The Future of Hepatocellular Carcinoma Incidence in the United States Forecast through 2030

Petrick, et al

Supplemental Methods

We define the probability of disease:

$$P(D) = P(E) * P(D|E) + P(\bar{E}) * P(D|\bar{E})$$

We define $\bar{\lambda}$ as the rate of HCC in any given age and cohort group, λ_0 as the baseline rate in the unexposed, and π as the prevalence of HCV in any given birth cohort. Finally, we define the relative risk of HCC among those infected with HCV of 40.0. Thus we rewrite the above equation as follows:

$$\bar{\lambda} = \pi * 40\lambda_0 + (1 - \pi) * \lambda_0$$

To demonstrate this example, we will use forecasted data for men aged 70 in 2030. The number of forecasted cases is 246, the population size is 243,139. Thus, the incidence rate OF HCC is 101.0 per 100,000 man-years. Utilizing NHANES 2011-2012 data, we applied a prevalence rate of 4,532 HCV infections per 100,000 men. We will assume a linear 50% uptake by 2030. That is, each year 3.7% of the remaining HCV infection would be treated. Thus, by 2030 the total amount of HCV infections treated would be 1-(1-0.037776)^{18}=0.5.

$$101.0 = 0.04532 * 40\lambda_0 + (1 - 0.04532) * \lambda_0$$
$$101.0 = (0.04532 * 40 + 0.95468) * \lambda_0$$
$$\lambda_0 = 101.0/(0.04532 * 40 + 0.95468)$$
$$\lambda_0 = 36.51$$

This is our baseline rate in the unexposed group, per 100,000 man-years. If we weight this by the proportion of man-years in the unexposed group (i.e., 1-π), we get 34.9 HCC cases in the unexposed group and 66.2 cases in the exposed group.

Now let's assume, as this is 2030 data, that we were able to treat 50% of those exposed with 100% efficacy leading to an HCC rate equal to unexposed individuals.

$$\bar{\lambda} = {}^{\pi}/_{2} * 40\lambda_0 + {}^{\pi}/_{2} * \lambda_0 + (1 - \pi) * \lambda_0$$
$$\bar{\lambda} = 0.02266 * 40 * 36.51 + 0.02266 * 36.51 + 0.95468 * 36.51$$
$$\bar{\lambda} = 68.8$$

We would be able to decrease the rate of HCC from 101.0 to 68.8 per 100,000 for males, aged 70, in 2030. With 80% uptake (i.e., 8.5% of remaining infections treated each year), the rate would decrease even further to 49.4 per 100,000 man-years.

	No Intervention		**Intervention 50%**		**Intervention 80%**	
	Cases	Man-Years	Cases	Man-Years	Cases	Man-Years
Exposed	66.2	4,532	33.1	2,266.2	13.2	906.5
Treated	0	0	0.8	2,266.2	1.3	3,625.9
Unexposed	34.9	95,467	34.9	95,467	34.9	95,467
TOTAL	101.0	100,000	68.8	100,000	49.4	100,000

Estimated Prevalence of Hepatitis C Antibody from NHANES 2011-2012.

Birth Cohort	**Sex**	**HCV Prevalence**
Silent Generation, ≤1945	Men	0.008419
	Women	0.00631
Baby Boomers, 1946-1965	Men	0.045324
	Women	0.023798
Generation X, 1966-1980	Men	0.015494
	Women	0.012335
Millenials, 1981-1995	Men	0.000594
	Women	0.000297

Table S1. Liver cancer incidence rates (per 100,000 person-years) and burden through 2030 by sex and race.

	2010*	2013		2020		2030		Burden % change	Rate EAPC	
	Rate	No.	Rate	No.	Rate	No.	Rate	2013-30	2000-12	2013-30
All	15.1	31,579	16.8	46,035	20.6	66,627	25.2	110.98	3.10	2.49
Male	23.6	23,566	26.4	34,219	32.4	47,732	38.7	102.55	3.13	2.38
Female	7.7	8,090	8.4	11,737	10.2	18,691	13.4	131.05	2.90	2.87
Asian	25.9	2,197	25.3	2,601	22.6	3,033	19.0	38.07	-1.14	-1.70
Hispanic	23.4	3,986	25.4	6,160	29.1	9,590	31.8	140.58	1.83	1.43
Black	18.9	4,686	21.7	6,783	26.2	8,758	28.5	86.92	2.87	1.65
White	11.4	18,662	13.1	28,051	17.0	42,201	22.2	126.14	3.61	3.29

*Number of HCC cases for 2010 are not provided, as these numbers are based on SEER data and not extrapolated to the entire US population.

Table S2. Hepatocellular carcinoma incidence rates (per 100,000 person-years) and burden through 2030 by age, sex, and race.

	Age 65+									
	2010*	2013		2020		2030		Burden % change	Rate EAPC	
	Rate	No.	Rate	No.	Rate	No.	Rate	2013-30	2000-12	2013-30
All	24.3	10,748	28.0	22,773	45.0	45,019	70.9	318.86	3.64	5.93
Males	37.6	7,807	44.6	17,439	74.4	33,855	116.7	333.64	3.65	6.13
Females	13.6	2,990	14.5	5,222	19.5	10,903	31.7	264.68	3.32	4.97
Asian	55.5	849	52.7	1,167	48.9	1,619	45.5	90.67	-1.14	-0.75
Hispanic	41.7	1,356	49.5	2,800	68.9	6,195	96.6	357.01	2.28	4.32
Black	26.8	1,269	33.1	3,465	63.3	6,023	84.8	374.53	3.37	5.80
White	17.4	6,293	20.8	14,311	37.0	30,201	65.3	379.92	4.22	7.34
	Age 50-64									
	2010*	2013		2020		2030		Burden % change	Rate EAPC	
	Rate	No.	Rate	No.	Rate	No.	Rate	2013-30	2000-12	2013-30
All	18.2	13,548	20.8	14,495	20.4	10,651	16.3	-21.38	3.64	-1.65
Males	31.4	11,219	35.5	11,614	33.6	8,188	25.7	-27.02	3.65	-2.18
Females	5.7	2,328	6.9	2,945	8.1	2,531	7.5	8.69	3.32	0.35
Asian	24.0	806	24.0	833	20.5	742	14.6	-7.95	-1.14	-2.95
Hispanic	26.9	1,730	28.6	2,241	27.3	2,009	18.1	16.14	2.28	-2.77
Black	28.9	2,581	33.1	2,460	27.1	1,784	20.6	-30.88	3.37	-3.20
White	13.8	7,817	16.3	8,180	16.3	4,800	11.5	-38.59	4.22	-2.28
	Age 35-49									
	2010*	2013		2020		2030		Burden % change	Rate EAPC	
	Rate	No.	Rate	No.	Rate	No.	Rate	2013-30	2000-12	2013-30
All	2.0	1,310	2.0	1,085	1.7	559	0.8	-57.36	3.64	-5.67
Males	3.2	1,046	3.2	828	2.6	368	1.0	-64.80	3.65	-6.83
Females	0.8	279	0.8	247	0.8	229	0.7	-18.08	3.32	-1.85
Asian	3.9	199	4.4	179	3.4	124	1.9	-37.33	-1.14	-5.19
Hispanic	2.9	273	2.8	252	2.2	107	0.8	-60.62	2.28	-8.25
Black	2.2	222	2.5	165	1.8	62	0.6	-72.24	3.37	-7.94
White	1.3	534	1.2	371	0.9	189	0.5	-64.49	4.22	-6.31

*Number of HCC cases for 2010 are not provided, as these numbers are based on SEER data and not extrapolated to the entire US population.

Figure S1. Fitted incidence rates of hepatocellular carcinoma by race for A) males and b) females, by birth cohort.

