level treatment effects separately for binary and continuous baseline characteristics. Each figure displays the predicted individual-level treatment effect decomposed into the cohort mean and the additive SHAP contribution of a focal baseline characteristic. The vertical axis therefore reflects how that characteristic shifts the predicted lifetime gain relative to the cohort average. For binary variables, color indicates baseline status (0/1); for continuous variables, color represents the

baseline value (e.g., BMI, age, or education level), facilitating visual identification of gradients and clustering across the distribution. The horizontal dashed line marks the cohort's mean lifetime treatment effect; points above or below that line represent larger or smaller predicted gains relative to the cohort average. The overlaid boxplot summarizes the distribution of predicted treatment effects, with the box indicating the interquartile range and the median.

Education Attainment

Educational attainment exhibits a clear monotonic gradient in the benefits of medically induced weight loss: as education increases, the estimated treatment effect declines. Individuals with less than a high school education consistently experience larger predicted gains than those with a college degree or higher (Table 1).

For lifetime net social value (Fig. 1), the cohort mean treatment effect is $192,735. Individuals with less than a high school education reach roughly $219,000–$220,000 (≈ 14% above the mean), whereas those with a college degree or higher fall to approximately $163,000 (≈ 15.4% below the mean). A similar gradient appears for discounted GRASA-QALYs (Fig. 2), where the cohort mean gain is 1.195. Individuals with less than a high school education reach roughly 1.39–1.40 GRASA-QALYs gained (≈ 16.3–17.2% above the mean), while those with a college degree or higher fall to approximately 0.99 (≈ 17.2% below). For life-years gained (Fig. 3), the cohort mean is 1.38 years. Individuals with less than a high school education reach roughly 1.65–1.66 years (≈ 20% above the mean), whereas those with a college degree or higher fall to approximately 1.01 years (≈ 26.8% below). In contrast to other outcomes, reductions in discounted lifetime medical spending (excluding treatment costs) are larger among individuals with higher educational attainment (Fig 4).

The same pattern appears for diabetes incidence (Fig. 5): relative to the cohort mean reduction of 15 percentage points, individuals with less than a high school education experience roughly ≈8% larger reductions, whereas those with a college degree or higher show ≈12% smaller reductions.

Education differences persist across the remaining outcomes (Appendix A, Figs. A1–A7). Larger long-run BMI reductions remain concentrated among lower-educated groups. For other outcomes, gradients are generally smaller, though higher-educated groups experience somewhat larger reductions in hypertension and heart disease person-years, and disability incidence.

Race and Ethnicity

All racial and ethnic subgroups experience positive lifetime benefits of medically induced weight loss, but Hispanic individuals frequently occupy the upper tail of predicted gains, Black individuals are above the cohort mean, and White individuals more often fall at or below the mean (Table 1).

For lifetime net social value (Fig. 1), the cohort mean treatment effect is $192,735. Hispanic individuals occupy an upper tail around $210k, approximately $17,265 above the cohort mean (≈9% higher), while Black individuals reach roughly $200k (≈4% above the mean). In contrast, White individuals cluster as low as $175k, about $17,735 below the mean (≈9% lower).

This pattern is similar for discounted GRASA-QALYs (Fig. 2), where the cohort mean gain is 1.195; Black and Hispanic individuals reach approximately 1.28 GRASA-QALYs gained (≈7% above the mean), and White individuals fall to roughly 1.15 (≈3.9% below). For life-years gained (Fig. 3), the cohort mean is 1.38 years; Black individuals reach approximately 1.52 years (≈10% above the mean), Hispanic individuals show modest gains above the cohort average, and White individuals decline to roughly 1.30 years (≈5.7% below).

These patterns extend across economic and clinical outcomes. Discounted lifetime medical spending (excluding treatment costs) (Fig. 4) shows a mean reduction of −$12,120; Hispanic individuals exhibit savings approaching −$22,000, representing roughly 82% greater savings than

the cohort mean reduction, whereas Black individuals cluster near −$11,000 (≈9.2% smaller savings than average) and White individuals exhibit smaller savings than the cohort mean.

For diabetes incidence (Fig. 5), the cohort mean reduction is 15 pp; Hispanic individuals reach approximately 17 points (≈13.3% larger reduction), Black individuals also experience reductions above the cohort mean, though smaller than those of Hispanic individuals, and White individuals cluster around 14 points (≈6.7% smaller reduction). Finally, for diabetes person-years averted (Fig. 6), the mean reduction is 3.53 person-years; Hispanic individuals reach roughly −4.7 person-years (≈33% greater reduction than the mean), Black individuals remain near average (≈−3.6), and White individuals cluster around −3.4 (≈3.7% smaller reduction).

Racial and ethnic differences persist across the remaining outcomes (Appendix A, Figs. A1–A7). Larger long-run BMI reductions are concentrated among Black individuals, while Hispanic individuals generally experience reductions close to the cohort average. For hypertension, the largest improvements occur among Hispanic individuals, who exhibit the greatest reductions in both incidence and cumulative duration of disease per person. For heart disease, gains are again concentrated among minority populations, with Black and Hispanic individuals experiencing larger reductions in incidence and Hispanic individuals the largest reductions in cumulative duration of disease per person. For disability, patterns are more mixed, but improvements remain concentrated among minority groups, including larger reductions in disability incidence among Black individuals and greater cumulative disability person-years averted among Hispanic individuals.

Sex

Both females and males experience positive lifetime benefits of medically induced weight loss relative to the status quo; however, a consistent sex gradient emerges, with females experiencing larger gains across most outcomes (Table 1).

For lifetime net social value (Fig. 1), the cohort mean treatment effect is $192,735. Females reach approximately $218,000, roughly $26,000 above the cohort mean (≈13% higher), whereas men cluster near $170,000, about $22,000 below the mean (≈12% lower). A similar pattern appears for gains in discounted GRASA-QALYs (Fig. 2), where the cohort mean gain is 1.195. Females reach approximately 1.35–1.40 GRASA-QALYs gained (≈13–17% above the mean), while men cluster near 1.10 (≈8% below). For life-years gained (Fig. 3), the cohort mean is 1.38 years. Females reach roughly 1.50–1.55 years (≈9–12% above the mean), whereas men cluster around 1.25 years (≈9% below).

Discounted lifetime medical spending (Fig. 4) shows a mean reduction of −$12,120. Females generate savings of roughly −$13,500 (≈10–12% greater savings than the mean), while men cluster around −$11,500 (≈5% smaller savings than average). For diabetes incidence (Fig. 5), the cohort mean reduction is 15 pp. Females reach approximately 15.5–16 pp (≈3–7% larger reduction), whereas men cluster closer to 14 pp (≈7% smaller reduction), although there is some overlap in the distribution. Finally, for diabetes person-years averted (Fig. 6), differences around the cohort mean are smaller and mixed.

