DYNAMIC TREATMENT SELECTION AND MODIFICATION FOR PERSONALIZED BLOOD PRESSURE THERAPY USING A MARKOV DECISION PROCESS MODEL: A COST-EFFECTIVENESS ANALYSIS

APPENDIX

eText 1. Model formulation

MDP formulation

Here we present the formulation of the MDP model. The simulation code is available at https://sdr.stanford.edu/. The MDP model is characterized by a state space, action space, transition probabilities, and rewards. A patient may enter one of 7 health states, as illustrated in eFigure 1: (1) Well; (2) Adverse event without CVD history; (3) MI; (4) Stroke; (5) Post CVD; (6) Adverse event with CVD history; (7) Death. Model notation is shown below. The action space consisted of a finite set of possible actions (treatment decisions). A patient could stop a medication treatment, remain on the current medication treatment(s) and dose level(s), or change medication treatment (by increasing a dosage of a current medication, and/or changing the medication). We did not include decreases in dosage in our action space to mimic how current clinical practice (including the protocol in randomized trials) is conducted. Usually blood pressure medication is prescribed, with increases in dosage if necessary, until the patient's blood pressure meets the target blood pressure goal. Once the target blood pressure is reached, the patient no longer changes medication dosage and typically stays on the same dosage for life. The objective of the MDP is to determine the optimal treatment strategy π^* for a single patient that maximizes the patient's expected discounted quality-adjusted life years (QALYs) over a simulated time horizon. The MDP chooses an action to maximize the expected gains by calculating transition probabilities and rewards (discounted QALYs) associated with each action as illustrated in eFigure 2.

Treatment effectiveness was modeled to be mediated through systolic blood pressure (SBP) reduction based on a meta-analysis of 147 randomized clinical trials, in which SBP reduction from treatment was found to be a function of the number of prescribed drugs and the

dosage level of the drugs.[1] The treatment dose scale and medications used in our model were based on that meta-analysis.[1] In our model, patients can take up to 4 different medications from among the following: angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), beta-blocker, calcium channel Blocker (CCB), and thiazide diuretic. The treatment dose scale is as follows:

0 – No treatment
0.5 – One drug, ½ dose
1 – One drug, 1 dose
1.5 – Two drugs, ½ doses
2 – Two drugs, 1 dose each
2.5 – Three drugs, ½ doses
3 – Three drugs, 1 dose each
3.5 – Four drugs, ½ doses
4 – Four drugs, 1 dose each

Transition probabilities $P_a(s, s')$, are functions of: the patient's post-treatment CVD risk, $r_a(s)$ → $r_a(s) = RR(s)*r(s)$; the likelihood of death from a CVD event, $\rho(s)$; the likelihood of non-CVD death, $\varphi(s)$; the likelihood of side effects from treatment, $\beta_{a,m}(s)$.

The transition probabilities $P_a(s, s')$ are updated in every time step (i.e., every month). At each time step, individuals are faced with either continuing with the current treatment option or advancing to the next level. When transitioning from s to s' state, rewards are given by:

$$R_a(s, s') = Q_a(s, s')$$

At each time step, π will contain the solution and $V(s)$ will contain the discounted sum of the rewards to be earned (on average) by following that solution from state s. The Bellman value function gives the maximized expected QALYs when in state s:

$$V(s) = \sum_{s'} P_a(s, s')(R_a(s, s') + \lambda V(s'))$$

The optimal policy maximizes the sum of expected QALYs over the time horizon:

$$\pi^*(s) = argmax_a\{\sum_{s'} P_a(s,s')(R_a(s,s') + \lambda V(s'))\}.$$

MDP Model Notation

Variable	Description
t	Time index; t = 0,1,…,T
$d \in D$	Treatment dose options A. A=(1,…,9)
$m \in M$	Number of treatment drugs M. M=(1,…,4)
$b_{min} \in R+$	Minimum allowable SBP
$g \in G$	Multidimensional state of the patient represented by the number of remaining decision epochs in the planning horizon, risk factors including demographic information for the patient (e.g. age, sex, smoking status), and CVD competing risk factors (pretreatment SBP, DBP, total cholesterol, HDL cholesterol, smoking status, hypertension treatment status, diabetes status, CVD history) n = 0,..., N, the number of remaining decision epochs p represents patient demographic information (age, sex, race, income) $b \in$ R+ denotes the pretreatment SBP c represents patient CVD competing risk factors. $s \in$ [1, …,7] denotes the patient health state g = (n; p; b; c; s)
$RR(s) \in [0,1]$	Relative-risk factor when in state s
$r(s) \in [0, 1]$	Patient's pretreatment risk of a CVD event in state s
$r_a(s) \in [0, 1]$	Patient's post treatment risk of a CVD event in state s with action a; $D(s)$*$r(s)$
$P_a(s,s')$	Transition probabilities from state s to s'
$\varphi(s) \in [0, 1]$	Probability of death from non-CVD cause given the patient's post-treatment CVD risk when in state s
$\rho(s) \in [0, 1]$	Probability of death from a CVD event when in state s, given that the patient had a CVD event
$\beta_{a,m}(s) \in [0, 1]$	Probability of experiencing side effects (adverse events) in state s
$Q_a(s,s')$	QALYs associated with transition from s to s'
λ	Discount rate for costs and health benefits

Microsimulation model formulation

We developed a microsimulation model at the level of the individual. The model is stochastic: we sample from probability distributions of input parameters to generate a distribution of outcomes. The model is run in discrete time steps over the life course of individuals from 2017. Key parameters and data sources are summarized in eTables 5-13.

We classified the synthetic population in this model by combinations of a few key demographic characteristics: age (18-39, 40-59, 60-85 years old), sex, and race/ethnicity (NHANES categories of non-Hispanic white, non-Hispanic black, Mexican-American or other). Because NHANES comprises repeated cross-sectional data, we had to construct a synthetic population to account for the survey weights. We generated 10,000 individuals, following pretreatment guidelines, for each cohort defined by the combinations of these characteristics. We re-ran the model 10,000 times while repeatedly Monte Carlo sampling from the probability distributions of all input parameters to capture uncertainties in our estimates.[2] Baseline characteristics between the simulated population and NHANES participants were compared using MANOVA (eTable 2).[3]

Baseline CVD risk factors and prevalent disease cases were assigned to each simulated individual by repeated Monte Carlo sampling from the probability distributions of each of these variables in NHANES, specific to each demographic group. The joint probability distributions of these risk factors were accounted for using multivariate sampling with copula functions, which allows us to capture how these factors are co-dependent. This procedure takes into account the correlation between risk factors. To account for individuals aging, we tracked the age of each simulated individual over the simulation period, and updated each individual's health metrics to account for age-specific health risks by preserving the individual's rank in the population

distribution to account for the stability of risk over time and differential survival probability.

eText 2. Effects of hypertension medication on blood pressure and CVD risks

We estimated the effect of blood pressure medications on lowering blood pressure as a function of dose based on a meta-analysis of 147 randomized placebo controlled trials of blood pressure-lowering drugs in fixed dose,[4] which showed that the five main classes of blood pressure-lowering drugs produce similar reductions in blood pressure. In our model, patients were allowed to take only up to full doses of 4 different medicines, given current data suggesting that increasing blood pressure medications beyond 4 full doses has been found to increase side-effects/adverse effects without providing any incremental benefit for patients.[5] In the JNC8 and Intensive JNC8 strategies, even if the patients' blood pressure levels do not meet the target blood pressure goals, they were not allowed to receive more than 4 full doses of medications. In the MDP-based treatment (MDPT) strategy, patients did not have an option to increase doses if they were receiving 4 full doses.

The blood pressure-lowering effect of the drugs was estimated as a function of treatment dose and pre-treatment blood pressure, and was not dependent on types of drugs, except for beta-blockers. Beta-blockers have been shown to be more effective than the other studied antihypertensive drugs in lowering blood pressure among patients with previous history of CVD (relative risk of 0.71, 95% confidence interval 0.66 to 0.78).[1] We included this effect in our model and found that for patients with CVD history the MDPT tended to favor beta-blockers over other types of drugs.

The estimated effect of one drug at standard dose in lowering blood pressure from a pre-treatment blood pressure P was calculated as $(9.1+0.10(P-154))$ systolic blood pressure. The estimated blood pressure reduction for a higher standard dose was calculated by applying this

equation to each drug in turn, allowing for the effect of the first in lowering pre-treatment blood pressure for the second, and the second for the third, and so on. The blood pressure reductions from half standard doses were calculated as (R+n*0.078(P−150)) systolic blood pressure, where R is the blood pressure reduction at 150 mm Hg systolic blood pressure, n is the number of drugs, and P is the pretreatment blood pressure. Using these equations yields the following estimates of R:

Number of drugs at standard dose	***R***
One drug half standard dose	6.7
Two drugs half standard dose	13.3
Three drugs half standard dose	19.9
Four drugs half standard dose	26.5

Given SBP changes from blood pressure medication, the relative risk reduction for MI and stroke was estimated using previously published equations (equations (1) and (2) below).[6] The equations were estimated by fitting curves to data from a meta-analysis of prospective patient-level data on blood pressure and CVD mortality.[7]

$$\text{Slope MI} = -1.1009\text{E-}05\ \text{age}^2 + 8.6305\text{ E -}04\ \text{age} + 3.5176\text{ E -}02 \quad (1)$$
$$\text{Relative risk of MI} = 2\text{^(change in SBP*slope MI)}$$

$$\text{Slope stroke} = -2.5946\text{E -}05\ \text{age}^2 + 2.3052\text{E -}03\ \text{age} + 2.2168\text{E -}02 \quad (2)$$
$$\text{Relative risk of stroke} = 2\text{^(change in SBP*slope stroke)}$$

eText 3. Risk of myocardial infarction (MI) or stroke

We used validated equations of monthly risks of MI and stroke estimated by fitting exponential curves to data on age- and sex-specific incidence of first MI and stroke from the Framingham Heart Study (1980-2003), published by the National Heart, Lung, and Blood Institute.[6, 8]

Given no history of MI (x = age in years), monthly risk of MI is:

$$\text{Male: } y = 0.0001 * e^{0.0312x} \quad (3)$$
$$\text{Female: } y = 8E-06 * e^{0.0599x} \quad (4)$$

Given no history of stroke (x = age in years), monthly risk of stroke is:

$$\text{Male: } y = 9E-06 * e^{0.0622x} \quad (5)$$

$$\text{Female: } y = 3E-06 * e^{0.0741x} \quad (6)$$

Given history of CVD, the risk of MI or stroke without a history of CVD was multiplied by a constant with a mean of 2, standard deviation 1.0204, gamma distribution (shape=3.84166, scale=0.520608).