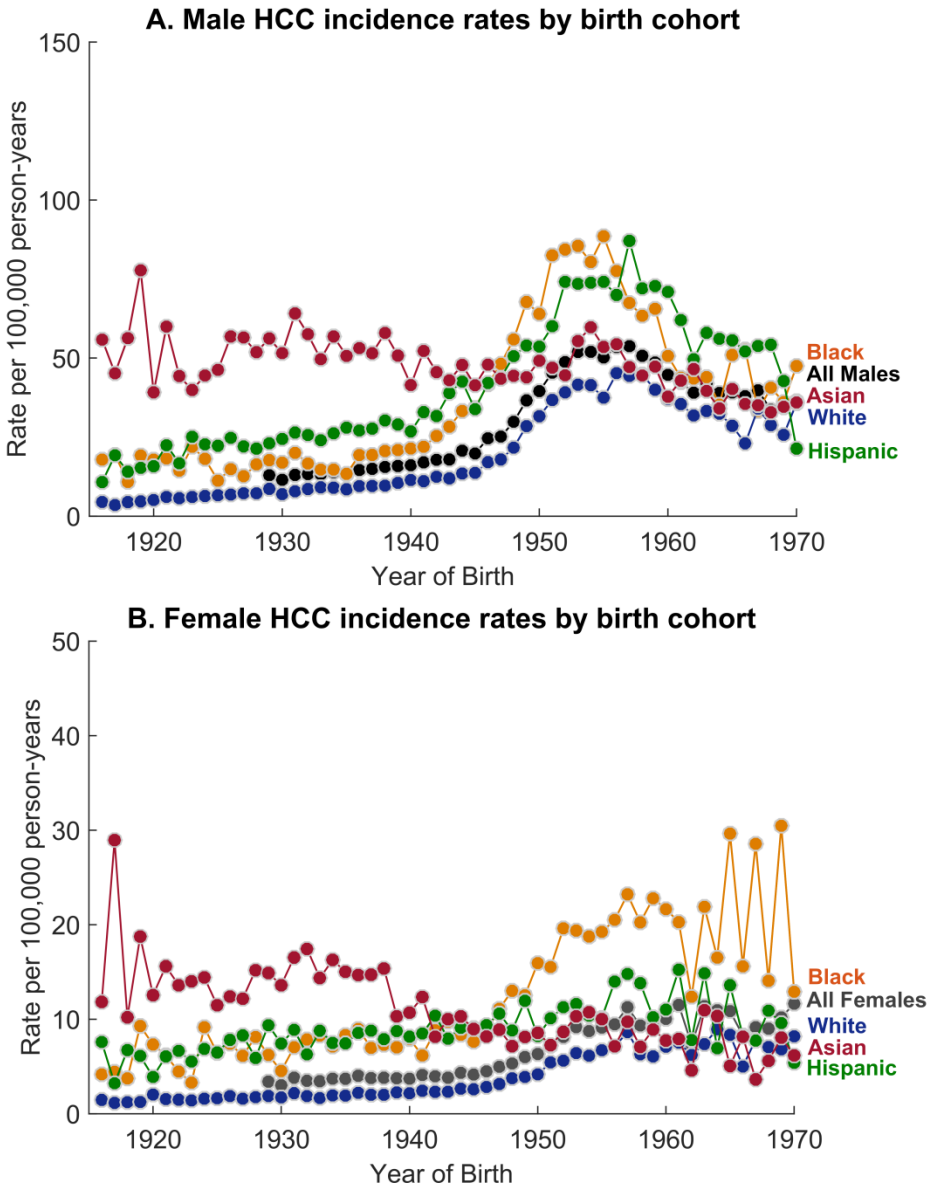


Figure S2. Observed and projected incidence of primary liver cancer (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, overall and by race in A) males and B) females. Shaded bands show point-wise 95% confidence limits.

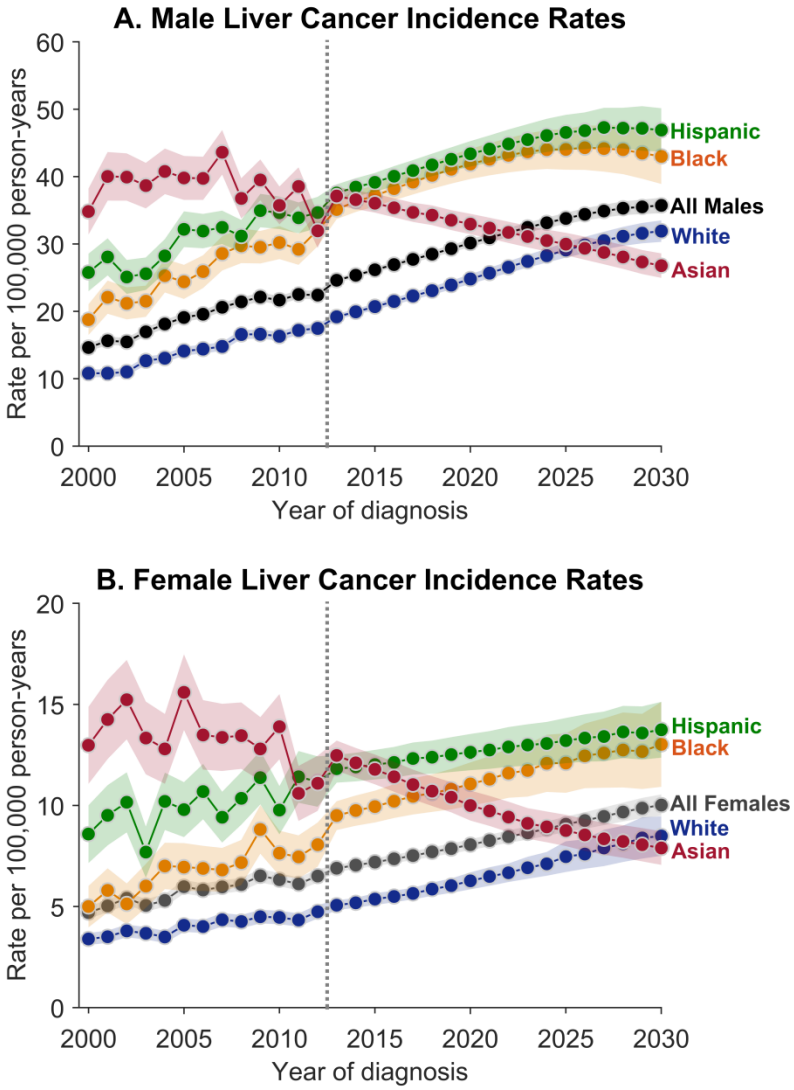


Figure S3. Observed and projected incidence of hepatocellular carcinoma (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, among 35-49 year olds overall and by race in A) males and B) females. Shaded bands show point-wise 95% confidence limits.