Sex differences persist across the remaining outcomes (Appendix A, Figs. A1–A7). Females exhibit larger long-run BMI reductions than the cohort average, whereas men show smaller sustained weight loss. For hypertension, men tend to experience slightly larger reductions in both incidence and cumulative person-years. For heart disease, females show slightly larger reductions in incidence and cumulative person-years. For disability, patterns are clearer. Females experience

substantially larger cumulative disability person-years averted, whereas men tend to show larger reductions in disability incidence.

Baseline BMI and Age
Differences arise in the magnitude of lifetime benefits of medically induced weight loss by baseline BMI and baseline age, as shown in Figs. 1–6. Higher baseline BMI is associated with larger lifetime net social value, greater discounted GRASA-QALY and life-year gains, and smaller reductions in lifetime medical spending. In contrast, lower baseline BMI is associated with larger reductions in diabetes incidence and cumulative years of diabetes per person. Baseline age also shapes the magnitude of gains: individuals who enter the treatment scenario at younger ages accrue larger lifetime net social value, survival gains, GRASA-QALY gains, spending reductions, and diabetes prevention. Results for additional outcomes are presented in Appendix A (Figs. A1–A7).

Larger Gains with Earlier Initiation
The same distributional structure persists in the younger simulated cohorts (See Appendices B and C). However, the mean lifetime effects increase when GLP-1 therapy is introduced earlier in adulthood. Mean lifetime net social value rises from $192,735 in the 40–50 cohort to $209,039 in the 30–40 cohort and $270,800 in the 25–30 cohort. Discounted GRASA-QALY gains increase from 1.20 to 1.28 and 1.63, respectively, while life-years gained rise from 1.38 to 1.68 and 2.38. Mean discounted lifetime medical spending reductions grow in magnitude from −$12,120 to −$15,994 and −$23,027. Diabetes incidence reductions also increase modestly across cohorts (−15%, −15%, and −17%), while diabetes person-years averted expand substantially in absolute terms (−3.53, −3.93, and −5.04).

Discussion

Weight loss due to potential use of GLP-1 receptor agonists generates substantial lifetime gains in survival, quality-adjusted life years, and reductions in chronic disease (1,4,23). However, the central contribution of this study lies not in the magnitude of these average effects, but in their structure. Because the central contribution of the study concerns the relative distribution of benefits across groups, uniform reductions in treatment persistence or effectiveness would primarily shift the overall level of benefits rather than materially alter the distributional patterns. Indeed, varying the magnitude of weight loss (e.g., 10–30%) changes the magnitude of the average effects but leaves the relative distribution across groups largely unchanged. The weight-loss benefits of GLP-1 therapy are distributed systematically and unequally across baseline characteristics. Individuals with lower educational attainment experience larger lifetime health benefits and greater improvements in net social value relative to more highly educated groups. Several historically disadvantaged racial and ethnic populations likewise cluster at or above the cohort mean in predicted gains across multiple outcomes. In contrast, more advantaged groups more often experience gains at or below the average. These patterns indicate that the distributional consequences of this biomedical innovation differ in important ways from many prior health technologies, which have frequently widened socioeconomic gradients in health (16,19,24).

Health outcomes often reflect the interaction of biological processes and behavioral inputs (25–27). Medically induced weight loss —such as that achieved with GLP-1 therapies— acts directly on biological pathways regulating appetite and metabolism, thereby reducing reliance on sustained behavioral self-management (28). In the canonical economic health-capital framework, individuals produce health using a combination of medical care, time, and behavioral inputs, with education increasing the efficiency with which those inputs are transformed into durable health improvements (17,29). A large empirical literature documents that more educated individuals are typically better able to adhere to treatment regimens, process health information, and sustain complex health behaviors, generating persistent socioeconomic gradients in health outcomes (18,20,21). Because weight management traditionally depends heavily on sustained behavioral

self-management, individuals with greater human capital may be better positioned to produce health through these behavioral inputs (18). By directly modifying physiological pathways that regulate appetite and metabolism, medically induced weight loss reduces reliance on these behavioral mechanisms (1,2). In doing so, pharmaceutical treatments partially substitute for inputs that are more efficiently deployed by individuals with greater educational and socioeconomic resources (16,24).

This substitution mechanism has broader implications for health equity. Health innovations differ in the extent to which they require information processing, sustained self-regulation, and complex adherence (18,24). Technologies that depend heavily on such inputs may amplify existing gradients in education, income, and health literacy, thereby widening inequality even when average outcomes improve (16,19). In contrast, innovations that act more directly on biological processes—reducing dependence on behavioral or informational capital—may compress disparities in realized lifetime health gains. The present results suggest that, under conditions of broad access, weight loss achieved through GLP-1 therapies falls closer to this latter class. As delivery options evolve, including the oral formulations and less frequent dosing, the behavioral burden of treatment may decline, further reinforcing this shift toward biological rather than behavioral determinants of health (30). Larger predicted gains among lower-education groups and several disadvantaged populations imply that the technology has the potential to attenuate, rather than exacerbate, long-standing socioeconomic gradients in obesity-related disease and survival. In this sense, biomedical innovation may partially substitute for self-management capital, attenuating the role of human capital in the health production process.

Importantly, these findings concern the distribution of health gains conditional on access, not patterns of uptake or diffusion. Historically, early access to medical innovation has often been concentrated among more advantaged groups, contributing to widening disparities (7,19,31). Our results suggest that, under broad access, the intrinsic structure of GLP-1–mediated weight loss does not inherently favor advantaged populations. Instead, larger marginal improvements emerge where baseline risk and behavioral constraints are greater, implying that the equity effects of innovation depend not only on who receives a technology first, but on how it interacts with the health production process (18,24).

Methodologically, this study provides a framework for identifying the drivers of heterogeneity in lifetime treatment effects. By integrating a nationally representative microsimulation model with Shapley-value decomposition, we decompose individual treatment gains into additive contributions from baseline characteristics (32–34). This approach moves beyond subgroup averages to quantify how traits such as education, race and ethnicity, baseline BMI, and age shift outcomes within the overall distribution of treatment gains, offering a tractable strategy for interpreting high-dimensional heterogeneity.

