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Research article

The dynamics of heroin and illicit opioid use disorder, casual use, treatment, and recovery: A mathematical modeling analysis

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Supplementary

S.1. Supplementary information

S.1.1. MIXING

The state variables E, T_E, I, and T are instantaneous in time, whereas the SAMHSA data is not. SAMHSA gives a count over the year of those respective classes. Therefore, we correct comparing the data to the variables. The following is a detailed explanation of how we added to the I variable and the T variable to approximate SAMHSA's yearly count.

There are two parts to this: (1) we need to incorporate those that left I in the last year since they would be counted in this data; (2) we then need to update this with an estimate of the number of people that left I in the last year, but came back to I (and thus are in I currently). While presumably each of these steps could happen multiple times within a year, we only consider each "correction" one time.

The reader should see the Mixing Model Flow Chart in Figure S.1 (modified from Figure 1 in main article) for the following explanations. First, we discuss how to find the corrected yearly number of individuals in the I class. In the flow diagram of Figure S.1, we see that the individuals over the year could leave I yearly by either going to the T class or the R class. We denote the number of individuals in the I class that flowed to the T class in one time period as $y06$. We denote the number of individuals in the I class that flowed to the R class in one time period as $y11$. Therefore we have:

$$\text{leave}I\text{yearly} = y06 + y11.$$

To get the the additional correction count we use the following equation:

$$\text{corrected leave}I\text{yearly} = y06 - \frac{Q_i}{T_i}y08 + y11 - \frac{P_i}{R_i}y09 \tag{S.1}$$

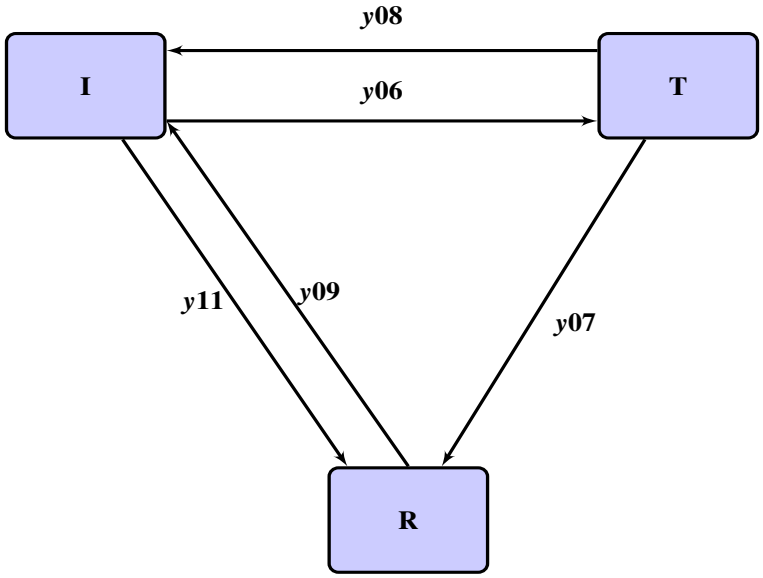

Figure S.1. Mixing Model Flow Chart. This Is Used Together with the Instantaneous Variables to Compare To SAMHSA's "use in Last Year" Data. An Analogous Flow Chart and Derivation Can Be Done for the Set of Variables S-E-T_E.

where $Q(t)$ denotes the number of former I in T from last year, $P(t)$ denotes the number of former I in R from last year, $y08$ denotes the number of individuals in the T class that flowed to the I class in one time period, and $y09$ denotes the number of individuals in the R class that flowed to the I class in one time period. Hence, $\frac{Q_i}{T_i}$ scales $y08$ by the proportion of T that are from I in the last year and $\frac{P_i}{T_i}$ scales $y09$ by the proportion of R that are from I in the last year. We then use the following equation to solve for Q:

$$\begin{cases} \dfrac{dQ(t)}{dt} = \text{rate in} - \text{rate out}, \\ \qquad = y06/\text{yr.} - (\text{concentration of former } I \text{ in } T) \times (\text{rate of flow out}), \\ \qquad = y06/\text{yr.} - \dfrac{Q}{T} \times (y08/\text{yr.} + y07/\text{yr.}), \\ \qquad = y06 - Q\left(\dfrac{y08 + y07}{T}\right) \end{cases} \tag{S.2}$$

where $y07$ denotes the number of individuals in the T class that flowed to the R class in one time period and $y08$ denotes the number of individuals in the T class that flowed back to the I class in one time period. We make the approximation/assumption that T, $y06$, $y07$, and $y08$ are constant over the time period of one year. With this simplifying assumption, this equation is now a standard linear ODE that can be solved explicitly. Solving for $Q(t)$,

$$Q(t) = \frac{y06}{y_c} + Ce^{-y_c t}$$

where $y_c = \dfrac{y08 + y07}{T}$. $Q(t)$ is the number of former individuals from I in T, to be updated each year.

This solution is continuous in time; however, we only receive a yearly number from SAMHSA. We thus consider a discrete version of this solution that will hold at time t_k (where k denotes the time period) and we will update this with the yearly output from our ODE model. The additional item that we need to determine is the initial condition, which is the number of from I in T from the last year for that initial year. We "guess" this is $\frac{1}{2}T_{t_k}$.

Hence we take our equation

$$Q(t_k) = \frac{y06}{y_{c_k}} + Ce^{-y_{c_k}t_k}$$

and substitute in the guess to obtain

$$\frac{1}{2}T_{t_k} = \frac{y06}{y_{c_k}} + Ce^{-y_{c_k}t_k}.$$

Solving for C gives us:

$$C = \left(\frac{1}{2}T_{t_k} - \frac{y06}{y_c}\right)e^{y_{c_k}t_k}$$

and thus

$$Q = \frac{y06}{y08 + y07}T + \left(\frac{1}{2}T_k - \frac{y06_k}{y08_k + y07_k}T_k\right)e^{y_{c_k}t_k - y_{c_{k+1}}t_{k+1}}$$

Because our derived equation utilizes the output from the ODE, we have the data for future time steps by keeping track of the yearly outputs. Recall, that the corrections are used to compare with the data and do not influence the dynamics of the equations. Thus, we write Q as an implicit equation where the subscript k denotes the current year and $k + 1$ denotes the next year:

$$Q_{k+1} = \frac{y06_{k+1}}{y08_{k+1} + t07_{k+1}}T_{k+1} + \left(\frac{1}{2}T_k - \frac{y06_k}{y08_k + t07_k}T_k\right)e^{-t_{k+1}\left(\frac{y08_{k+1} + t07_{k+1}}{T_{k+1}}\right) + y_c t_k}$$

In a typical mixing model, the rate in and rate out remain constant over time and thus we approach an equilibrium with the exponential term rapidly decreasing over time. In our situation, the rate in and rate out may change each year according to our model output. Thus we reset our time step each year: $t_k = 0$ and $t_{k+1} = 1$. Hence, our equation for Q, the number of former I in T from last year, is

$$Q_{k+1} = \frac{y06_{k+1}}{y08_{k+1} + t07_{k+1}}T_{k+1} + \left(\frac{1}{2}T_k - \frac{y06_k}{y08_k + t07_k}T_k\right)e^{-(y08_{k+1} + t07_{k+1})/T_{k+1}}$$

In order to not make the first data comparison too dependent on our initial "guess" of $\frac{1}{2}T_{t_k}$, we iterate the formula twice at the first year to "correct" this guess and then the formula is used with the output for remaining years. In this way, we try to account for those that left I and those that possibly left I but returned to I.

Similarly, we compute an equation for $P(t)$, the number of former I in R from last year:

$$\begin{cases} \dfrac{dP(t)}{dt} = \text{rate in} - \text{rate out}, \\ \qquad = y11/\text{yr.} - (\text{concentration of former } I \text{ in } R) \times (\text{rate of flow out}), \\ \qquad = y11/\text{yr.} - \dfrac{P}{R} \times (y09/\text{yr.}), \\ \qquad = y11 - P\dfrac{y09}{R} \end{cases} \tag{S.3}$$

where $y09$ denotes the number of individuals in the R class that flowed back to the I class in one time period. We make the approximation/assumption that R, $y11$, and $y09$ are constant over the time period of one year. With this simplifying assumption, this equation is now a standard linear ODE that can be solved explicitly. Solving for $P(t)$,

$$P(t) = \frac{y11}{y09}R + Ce^{-t\dfrac{y09}{R}}$$

where $P(t)$ is the number of former individuals from I in R, to be updated each year.

This solution is continuous in time; however, we only receive a yearly number from SAMHSA. As with Q, we thus consider a discrete version of this solution that will hold at time t_k and we will update this with the yearly output from our model. The additional item that we need to determine is the initial condition, which is the number of from I in R from the last year for that initial year. We "guess" this is $\frac{1}{10}R_{t_k}$.

Hence we substitute our guess into our equation to obtain:

$$\frac{1}{10}R_{t_k} = \frac{y11}{y09}R_{t_k} + Ce^{-t_k\dfrac{y09}{R_{t_k}}}$$

Solving for C gives us:

$$C = \left(\frac{1}{10}R_{t_k} - \frac{y11_k}{y09_k}R_{t_k}\right)e^{t_k\dfrac{y09_k}{R_k}}$$

and $P = \dfrac{y11}{y09}R_{t_k} + \left(\dfrac{1}{10}R_{t_k} - \dfrac{y11_k}{y09_k}R_{t_k}\right)e^{-t_{k+1}\dfrac{y09_{k+1}}{R_{k+1}}t_k\dfrac{y09_k}{R_{t_k}}}$

As with Q, we write P as an implicit equation where the subscript k denotes the current year and $k+1$ denotes the next year.

$$P_{k+1} = \frac{y11_{k+1}}{y09_{k+1}}R_{k+1} + \left(\frac{1}{10}R_k - \frac{y11_k}{y09_k}R_k\right)e^{-t_{k+1}\dfrac{y09_{k+1}}{R_{k+1}}+t_k\dfrac{y09_k}{R_k}}$$

As with Q, we set $t_k = 0$ and $t_{k+1} = 1$. Hence, our final equation for P:

$$P_{k+1} = \frac{y11_{k+1}}{y09_{k+1}}R_{k+1} + \left(\frac{1}{10}R_k - \frac{y11_k}{y09_k}R_k\right)e^{-\dfrac{y09_{k+1}}{R_{k+1}}}$$

Our "guess" of $\frac{1}{10}R_{t_k}$ is then iterated twice at the first year to "correct" this guess and then the formula is used with the output for remaining years. In this way, we try to account for those that left I and those that possibly left I but returned to I in the year. We now have expressions for P and Q and can use this in Eq (S.1) together with our instantaneous model output in order to compare with the SAMHSA data.

Next, we discuss finding the corrected yearly number of individuals in the T class. In the flow diagram S.1, we see that the individuals over the year could leave T early by either going to the I class

or the R class. We denote the number of individuals in the T class that flowed to the R class in one time period as $y07$. We denote the number of individuals in the T class that flowed to the I class in one time period as $y08$. Therefore, we obtain:

$$\text{leave}T\text{yearly} = y07 + y08$$

To get the the additional correction count we use the following equation:

$$\text{corrected leave}T\text{yearly} = y07 + y08 - \frac{B_i}{I_i}y06$$

where $B(t)$ denotes the number of former T in I from last year. Hence, $\frac{B_i}{I_i}$ scales $y06$ by the proportion of I that are from T in the last year. We then use the following equation to solve for B:

$$\begin{cases} \dfrac{dB(t)}{dt} = \text{rate in} - \text{rate out}, \\ \qquad = y08/\text{yr.} - (\text{concentration of former } T \text{ in } I) \times (\text{rate of flow out}), \\ \qquad = y08/\text{yr.} - \dfrac{B}{I} \times (y06/\text{yr.} + y11/\text{yr.}), \\ \qquad = y08 - B\dfrac{y06 + y11}{I} \end{cases} \tag{S.4}$$

We make the approximation/assumption that I, $y06$, $y08$, and $y11$ are constant over the time period of one year. With this simplifying assumption, this equation is now a standard linear ODE that can be solved explicitly. Solving for $B(t)$,

$$B(t) = \frac{y08}{y06 + y11}I + Ce^{-t\dfrac{y06 + y11}{I}}$$

where $B(t)$ is the number of former individuals from T in I, to be updated each year.

This solution is continuous in time; however, we only receive a yearly number from SAMHSA. We thus consider a discrete version of this solution that will hold at time t_k and we will update this with the yearly output from our model. The additional item that we need to determine is the initial condition, which is the number of from I in T from the last year for that initial year. We "guess" this is $\frac{1}{3}I_{t_k}$.

Hence we substitute our guess $B(t_k) = \frac{1}{3}I_{t_k}$ into our equation to obtain:

$$\frac{1}{3}I_{t_k} = \frac{y08_k}{y06_k + y11_k}I_k + e^{t_k\dfrac{y06 + y11}{I}}$$

Solving for C gives us:

$$C = \left(\frac{1}{3}I_{t_k} - \frac{y08_k}{y06_k + y11_k}I_k\right)e^{t_k\dfrac{y06_k + y11_k}{I_k}}$$

and

$$B = \frac{y08}{y06 + y11}I + \left(\frac{1}{3}I_{t_k} - \frac{y08_k}{y06_k + y11_k}I_k\right)e^{t_k\dfrac{y06_k + y11_k}{I_k} - t_{k+1}\dfrac{y06_{k+1} + y11_{k+1}}{I_{k+1}}}$$

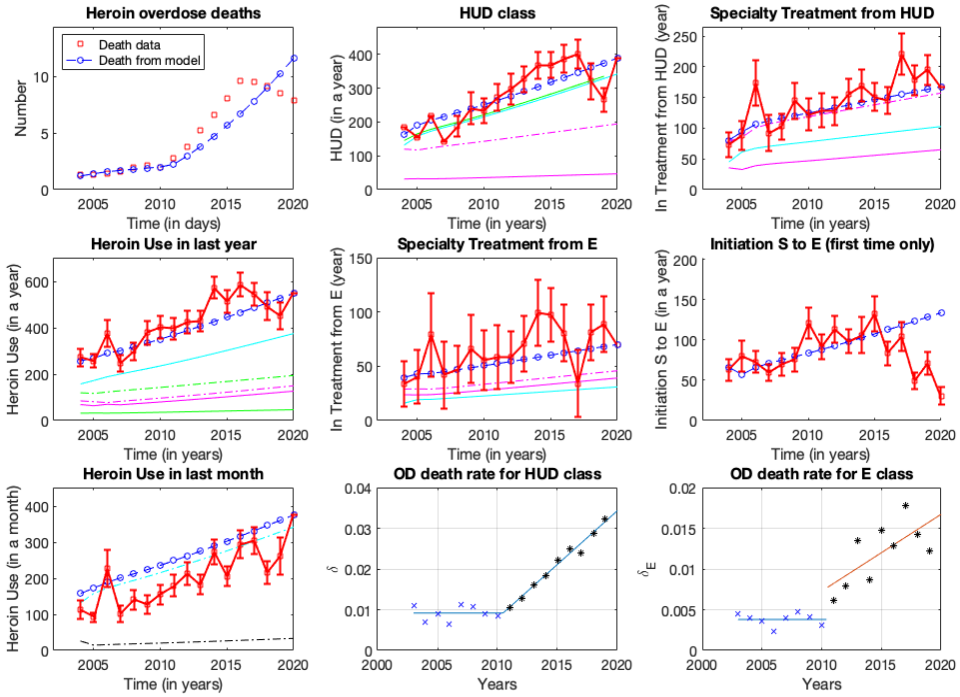

Figure S.2. Fitting Model Output to Scaled Data (Error Bars When given) for Heroin. (Top Left): Heroin Overdose Deaths: Red Squares Depict CDC Data, Blue Curve Depicts Model Output; (Top Middle) HUD Class: Red Curve Depicts Data, Magenta Dash-dot Curve Depicts Leave I Yearly, Magenta Solid Curve Depicts Leave I Yearly "corrected", Cyan Depicts the Model Output for I, Green Depicts This Model Output Averaged over Successive Years, Blue Curve with Circles Is the Model Approximation. (Top Right) Specialty Treatment from HUD: Red Curve Depicts Data, Cyan Depicts the Model Output for T, Magenta Dash-dot Curve Depicts Leave T Yearly, Magenta Solid Curve Depicts Leave T Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Left) Heroin Use: Red Curve Depicts Data, Cyan Depicts the Model Output for $E + I$, Magenta Dash-dot Curve Depicts Leave E Yearly, Magenta Solid Curve Depicts Leave E Yearly "corrected", Green Dash-dot Is Leave I Yearly, Green Is Leave I Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Middle) Specialty Treatment from E: Red Curve Depicts Data, Cyan Curve Depicts the Model Output for T_E, Magenta Dash-dot Curve Depicts Leave T_E Yearly, Magenta Solid Curve Depicts Leave T_E Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Right) Initiation from S to E (First-time Only): Red Curve Depicts Data, Blue Curve with Circles Is the Model Output $I+E$. (Bottom Left) Heroin Use in Last Mo: Red Curve Depicts Data, Cyan Depicts the Model Output for I, Black Depicts the Model Output for E, Blue Curve with Circles Is the Model Approximation. (Bottom Middle) OD Death Rate for HUD Class: Asterisks and X-marks Are Calculated from Data (See main article and equation for δ).) with Blue X-marks Used to Obtain the Horizontal (Constant) Line and Black Asterisks Used to Obtain the Non-zero Sloped Line; Both Lines Are Calculated with a Least Squares Fit. (Bottom Right) OD Death Rate for E Class.: Asterisks and X-marks Are Calculated from Data (See main article and equation for δ_E).