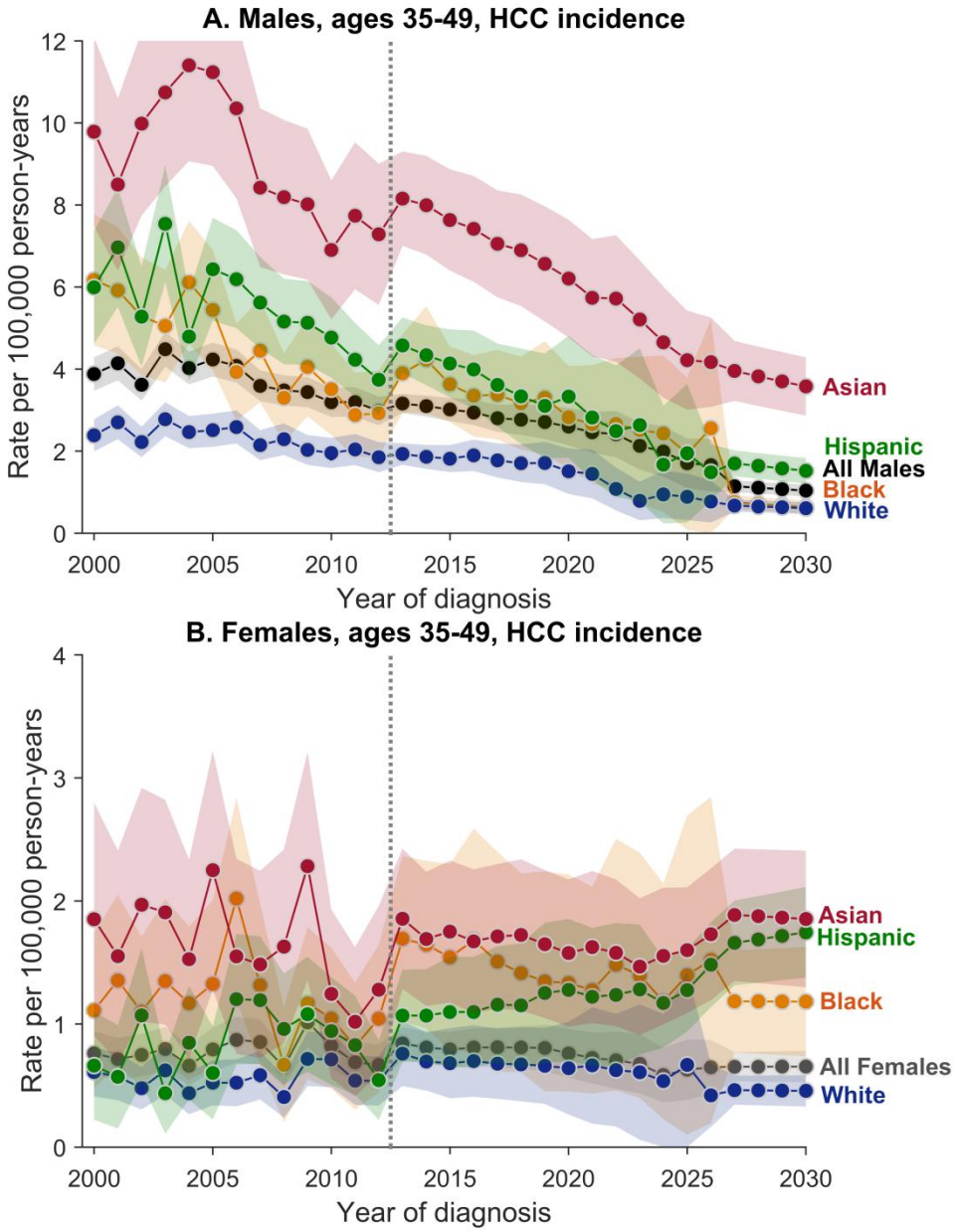


Figure S4. Observed and projected incidence of hepatocellular carcinoma (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, among 50-64 year olds overall and by race in A) males and B) females. Shaded bands show point-wise 95% confidence limits.

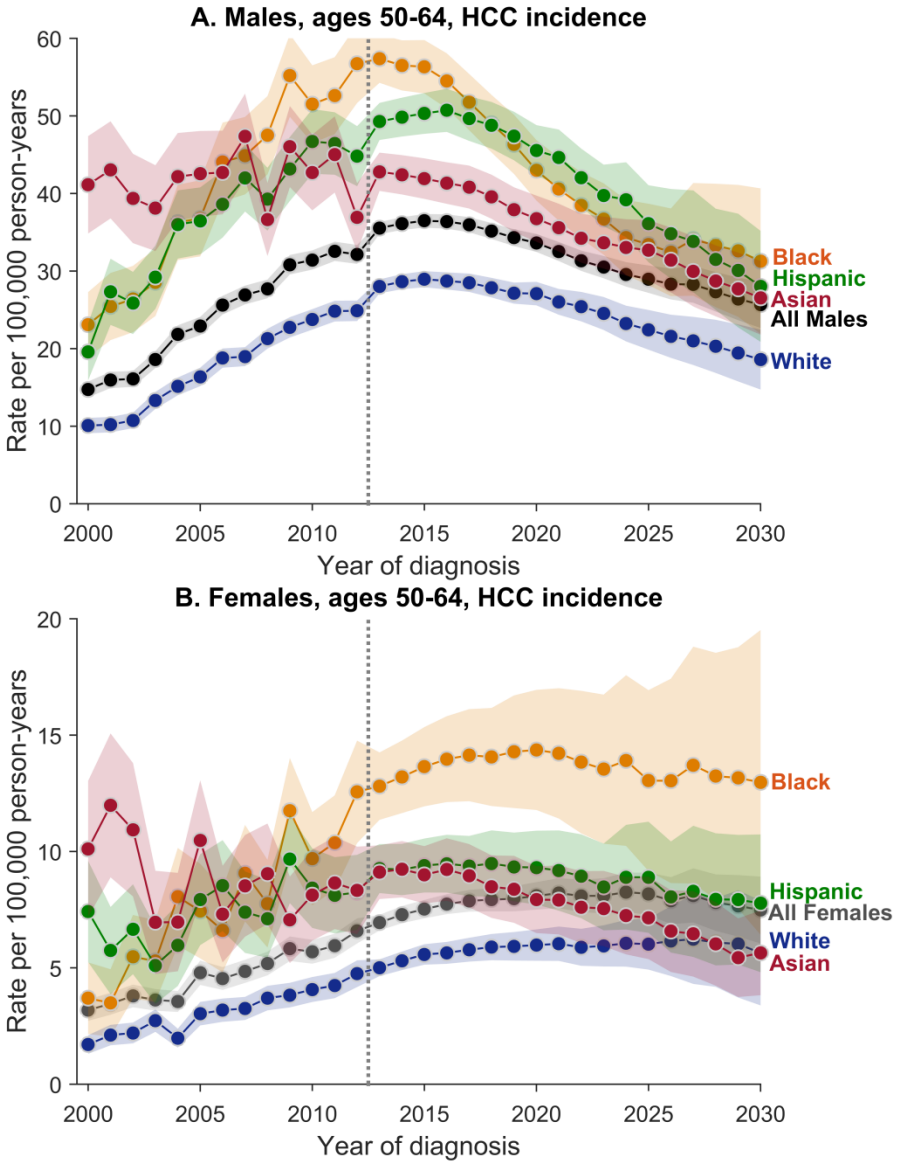


Figure S5. Observed and projected incidence of hepatocellular carcinoma (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, among 65-84 year olds overall and by race in A) males and B) females. Shaded bands show point-wise 95% confidence limits.