To account for other CVD risk factors, we adopted a previously published approach in which weights are assigned to each individual based on the following risk factors used in the Framingham risk equations[9, 10]: age, total cholesterol, HDL cholesterol, hypertension treatment status, smoking, and diabetes. Individual Framingham risks were divided by the mean Framingham risk of each cohort (defined by age, sex, race, and income), then used to weight each individual's baseline MI and stroke risk equations, equations (3)-(6). The Framingham risk equations are as follows:

For males:

Individual_FHS_risk = (1-0.88936)*exp((3.06117*log(age)+1.12370*log(total_cholesterol)-0.93263*log(HDL_cholesterol)+1.99881*log(SBP_treated)+1.93303*log(SBP_untreated)+0.65451*smoking+0.57367*diabetes)- 23.9802)

For females:

Individual_FHS_risk = (1-0.95012)*exp((2.32888*log(age)+1.20904*log(total_cholesterol)-0.70833*log(HDL_cholesterol)+2.82263*log(SBP_treated)+2.76157*log(SBP_untreated)+0.52873*smoking+0.69154*diabetes)-26.1931)

$$\text{Weights assigned to individual} = \frac{\text{Individual FHS risk}}{\text{Mean FHS risk of each cohort}}$$

eText 4. Mortality after myocardial infarction (MI) or stroke

We used validated equations of age- and sex-specific risk of mortality after MI and stroke developed by fitting exponential curves to the ratio of incidence of fatal events to total incidence of events. Data on fatal MI and total incidence of MI was obtained from the Framingham Heart Study. The ratio of fatal stroke to stroke incidence was obtained from the Cardiovascular Health Study.[6, 8] This yields the following estimated mortality risks.

Risk of mortality after MI (x = age in years):

Male: $y = 0.0289 * e^{0.0269x}$

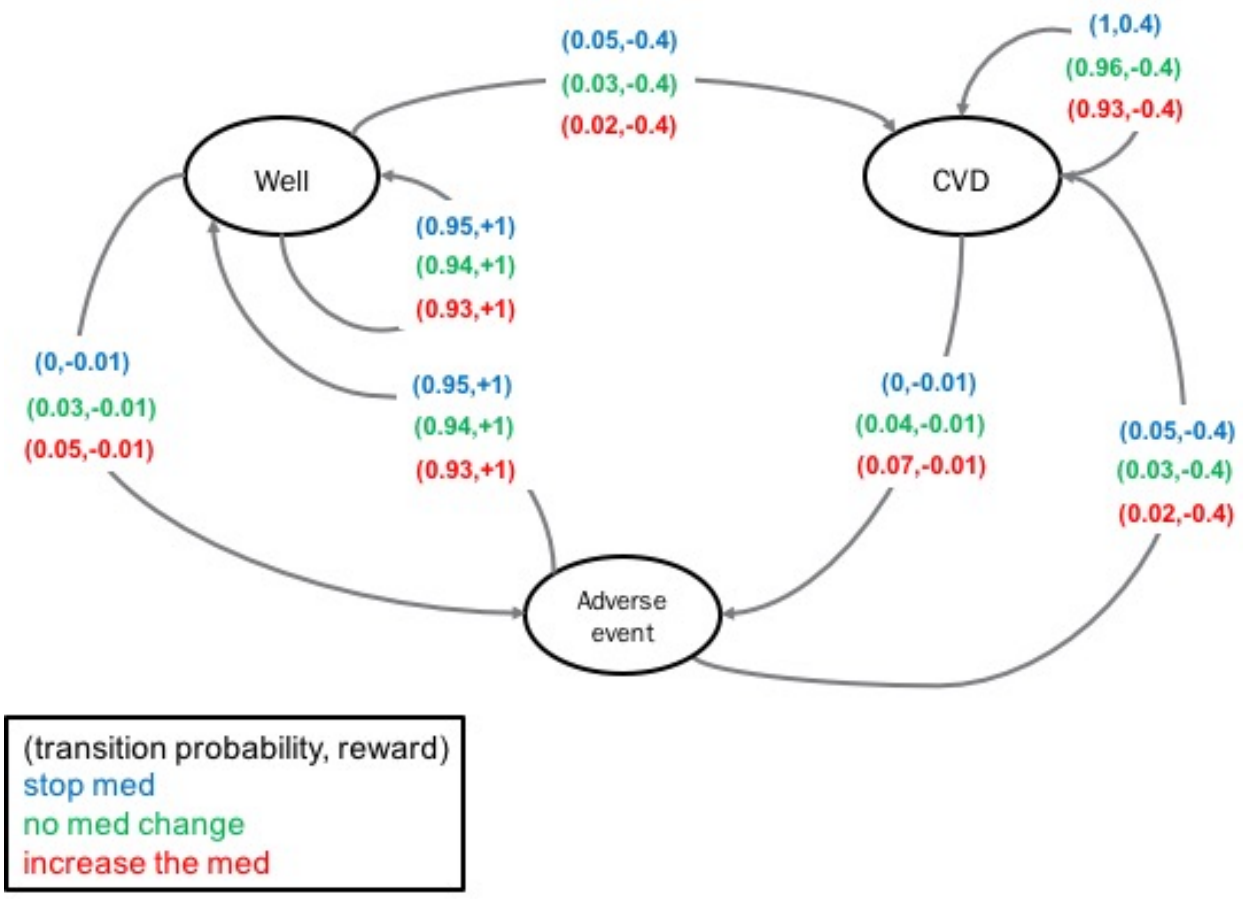
Female: $y = 0.0004 * e^{0.0706x}$

Risk of mortality after stroke (x = age in years):

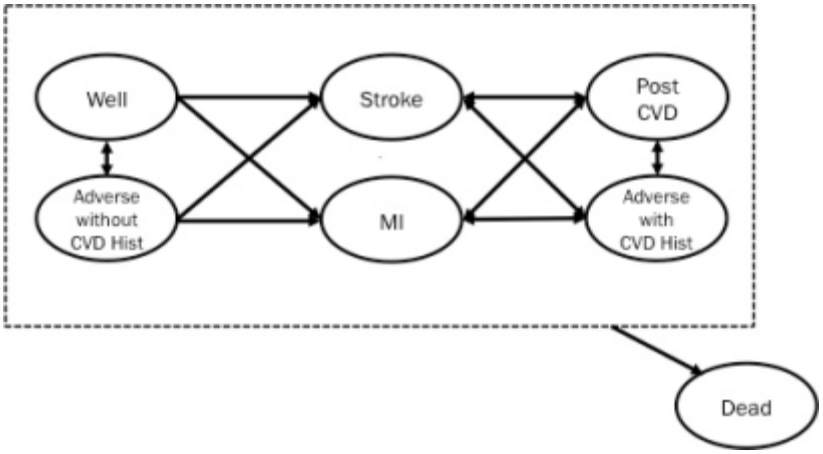
Male: $y = 0.0003 * e^{0.0782x}$

Female: $y = 0.0034 * e^{0.0428x}$

eFigure 1. Illustration of decision making process in the Markov Decision Process. This figure illustrates how the MDP chooses the optimal action (treatment decision) at each decision epoch. The transition probabilities from the current state to the next are determined by which action is taken, and each transition is associated with corresponding rewards. This illustration has three actions in different colors. The numbers in each parenthesis are the transition probability and reward associated with each action. The MDP chooses an action that will maximize total rewards by calculating expected rewards from each action over the simulated horizon.