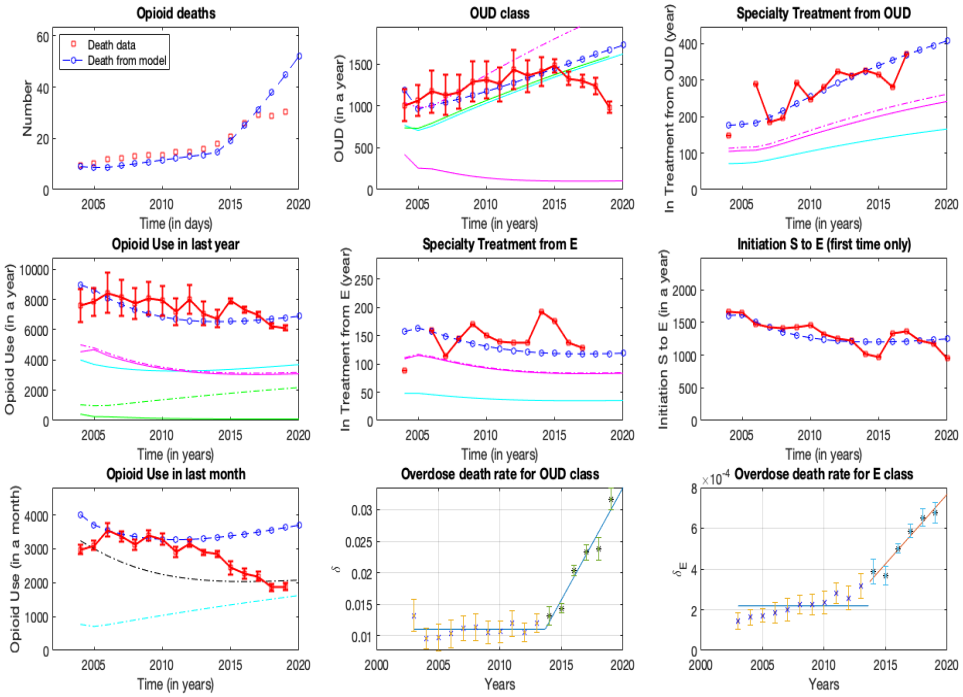

Figure S.3. Fitting Model Output to Scaled Data (Error Bars When given) for All-illicit Opioids. (Top Left): Illicit Opioids Overdose Deaths: Red Squares Depict CDC Data, Blue Curve Depicts Model Output. (Top Middle) OUD Class: Red Curve Depicts Data, Magenta Dash-dot Curve Depicts Leave I Yearly, Magenta Solid Curve Depicts Leave I Yearly "corrected", Cyan Depicts the Model Output for I, Green Depicts This Model Output Averaged over Successive Years, Blue Curve with Circles Is the Model Approximation. (Top Right) Specialty Treatment from OUD: Red Curve Depicts Data, Cyan Depicts the Model Output for T, Magenta Dash-dot Curve Depicts Leave T Yearly, Magenta Solid Curve Depicts Leave T Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Left) Opioid Use in Last Yr: Red Curve Depicts Data, Cyan Depicts the Model Output for $E + I$, Magenta Dash-dot Curve Depicts Leave E Yearly, Magenta Solid Curve Depicts Leave E Yearly "corrected", Green Dash-dot Is Leave I Yearly, Green Is Leave I Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Middle) Specialty Treatment from E: Red Curve Depicts Data, Cyan Curve Depicts the Model Output for T_E, Magenta Dash-dot Curve Depicts Leave T_E Yearly, Magenta Solid Curve Depicts Leave t_e Yearly "corrected", Blue Curve with Circles Is the Model Approximation. (Middle Right) Initiation from S to E (First-time Only): Red Curve Depicts Data, Blue Curve with Circles Is the Model Output. (Bottom Left) Opioid Use in Last Mo: Red Curve Depicts Data, Cyan Depicts the Model Output for I, Black Depicts the Model Output for E, Blue Curve with Circles Is the Model Output $I + E$. (Bottom Middle) OD Death Rate for OUD Class: Asterisks and X-marks Are Calculated from Data (See main article and equation for δ). With Blue X-marks Used to Obtain the Horizontal (Constant) Line and Black Asterisks Used to Obtain the Non-zero Sloped Line; Both Lines Are Calculated with a Least Squares Fit. (Bottom Right) OD Death Rate for E Class.: Asterisks and X-marks Are Calculated from Data (See main article and equation for δ_E). With Blue X-marks Used to Obtain the Horizontal (Constant) Line and Black Asterisks Used to Obtain the Non-zero Sloped Line; Both Lines Are Calculated with a Least Squares Fit.

Because our derived equation utilizes the output from the ODE, we have the data for future time

steps by keeping track of the yearly outputs. Recall, that the corrections are to compare with the data and do not influence the dynamics of the equations. Thus, we write B as an implicit equation where the subscript k denotes the current year and $k+1$ denotes the next year.

$$B_{t_{k+1}} = \frac{y08_{k+1}}{y06_{k+1}+y11_{k+1}} I_{k+1} + \left(\frac{1}{3}I_k - \frac{y08_k}{y06_k+y11_k}I_k\right) e^{-t_{k+1}\frac{y06_{k+1}+y11_{k+1}}{I_{k+1}}+t_k\frac{y06_k+y11_k}{I_k}}$$

We set $t_k = 0$ and $t_{k+1} = 1$. Hence, our final equation for B is

$$B_{t_{k+1}} = \frac{y08_{k+1}}{y06_{k+1}+y11_{k+1}} I_{k+1} + \left(\frac{1}{3}I_k - \frac{y08_k}{y06_k+y11_k}I_k\right) e^{-(y06_{k+1}+y11_{k+1})/I_{k+1}}$$

Our "guess" of $\frac{1}{3}I_{t_k}$ is then iterated twice at the first year to "correct" this guess and then the formula is used with the output for remaining years. In this way, we try to account for those that left T and those that possibly left T but returned to T.

Similarly, we use the previous tools and analysis to find the corrections for the S, E, and T_E variables.

We give the "correction" plots on the curves of data match for illustration; see Figures S.2 and S.3.

S.1.2. Additional PRCC results for heroin and illicit opioid use

The following plots and tables are for the IOUD model with casual user class. These results continue from what was done.

S.2. Heroin only: Additional PRCC plots and tables

Other variables and the sensitivity of the state variables for the heroin dataset are presented only in terms of plots and tables.

Checking the monotonicity results as was done in the previous sections, although some potential issues arose, after checking we see that those parameters were either not significant during the time period of non-monotonicity or did not even show up on the PRCC graph. Therefore, we conclude that our results are valid.

Table S.1. Heroin Only Data: PRCC Results for the S Population, for the E Population, and the T_E Population Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.4–S.6.

Param	S				E				T_E			
	Constant		Variable		Constant		Variable		Constant		Variable	
years	10	20	10	20	10	20	10	20	10	20	10	20
μ	-0.96	-0.93	-0.93	-0.92	-	-	-	-0.44	-	-	-	-
β	-	-	-	-	0.98	0.97	0.98	0.98	0.97	0.97	0.98	0.98
δ	-	-	-	-	-0.61	-0.62	-	-	-0.41	-0.53	-	-
m	-	-	-	-	-		-	-0.53	-	-	-	-
b	-	-	-	-	-		-0.52	-0.67	-	-	-0.42	-0.55
Λ	0.96	0.94	0.93	0.93	-	-	-	-	-	-	-	-
k	-	-	-	-	-	-	-	-	0.6	0.45	0.67	0.53
ρ	-	-	-	-	-	-	-	-	-	-	-	-
η_1	-	-	-	-	-	-	-	-	-0.56	-0.47	-0.7	-0.52
η_2	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-	-	-	-	-	-	-	-	-0.48	-
α_1	-	-	-	-	0.58	-	0.51	0.42	-	-	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-	-	-	-	-	-	-	-	-	-	-
ϵ	-	-	-	-	0.6	0.41	0.57	0.56	-0.42	-	-0.47	-
β_E	-	-	-	-	-	-	-	-	-	-	-	-
δ_E	-	-	-	-	-	-	-	-	-	-	-	-
m_E	-	-	-	-	-		-	-			-	-
b_E			-	-	-		-	-			-	-
k_E	-	-	-	-	-	-	-	-	-0.72	-0.48	-0.71	-0.54
ρ_E	-	-	-	-	-0.45	-	-	-	-0.85	-0.74	-0.87	-0.81
ψ_1	-	-	-	-	-0.41	-	-	-	0.67	0.6	0.75	0.58
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	0.71	0.54	0.76	0.51
ζ	-	-	-	-	-0.97	-0.92	-0.95	-0.95	-0.94	-0.92	-0.95	-0.94
χ	-	-	-	-	0.78	0.83	0.7	0.91	0.46	0.71	-	0.81
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	1	1	1	0.99	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$A(0)$	-	-	-	-	0.92	0.72	0.9	0.85	0.79	0.64	0.84	0.74
$T(0)$	-	-	-	-	0.59	-	0.45	-	0.47	-	-	-
$R(0)$	-	-	-	-	0.43	-	-	-	-	-	-	-

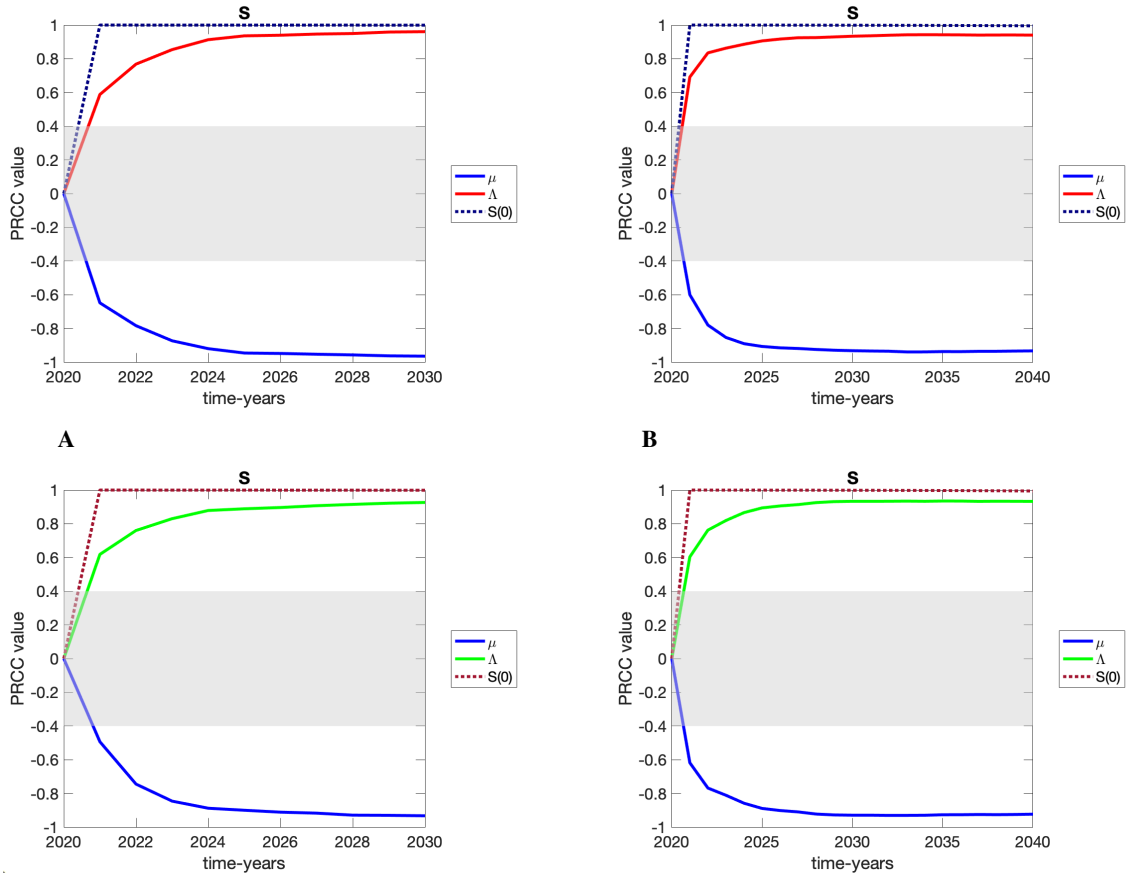

Figure S.4. Heroin: PRCC Results over Time for the Number of Individuals in the S Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.1. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

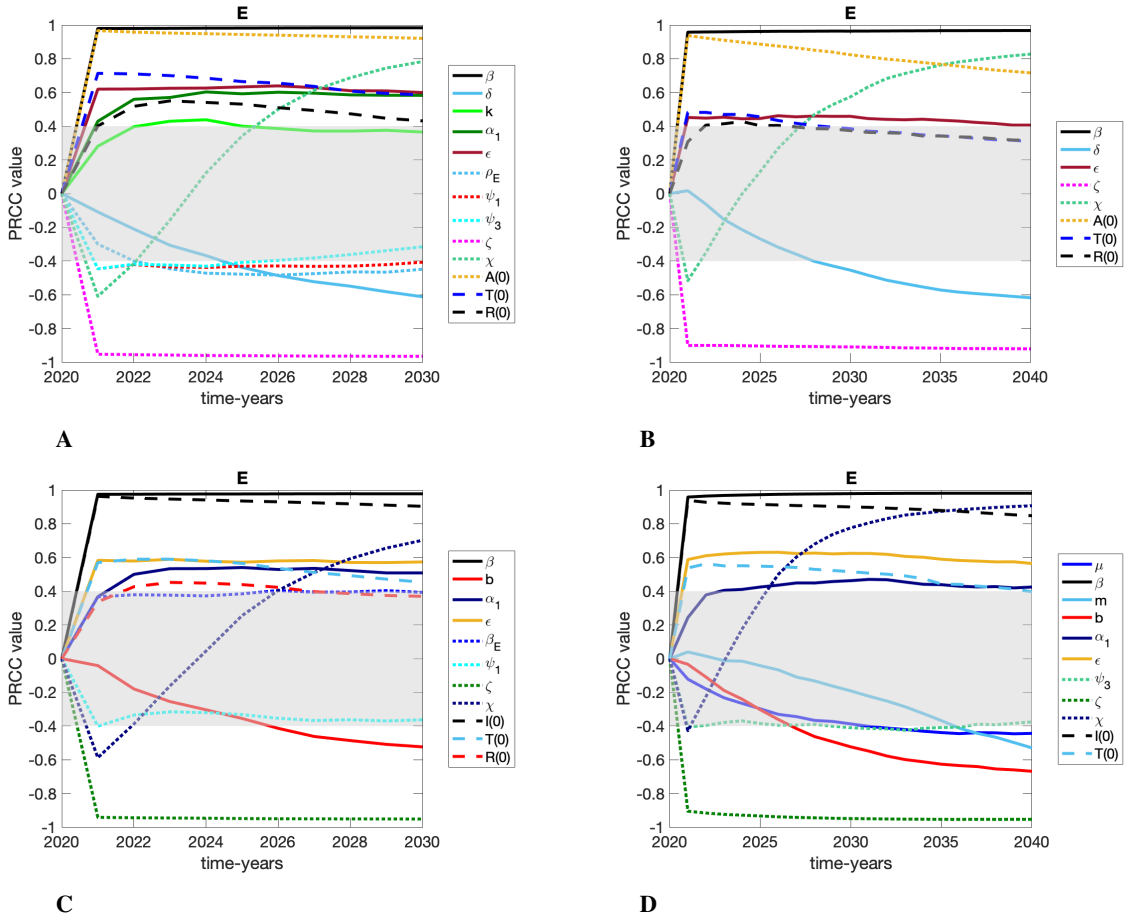

Figure S.5. Heroin: PRCC Results over Time for the Number of Individuals in the E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.1.The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