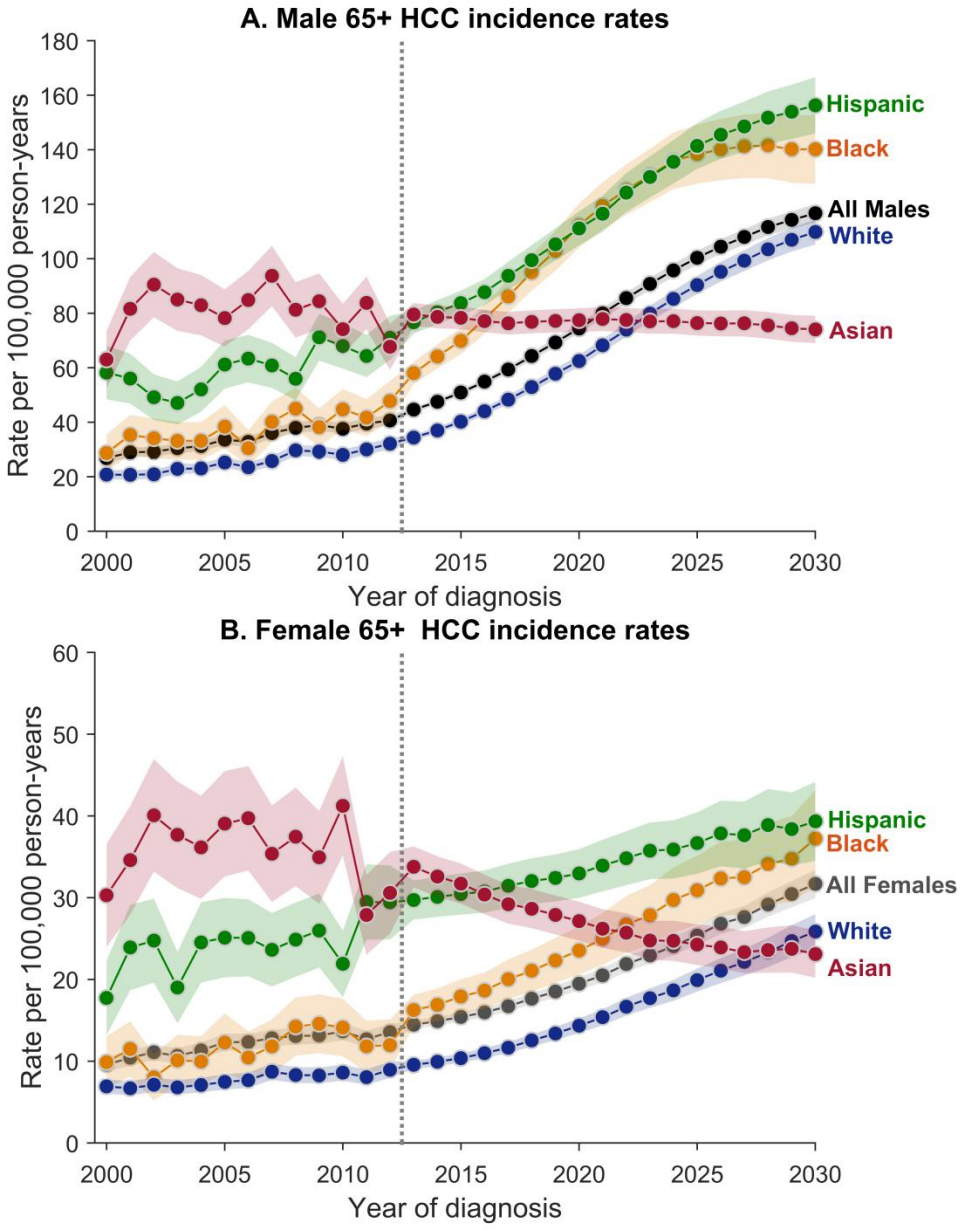
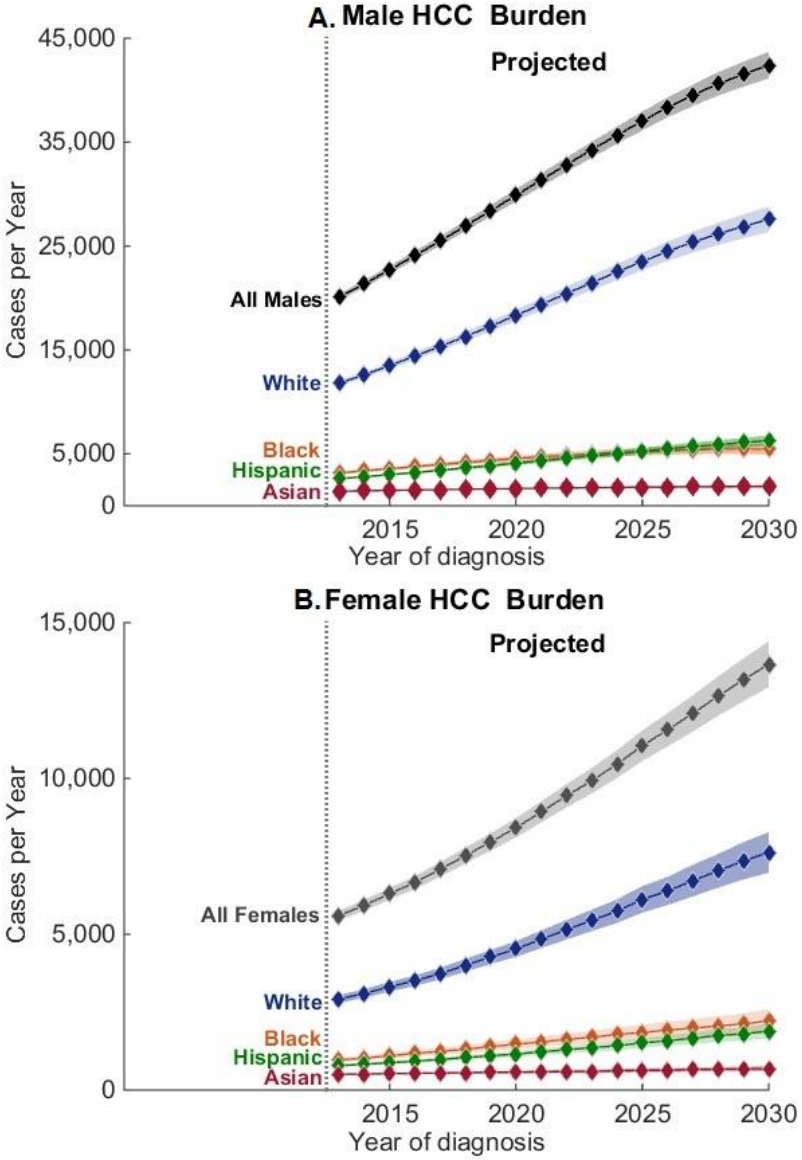
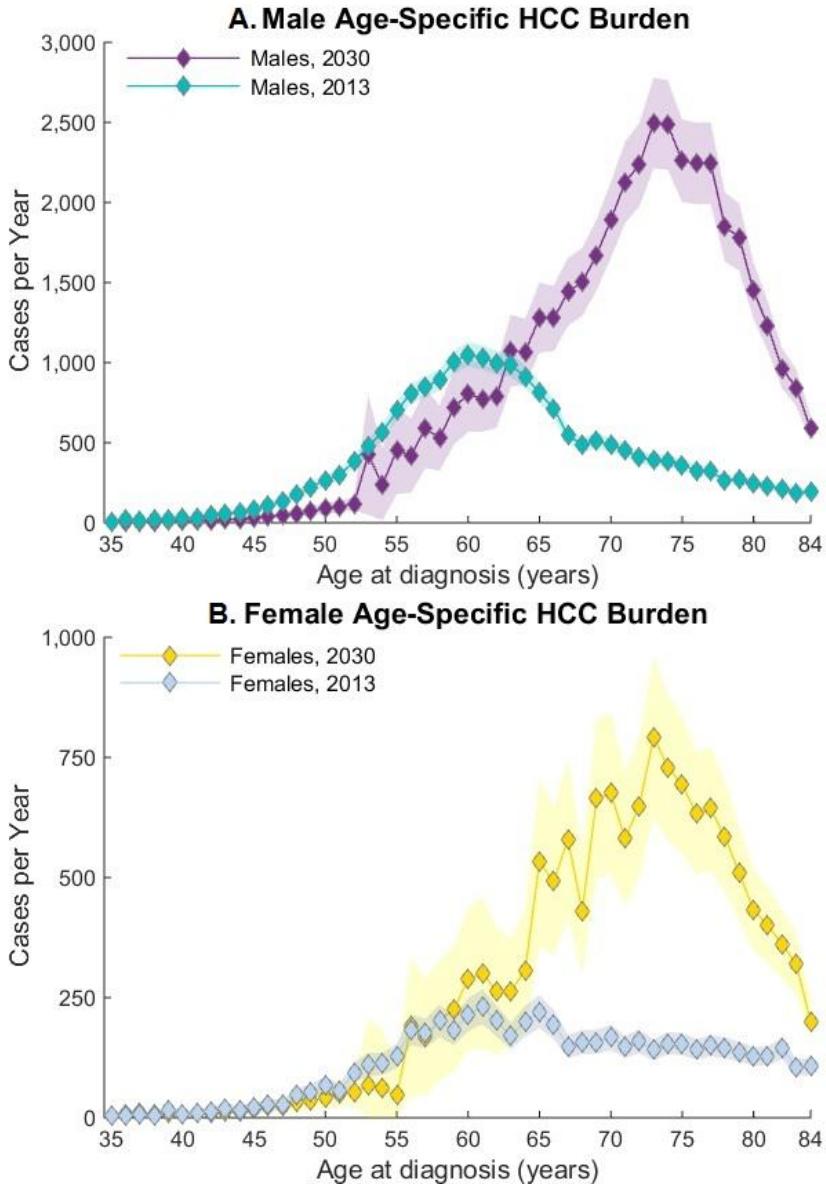