Several limitations merit consideration. First, projections rely on assumptions regarding the durability of weight loss and treatment adherence over extended horizons. Although grounded in clinical evidence, long-run real-world persistence remains uncertain, and empirical evidence on adherence patterns, particularly across socioeconomic groups, is limited given the recent diffusion of these therapies. Accordingly, the analysis focuses on the distribution of treatment effects under sustained use, providing a characterization of potential benefits under continued therapy. Second, the analysis models clinically eligible populations under broad treatment uptake and therefore does not incorporate real-world barriers to access that may influence who receives treatment and, in turn, the realized distribution of benefits. At the same time, the treatment landscape is evolving rapidly, including changes in pricing, expanding coverage, and the development of alternative formulations, which are likely to expand access over time (35). Third, the Shapley decomposition characterizes how observed baseline traits structure variation in simulated treatment effects; it does not establish causal effects of those traits.

Biomedical innovation is often evaluated in terms of average efficacy or aggregate cost-effectiveness. Our findings underscore the importance of examining how new technologies reshape the distribution of health gains across populations. If certain innovations substitute for behavioral or informational capital, they may alter the longstanding relationship between socioeconomic status and health (18,24). Understanding whether and how emerging therapies compress or widen health gradients is therefore central to assessing their broader scientific and societal significance.

Materials and Methods

The Future Adult Model

We used the Future Adult Model (FAM), a dynamic microsimulation model of the U.S. adult population, to estimate the lifetime health and economic effects of expanded access to GLP-1 anti-obesity medications. Microsimulation models are commonly used to project long-run health and economic outcomes when direct lifetime evidence is not available (36,37). FAM simulates transitions in health, functional status, medical spending, and mortality for nationally representative cohorts of adults beginning at age 25 and continuing through death (38). The model has been previously applied to study the long-term consequences of chronic disease, medical innovation, and preventive interventions in aging populations (5,11,39).

FAM integrates data from several large, nationally representative surveys, including the Panel Study of Income Dynamics (PSID), the Health and Retirement Study (HRS), the Medical Expenditure Panel Survey (MEPS), and the Medicare Current Beneficiary Survey (MCBS). The PSID provides longitudinal information on demographics, health conditions, body mass index (BMI), and socioeconomic characteristics beginning in early adulthood. Supplemental surveys provide validated measures of mortality risk (HRS), healthcare expenditures (MEPS and MCBS), and generalized risk- and severity-adjusted QALYs (GRASA-QALYs) constructed using Generalized Risk-Adjusted Cost-Effectiveness (GRACE), which extend conventional QALY measures by accounting for differences in baseline health and risk preferences, based on predicted health states and functional status (40,41).

Health transitions in FAM are modeled as first-order Markov processes estimated from regression models. In each two-year cycle, an individual's probability of developing new chronic conditions—such as diabetes, hypertension, heart disease, stroke, cancer, or lung disease—depends on age, sex, race, education, BMI, prior health status, and functional limitations. Chronic conditions are treated as absorbing states once diagnosed. Mortality risk evolves as a function of age and accumulated comorbidities.

BMI is modeled dynamically and influences disease incidence. Because self-reported height and weight are known to contain systematic bias, we adjust BMI distributions using external validation data from the National Health and Nutrition Examination Survey (NHANES), following prior FAM applications (39). To capture persistence in weight trajectories, current BMI projections depend on prior BMI realizations over multiple cycles.

At each cycle, FAM projects medical spending, disability, and GRASA-QALYs based on predicted health states. Healthcare spending for individuals under age 65 is estimated using MEPS; spending for Medicare beneficiaries is calibrated using MCBS data. GRASA-QALYs are derived from predicted health states and functional status using validated preference weights.

Model projections are calibrated to national demographic and epidemiologic trends and have been validated through cross-validation and external corroboration exercises. FAM and its predecessor, the Future Elderly Model, have been extensively validated in prior work for projections of risk factors, chronic disease, and both quantity and quality of life (38,42). In out-of-

sample comparisons, FAM mortality, disease prevalence, and population forecasts closely track observed survey data and U.S. Census projections, remaining within approximately 2% of Census population estimates through mid-century (43).

Intervention Scenarios

We simulated two scenarios: a status quo scenario and a GLP-1 weight-loss intervention scenario.

Status Quo: Under the status quo scenario, individuals evolve according to the estimated FAM transition equations without GLP-1 exposure. BMI trajectories, disease incidence, mortality, medical spending, and quality-of-life outcomes are determined entirely by the empirically estimated transition processes described above. This scenario serves as the counterfactual baseline.

GLP-1 Intervention: In the intervention scenario, we simulate weight loss for individuals who meet GLP-1 clinical eligibility criteria during the simulation. Individuals are eligible if their BMI is ≥30 kg/m², or ≥27 kg/m² in the presence of an obesity-related comorbidity (hypertension or heart disease), and if they are between ages 25 and 75 inclusive. Weight-reduction is calibrated to reflect the magnitude and duration of effects observed in clinical trials of GLP-1 therapies (1,4). "GLP-1 initiation" results in a 20% reduction in BMI. To estimate the potential long-term value of GLP-1 therapy under sustained use, we assume that individuals remain on continuous treatment over their lifetime. Thereafter, BMI evolves according to the empirically estimated transition equations. In addition to weight reduction, GLP-1 therapies have been shown to improve glycemic control through mechanisms not fully mediated by weight change. Following prior literature on diabetes incidence-reduction, we incorporate an additional 94% reduction in the risk of incident diabetes over a four-year period, independent of BMI reduction (44).

Study Design and Projection Horizon

Simulations begin in 2019 and follow each individual forward until death. To examine how the timing of treatment initiation shapes lifetime outcomes, we simulated three baseline age cohorts separately: individuals aged 25–30, 30–40, and 40–50 in 2019. Each scenario was simulated 100 times to incorporate stochastic variation in individual health and mortality transitions. Reported effects are the average results across those replications, meaning that lifetime outcomes are computed in each run and then averaged to obtain expected effects under each scenario.

For each individual, the simulation generates two counterfactual lifetime trajectories: one under the GLP-1 intervention and one under the status quo. Because the same individual is projected forward under both scenarios, we directly compute that person's lifetime treatment effect as the difference between outcomes with and without GLP-1 exposure:

$$\Delta Y_i = Y_i^{GLP-1} - Y_{i,}^{SQ}$$

Population-level effects are reported as the average of these individual treatment effects within each cohort.

We evaluate outcomes across three domains. Anthropometric outcomes include absolute BMI change over 20 years. Health outcomes include both the extensive and intensive margins of disease. For each condition (diabetes, hypertension, heart disease, and disability), we compute (i) whether the individual ever develops the condition during the horizon and (ii) the total years lived with the condition (person-years). We also compute life-years gained. Economic and welfare outcomes discounted at 3% include discounted lifetime GRASA-QALYs, discounted cumulative medical spending (excluding treatment cost), and lifetime net social value (defined as monetized discounted GRASA-QALYs plus disability savings plus medical spending savings).