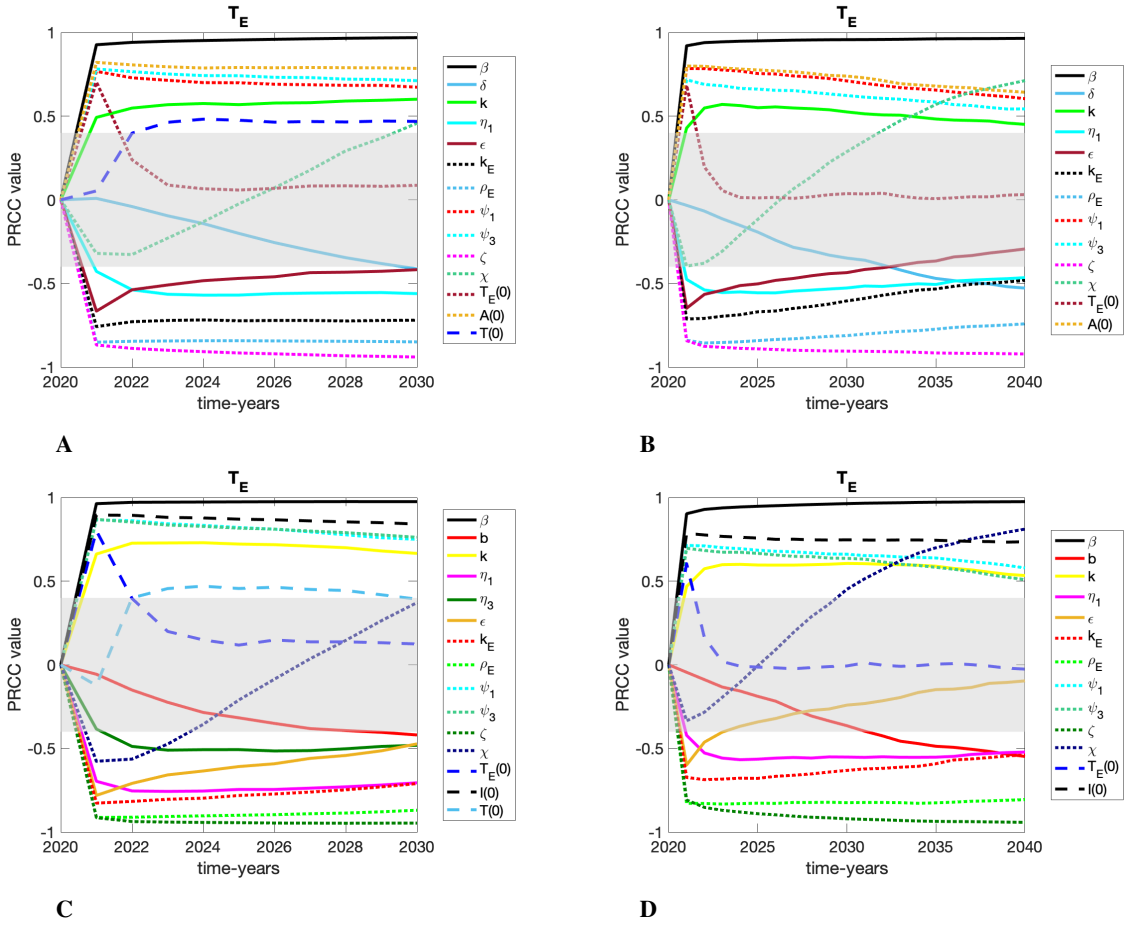

Figure S.6. Heroin: PRCC Results over Time for the Number of Individuals in the T_E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.1. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.2. Heroin Only Data: PRCC Results for the I Population, for the T Population, and the R Population Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.7-S.9. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Param	I				T				R			
	Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20
μ	-0.41	-	-0.51	-0.58	-	-0.41	-0.45	-0.56	-0.46	-0.49	-	-0.55
β	0.94	0.94	0.94	0.97	0.92	0.95	0.89	0.97	0.91	0.96	0.87	0.96
δ	-0.61	-0.67	-	-	-0.62	-0.74	-	-	-0.58	-0.75	-	
m	-	-	-	-0.62	-	-	-	-0.66	-	-	-	-0.52
b	-	-	-0.67	-0.76	-	-	-0.57	-0.79	-	-	-0.55	-0.71
Λ	-	-	-	-	-	-	-	-	-	-	-	-
k	0.43	-	0.44	-	-0.88	-0.72	-0.84	-0.81	-	-	-	-
ρ	-	-	-	-	-0.78	-0.63	-0.66	-0.63	0.85	0.54	0.77	0.69
η_1	-0.48	-	-	-	0.86	0.69	0.8	0.78	-	-	0.41	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-0.43	-	0.74	0.55	0.6	0.63	-	-	-	-
α_1	0.6	-	0.65	0.52	0.54	0.43	0.54	0.53	-0.95	-0.86	-0.93	-0.86
α_2	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-	-	-	-	-	-	-	0.84	0.65	0.78	0.67
ϵ	0.55	0.41	0.59	0.56	-0.8	-0.62	-0.75	-0.63	-	-	-	-
β_E	-	-	-	-	-	-	-	-	-	-	-	-
δ_E	-	-	-	-	-	-		-	-	-	-	-
m_E	-	-	-	-			-	-	-	-	-	-
b_E	-	-	-	-			-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-	-	-	-
ρ_E	-	-	-	-	-	-	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	-	-	-	-
ζ	-0.89	-0.88	-0.89	-0.93	-0.86	-0.89	-0.78	-0.93	-0.84	-0.9	-0.77	-0.89
χ	0.91	0.91	0.91	0.95	0.9	0.93	0.86	0.96	0.89	0.93	0.82	0.93
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$A(0)$	0.93	0.77	0.94	0.89	0.93	0.82	0.91	0.89	0.93	0.84	0.9	0.86
$T(0)$	0.61	-	0.6	0.44	0.57	0.46	0.54	0.54	0.62	0.43	0.56	0.43
$R(0)$	0.53	-	0.46	-	0.48	0.4	-	-	0.44	-	-	-

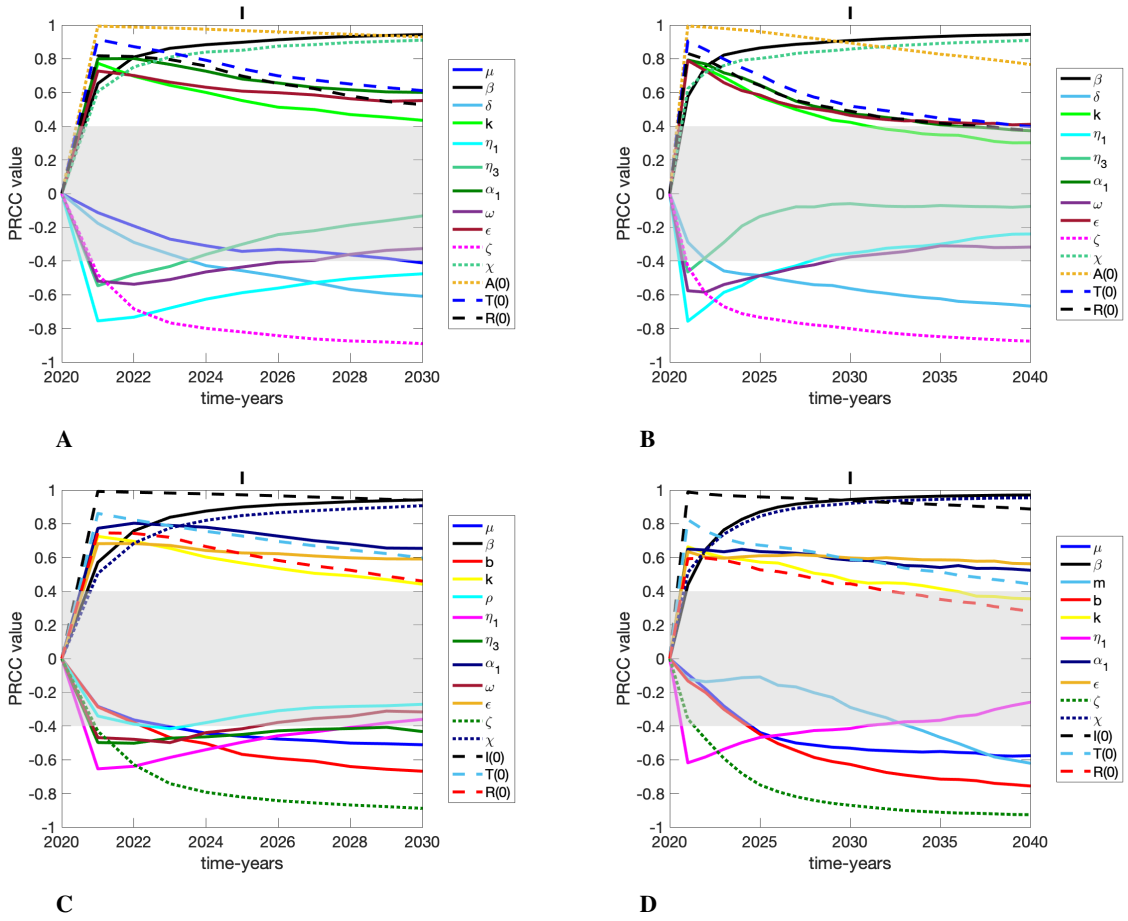

Figure S.7. Heroin: PRCC Results over Time for the Number of Individuals in the I Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.2. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

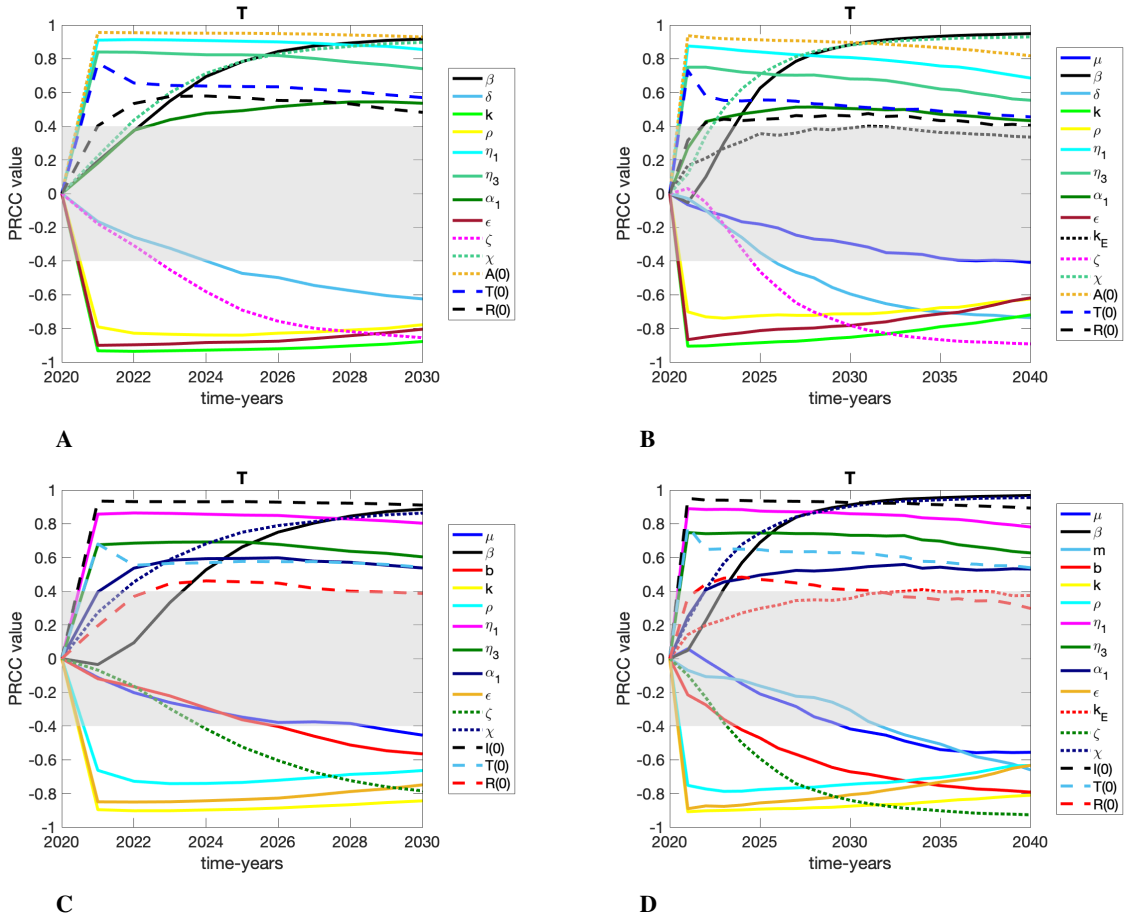

Figure S.8. Heroin: PRCC Results over Time for the Number of Individuals in the T Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.2. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

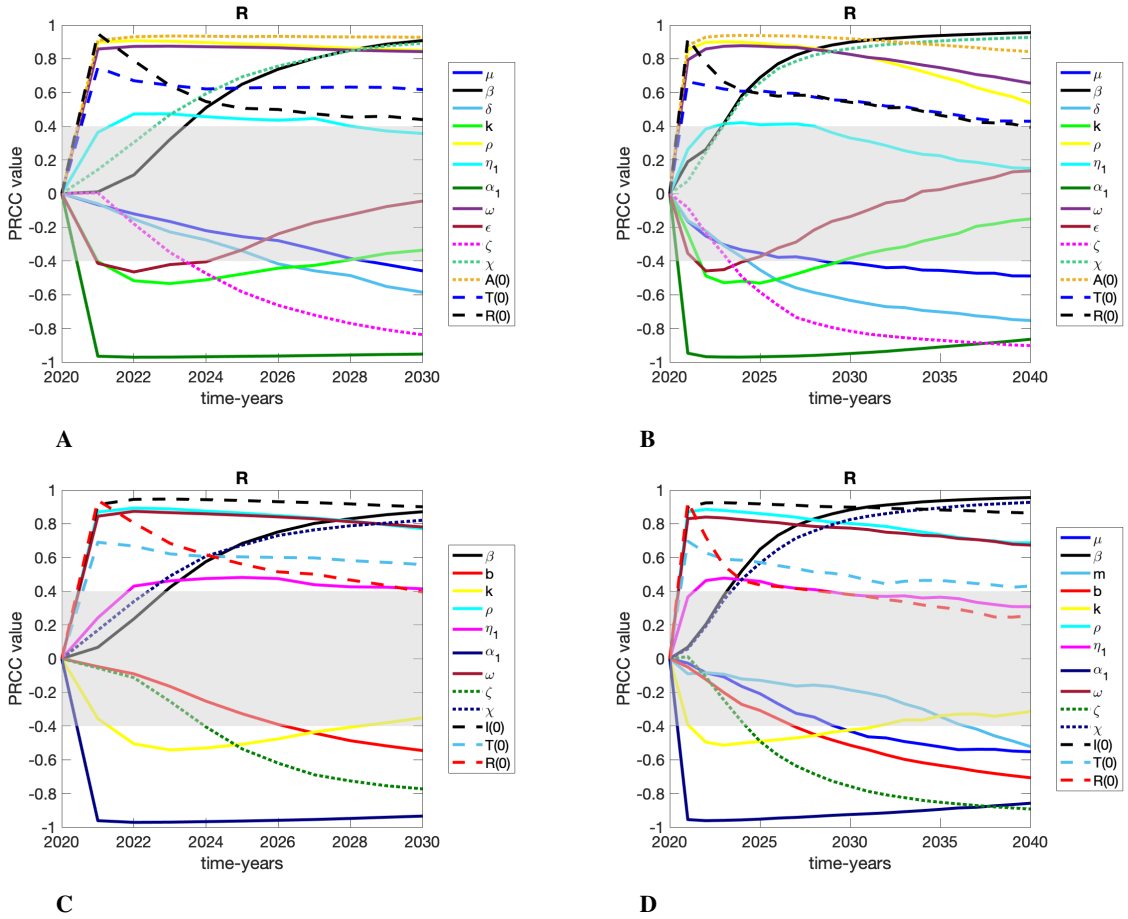

Figure S.9. Heroin: PRCC Results over Time for the Number of Individuals in the R Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.2. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.3. Heroin Only Data: PRCC Results for the Movement into Treatment T, Completed Treatment T, the Movement from I to R, and the Movement from S to E Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.10-S.13. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