Figure S6. Projected burden of hepatocellular carcinoma (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, overall and by race in A) males and B) females. Shaded bands show point-wise 95% confidence limits*.



*Population projections are provided as point estimates, without confidence intervals, for planning purposes. Thus, these confidence intervals incorporate some but not all sources of variation.

Figure S7. Projected burden of hepatocellular carcinoma in Surveillance, Epidemiology, and End Results (SEER) 18 by calendar period, 2000-2012 and 2013-2030 in A) males and B) females. Shaded bands show point-wise 95% confidence limits*.



*Population projections are provided as point estimates, without confidence intervals, for planning purposes. Thus, these confidence intervals incorporate some but not all sources of variation.

Figure S8. Projected burden of hepatocellular carcinoma (per 100,000 person-years) in Surveillance, Epidemiology, and End Results (SEER) 18, by age group in A) males and B) females. Shaded bands show point-wise 95% confidence limits*.

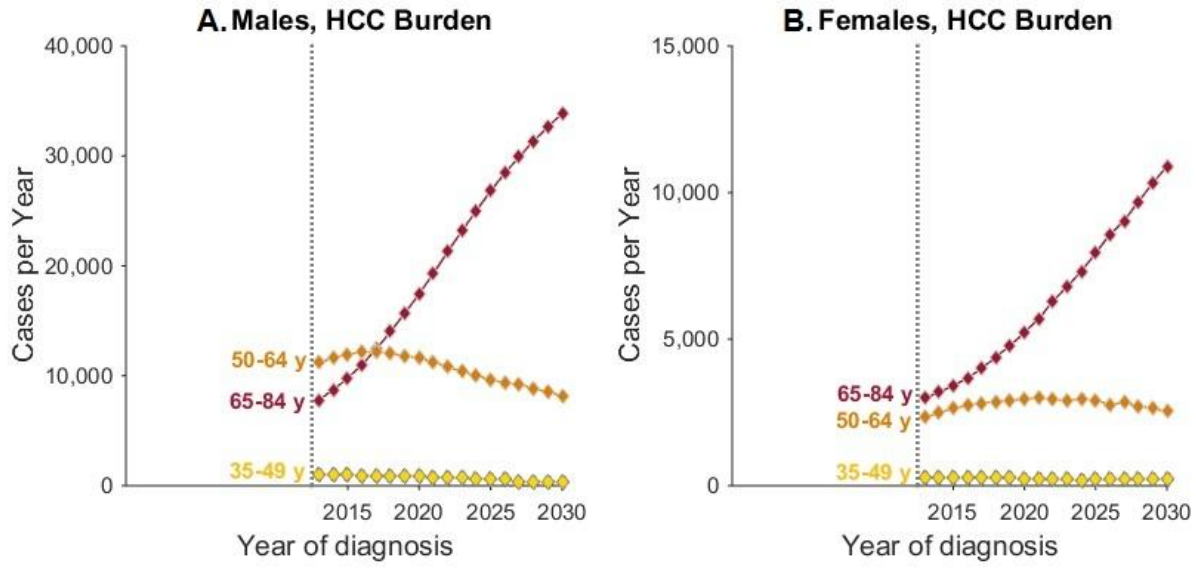
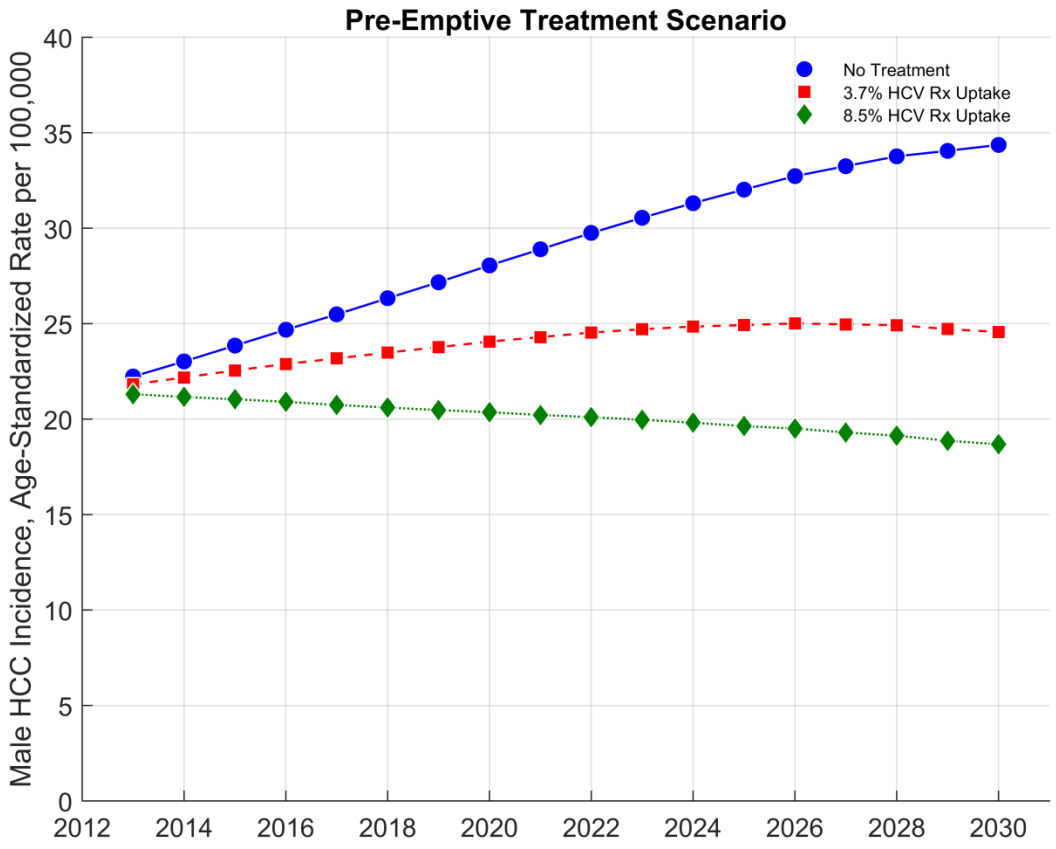


Figure S9. Sensitivity analysis showing potential scenarios of the impact of HCV treatment with second generation direct-acting antivirals among A) Males and B) Females. This model uses the assumptions of linear uptake in antivirals, with 50% and 80% of infections treated by 2030. Thus, each year 3.7% and 8.5% of remaining HCV infections would be treated, respectively.