Decomposing Treatment Effects Using Shapley Values

The central aim of this analysis is to identify which baseline characteristics shape the distribution of GLP-1 treatment benefits across individuals. To do so, we apply Shapley additive explanations (SHAP) to decompose individual-level treatment effects into contributions from observed baseline attributes (32–34,45). Shapley-value decompositions are increasingly used in biomedical and health research to attribute predicted outcomes to underlying risk factors and patient characteristics (46,47).

For each cohort, simulated individual treatment effects serve as the outcome, and baseline characteristics measured in 2019 serve as predictors. We estimate a separate prediction model for each outcome and cohort. Outcomes include lifetime net social value (monetized discounted GRASA-QALYs combined with disability and medical spending effects), discounted lifetime GRASA-QALYs, life-years gained, discounted lifetime medical spending, disease incidence (onset of diabetes, hypertension, heart disease, or disability), disease-specific person-years, and long-run changes in body mass index. For incidence and person-year outcomes, individuals with the condition at baseline are excluded to ensure that estimated heterogeneity reflects differences in risk of onset rather than pre-existing disease status.

Baseline predictors span four domains measured prior to treatment initiation: demographic characteristics (age, sex, race and ethnicity, marital status, labor force participation, and education), health behaviors (smoking and physical activity), pre-existing clinical conditions (body mass index and prior diagnoses of chronic disease and disability), and socioeconomic resources (insurance type, earnings, wealth, and insurance coverage). Educational attainment is categorized as less than high school, high school or some college, college graduate, and more than college. These variables represent information available before treatment and are held fixed when explaining variation in simulated treatment effects.

SHAP values quantify how each predictor shifts an individual's predicted treatment effect relative to the cohort's average effect. A positive SHAP value indicates that a given characteristic increases the predicted treatment effect relative to the cohort mean, while a negative value indicates that it decreases it. The substantive interpretation of these shifts depends on the outcome analyzed—for example, whether larger values represent greater health gains or greater reductions in risk or spending. Because SHAP values are computed for each individual and each outcome, the predicted treatment effect can be expressed as the sum of the cohort average and additive contributions from that individual's characteristics. We present the full distribution of these contributions for each predictor to visualize how baseline traits shape treatment responsiveness across the population.

Gradient-boosted decision trees (XGBoost) are used as a flexible nonlinear prediction model to map baseline characteristics to simulated treatment effects. To assess predictive stability and guard against overfitting, we evaluate model performance using 5-fold cross-validation; results reported in Appendix D (Table D.1) indicate that prediction errors are small relative to the magnitude of the outcomes and that the emulator models explain a substantial share of variation in treatment effects for key outcomes. SHAP values are derived from the fitted models to obtain the additive decomposition. Full model specifications are provided in the Supporting Information.

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Table 1. Summary of heterogeneity in lifetime health and economic effects of GLP-1 therapy across baseline characteristics

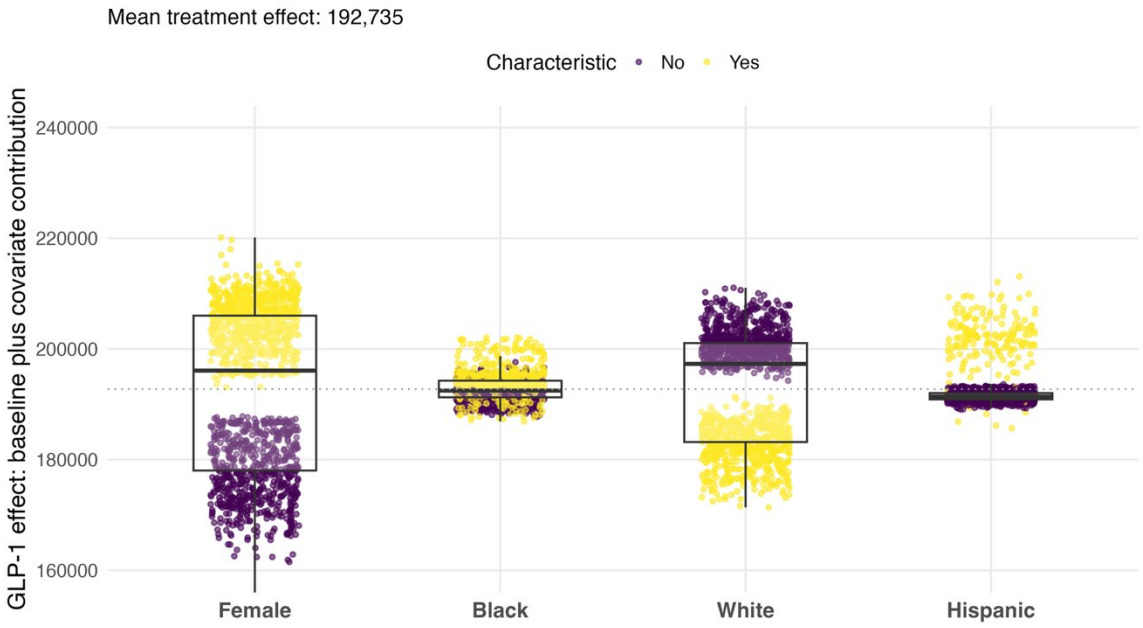
Note: Arrows indicate the direction of treatment effects relative to the cohort mean. "↑" denotes more favorable outcomes, "↓" denotes less favorable outcomes, and "≈" denotes values close to the cohort mean or cases where no clear gradient is observed

Characteristic	Net social value	GRASA-QALYs	Life-years	Discounted Lifetime Medical Spending (savings)	Diabetes incidence (reduction)	Diabetes Person-Years (reduction)
Mean effect	$192,735	1.195	1.38	−$12,120	−15 pp	−3.53
Education (low → high)	↓	↓	↓	↑	↓	≈
Race: Hispanic	↑	↑	↑	↑	↑	↑
Race: Black	↑	↑	↑	↓	↑	≈
Race: White	↓	↓	↓	↓	↓	↓
Sex: Female	↑	↑	↑	↑	↑	≈
Baseline BMI (low → high)	↑	↑	↑	↓	↓	↓
Age (younger → older)	↓	↓	↓	↓	↓	↓

Figures and Tables

Figure 1. GLP-1 Intervention Effect on Lifetime Net Social Value (Relative to Status Quo)
Monetized discounted GRASA-QALY gains plus lifetime medical spending and disability savings.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)