	Treatment				Completed Treatment				Yearly I to R				Yearly S to E			
	Constant		Variable		Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
μ	-	-	-	-0.57	-	-	-0.43	-0.49	-	-	-0.51	-0.57	-	-	-0.48	-0.56
β	0.87	0.94	0.88	0.97	0.89	0.94	0.9	0.96	0.93	0.94	0.93	0.96	0.99	0.98	0.99	0.99
δ	-0.44	-0.69			-0.59	-0.69	-	-	-0.61	-0.67	-		-0.59	-0.67	-	-
m	-	-	-	-0.67	-	-	-	-0.68	-	-	-	-0.56	-	-	-	-0.61
b	-	-	-0.42	-0.79	-		-0.64	-0.72	-	-	-0.67	-0.72	-	-	-0.62	-0.75
Λ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k	0.81	0.72	0.83	0.81	-0.84	-0.7	-0.89	-0.77	0.53	-	0.49	-	0.44	-	-	-
ρ	-	-	-	-	0.97	0.91	0.97	0.94	-	-	-	-	-	-	-	-
η_1	0.81	0.68	0.78	0.8	0.81	0.64	0.84	0.74	-	-	-	-	-	-	-	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_3	0.61	0.53	0.56	0.61	0.68	0.52	0.68	0.61	-	-	-	-	-	-	-	-
α_1	0.48	0.4	0.45	0.56	0.57	0.48	0.52	0.56	0.55	-	0.61	0.51	0.59	-	0.63	0.5
α_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-	-	-	-	-	-0.4	-	0.93	0.76	0.94	0.86	-	-	-	-
ϵ	-0.71	-0.54	-0.71	-0.62	-0.77	-0.57	-0.82	-0.65	0.51	-	0.61	0.54	0.54	0.44	0.55	0.56
β_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.47	-
δ_E	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-
m_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ρ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ζ	-0.77	-0.88	-0.75	-0.93	-0.78	-0.86	-0.78	-0.9	-0.85	-0.87	-0.86	-0.92	-0.88	-0.88	-0.88	-0.93
χ	0.85	0.92	0.83	0.96	0.87	0.91	0.9	0.94	0.89	0.9	0.89	0.95	0.88	0.9	0.88	0.96
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$I(0)$	0.88	0.81	0.9	0.9	0.9	0.8	0.93	0.87	0.91	0.75	0.93	0.88	0.92	0.76	0.93	0.89
$T(0)$	0.48	0.49	0.49	0.53	0.54	0.5	0.56	0.53	0.52	-	0.59	-	0.59	-	0.55	0.43
$R(0)$	0.43	-	0.43	-	-	-	-	-	0.56	-	0.47	-	0.48	-	0.47	-

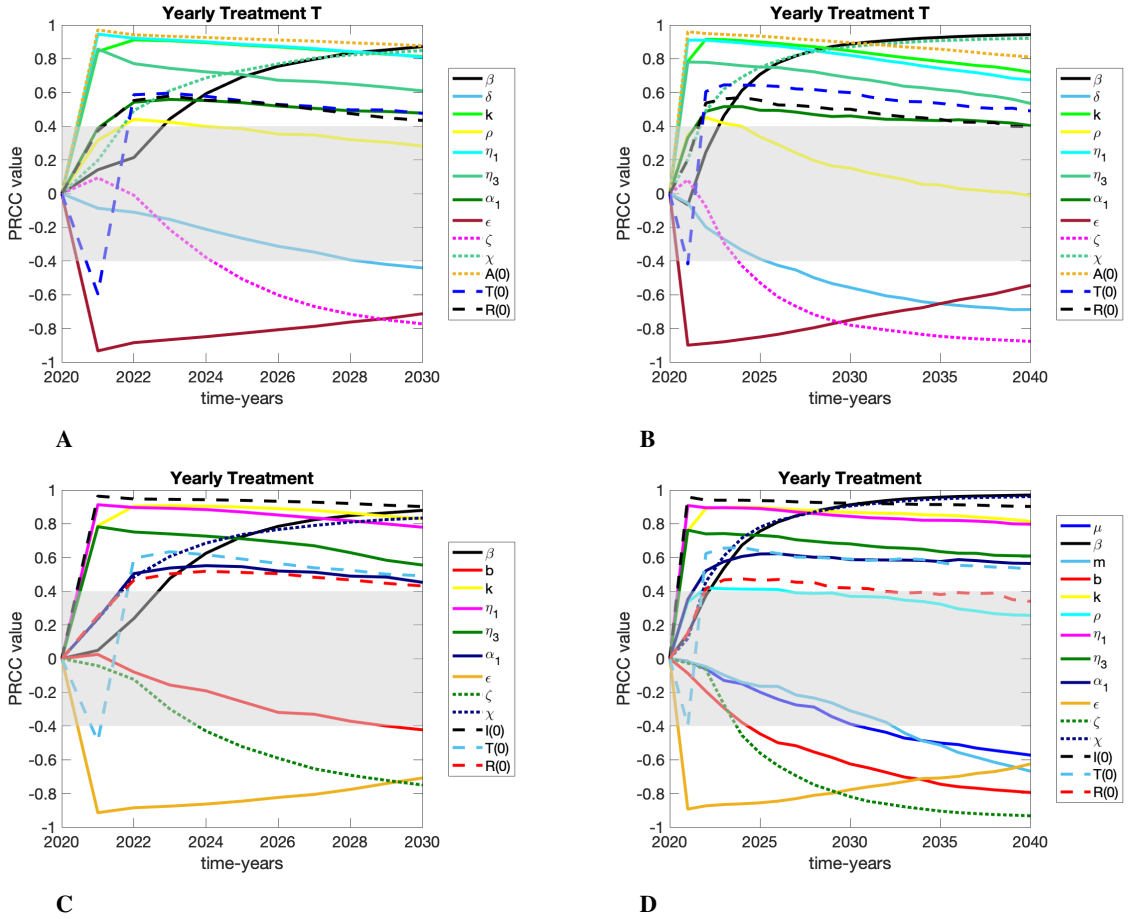

Figure S.10. Heroin: PRCC Results over Time for Those Who Went to Treatment from the I Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.3. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

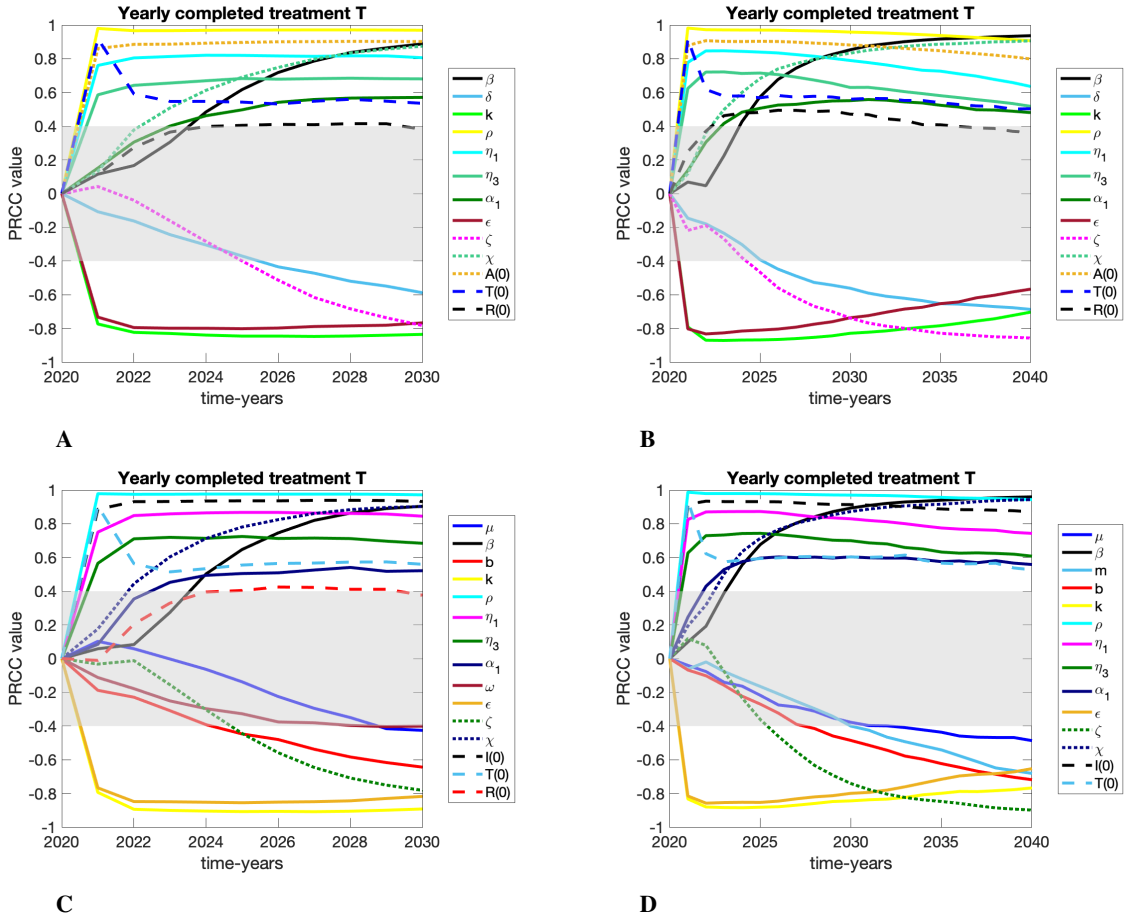

Figure S.11. Heroin: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T Class, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.3. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

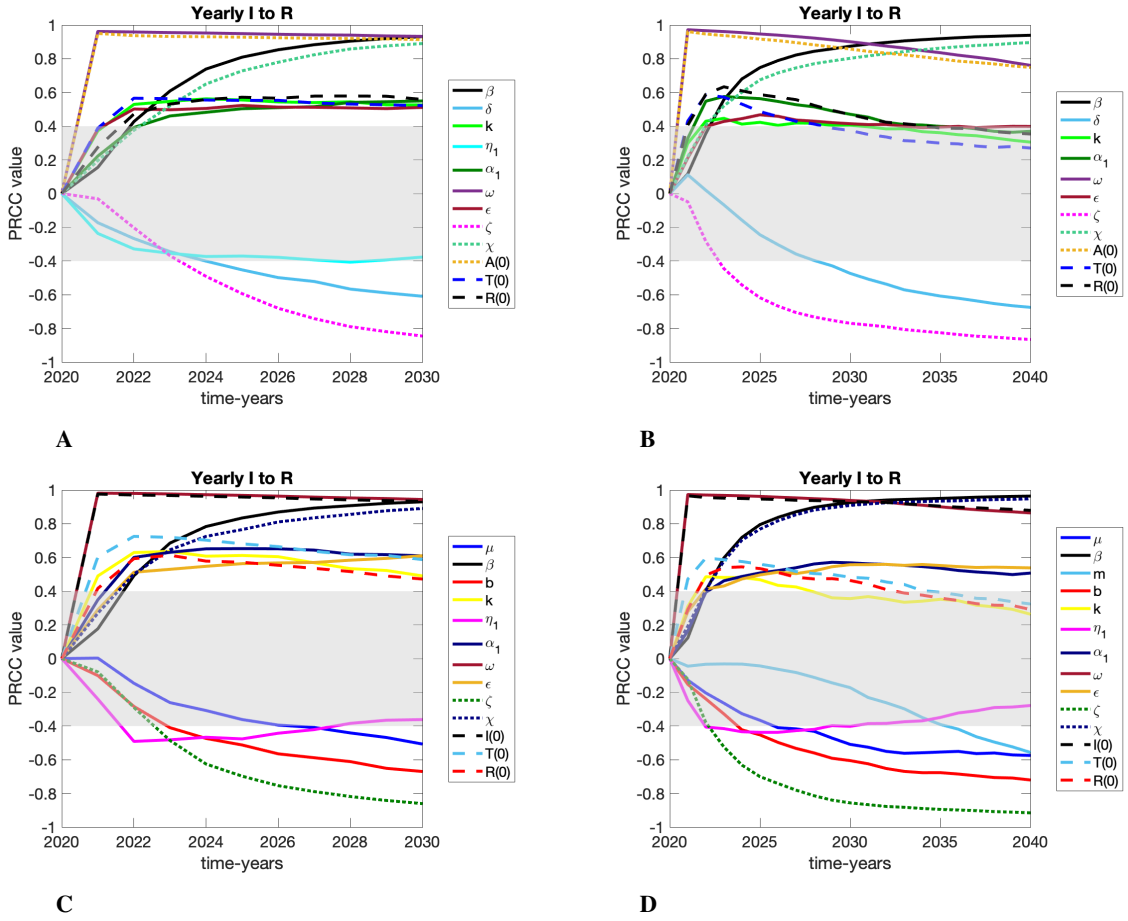

Figure S.12. Heroin: PRCC Results over Time for the Number of Individuals Who Went to the R Class Directly from I, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in Table S.3.