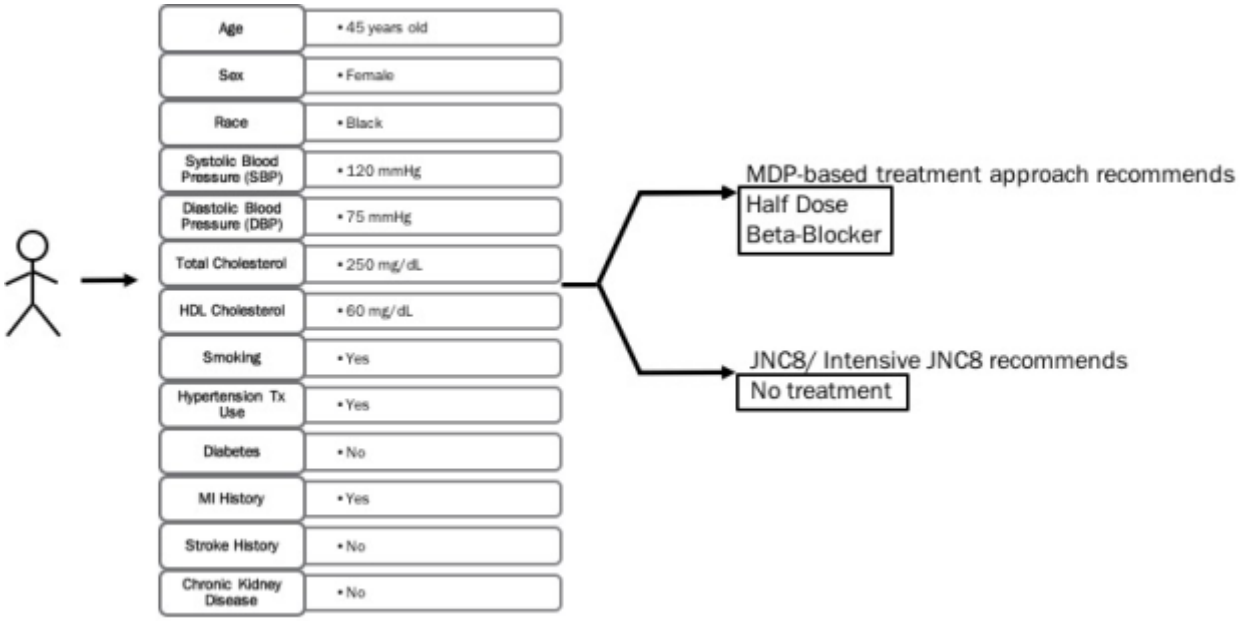


eFigure 2. Schematic of health states in the Markov Decision Process

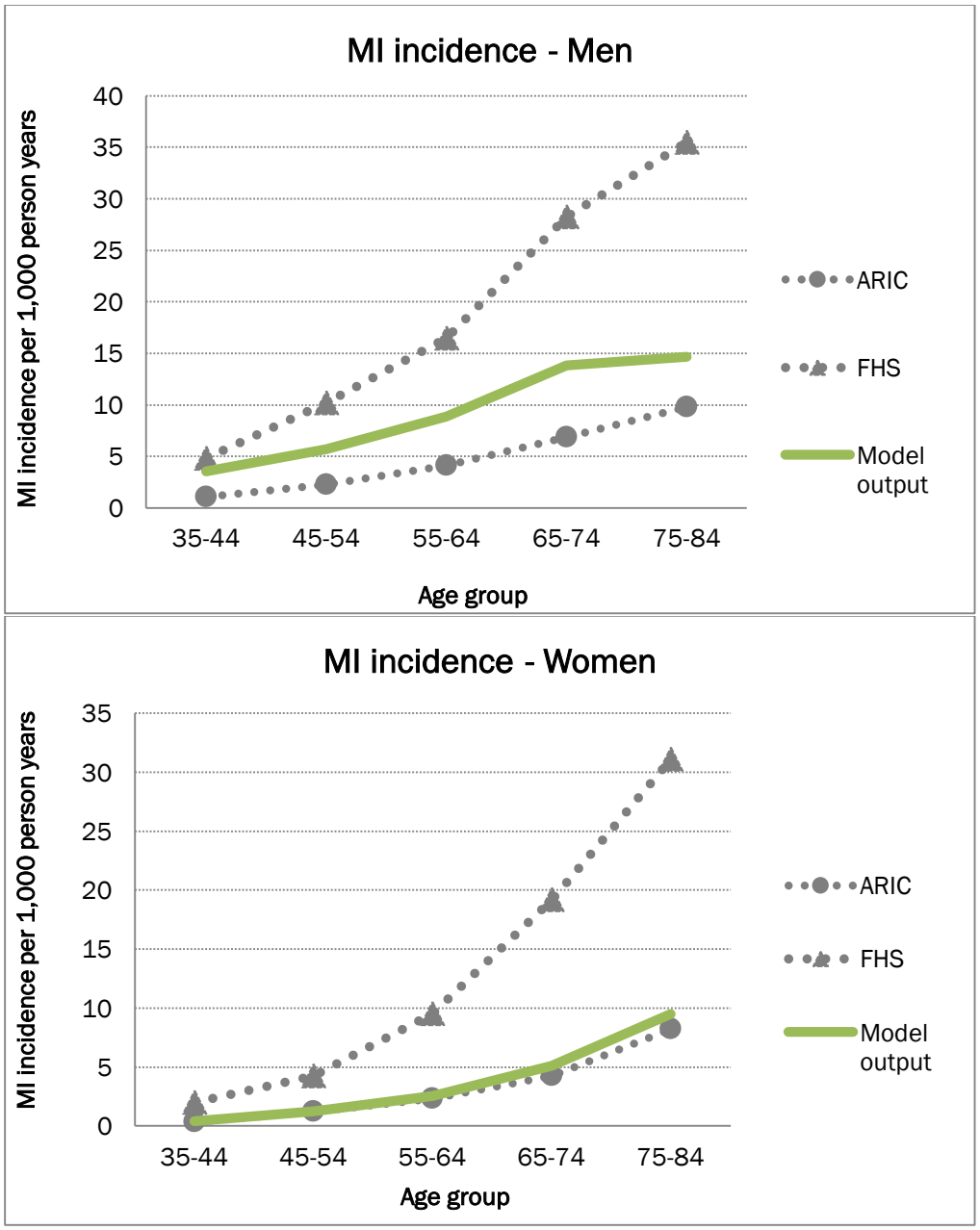


CVD: Cardiovascular disease; CVD Hist: CVD History

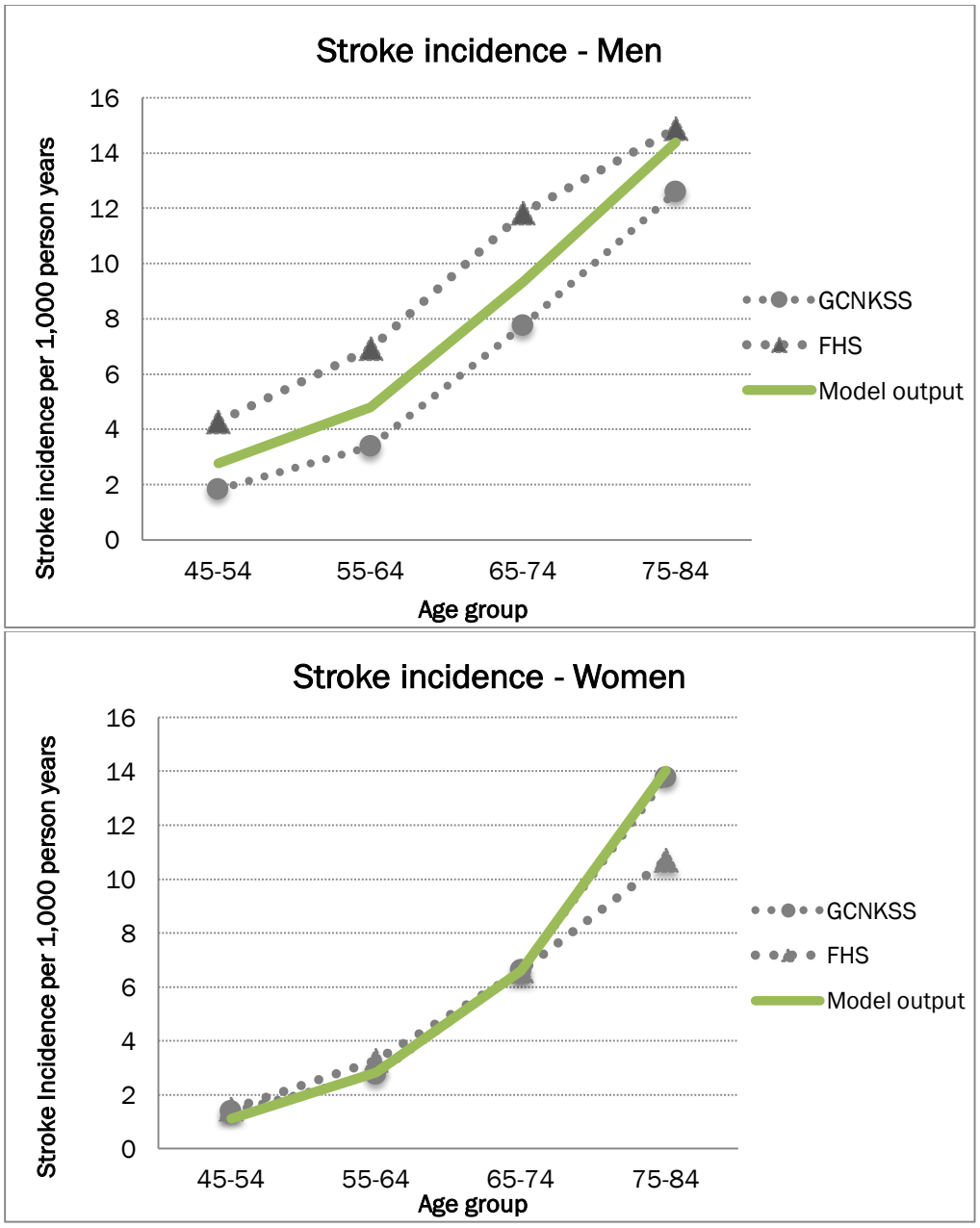
eFigure 3: Illustration of a single patient receiving different treatments under MDP-based treatment (MDPT) versus current guidelines. A single patient with a certain set of demographic features and CVD-related covariates is recommended for different treatment regimens. JNC8 and Intensive JNC8 recommend no treatment. MDPT recommends a half-dose of beta-blocker for this patient with a blood pressure that is below the current targets due to his/her CVD-related covariates that indicate high risk of CVD.