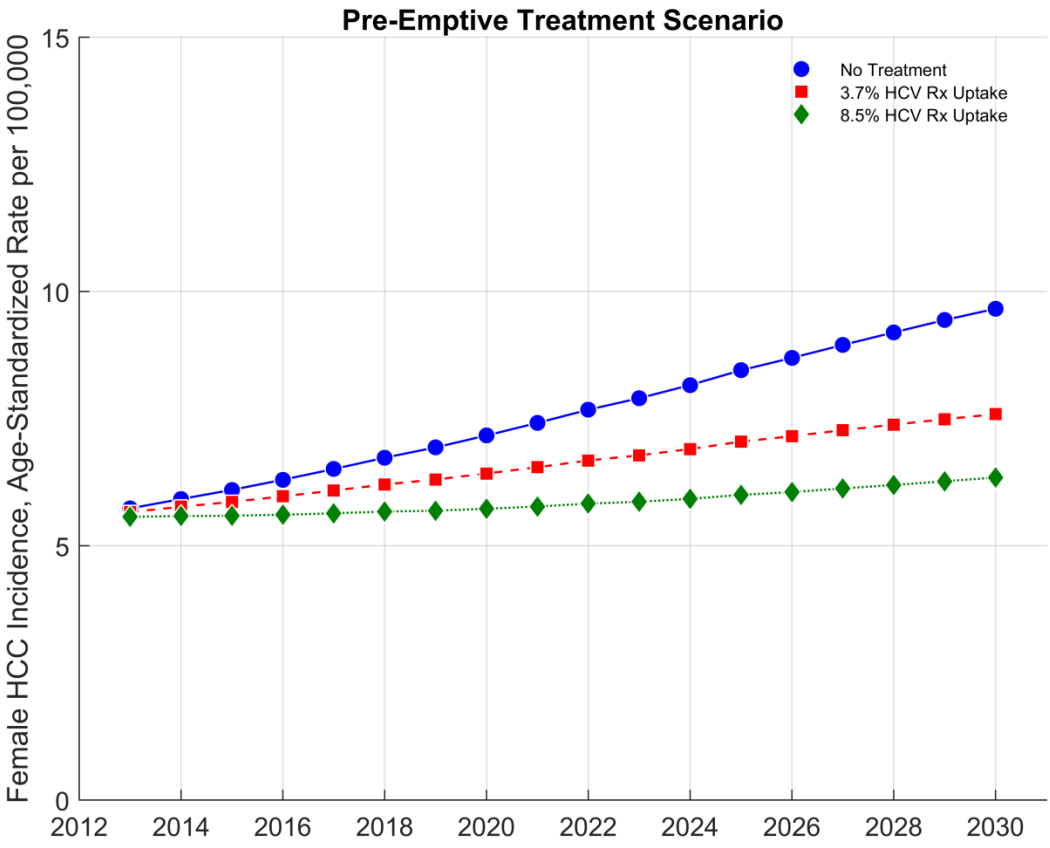
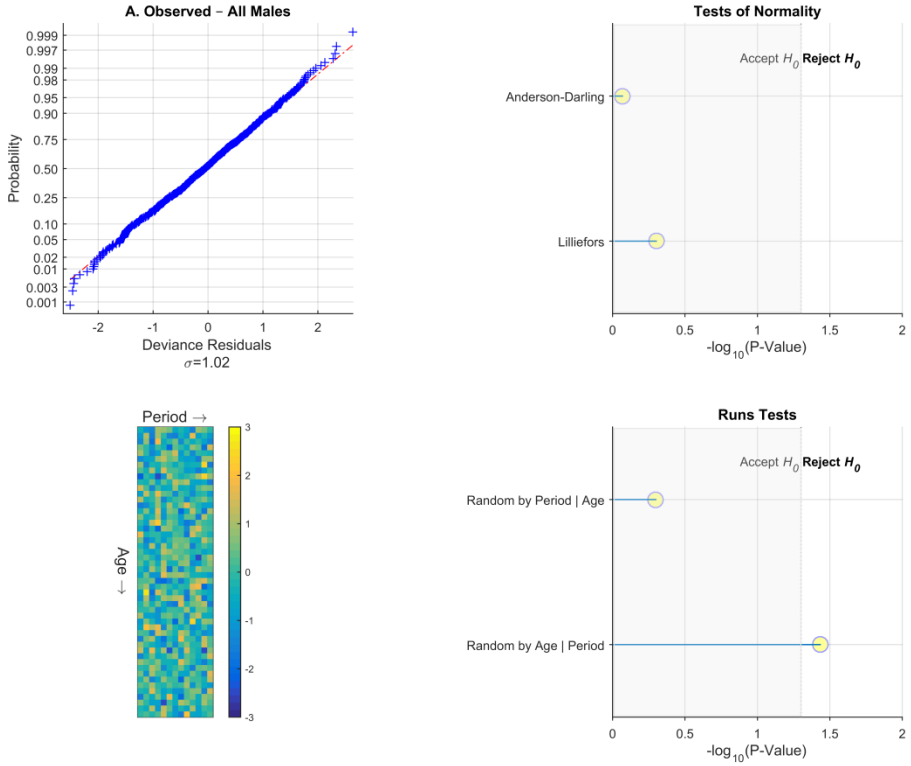
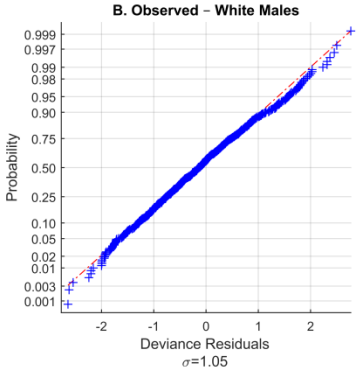
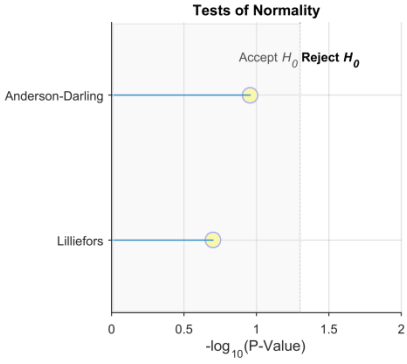
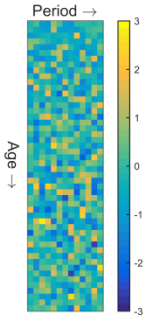

Pre-Emptive Treatment Scenario
Female HCC Incidence, Age-Standardized Rate per 100,000
15
10
5
0
2012
2014
2016
2018
2020
2022
2024
2026
2028
2030
No Treatment
3.7% HCV Rx Uptake
8.5% HCV Rx Uptake

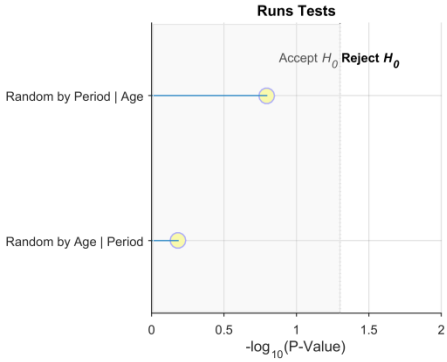
Figure S10. Goodness of fit tests for males: A) all males, B) White, C) Black, D) Hispanic, and E) Asian.