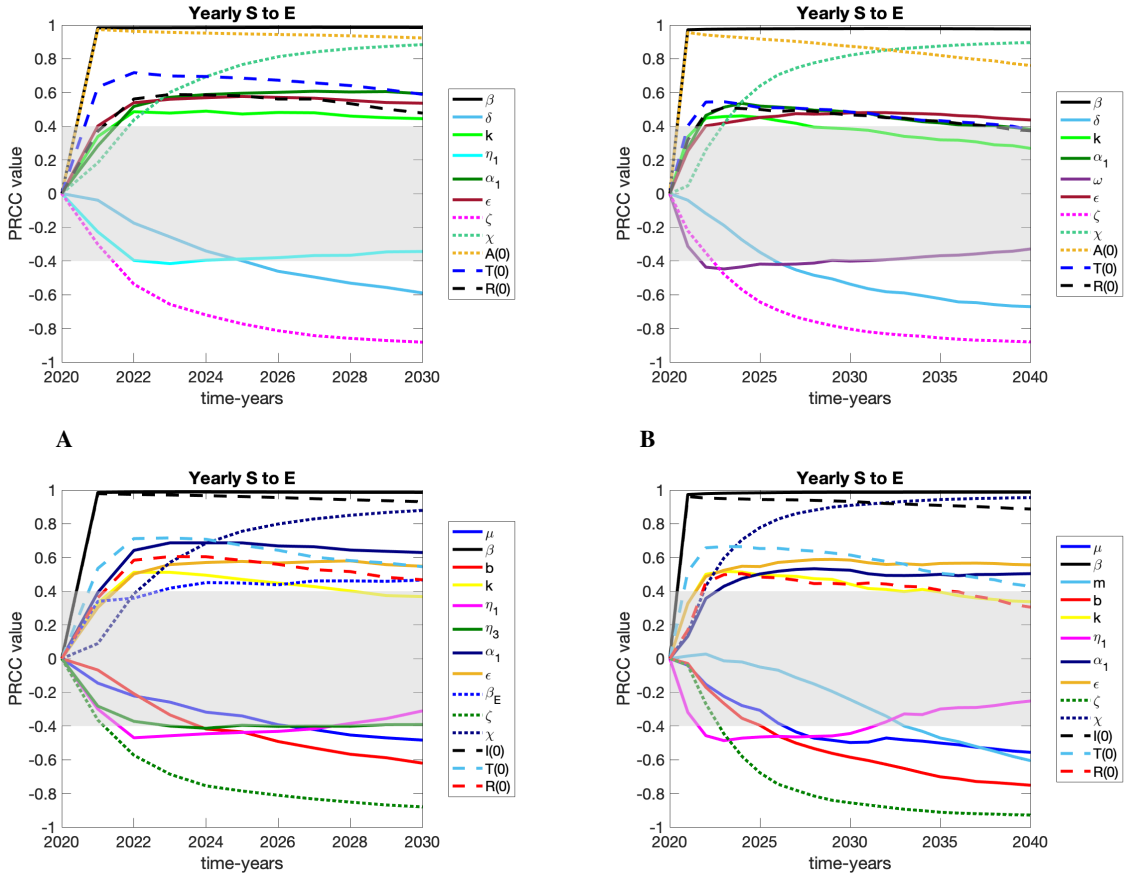

Figure S.13. Heroin: PRCC Results over Time for Those Who Are Entering E from S, with Greyed Region Denoting a Lack of Significance. These Results Are Also Found in S.3. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.4. Heroin Only Data: PRCC Results for the Movement from E to S, the Movement into Treatment T_E, Completed Treatment T_E, and Relapse from T_E Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.14-S.17. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Param	E2S				E2TE				CTE				RTE			
	Constant		Variable		Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
μ	-	-0.41	-0.52	-0.61	-	-	-0.48	-	-	-	-0.52	-	-	-	-	-
β	0.99	0.98	0.99	0.99	0.99	0.97	0.99	0.98	0.99	0.97	0.99	0.97	0.95	0.96	0.97	0.97
δ	-0.62	-0.71	-	-	-0.59	-0.57	-	-	-0.62	-0.56	-	-	-	-0.54	-	-
m	-	-	-	-0.66	-	-	-	-0.46	-	-	-	-0.4	-	-	-	-0.46
b	-	-	-0.67	-0.79	-	-	-0.62	-0.58	-	-	-0.67	-0.57	-	-	-0.41	-0.55
Λ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k	-	-	-	-	0.44	0.45	-	0.59	-	0.47	-	0.6	0.46	0.45	0.59	0.55
ρ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_1	-	-	-	-	-	-0.42	-	-0.51	-	-0.47	-	-0.49	-0.48	-0.45	-0.59	-0.47
η_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-0.48	-
α_1	0.6	0.47	0.7	0.54	0.59	-	0.63	-	0.6	-	0.7	-	-	-	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ϵ	0.66	0.55	0.71	0.66	0.54	-	0.55	-	0.66	-	0.71	-	-	-	-0.45	-
β_E	-	0.4	0.51	0.4	-	-	0.47	-	-	-	0.51	-	-	-	-	-
δ_E	-	-	-	-	-	-	-	-	-	-	-		-	-		
m_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k_E	-	-	-	0.44	-	-	-	-	-	-0.52	-	-0.55	0.8	0.76	0.86	0.81
ρ_E	-	-	-	-0.42	-	-	-	-	-	0.66	-	0.63	-0.75	-0.75	-0.85	-0.8
ψ_1	-	-	-	-	-	0.59	-	0.63	-	0.62	-	0.57	0.59	0.58	0.66	0.62
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-0.48	-	0.57	-	0.53	-	0.56	-	0.51	0.64	0.55	0.71	0.51
ζ	-0.66	-0.84	-0.65	-0.88	-0.88	-0.93	-0.88	-0.95	-0.66	-0.93	-0.65	-0.94	-0.91	-0.91	-0.93	-0.94
χ	0.8	0.89	0.81	0.95	0.88	0.71	0.88	0.82	0.8	0.7	0.81	0.8	-	0.68	-	0.79
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$I(0)$	0.93	0.81	0.95	0.91	0.92	0.66	0.93	0.76	0.93	0.67	0.95	0.73	0.74	0.61	0.81	0.71
$T(0)$	0.64	0.43	0.66	0.49	0.59	-	0.55	-	0.64	-	0.66	-	-	-	-	-
$R(0)$	0.54	0.43	0.49	0.43	0.48	-	0.47	-	0.54	-	0.49	-	-	-	-	-

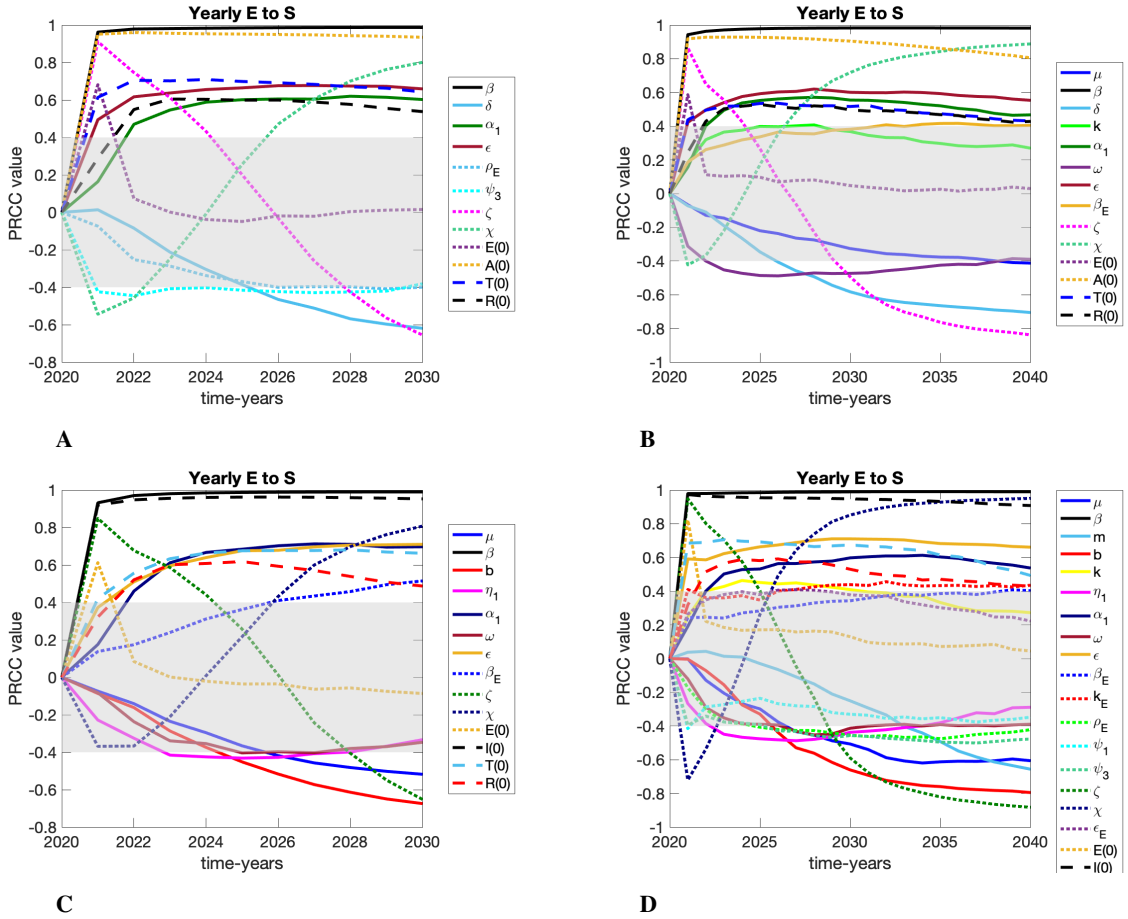

Figure S.14. Heroin: PRCC Results over Time for the Number of Those Leaving from the E Class Back to the S Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.4. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

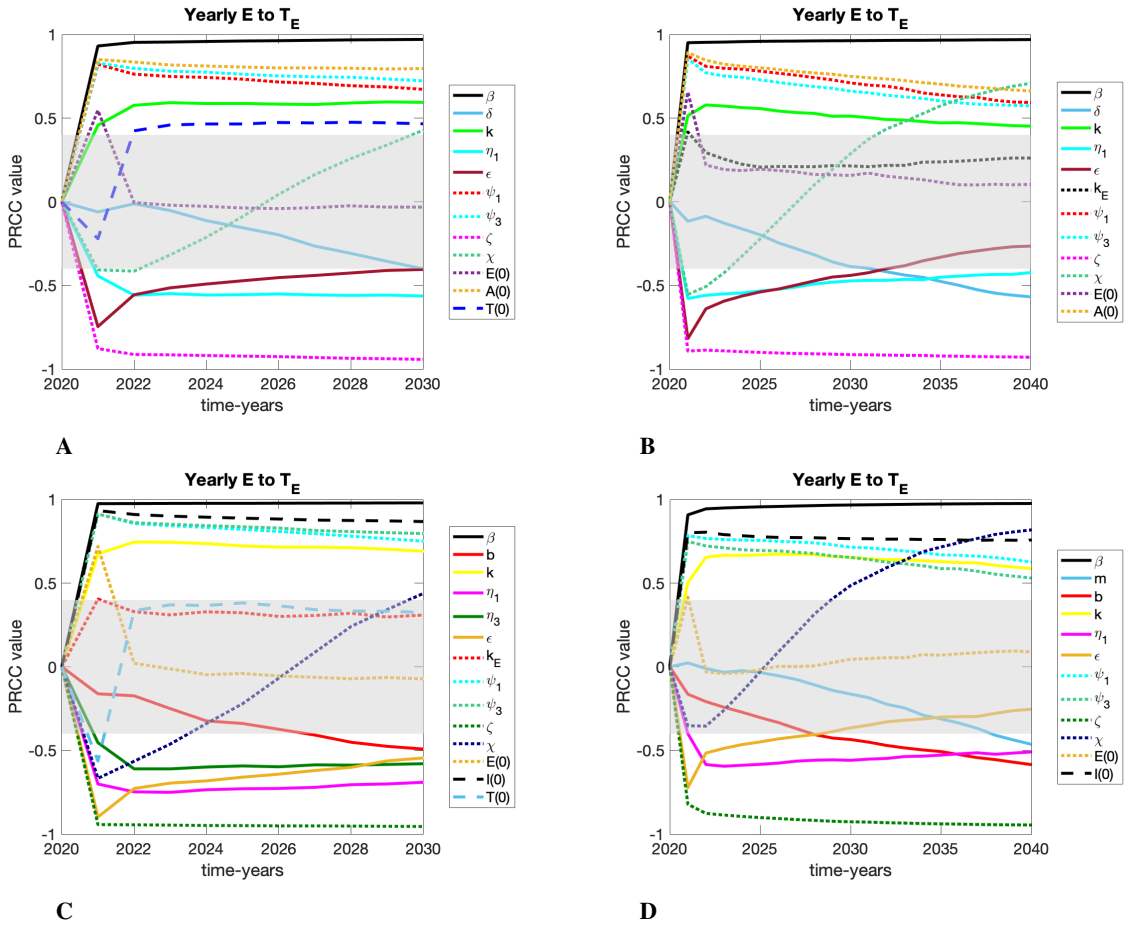

Figure S.15. Heroin: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.4. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

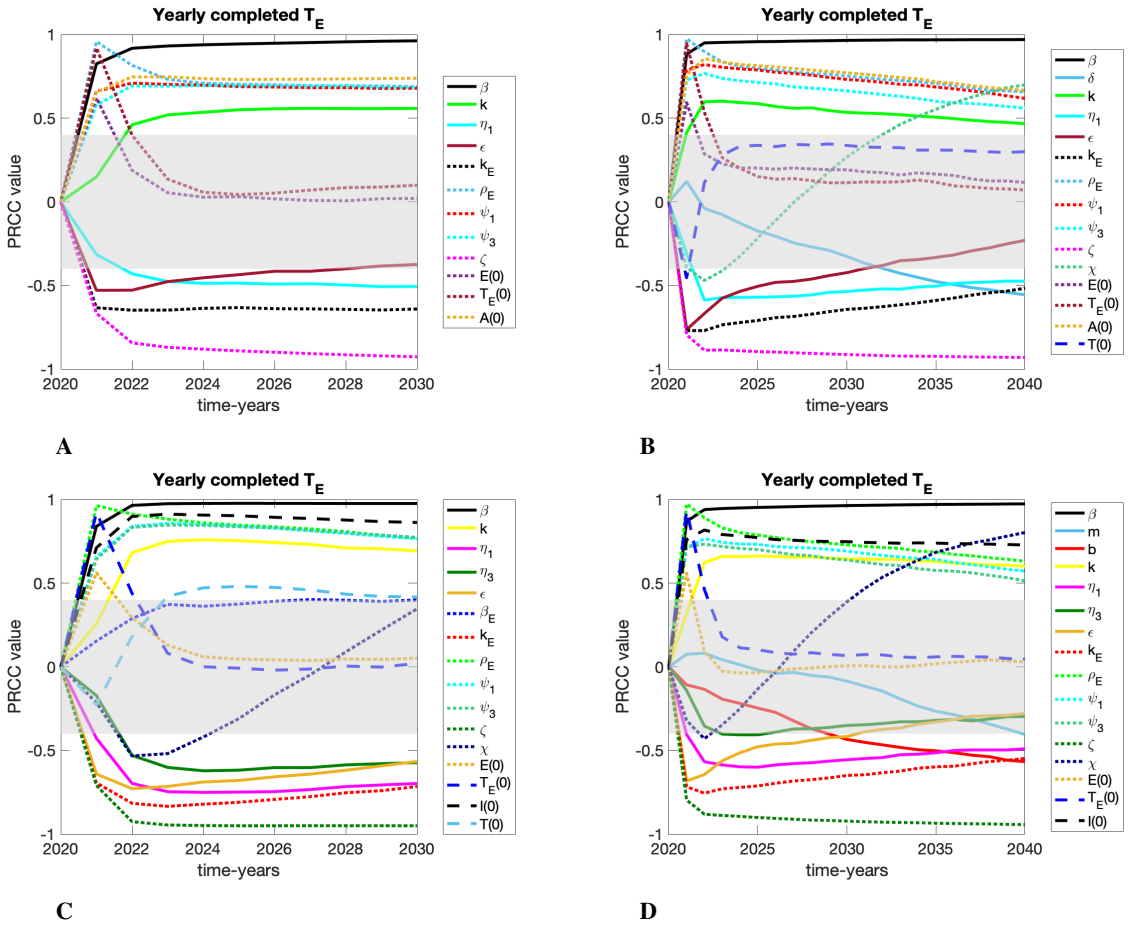

Figure S.16. Heroin: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T_E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.4.

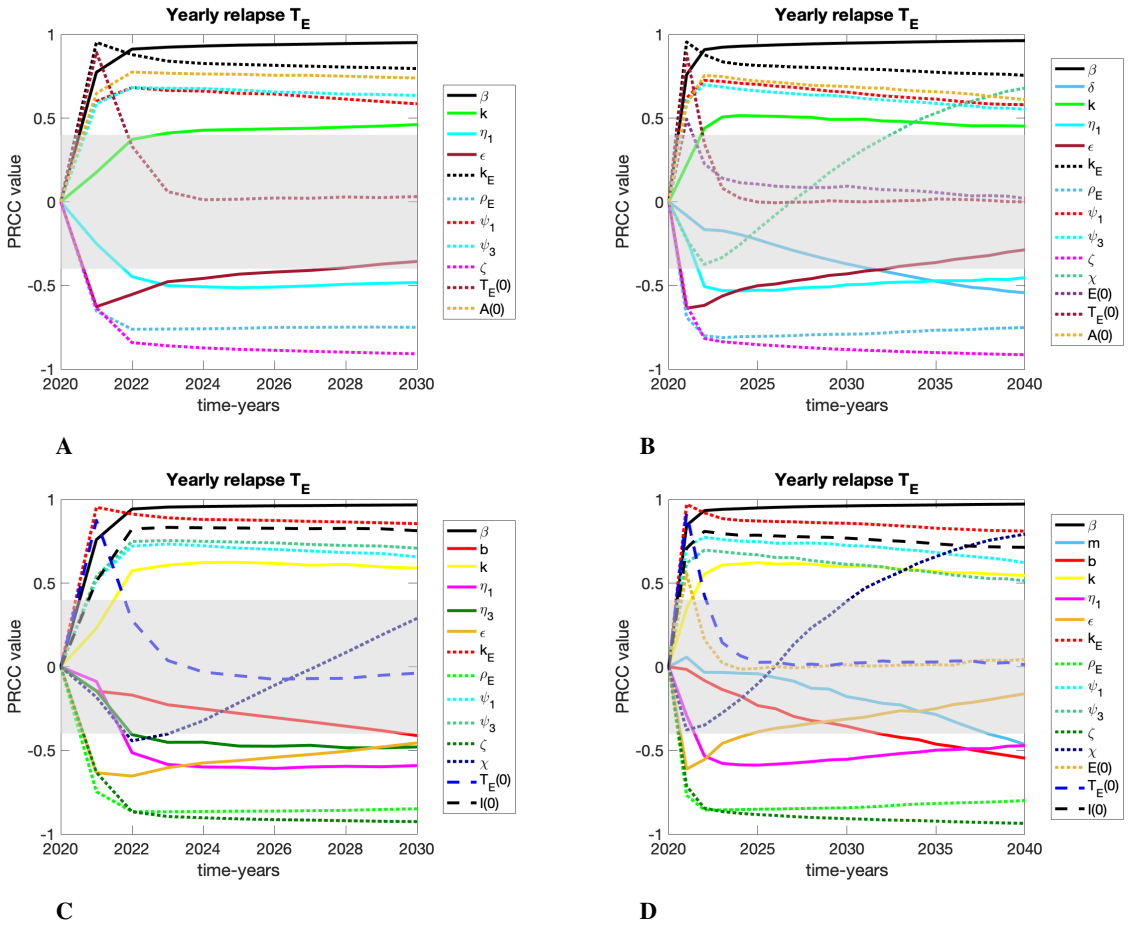

Figure S.17. Heroin: PRCC Results over Time for Those Who Are Entering I for the First Time, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.4. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

S.3. All illicit opioids: Additional PRCC plots and tables

Other variables and the sensitivity of the state variables for the all-illicit opioids dataset are presented only in terms of plots and tables.