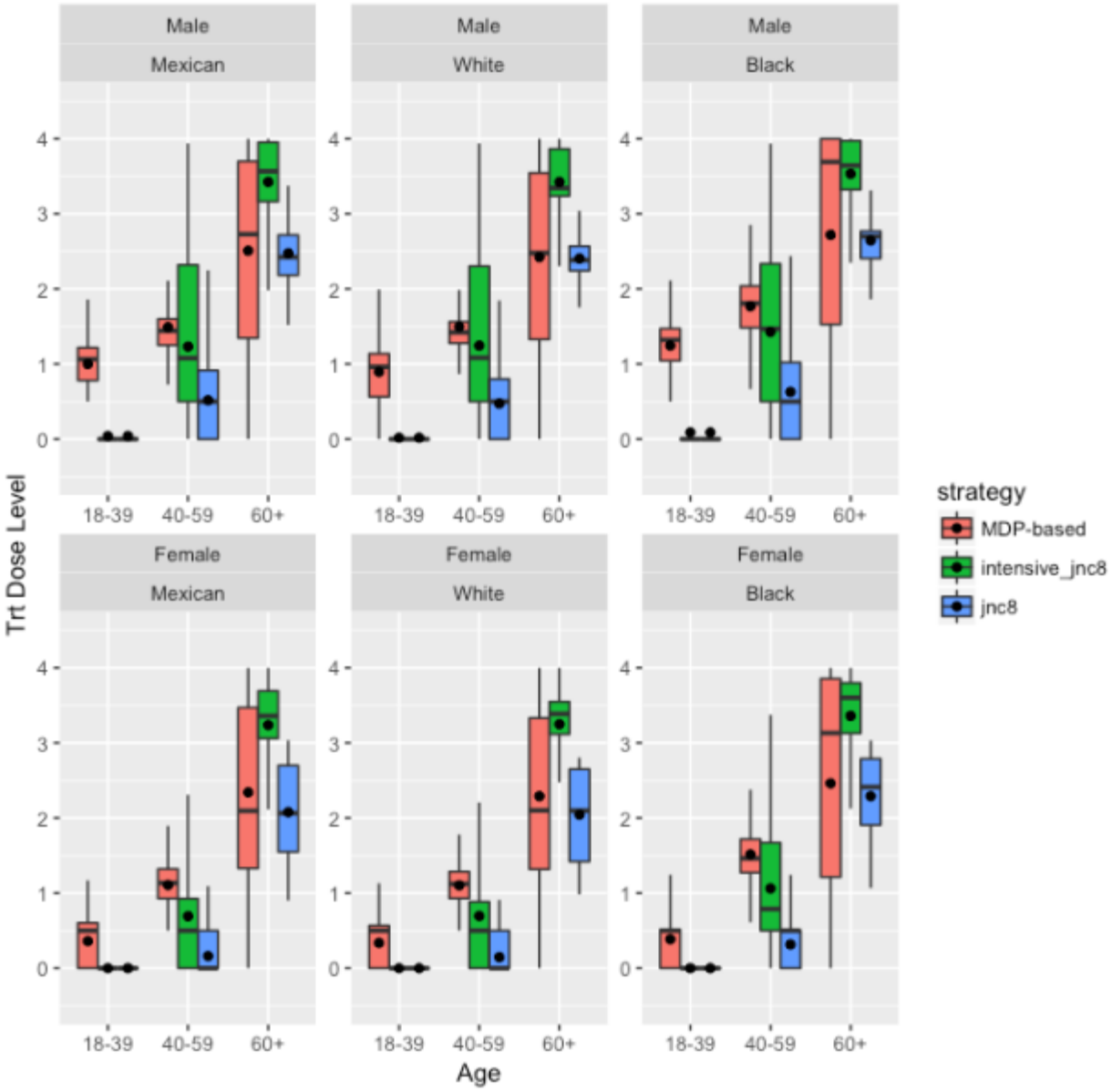
eFigure 4. Calibration results: MI incidence. We considered our targets were met if the projected incidence fell within the interval between the estimates from the Framingham Heart Study (FHS) and the Atherosclerosis Risk in Communities study (ARIC) which are, respectively more-inclusive and less-inclusive measures of composite CVD outcomes.



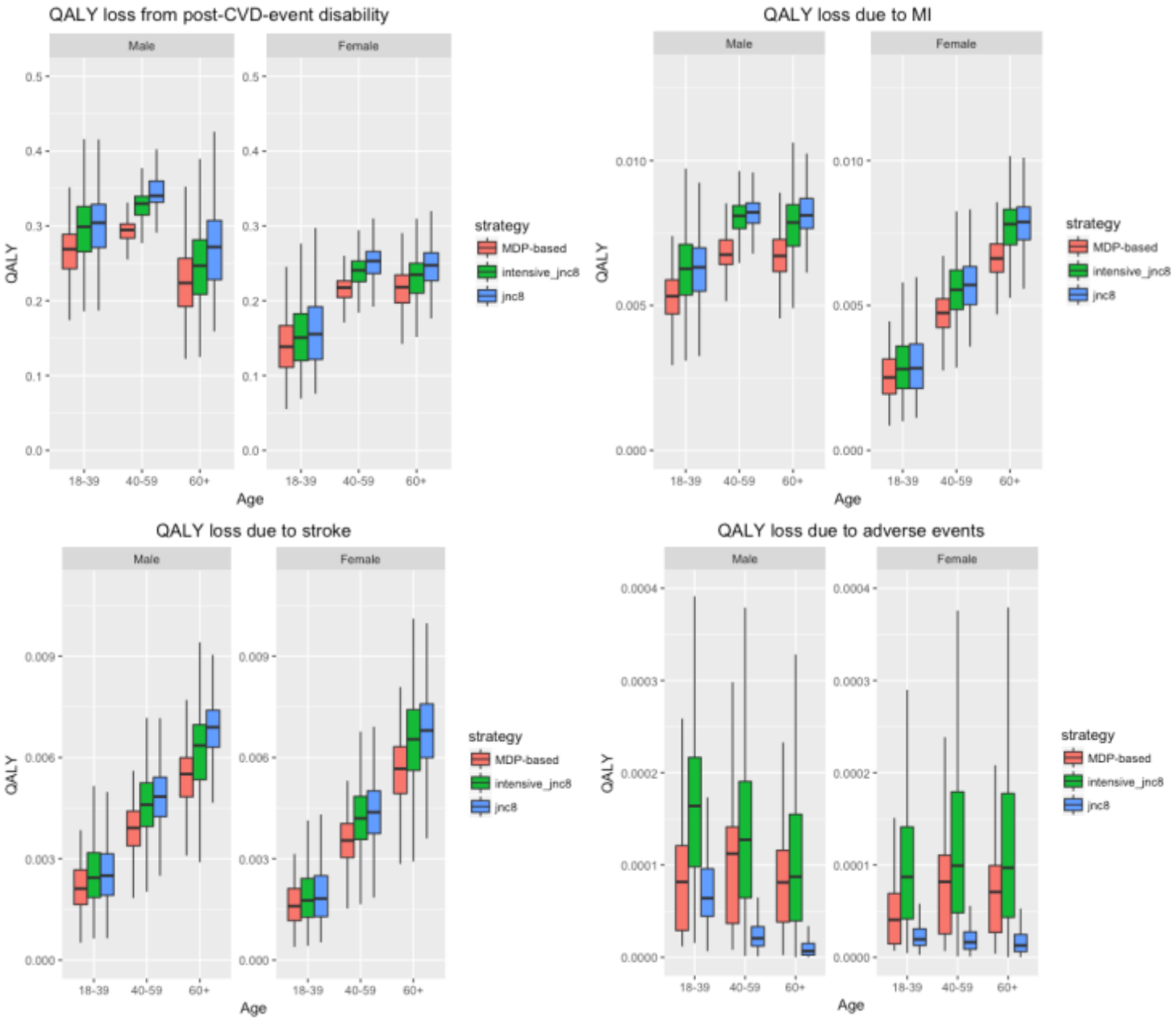
eFigure 5. Calibration results: stroke incidence. We considered our targets were met if the projected incidence fell within the interval between the estimates from Framingham Heart Study (FHS) and the Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS)



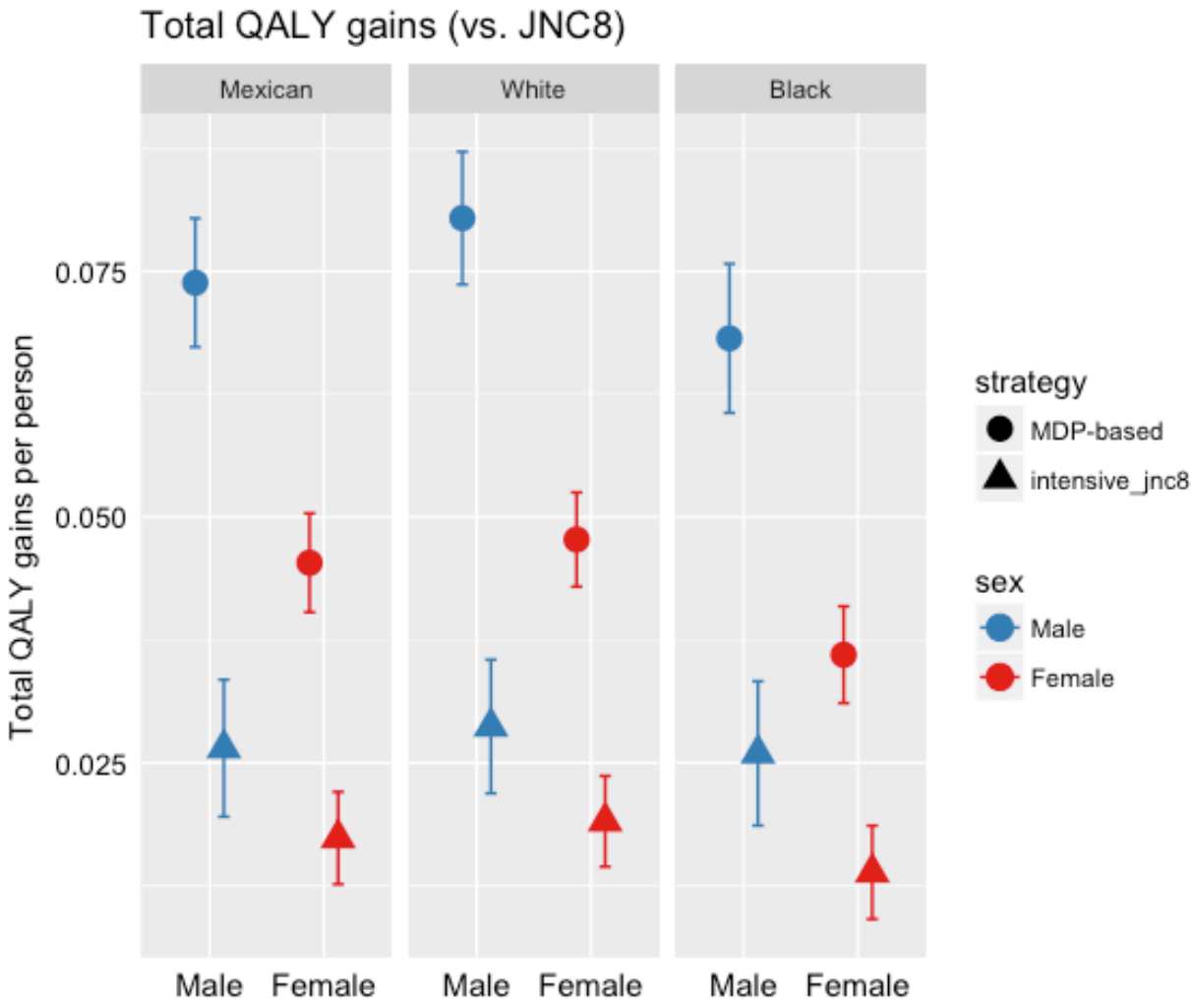
eFigure 6. Treatment dose levels by age, sex, and race under each treatment strategy