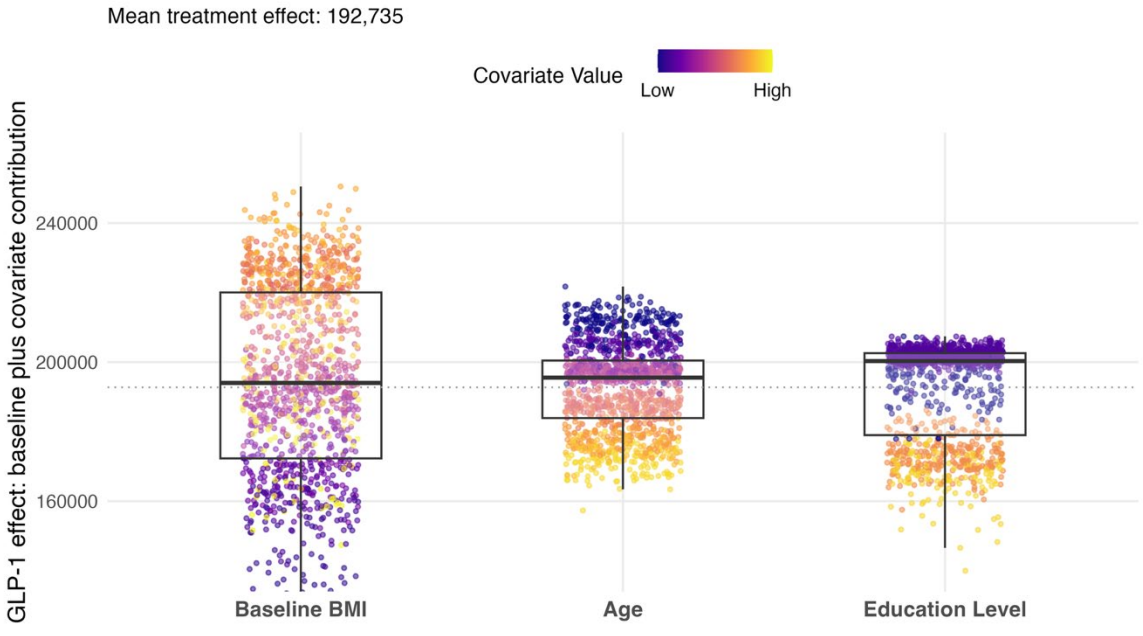
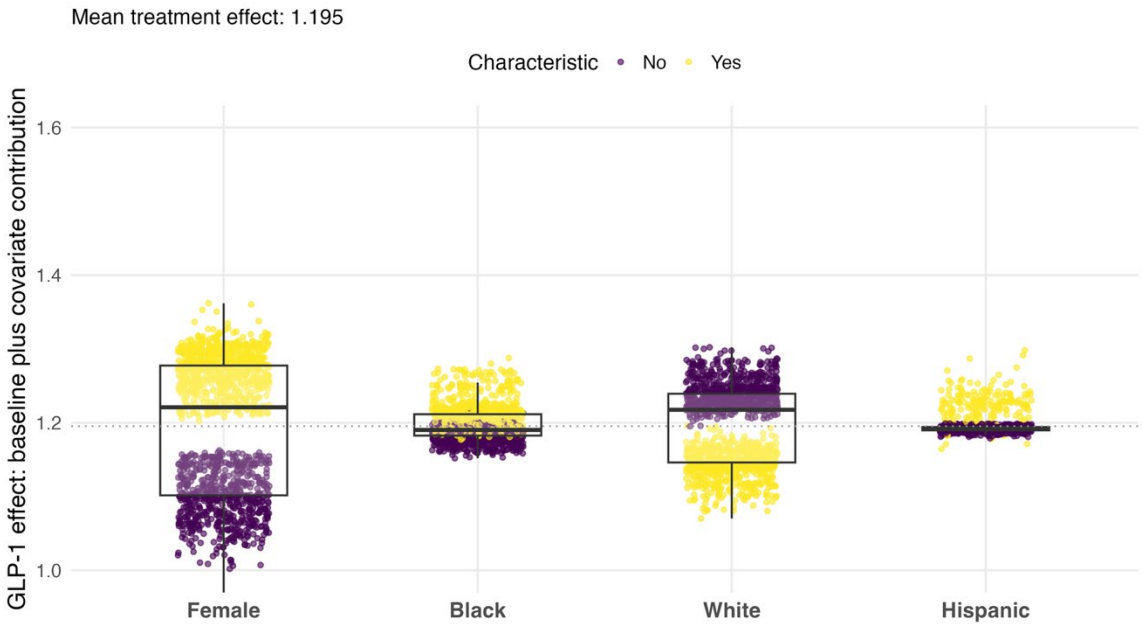


Figure 2. GLP-1 Intervention Effect on Discounted Lifetime GRASA-QALYs (Relative to Status Quo)

Change in present-value quality-adjusted life years over the remaining lifetime.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)