Checking the monotonicity results as was done in the previous sections, although some potential issues arose, after checking we see that those parameters were either not significant during the time period of non-monotonicity or did not even show up on the PRCC graph. Therefore, we conclude that our results are valid.

Table S.5. All Illicit Opioids Data: PRCC Results for the S Population, for the E Population, and the T_E Population Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.18–S.20.

Param	S				E				TE			
	Constant		Variable		Constant		Variable		Constant		Variable	
Years	10	20	10	20	10	20	10	20	10	20	10	20
μ	-0.55	-0.57	-0.57	-0.57	-	-	-	-	-	-	-	-
β	-	-	-	-	0.62	0.67	0.55	0.46	0.58	0.63	0.53	0.47
δ	-	-	-	-	-	-	-	-	-	-	-	
m	-	-	-	-	-	-	-	-	-	-	-	-
b	-	-	-	-	-	-	-	-	-	-	-	-
Λ	0.58	0.6	0.63	0.67	-	-	-	-	-	-	-	-
k	-	-	-	-	-	-	-	-	-	-	-	-
ρ	-	-	-	-	-	-	-	-	-	-	-	-
η_1	-	-	-	-	-	-	-	-	-	-	-	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-	-	-	-	-	-	-	-	-	-
α_1	-	-	-	-	-	0.43	-	-	-	-	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-	-	-	-	-0.49	-	-0.43	-	-0.42	-	-
ϵ	-	-	-	-	-	-	-	-	-	-	-	-
β_E	-0.8	-0.85	-0.81	-0.84	0.98	0.98	0.97	0.97	0.98	0.98	0.97	0.97
δ_E	-	-			-	-	-	-	-	-	-	
m_E	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-0.45	-	-	-
ρ_E	-	-	-	-	-	-	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	-	0.41	0.42	-
ζ	0.79	0.85	0.81	0.83	-0.98	-0.98	-0.97	-0.97	-0.98	-0.98	-0.97	-0.96
χ	-	-	-	-	-0.48	-0.48	-	-	-0.5	-0.48	-	-
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	0.98	0.94	0.98	0.94	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$A(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$T(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$R(0)$	-	-	-	-	-	-	-	-	-	-	-	-

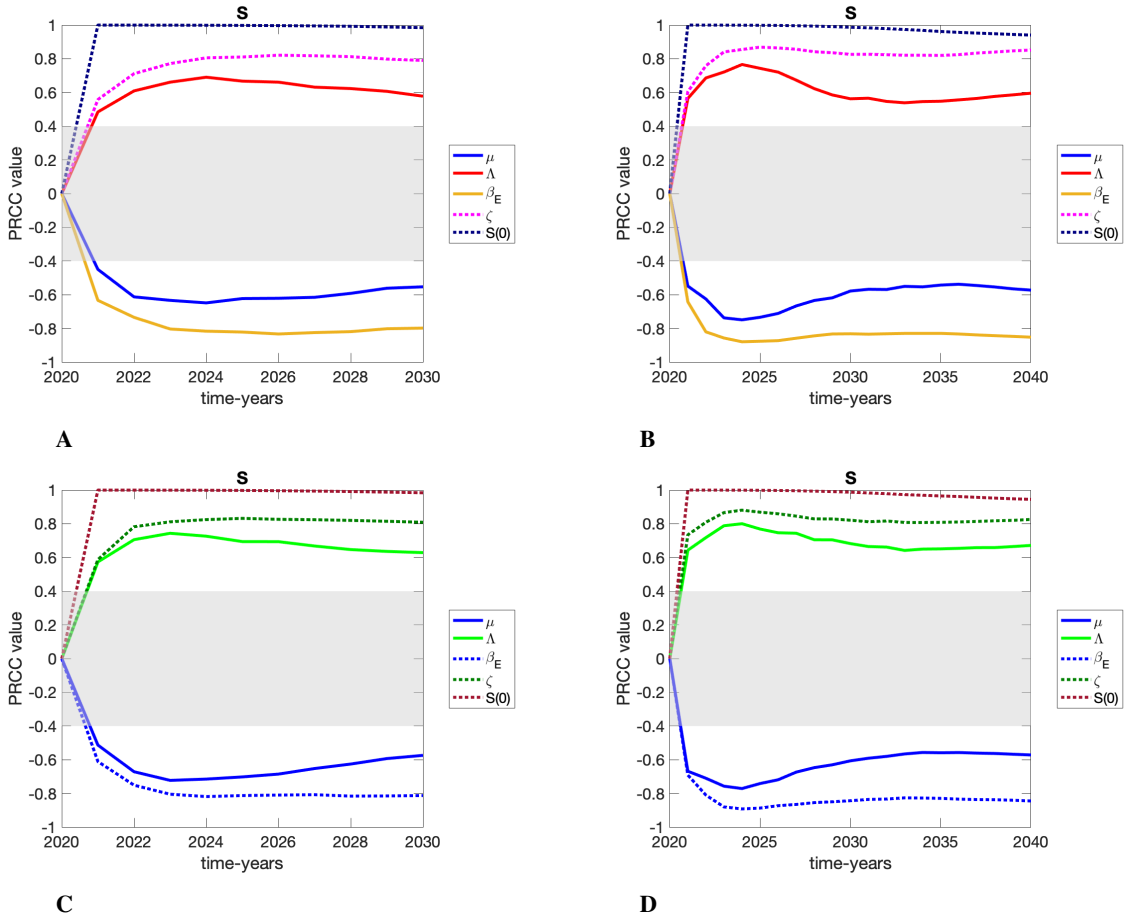

Figure S.18. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the S Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.5. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

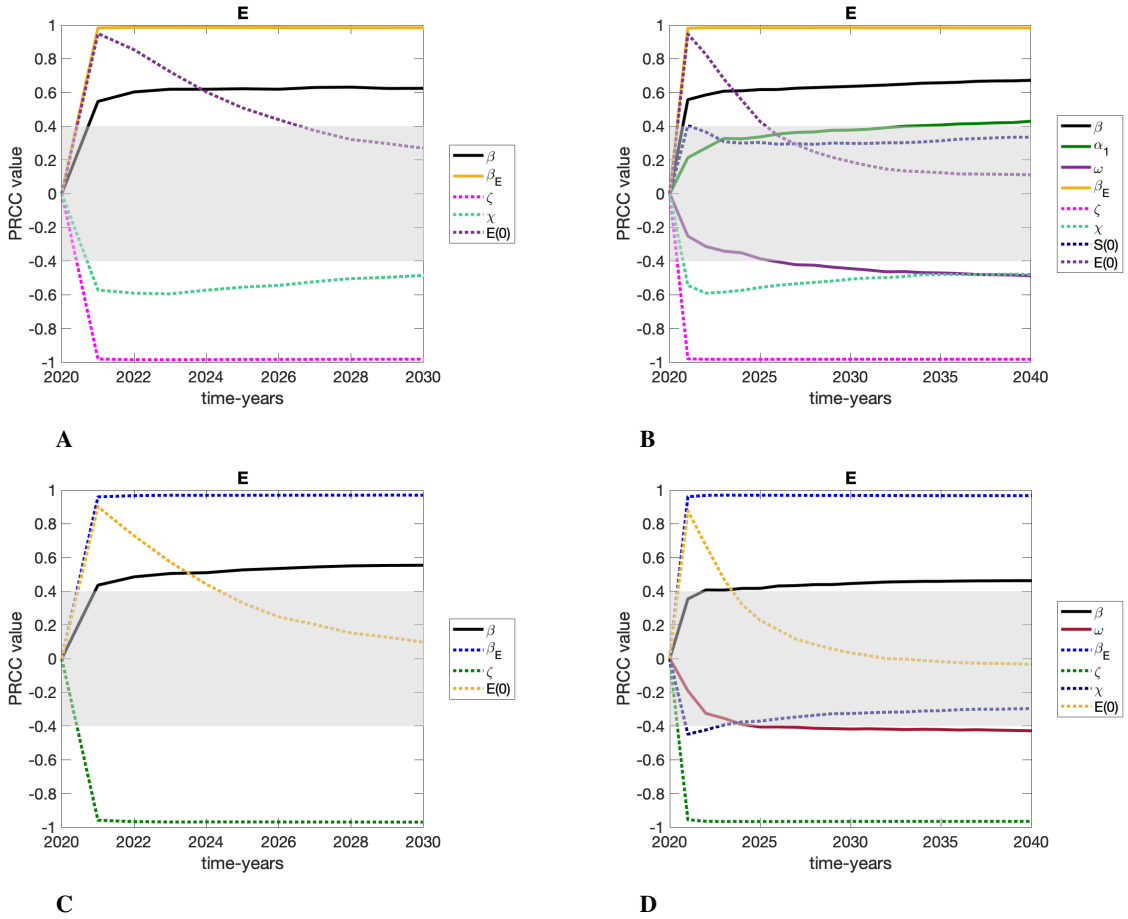

Figure S.19. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.5. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

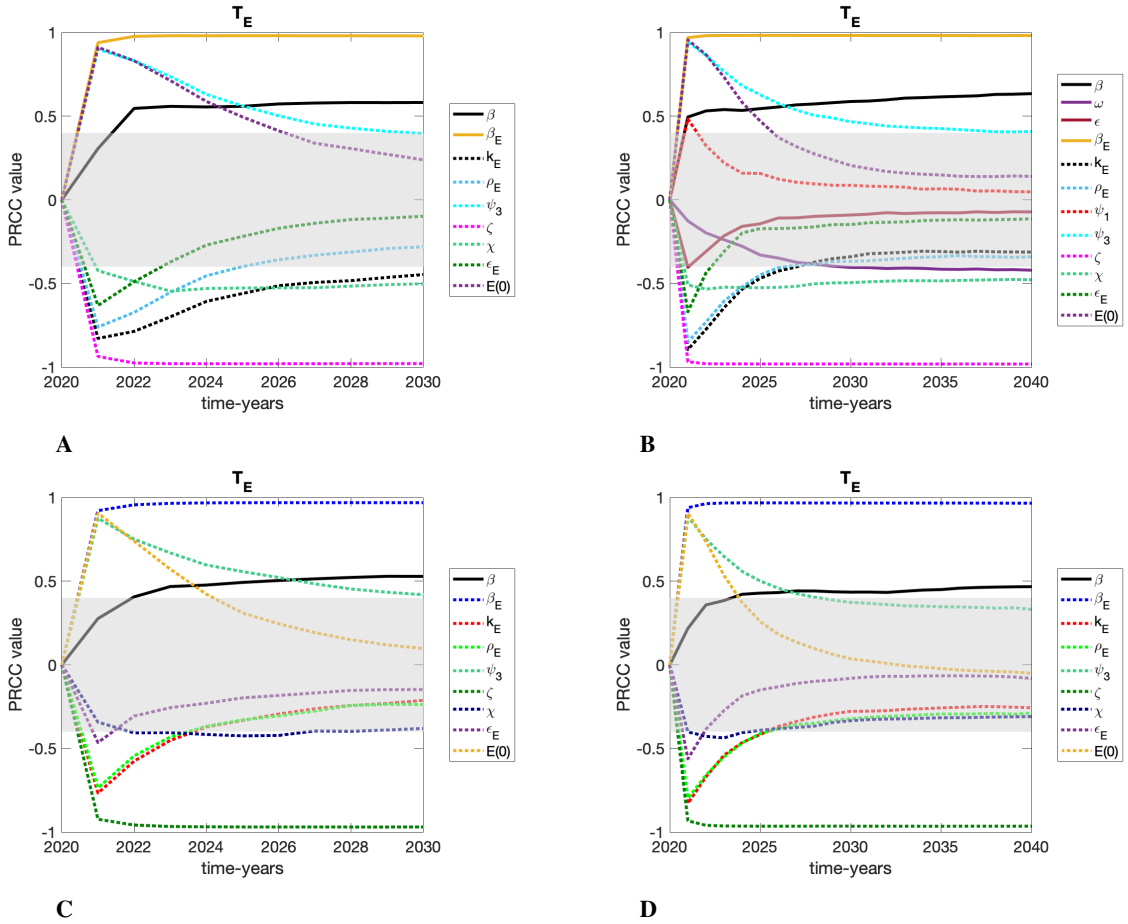

Figure S.20. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the T_E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.5. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.6. All Illicit Opioids Data: PRCC Results for the I Population, for the T Population, and the R Population Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.21-S.23.

Param	I				T				R			
	Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20
μ	-	-	-	-	-	-	-	-	-0.42	-	-	-
β	-	0.6	0.5	0.42	-	0.45	-	-	0.5	0.59	0.5	0.47
δ	-	-	-	-	-	-			-	-	-	
m	-	-	-	-	-	-	-	-	-	-	-	-
b	-	-	-	-	-	-	-	-	-	-	-	-
Λ	-	-	-	-	-	-	-	-	-	-	-	-
k	-	-	-	-	-0.82	-0.57	-0.67	-0.68	-	-	-	-
ρ	-	-	-	-	-0.72	-0.42	-0.54	-0.53	-	-	-	-
η_1	-	-	-	-	0.8	0.63	0.6	0.65	-	-	-	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-	-	0.73	0.5	0.57	0.55	-	-	-	-
α_1	0.74	0.69	0.73	0.62	0.85	0.76	0.74	0.75	-	-	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-
ω	-0.75	-0.73	-0.78	-0.66	-0.85	-0.76	-0.8	-0.76	-	-	-	-
ϵ	-	-	-	-	-	-	-	-	-	-	-	-
β_E	0.96	0.97	0.96	0.96	0.92	0.96	0.88	0.96	0.97	0.98	0.96	0.97
δ_E	-	-			-	-			-	-	-	
m_E	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-	-	-	-
ρ_E	-	-	-	-	-	-	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	-	-	-	-
ζ	-0.96	-0.97	-0.96	-0.96	-0.9	-0.96	-0.87	-0.96	-0.97	-0.98	-0.96	-0.97
χ	-	-	-	-	0.67	-	0.52	0.44	0.46	-	-	-
ϵ_E	-	-	-	-	-0.44	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	0.41	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$A(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$T(0)$	-	-	-	-	-	-	-	-	-	-	-	-
$R(0)$	0.58	-	0.53	0.44	0.71	-	0.54	0.48	0.81	0.46	0.71	0.51