eFigure 7. QALYs in each disease state over patient lifetimes

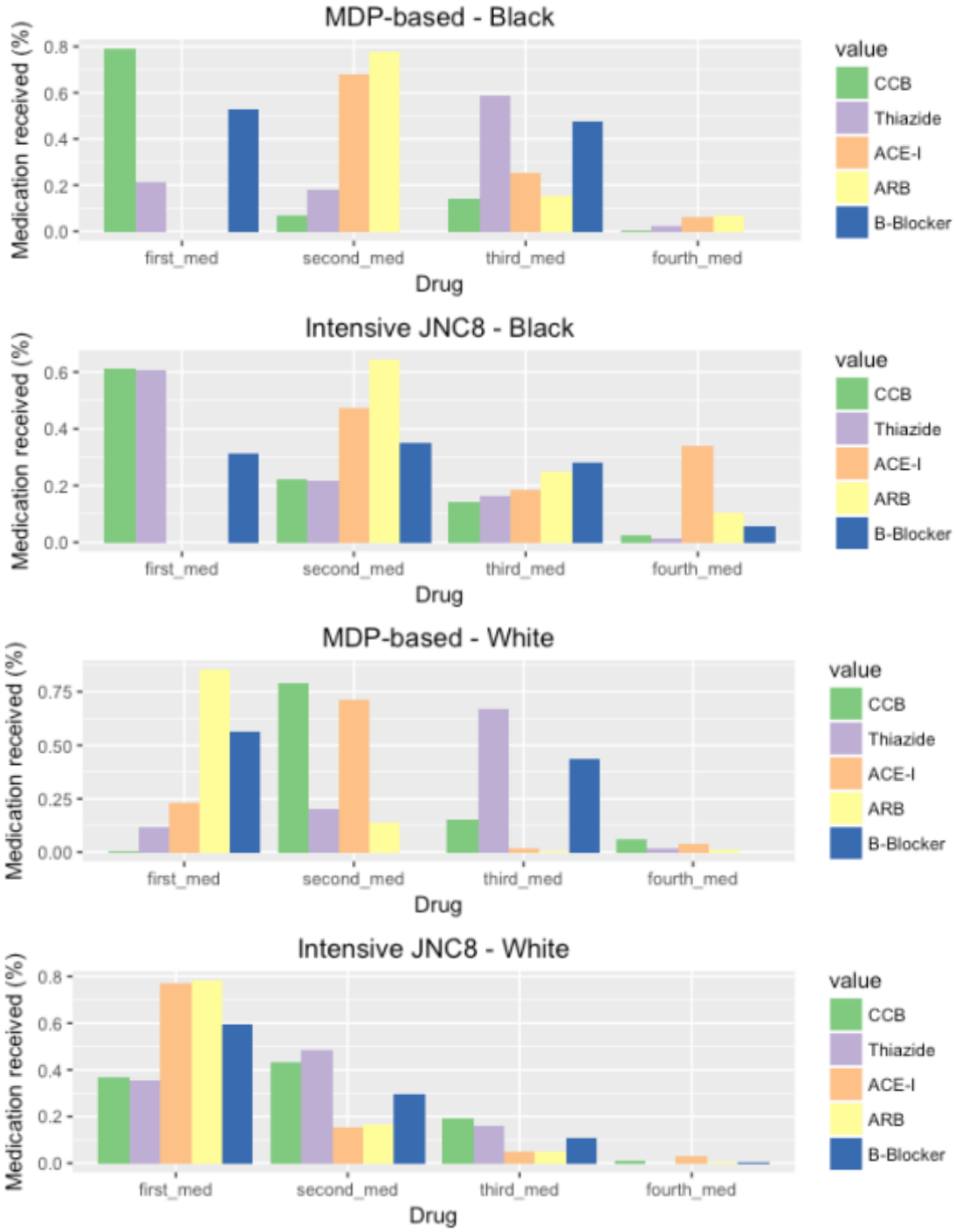


eFigure 8. Total QALY gains over patient lifetimes for the Intensive JNC8 strategy and the MDP-based treatment strategy compared to the JNC8 strategy

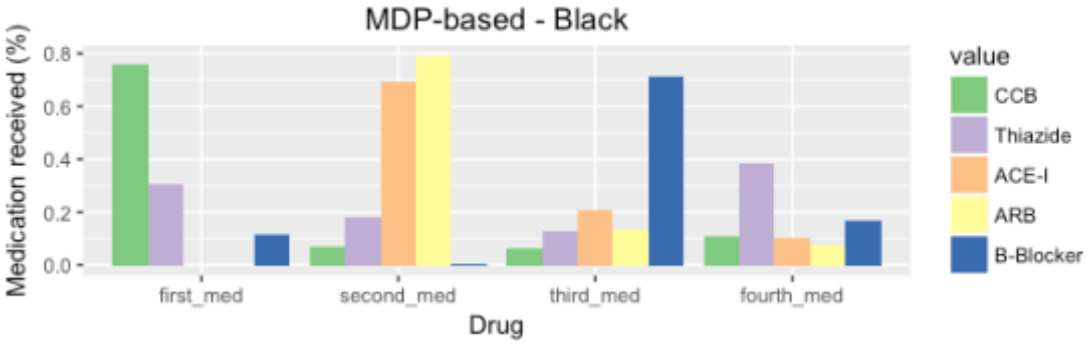


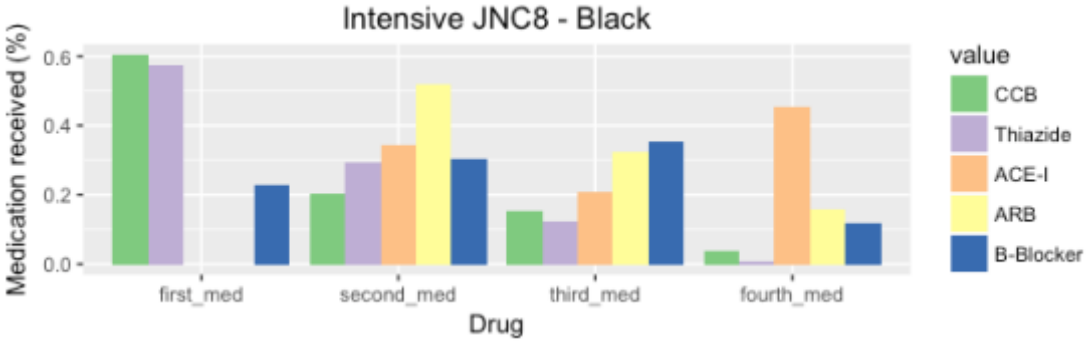
eFigure 9. Comparison of medications selected by MDP-based treatment (MDPT) approach vs. current guidelines