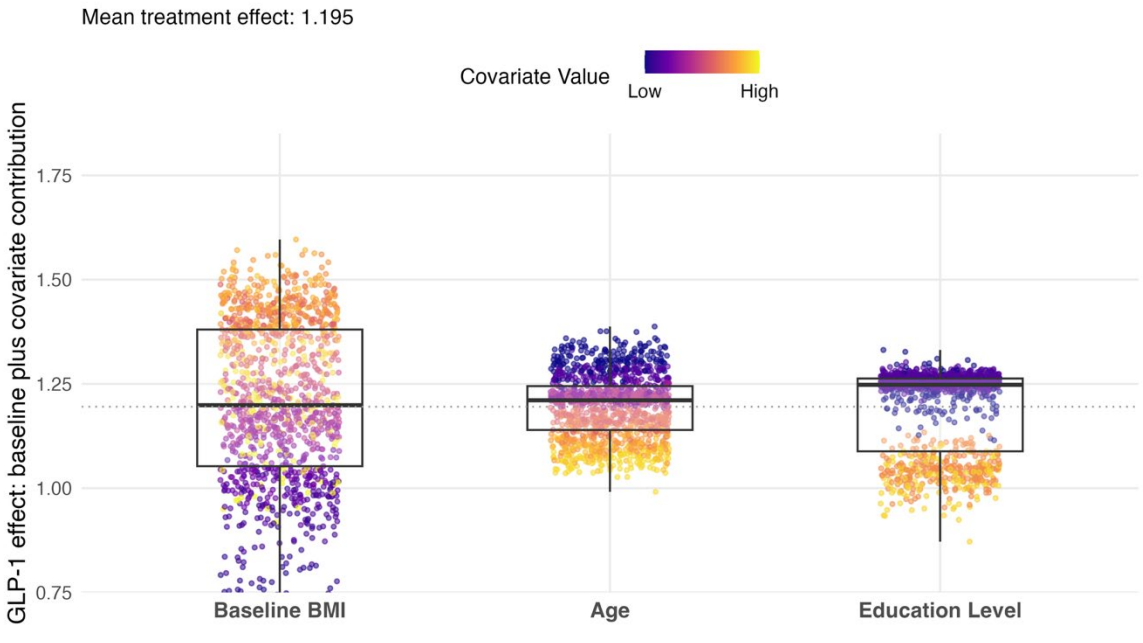
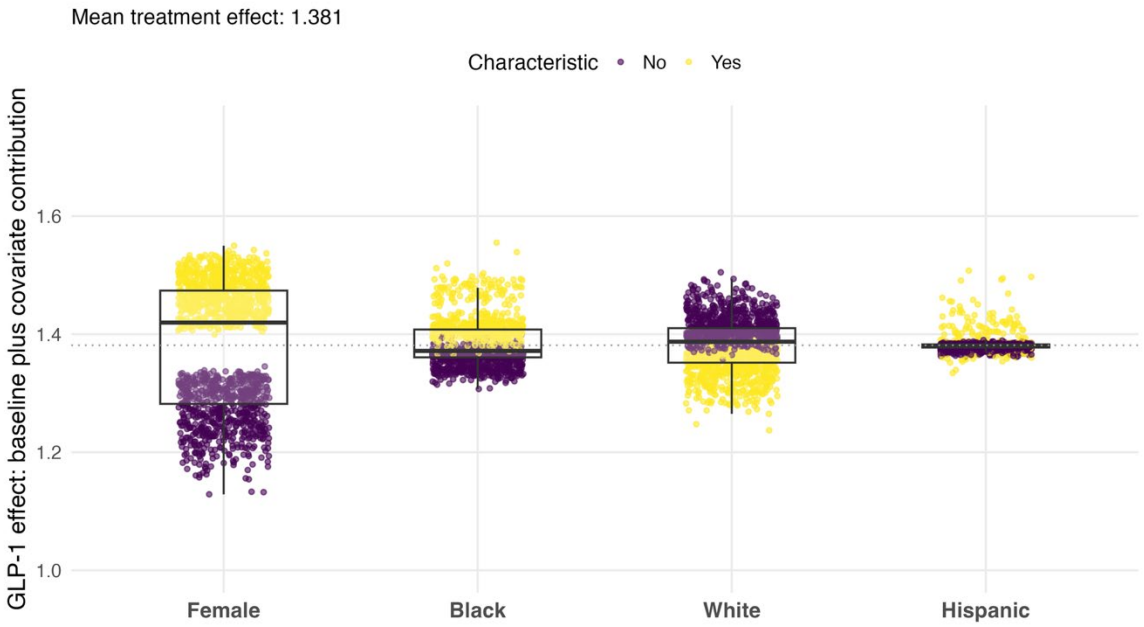


Figure 3. GLP-1 Intervention Effect on Life-Years Gained (Relative to Status Quo)
Change in total survival time over the remaining lifetime.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)

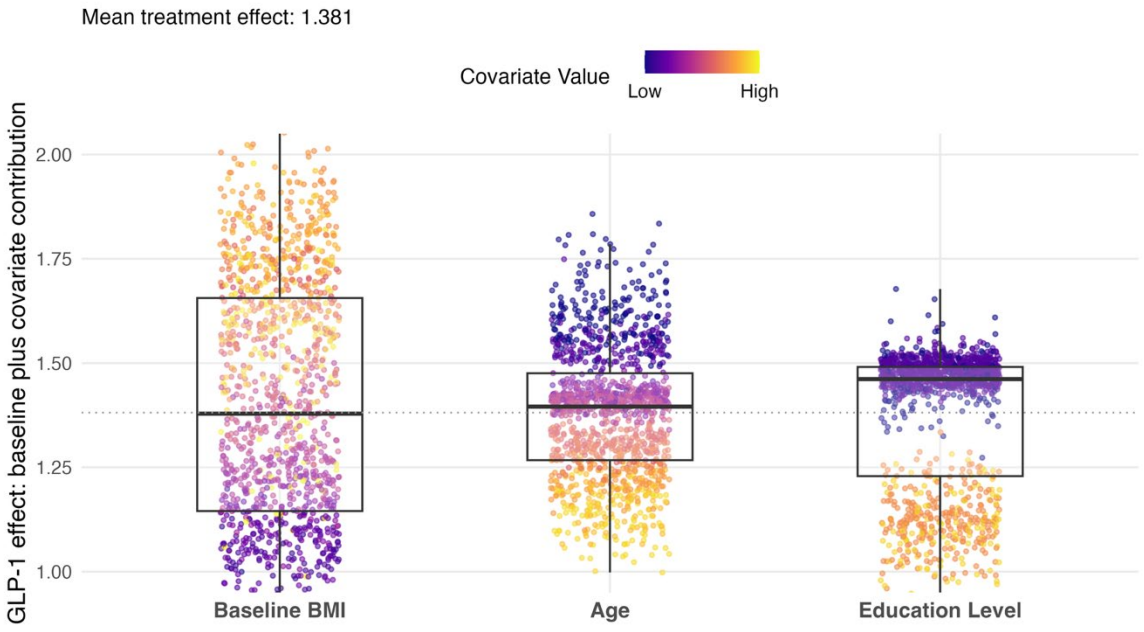
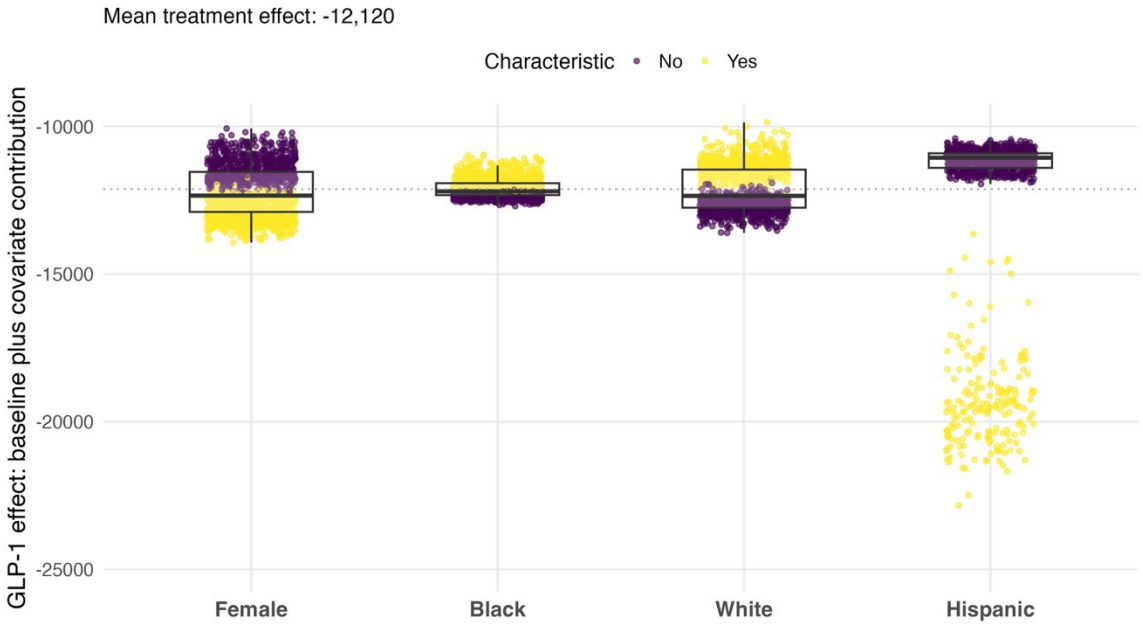