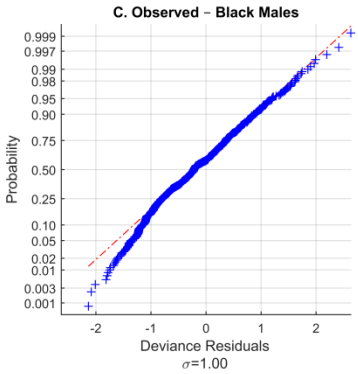


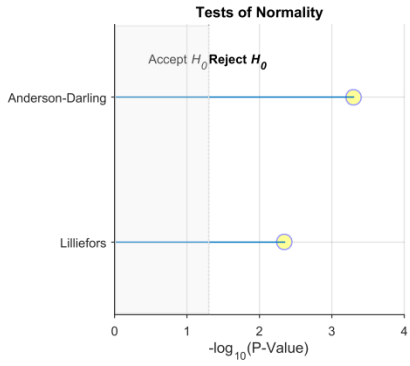

B. Observed – White Males
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.05

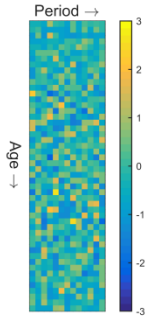

Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
0.5
1
1.5
2
-log10(P-Value)

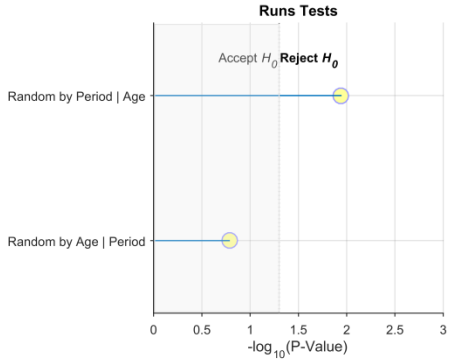

Period →
Age →
3
2
1
0
-1
-2
-3

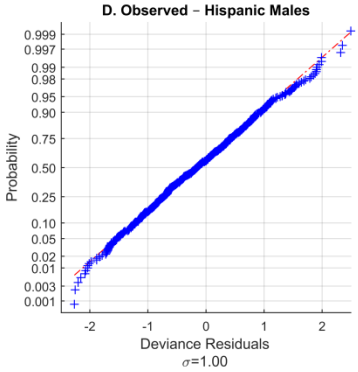

Runs Tests
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)

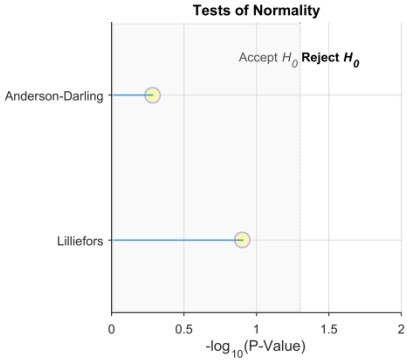

C. Observed – Black Males
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00

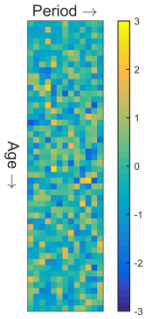

Tests of Normality
Accept H_0
Reject H_0
Anderson-Darling
Lilliefors
0
1
2
3
4
-log10(P-Value)


Period →
Age →
3
2
1
0
-1
-2
-3


Runs Tests
Accept H_0
Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
2.5
3
-log10(P-Value)


D. Observed – Hispanic Males
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00


Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
0.5
1
1.5
2
-log10(P-Value)


Period →
Age ↓
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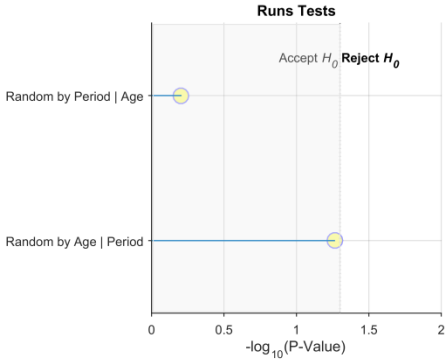
2
1
0
-1
-2
-3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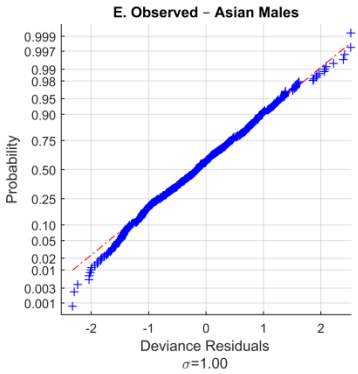
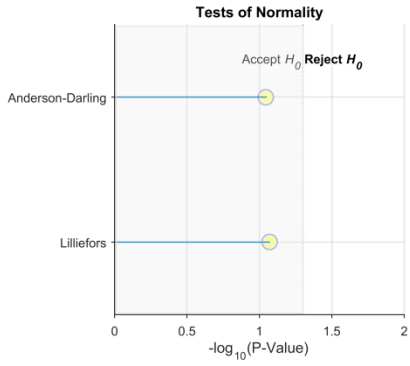
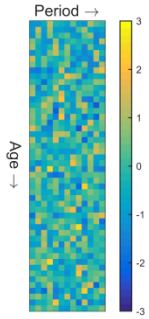
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)


E. Observed – Asian Males
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00


Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
0.5
1
1.5
2
-log10(P-Value)


Period →
Age ↓
3
2
1
0
-1
-2
-3

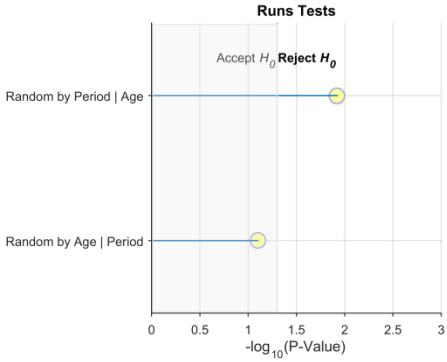
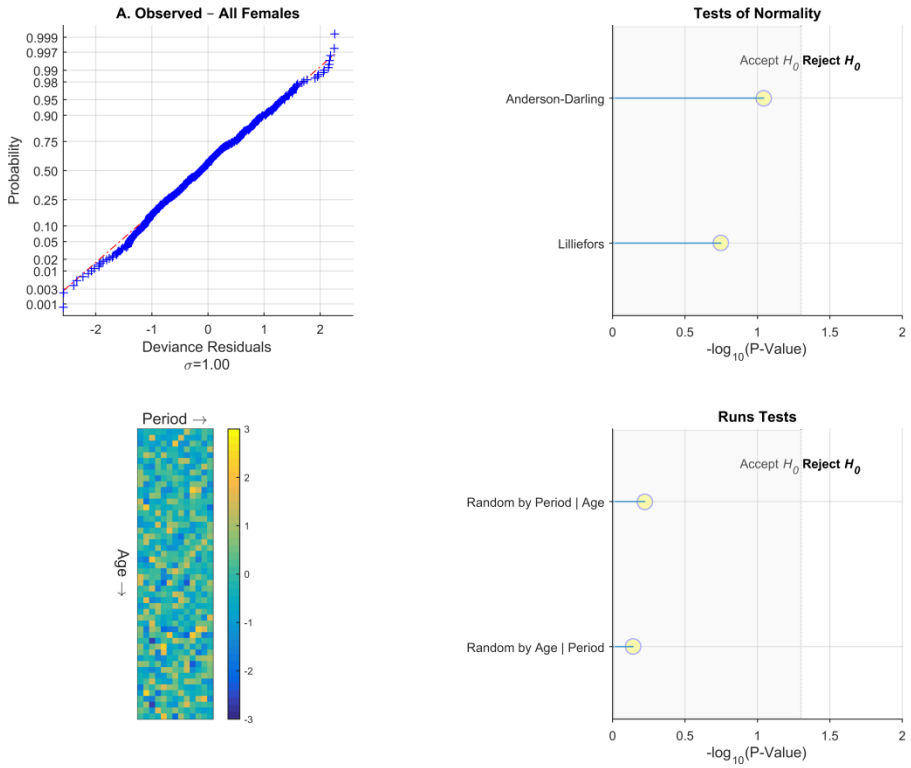
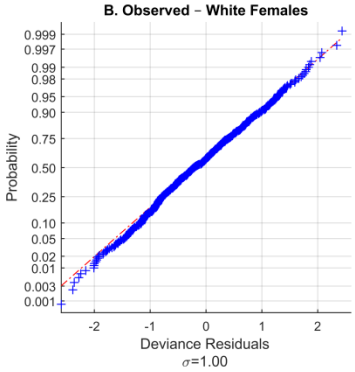
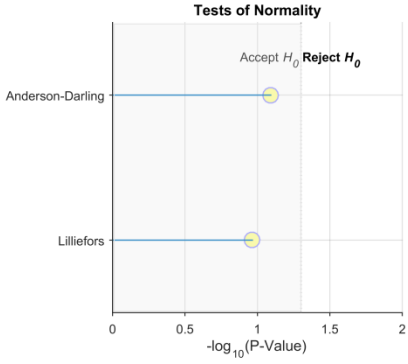
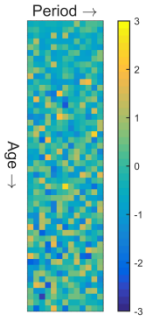