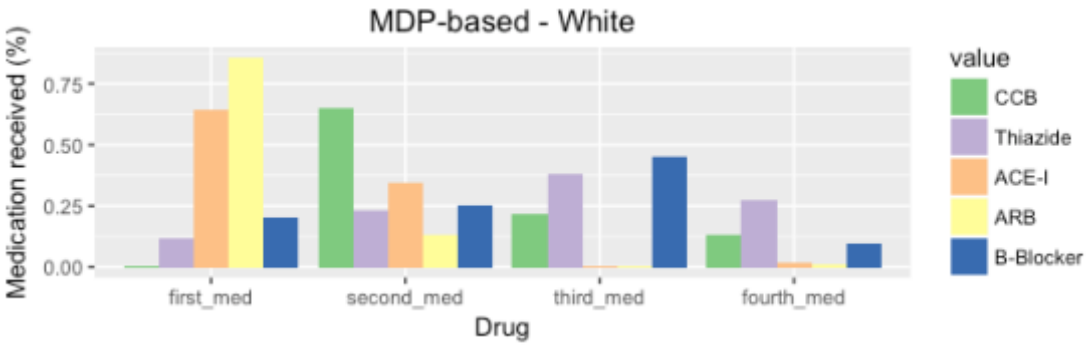
Without CVD History

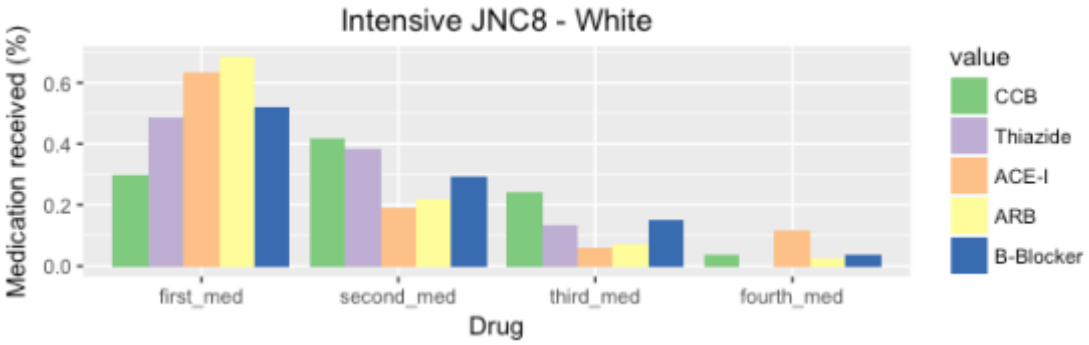


With CVD History

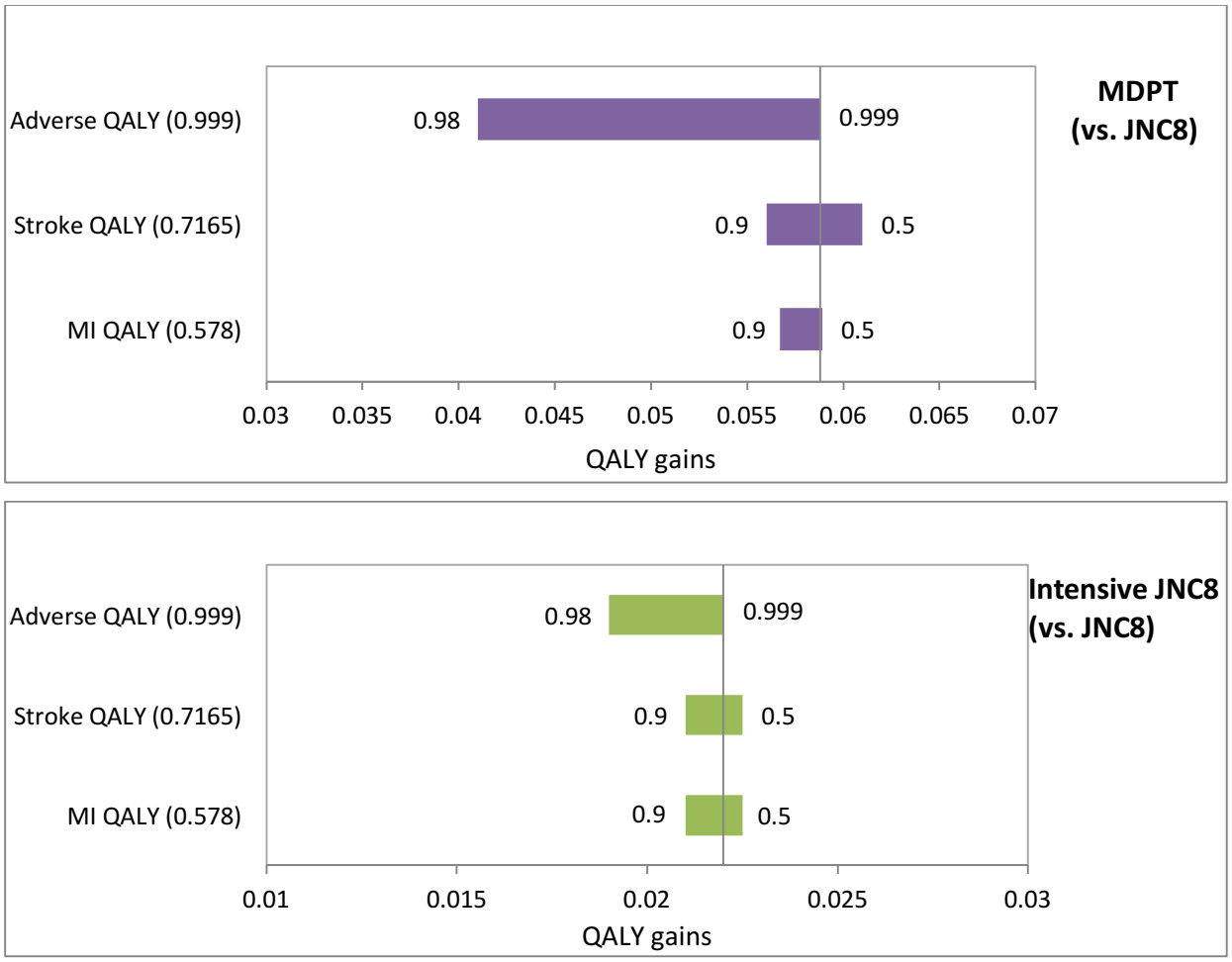






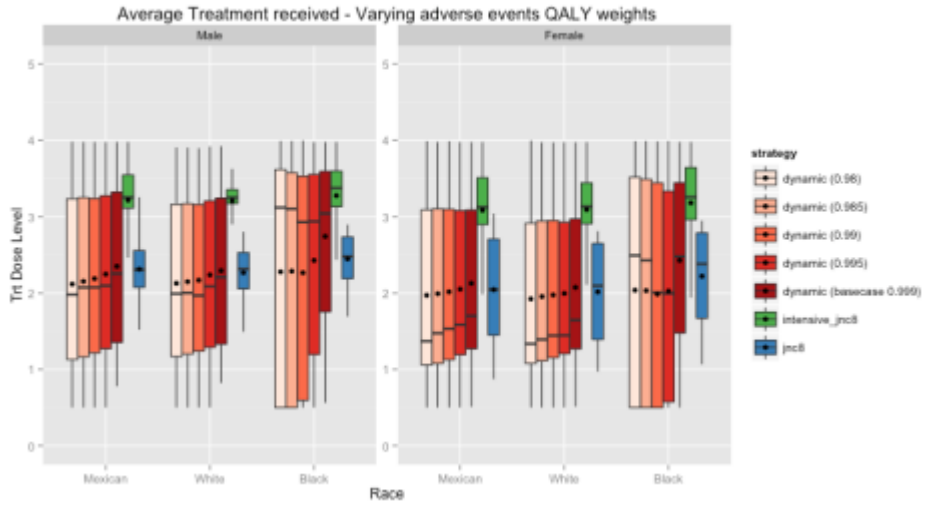


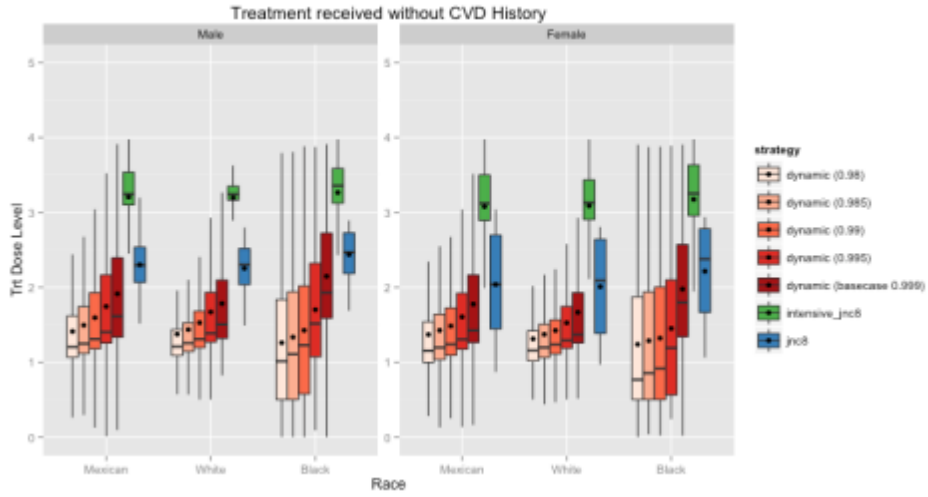
eFigure 10. Sensitivity analysis: QALY gains from the MDP-based treatment (MDPT) strategy and the Intensive JNC8 strategy (vs. JNC8). The vertical lines represent the QALY gains in the base case analysis, and the horizontal bars represent the variation of the QALY gains given variations of parameters. The numbers at each end of the bars represent the lower and upper bounds of the value used for each parameter.

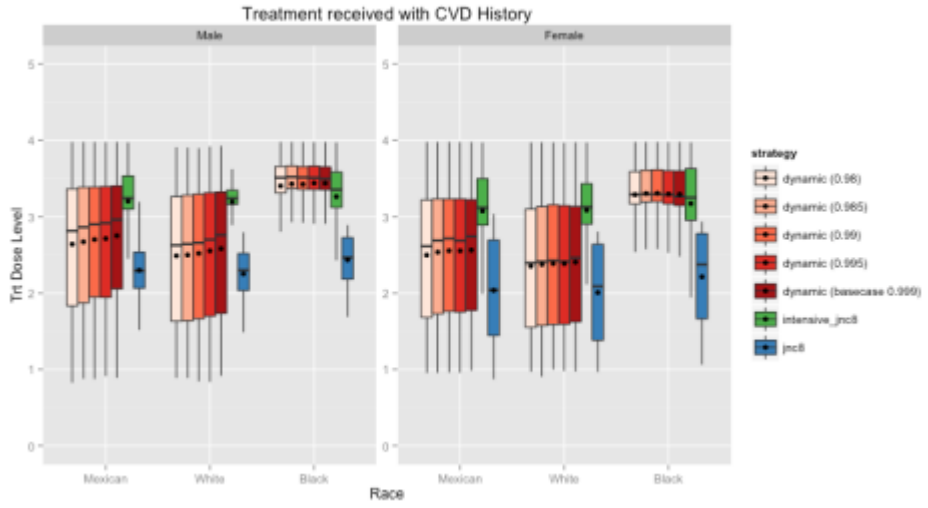


eFigure 11. Sensitivity analyses: Treatment dose levels for different adverse event QALY weights

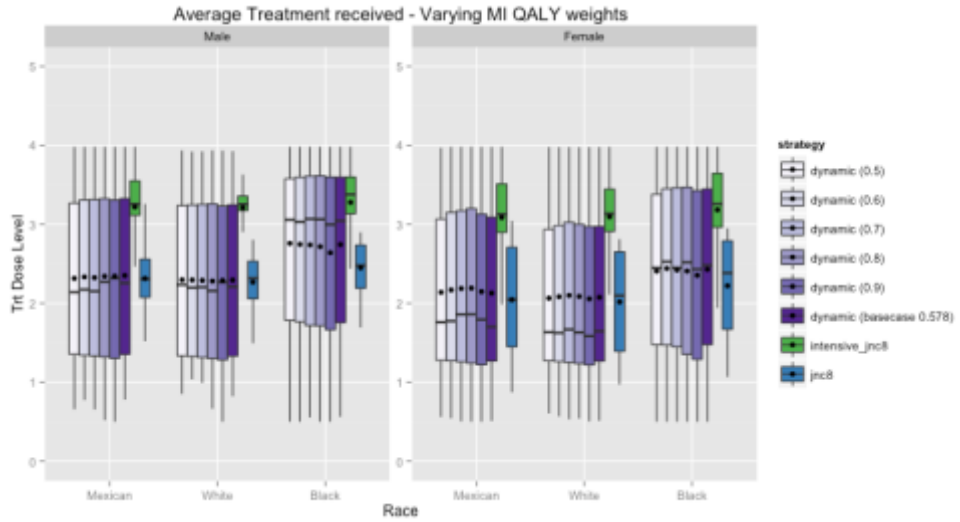
Treatment side effect QALY weights (dynamic: MDP-based)