Figure 4. GLP-1 Intervention Effect on Discounted Lifetime Medical Spending (Relative to Status Quo)

Change in present-value cumulative healthcare expenditures.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)

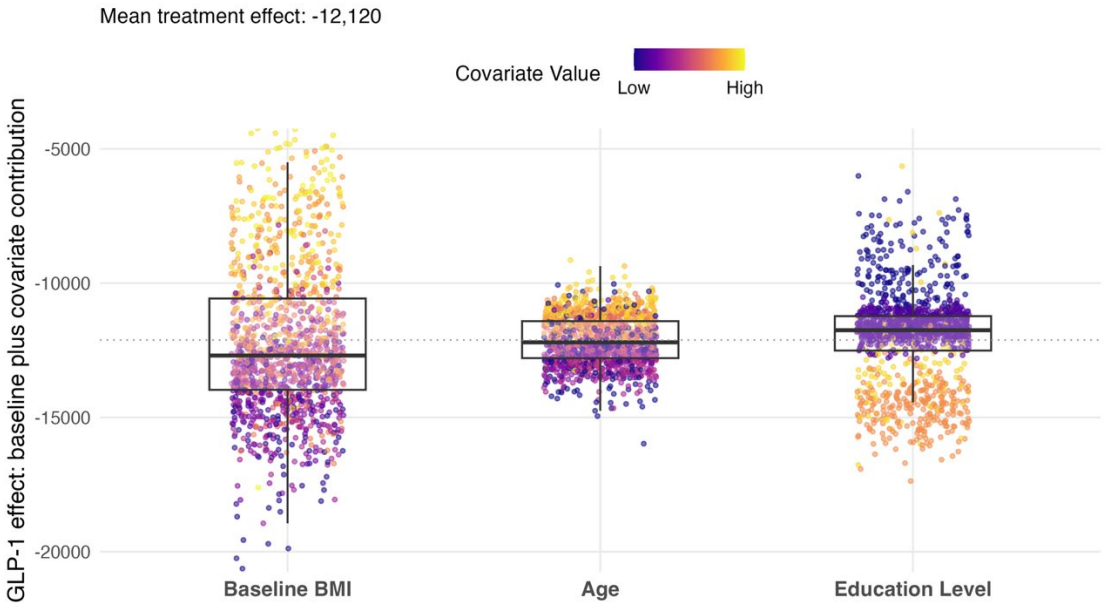
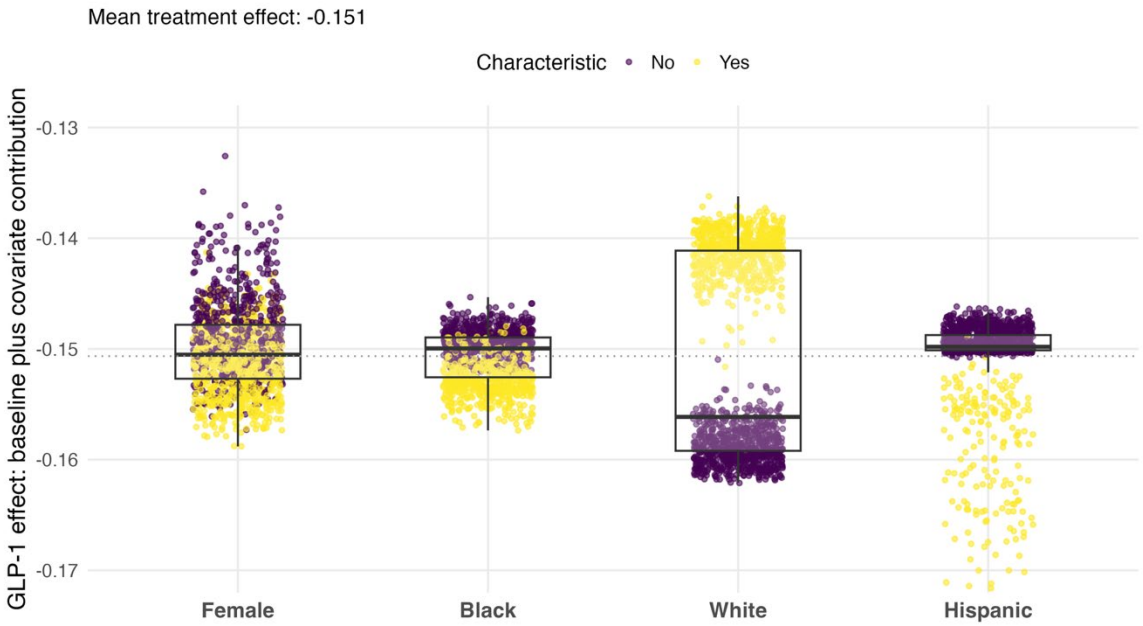


Figure 5. GLP-1 Intervention Effect on Diabetes Cases Averted (Relative to Status Quo)
Change in the probability of ever developing diabetes.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)