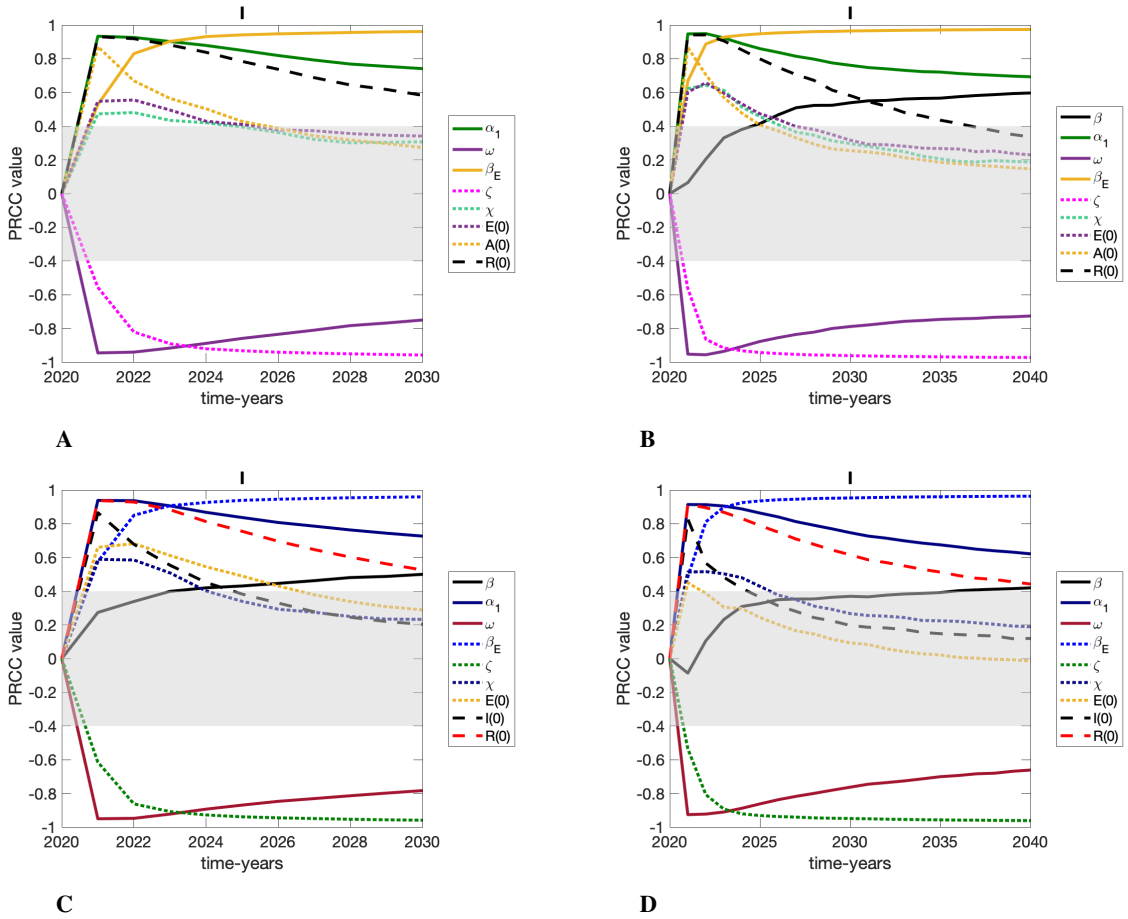

Figure S.21. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the R Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.6. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

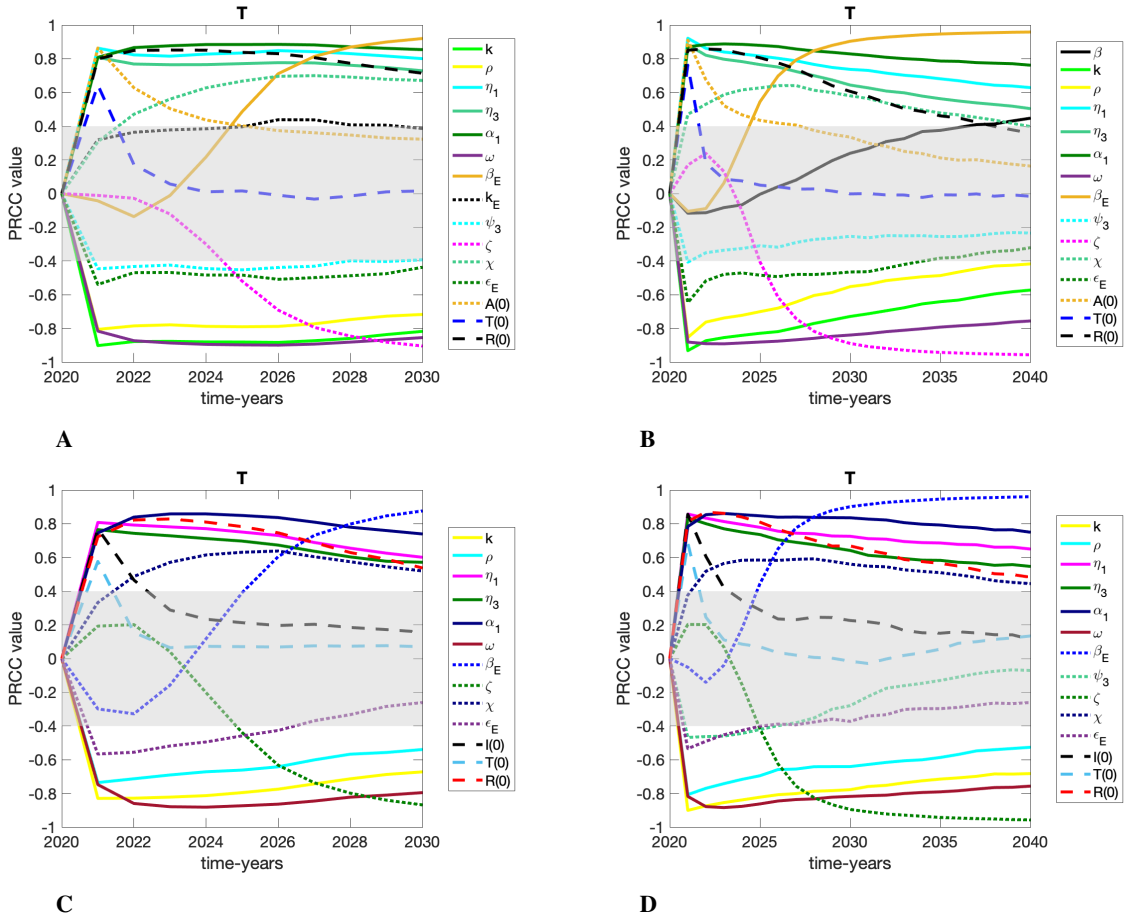

Figure S.22. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the T Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.6. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

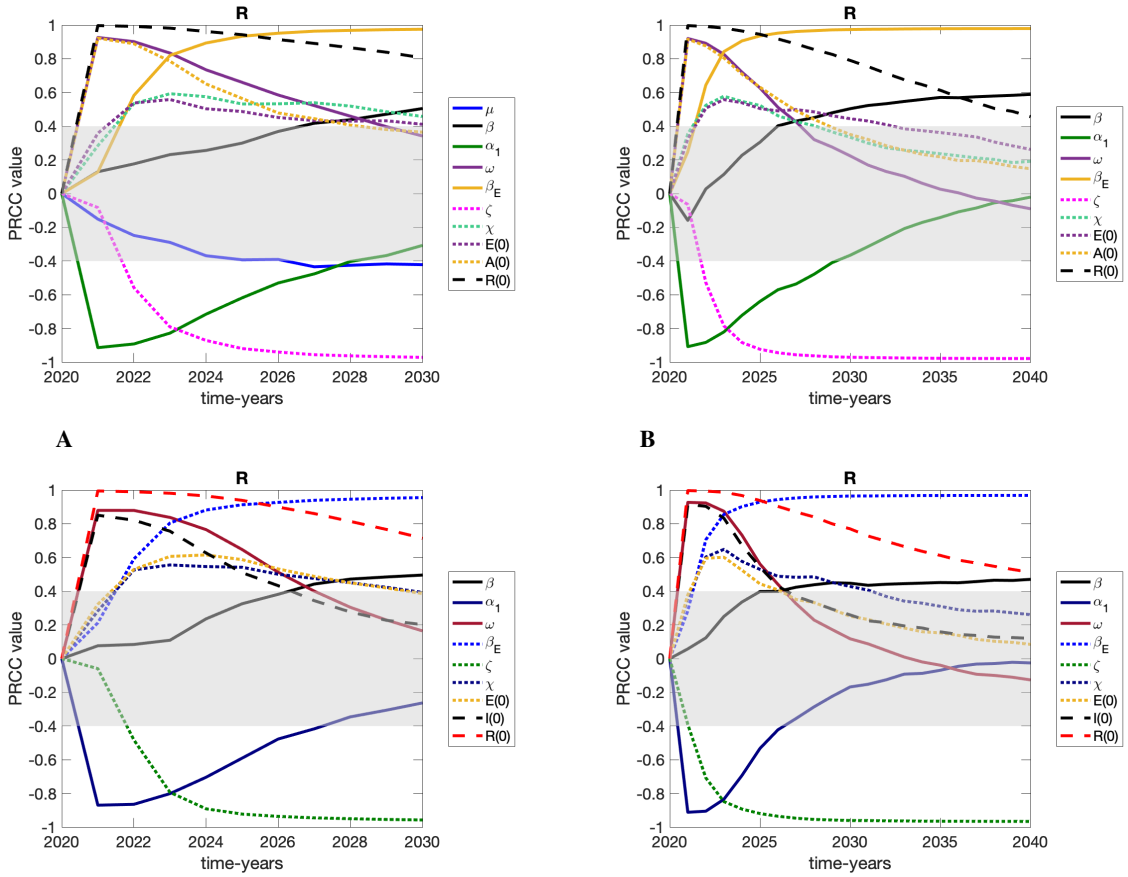

Figure S.23. Illicit Opioids: PRCC Results over Time for the Number of Individuals in the I Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.6. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.7. All Illicit Opioids Data: PRCC Results for the Movement into Treatment T, Completed Treatment T, the Movement from I to R, and the Movement from S to E Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.24–S.27.

Param	GoT				CT				I2R				S2E			
	Constant		Variable		Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
μ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
β	-	0.52	-	-	-	0.48	-	-	0.5	0.59	0.53	0.46	0.66	0.7	0.58	0.49
δ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
m	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Λ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k	-	-	-	-	-0.72	-0.58	-0.72	-0.62	-	-	-	-	-	-	-	-
ρ	-	-	-	-	0.77	0.72	0.81	0.63	-	-	-	-	-	-	-	-
η_1	0.79	0.65	0.68	0.63	0.7	0.67	0.66	0.6	-	-	-	-	-	-	-	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_3	0.72	0.48	0.65	0.5	0.62	0.49	0.6	0.47	-	-	-	-	-	-	-	-
α_1	0.85	0.78	0.79	0.71	0.78	0.77	0.78	0.7	0.79	0.71	0.77	0.62	0.42	0.44	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ω	-0.84	-0.77	-0.82	-0.74	-0.78	-0.76	-0.81	-0.72	-	-	-	-	-	-0.5	-0.43	-0.45
ϵ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
β_E	0.91	0.96	0.89	0.95	0.85	0.96	0.86	0.95	0.97	0.98	0.96	0.96	0.99	0.98	0.98	0.97
δ_E	-	-	-	-	-	-	-		-	-	-		-	-	-	
m_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ρ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ζ	-0.9	-0.96	-0.9	-0.95	-0.82	-0.96	-0.87	-0.95	-0.97	-0.98	-0.96	-0.96	-0.98	-0.98	-0.97	-0.96
χ	0.61	0.51	0.54	0.41	0.58	0.48	0.54	-	-	-	-	-	-0.45	-0.46	-	-
ϵ_E	-0.42	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	0.42	-	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$I(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$T(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$R(0)$	0.69	0.43	0.56	0.46	0.59	-	0.57	0.46	0.64	-	0.56	0.44	-	-	-	-

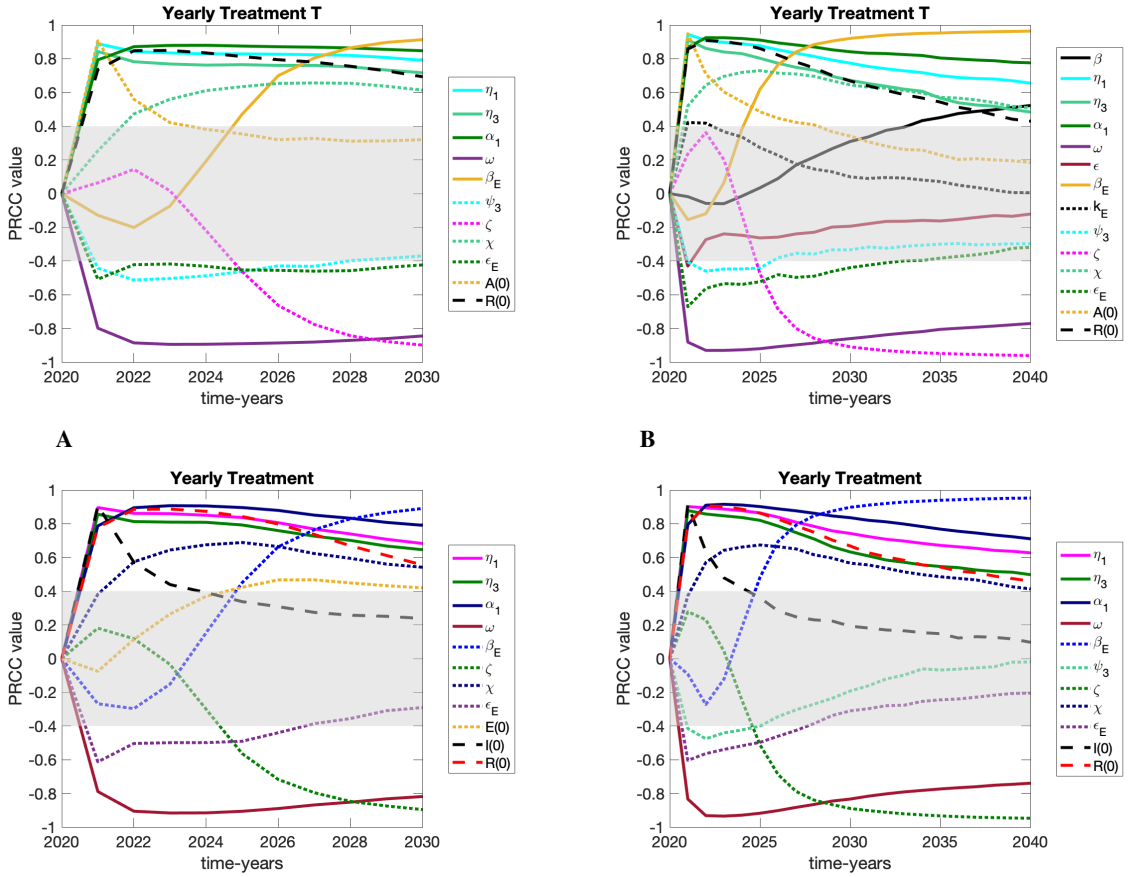

Figure S.24. Illicit Opioids: PRCC Results over Time for Those Who Are Entering i for the First Time, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.7. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

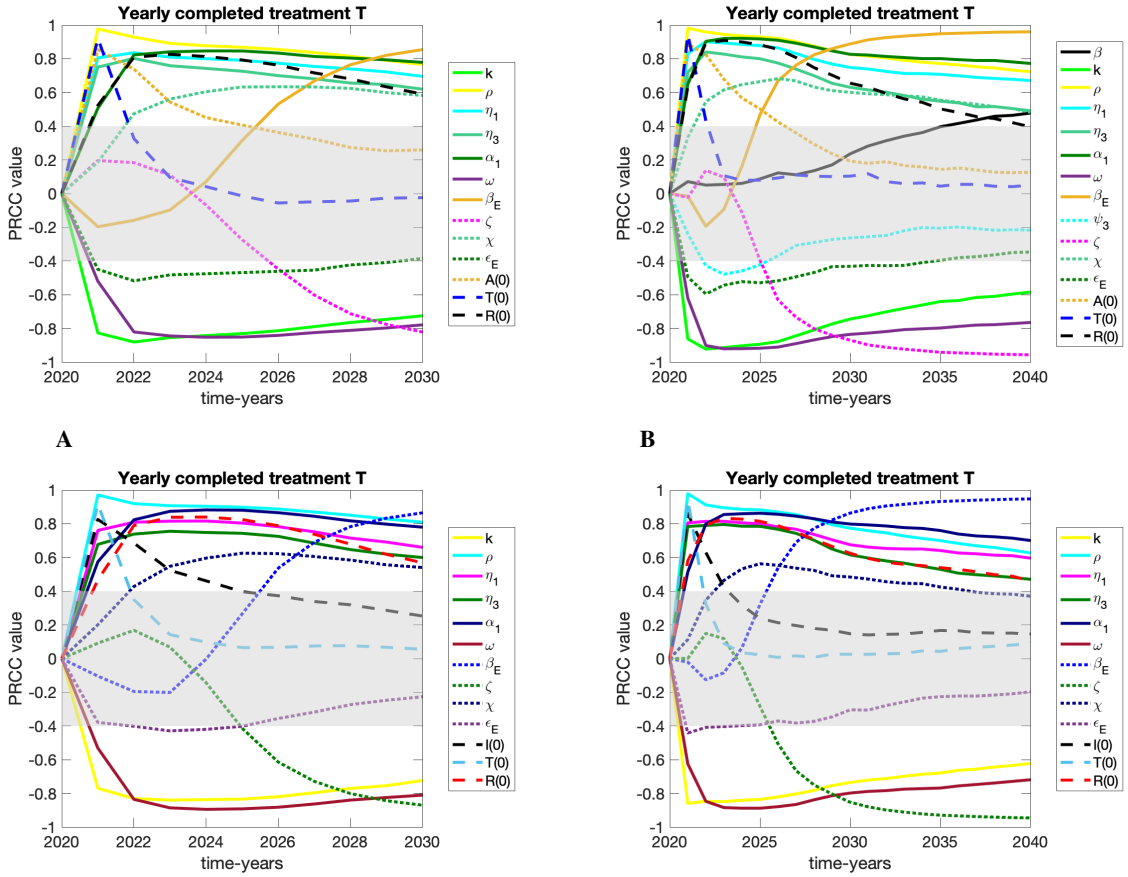

Figure S.25. Illicit Opioids: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T_E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.7. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