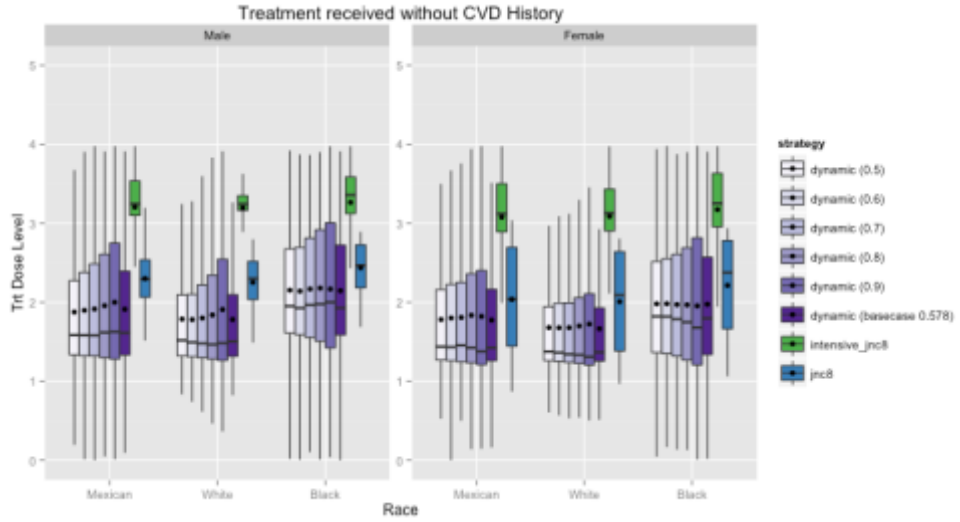


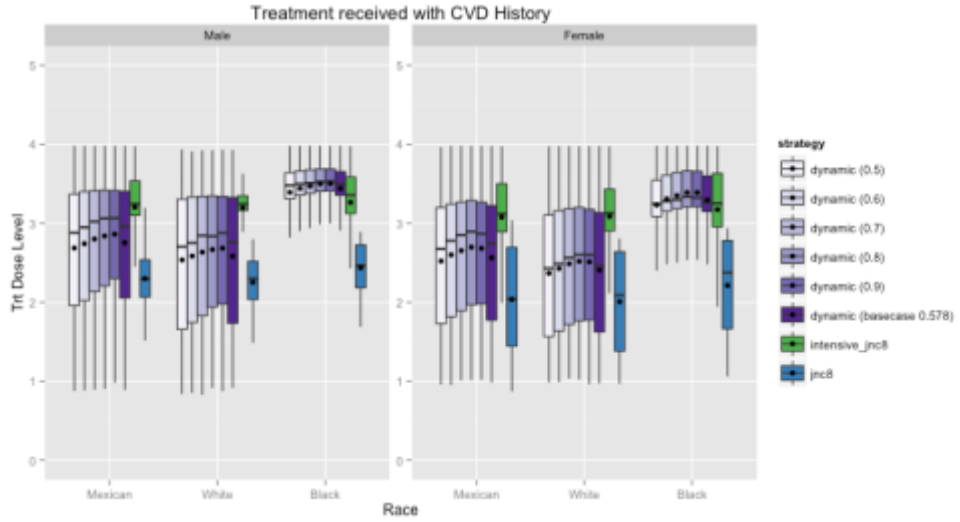




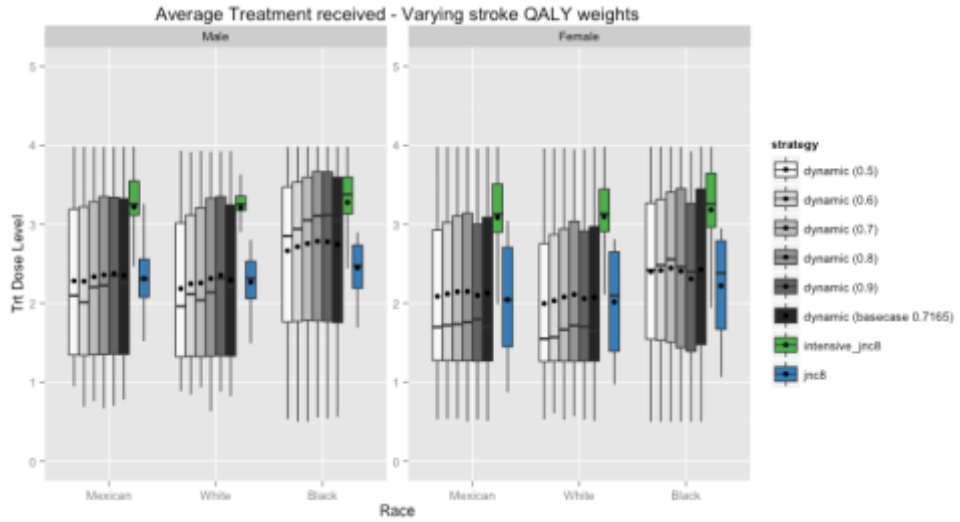
MI QALY weights (dynamic: MDP-based)

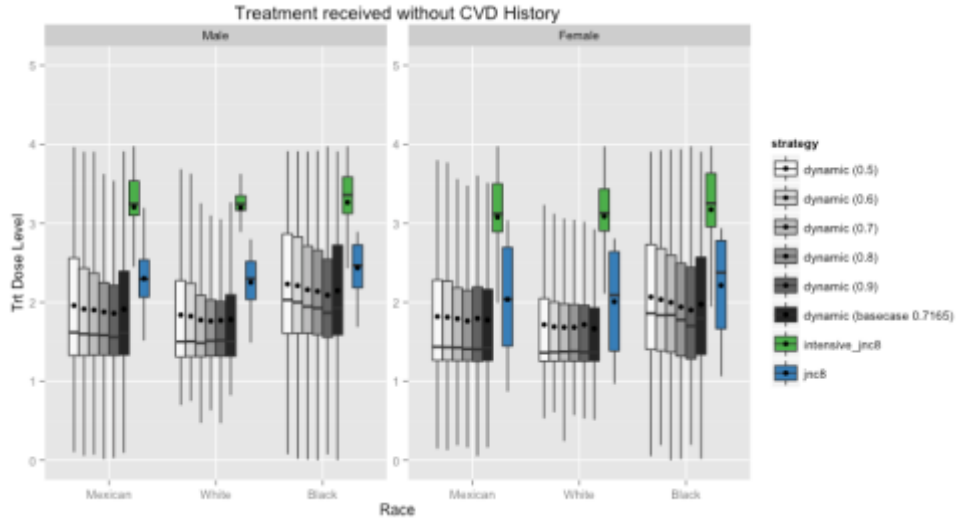


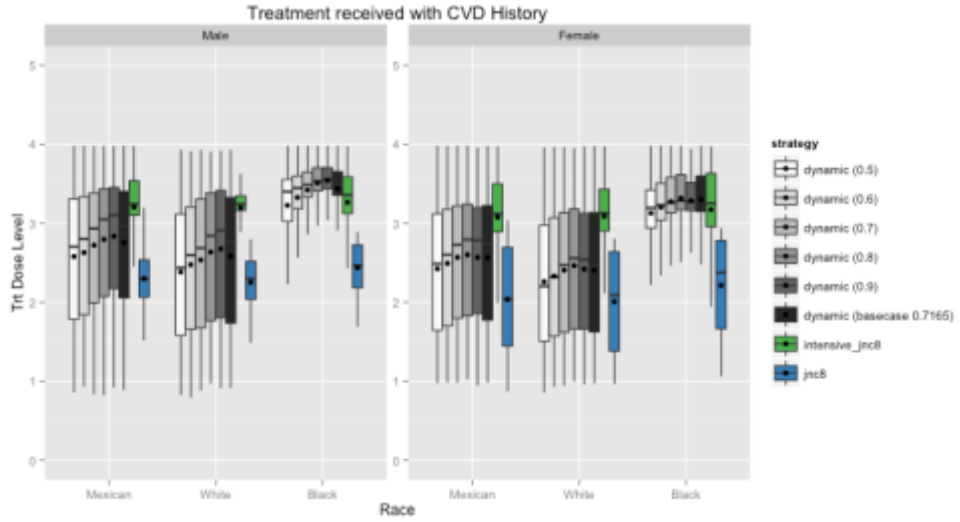




Stroke QALY weights (dynamic: MDP-based)







eTable 1. Risk of Adverse Events from Medications: Percentage of Patients with One or More Symptoms Attributable to Treatment*[1]

Medication	Half dose		Standard dose		Twice standard dose	
	Mean	SD	Mean	SD	Mean	SD
ACE- I	3.9	3.88	3.9	2.24	3.9	2.09
ARB	-1.8	4.28	0	1.79	1.9	3.83
Beta-blocker	5.5	2.6	7.5	1.79	9.4	2.6
CCB	1.6	2.65	8.3	1.79	14.9	2.95
Thiazide	2	2.14	9.9	1.68	17.8	3.21

*Calculated as difference between treated and placebo groups in proportion of participants who developed one or more symptoms, excluding headaches, which were significantly less common in people receiving treatment

Note: The adverse event rates from higher doses were linearly extrapolated up to 4 standard doses.

eTable 2. Comparison of Simulated Population and NHANES, 2003-2014

Characteristics [Mean or N (%)]	Simulated population	NHANES
Age (years)	50.52	49.20
Male	50.2 %	50.9 %
Race/ethnicity		
Mexican American	11.0%	11.5%
Non-Hispanic White	63.4%	62.9%
Non-Hispanic Black	25.4%	25.5%
MI History	4.26%	4.26%
Stroke History	3.26%	3.10%
SBP	124.1	122.7
Total cholesterol	197.1	195.0
HDL cholesterol	52.73	53.01
Smoking prevalence	21.0%	20.8%
Type 2 diabetes prevalence	13.5%	13.1%
Kidney disease history	18.9%	22.3%
MANOVA testing	p-value : 0.4268	