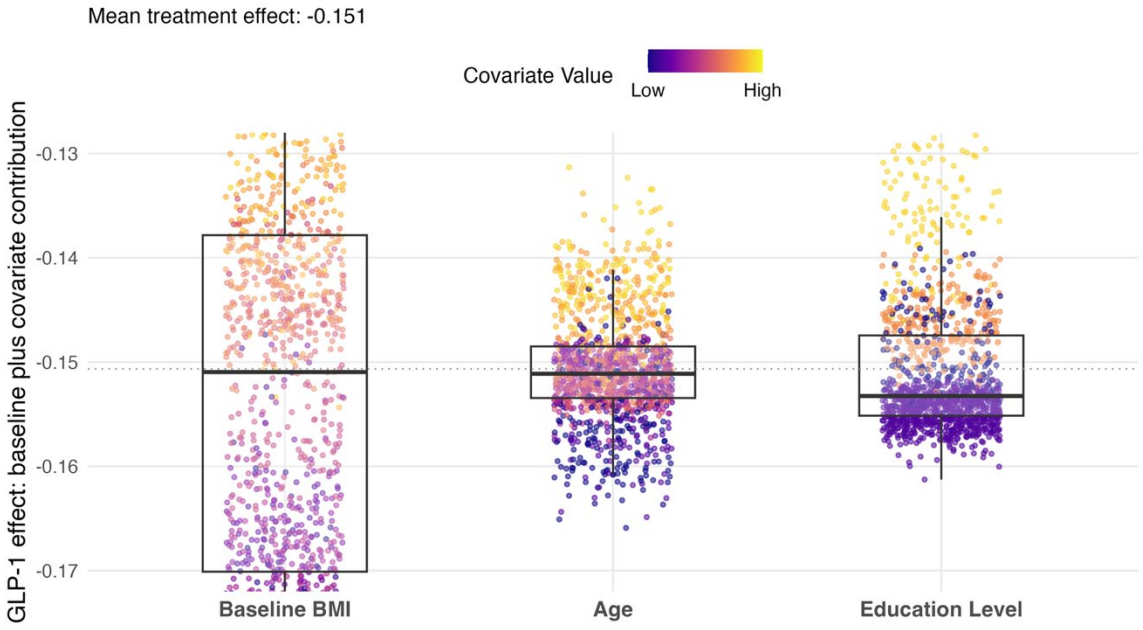
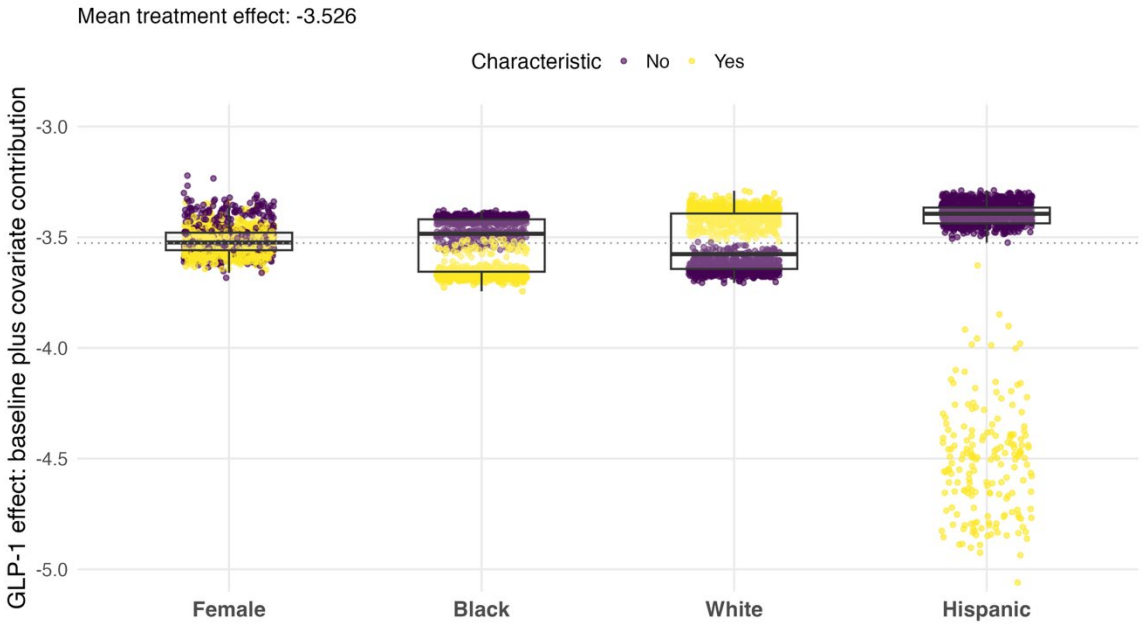


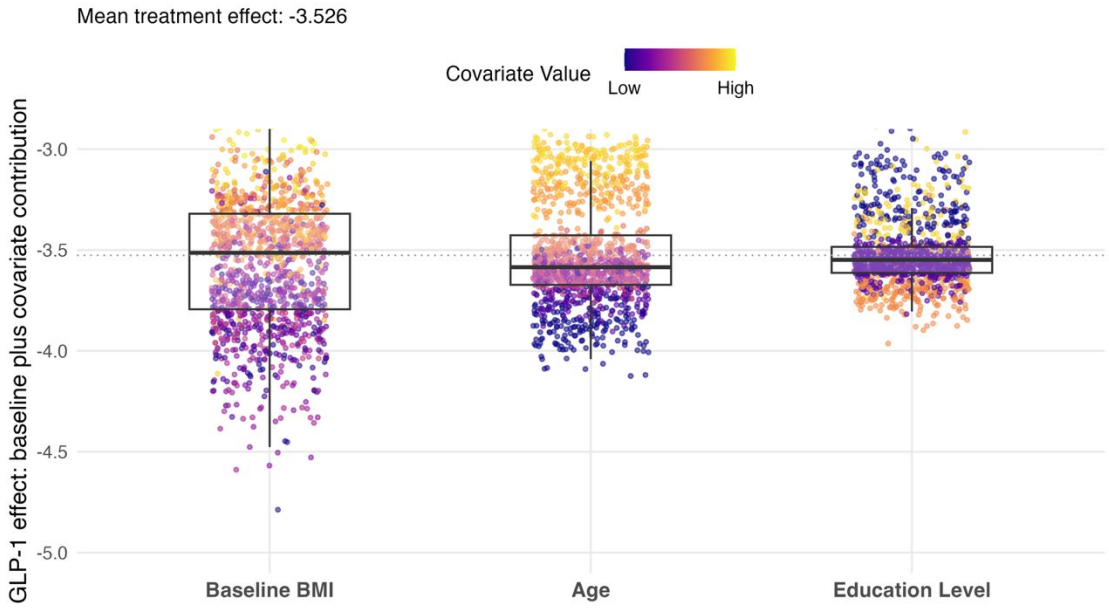
Figure 6. GLP-1 Intervention Effect on Diabetes Person-Years Averted (Relative to Status Quo)

Change in total years lived with diabetes over the lifetime.

Panel A: Binary baseline characteristics (female, race/ethnicity)



Panel B: Continuous baseline characteristics (BMI, age, education)



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