Runs Tests
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
2.5
3
-log10(P-Value)

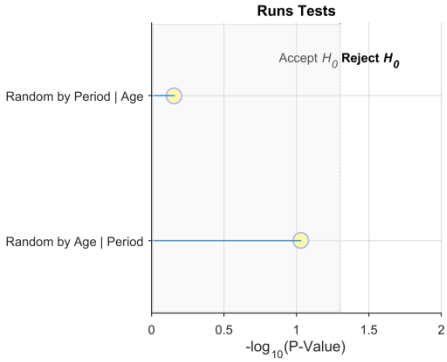
Figure S11. Goodness of fit tests for females: A) all females, B) White, C) Black, D) Hispanic, and E) Asian.

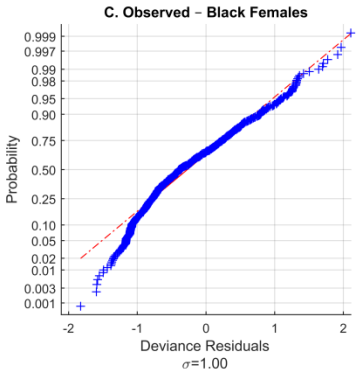


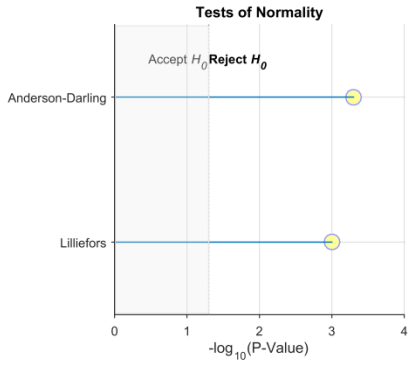

B. Observed – White Females
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00

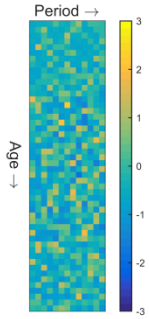

Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
0.5
1
1.5
2
-log10(P-Value)

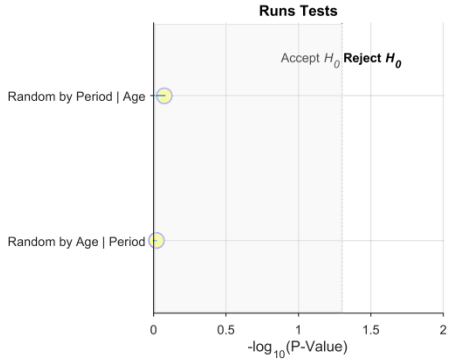

Period →
Age ↓
3
2
1
0
-1
-2
-3

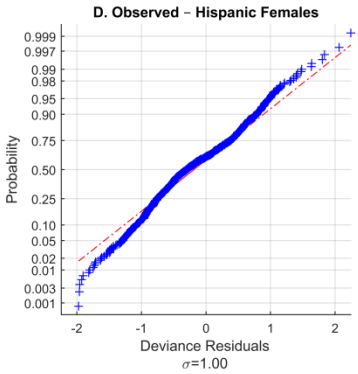

Runs Tests
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)

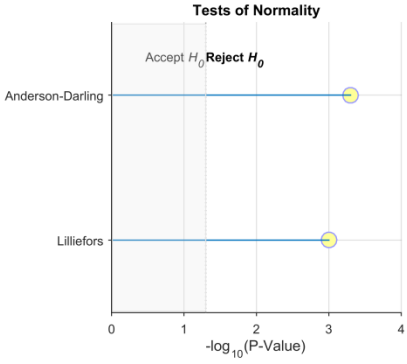

C. Observed – Black Females
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00

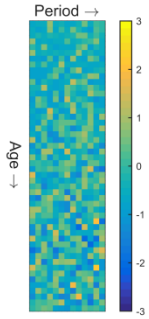

Tests of Normality
Accept H_0
Reject H_0
Anderson-Darling
Lilliefors
0
1
2
3
4
-log10(P-Value)

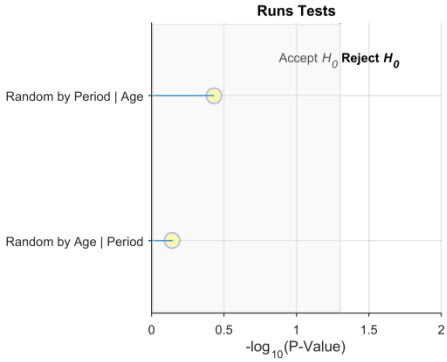

Period →
Age ↓
3
2
1
0
-1
-2
-3

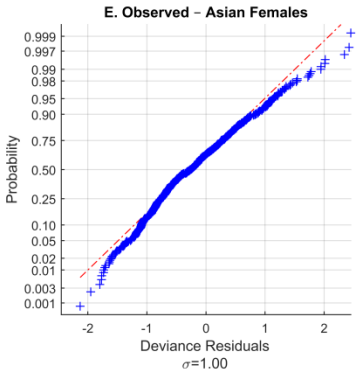

Runs Tests
Accept H_0
Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)

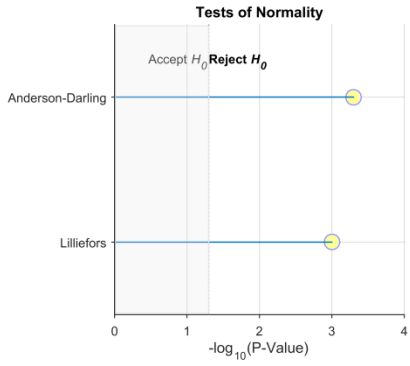

D. Observed – Hispanic Females
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00

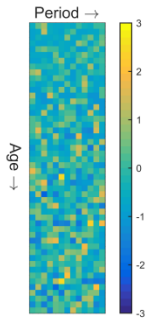

Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
1
2
3
4
-log10(P-Value)

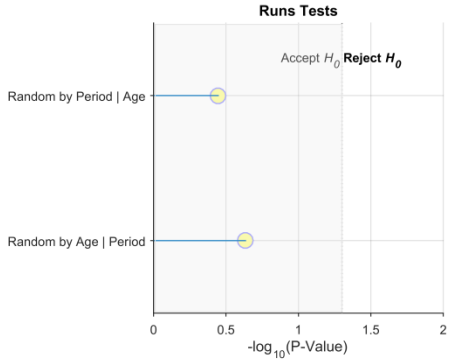

Period →
Age ↓
3
2
1
0
-1
-2
-3


Runs Tests
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)


E. Observed – Asian Females
Probability
0.999
0.997
0.99
0.98
0.95
0.90
0.75
0.50
0.25
0.10
0.05
0.02
0.01
0.003
0.001
-2
-1
0
1
2
Deviance Residuals
σ=1.00


Tests of Normality
Accept H_0 Reject H_0
Anderson-Darling
Lilliefors
0
1
2
3
4
-log10(P-Value)


Period →
Age ↓
3
2
1
0
-1
-2
-3


Runs Tests
Accept H_0 Reject H_0
Random by Period | Age
Random by Age | Period
0
0.5
1
1.5
2
-log10(P-Value)