R outputs

```
> summary(manova(cbind(log_sbp,log_tchol,log_hdl,smoke,
hbp_tx,diab,premi,prestroke,ckd) ~ pop, data = comb.data),test =
"Hotelling-Lawley")
               Df Hotelling-Lawley approx F num Df den Df Pr(>F)
pop             1       2.5318e-05   1.0127      9 359990 0.4268
Residuals 359998
```

Based on the outputs from MANOVA test above, it can be seen that the patient covariates are not statistically different between the simulated population and NHANES population (real population data).

eTable 3. Quality-of-Life and Cost Estimates for Disease States and Adverse Events

By disease states and adverse events, mean (sd)

Disease states	Quality of life	Sources
MI	0.578	[5, 11]
Stroke	0.7165	[5, 11, 12]
Post CVD	0.9	[5, 11]
Adverse event	0.999	[5]

Disease states	Annual cost	Sources
MI	$44,267	[12]
Stroke	$23,254 (1400)	[12]
Post CVD	$5,208 (356)	[13]
Adverse event	(see below)	

Annual costs of medications and associated adverse events [12, 14]

Dose	Antihypertensive drug costs	Costs of adverse events*
0.5 standard doses	gamma(1.24, rate = 0.01)	$65.92
1.0 standard dose	gamma(1.66, rate = 0.01)	$131.40
1.5 standard doses	gamma(0.216, rate = 0.001)	$162.63
2.0 standard doses	gamma(0.238, rate = 0.001)	$193.87
2.5 standard doses	gamma(0.298, rate = 0.001)	$225.93
3.0 standard doses	gamma(0.357, rate = 0.001)	$258.05
3.5 standard doses	gamma(0.430, rate = 0.001)	$258.05
4.0 standard doses	gamma(0.496, rate = 0.001)	$258.05

* Costs of adverse events were estimated based on hospitalization cost – average cost (used for infrequent hospitalized drug-related adverse events) and high costs (used for rare hospitalized drug-related adverse events) – and incidence rates of serious adverse effects of medication (common, infrequent, and rare).

eTable 4. Comparison of MDP-based treatment (MDPT) vs. Intensive JNC8 Strategies

	Patients treated similarly by both Intensive JNC8 and MDPT strategies	Patients treated more intensively by MDPT strategy	Patients treated more intensively by Intensive JNC8 strategy
% of population	19.1	17.6	63.3
Mean initial 10-year CVD risk (%)	14.5	18.6	12.7
Mean post-10 years of treatment 10-year CVD risk (%)	14.6	14.8	14.6
QALY loss saved from CVD events, per 1000 patients treated, compared to Intensive JNC8	1.85	2.17	1.25
QALY loss saved from adverse events, per 1000 patients treated, compared to Intensive JNC8	0.03	-0.04	0.07
Total QALYs saved, per 1000 patients treated, compared to Intensive JNC8	43.4	46.8	31.7

eTable 5. Baseline MI History Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	0.00	NA	0.72	0.25	6.92	1.04
	NH White	0.21	0.04	2.31	0.18	15.42	0.48
	NH Black	0.00	NA	4.43	0.61	12.11	0.75
Female	Mexican	0.00	NA	1.26	0.29	4.11	0.60
	NH White	1.34	0.22	1.32	0.16	8.71	0.38
	NH Black	0	NA	0	NA	5.91	0.06

eTable 6. Baseline Stroke History Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	0.00	NA	1.91	1.89	9.43	3.94
	NH White	0.14	0.13	0.42	0.24	6.51	1.48
	NH Black	0.00	NA	1.98	1.72	12.61	3.76
Female	Mexican	0.00	NA	1.51	8.66	2.68	2.30
	NH White	1.05	1.04	1.69	0.61	7.95	1.72
	NH Black	0.33	0.32	4.49	2.32	8.02	2.95

eTable 7. Baseline Hypertension Medication Use Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	1.46	1.48	9.75	5.26	41.66	8.53
	NH White	3.95	1.49	14.25	2.35	52.41	2.41
	NH Black	5.76	1.41	33.54	4.48	62.41	3.91
Female	Mexican	7.88	5.24	6.47	3.48	47.86	10.54
	NH White	0.81	0.64	24.70	3.30	54.23	3.42
	NH Black	9.48	3.41	43.57	4.95	75.36	6.23

eTable 8. Baseline Systolic Blood Pressure (mmHg)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	121.4	1.2	124.1	3.2	135.1	7.6
	NH White	120.5	1.2	124.4	1.2	131.1	1.1
	NH Black	123.5	1.0	128.5	1.4	136.8	1.2
Female	Mexican	110.6	1.4	120.3	2.4	138.5	3.9
	NH White	109.9	0.7	121.2	1.1	135.3	1.3
	NH Black	113.8	1.3	128.5	1.9	140.4	1.9

eTable 9. Baseline Total Cholesterol (mmol/L)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	179.1	5.4	208.8	6.8	187.8	8.1
	NH White	191.5	4.4	206.4	2.1	187.8	1.4
	NH Black	182.3	3.3	190.8	5.0	184.9	4.6
Female	Mexican	187.2	5.6	208.9	6.7	208.6	9.5
	NH White	189.8	2.9	209.6	2.9	208.5	2.4
	NH Black	182.9	2.8	201.4	3.9	206.9	5.6

eTable 10. Baseline HDL Cholesterol (mmol/L)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	44.8	1.8	52.8	3.7	48.4	4.4
	NH White	47.3	1.1	49.1	0.8	51.2	0.6
	NH Black	49.5	1.5	54.9	2.7	53.0	0.7
Female	Mexican	58.7	2.4	55.7	4.1	53.3	2.4
	NH White	58.5	1.0	60.0	0.9	63.0	1.0
	NH Black	59.4	1.6	62.4	1.7	64.7	3.2

eTable11. Baseline Smoking Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	26.7	6.1	18.4	10.6	16.9	4.3
	NH White	30.9	3.1	24.1	3.6	11.9	2.8
	NH Black	27.6	4.5	35.5	6.8	22.1	5.0
Female	Mexican	9.5	4.5	26.2	9.0	9.9	3.1
	NH White	27.2	4.5	16.4	3.0	12.7	2.5
	NH Black	23.7	6.6	22.7	4.6	15.1	4.5

eTable 12. Baseline Type 2 Diabetes Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	0	NA	19.4	7.3	37.2	9.3
	NH White	1.3	0.7	4.9	1.3	14.7	2.2
	NH Black	5.1	1.5	14.2	5.7	32.9	5.0
Female	Mexican	2.7	1.2	5.2	2.1	30.7	4.8
	NH White	2.8	1.7	4.3	1.1	12.9	1.6
	NH Black	2.6	1.6	15.8	4.5	34.1	3.8

eTable 13. Baseline Chronic Kidney Disease (CKD) Prevalence (%)

		Age					
Sex	**Race**	**20-39**	**20-39**	**40-59**	**40-59**	**60-85**	**60-85**
		Mean	**SE**	**Mean**	**SE**	**Mean**	**SE**
Male	Mexican	10.5	3.3	2.6	2.3	19.4	5.9
	NH White	14.5	2.0	17.6	2.1	14.7	2.9
	NH Black	1.4	0.7	4.2	2.1	10.6	3.3
Female	Mexican	25.8	6.9	22.5	6.6	48.5	4.4
	NH White	23.2	4.3	41.1	2.4	42.8	3.2
	NH Black	6.9	1.7	6.8	1.8	13.6	3.4

References

1. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *Bmj-British Medical Journal*. 2009; 338. doi:ARTN b1665
10.1136/bmj.b1665.
2. Ramsey S, Willke R, Briggs A, et al. Good research practices for cost-effectiveness analysis alongside clinical trials: the ISPOR RCT-CEA Task Force report. *Value Health*. 2005; 8: 521-33. doi:10.1111/j.1524-4733.2005.00045.x.
3. Carey G. Multivariate Analysis of Variance (MANOVA): I. Theory. http://ibgwww.colorado.edu/~carey/p7291dir/handouts/manova1.pdf. (accessed Oct 25 2017).
4. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ*. 2009; 338: b1665. doi:10.1136/bmj.b1665.
5. Sussman J, Vijan S, Hayward R. Using benefit-based tailored treatment to improve the use of antihypertensive medications. *Circulation*. 2013; 128: 2309-17. doi:10.1161/CIRCULATIONAHA.113.002290.
6. Smith-Spangler CM, Juusola JL, Enns EA, et al. Population strategies to decrease sodium intake and the burden of cardiovascular disease: a cost-effectiveness analysis. *Ann Intern Med*. 2010; 152: 481-7, W170-3. doi:10.7326/0003-4819-152-8-201004200-00212.
7. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002; 360: 1903-13.
8. National Heart Lung and Blood Institute. Incidence and prevalence: 2006 chart book on cardiovascular and lung diseases. http://www.nhlbi.nih.gov/resources/docs/cht-book_ip.htm. (accessed May 15 2017).
9. Lim SS, Gaziano TA, Gakidou E, et al. Chronic diseases 4 - Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs. *Lancet*. 2007; 370: 2054-62. doi:Doi 10.1016/S0140-6736(07)61699-7.
10. National Heart Lung and Blood Institute. Cardiovascular Disease (10-year risk), Framingham Heart Study. https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php. (accessed Feb 2 2016).
11. Schell GE, Marrero WJ, Lavieri MS, et al. Data-driven Markov Decision Process approximations for personalized hypertension treatment planning. *MDM Policy & Practice*. 2016; 1: 1-9. doi:10.1177/2381468316674214.
12. Khoury MJ, Galea S. Will Precision Medicine Improve Population Health? *JAMA*. 2016; 316: 1357-8. doi:10.1001/jama.2016.12260.
13. Bayer R, Galea S. Public health in the precision-medicine era. *N Engl J Med*. 2015; 373: 499-501. doi:10.1056/NEJMp1506241.

14. RED BOOK Drug References. http://www.micromedexsolutions.com/micromedex2/4.34.0/WebHelp/MICROMEDEX_2.htm - RED_BOOK/Introduction_to_REDB_BOOK_Online.htm. (accessed April 17 2017).