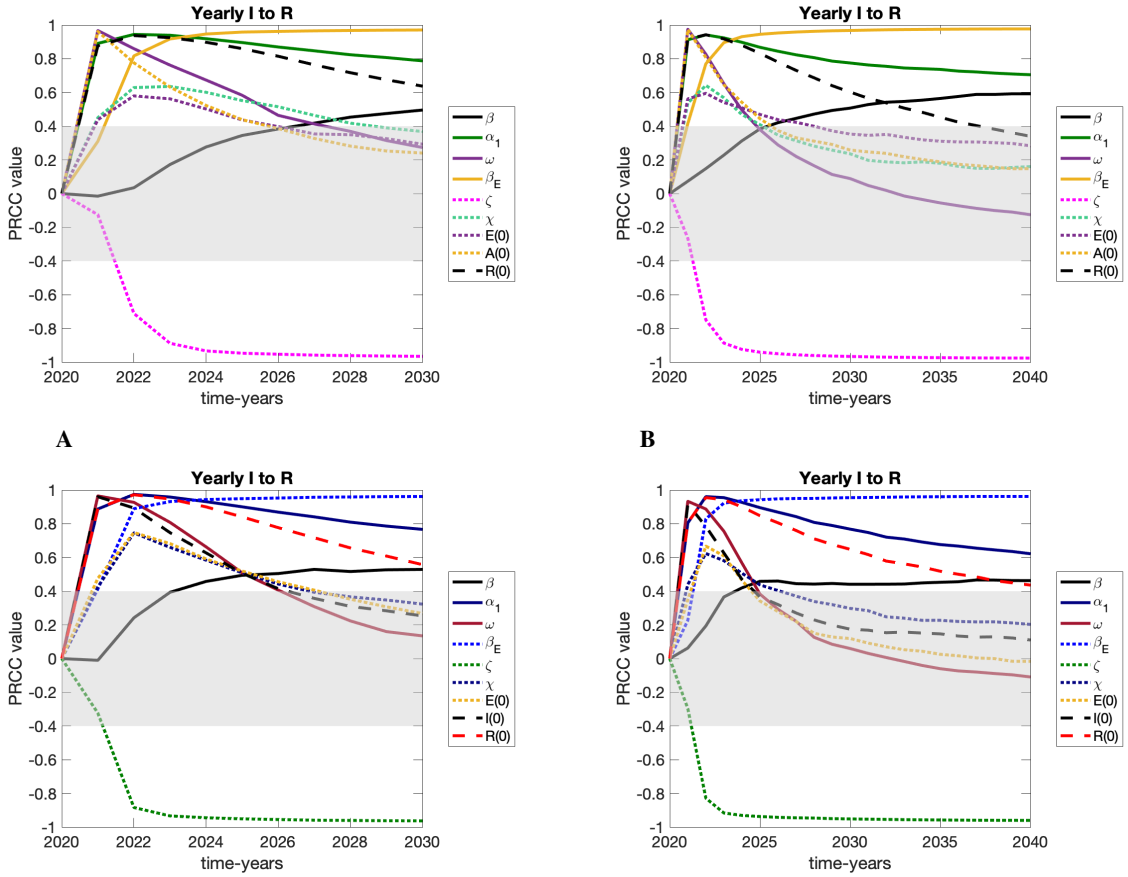

Figure S.26. Illicit Opioids: PRCC Results over Time for Those Who Are Entering I for the First Time, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.7. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

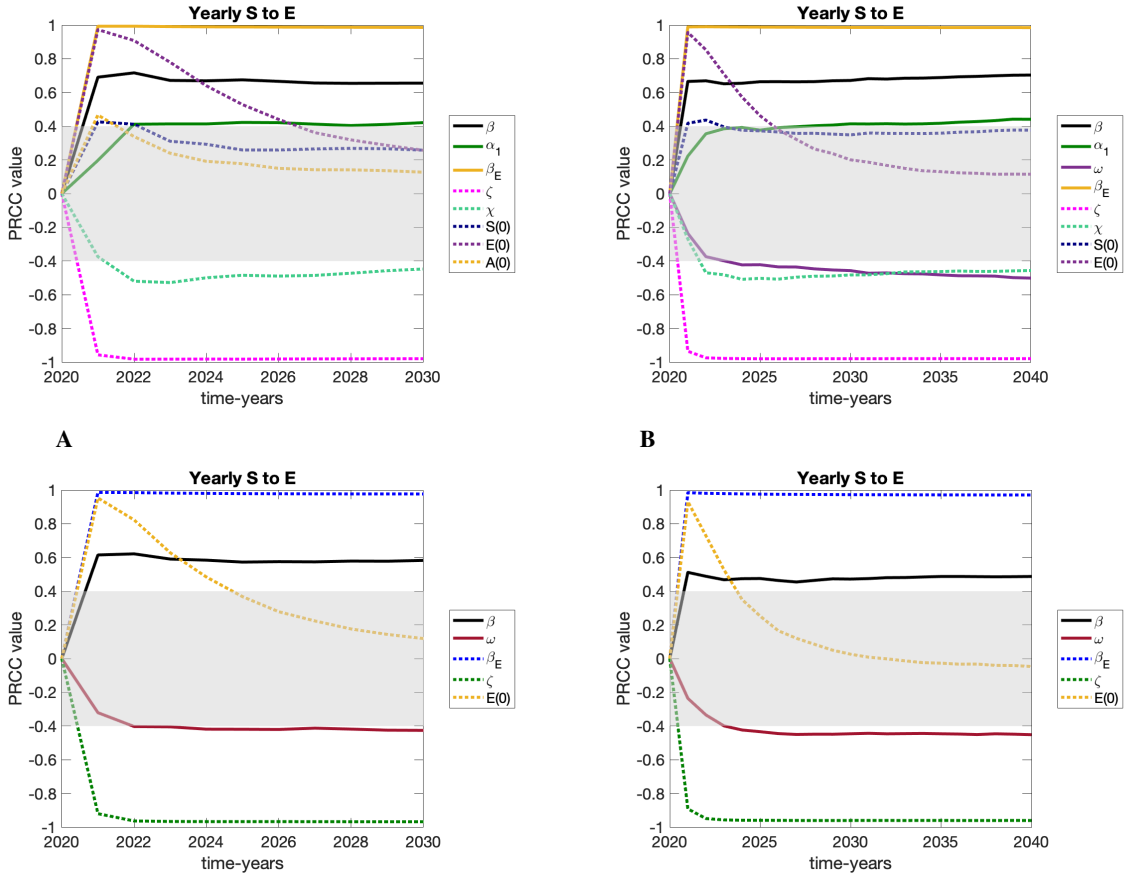

Figure S.27. Illicit Opioids: PRCC Results over Time for Those Who Are Entering I for the First Time, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.7. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

Table S.8. All Illicit Opioids data: PRCC Results for the Movement from E to S, the Movement into Treatment T_E, Completed Treatment T_E, and Relapse from T_E Using the Baseline Parameters and Initial Conditions and Using Either the Constant Delta or the Variable Delta. The PRCC Values Are given at Year End Time of 2030 and Year End Time of 2040. Table Values Without an Entry Are Either Not Significant or Undefined (in the Case of m and b for the Constant Death Rate and δ and δ_E for the Variable Death Rate). The Corresponding Graphs for This Table Are given in Figures S.28–S.31.

Param	E2S				E2TE				CTE				RTE			
	Constant		Variable		Constant		Variable		Constant		Variable		Constant		Variable	
	10	20	10	20	10	20	10	20	10	20	10	20	10	20	10	20
μ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
β	0.66	0.71	0.58	0.49	0.66	0.65	0.58	0.45	0.66	0.61	0.58	0.43	0.58	0.65	0.54	0.48
δ	-	-	-	-	-	-	-	-	-	-			-	-	-	
m	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Λ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
k	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ρ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
η_3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
α_1	0.43	0.44	-	-	0.42	-	-	-	0.43	-	-	-	-	-	-	-
α_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ω	-	-0.5	-0.44	-0.45	-	-	-0.43	-	-	-	-0.44	-	-	-	-	-
ϵ	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
β_E	0.99	0.99	0.98	0.97	0.99	0.98	0.98	0.97	0.99	0.98	0.98	0.97	0.98	0.98	0.97	0.97
δ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
m_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
b_E	-	-	-	-	-	-	-	-			-	-	-	-	-	-
k_E	-	-	-	-	-	-	-	-	-	-	-	-	-	0.46	0.45	-
ρ_E	-	-	-	-	-	-	-	-	-	0.42	-	-	-	-	-	-
ψ_1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
ψ_3	-	-	-	-	-	0.42	-	-	-	0.43	-	-	-	0.41	0.42	-
ζ	-0.98	-0.98	-0.97	-0.96	-0.98	-0.98	-0.97	-0.97	-0.98	-0.98	-0.97	-0.96	-0.98	-0.98	-0.97	-0.96
χ	-0.54	-0.52	-0.41	-	-0.45	-0.46	-	-	-0.54	-0.44	-0.41	-	-0.46	-0.49	-	-
ϵ_E	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$S(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$T_E(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$I(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$T(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$R(0)$	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

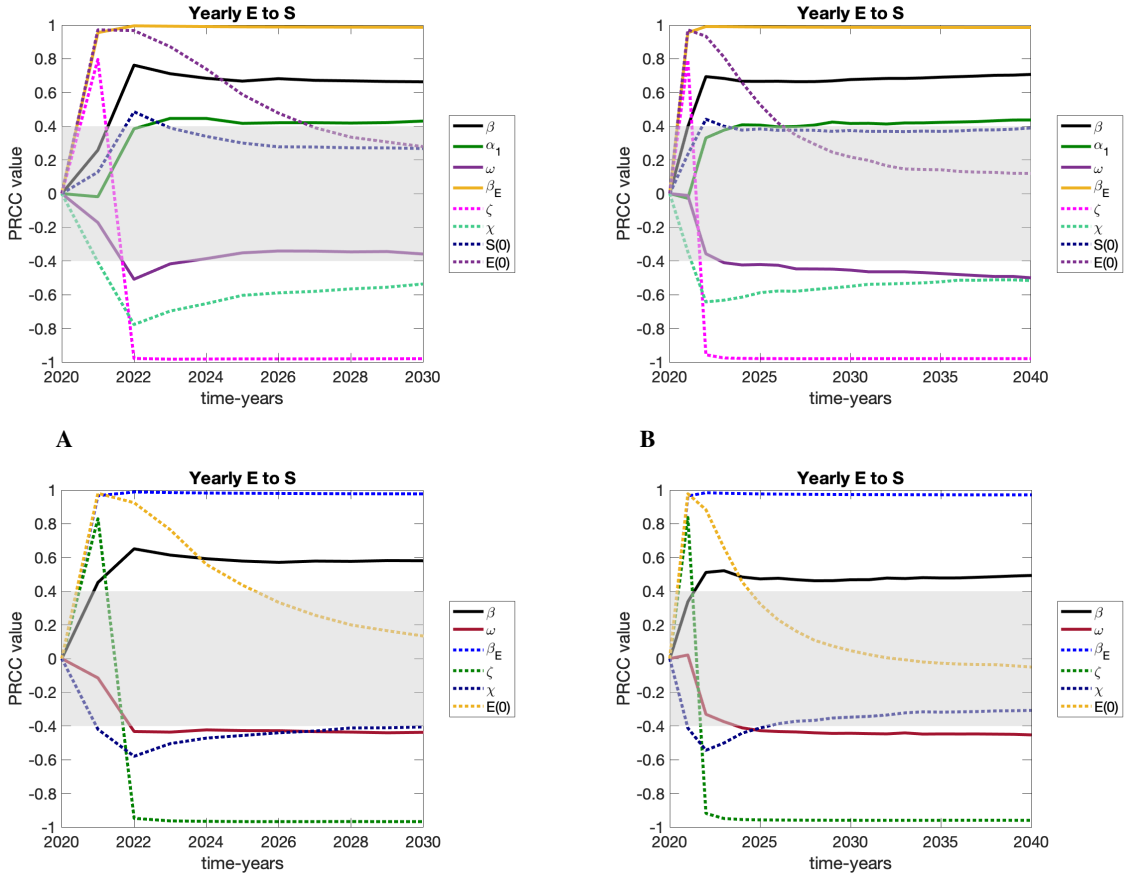

Figure S.28. Illicit Opioids: PRCC Results over Time for the Number of Those Leaving from the E Class Back to the S Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.8. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

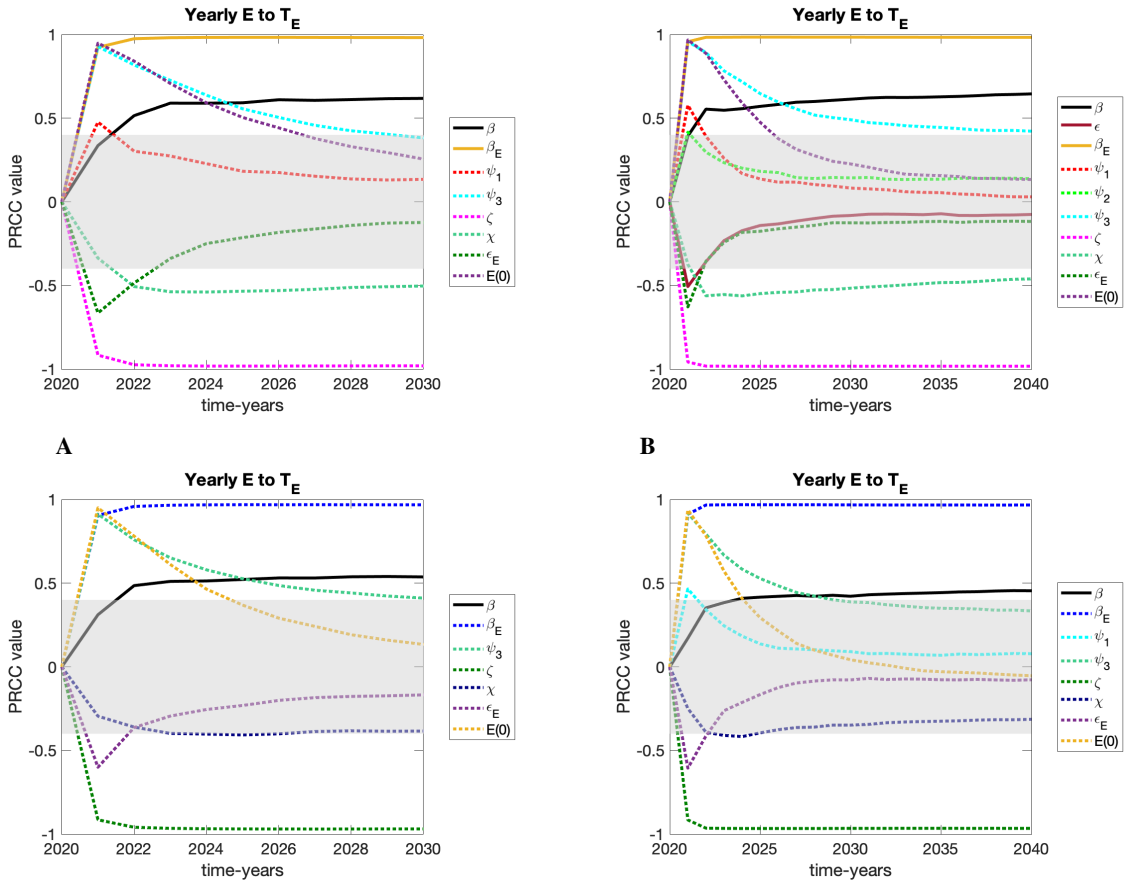

Figure S.29. Illicit Opioids: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.8. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

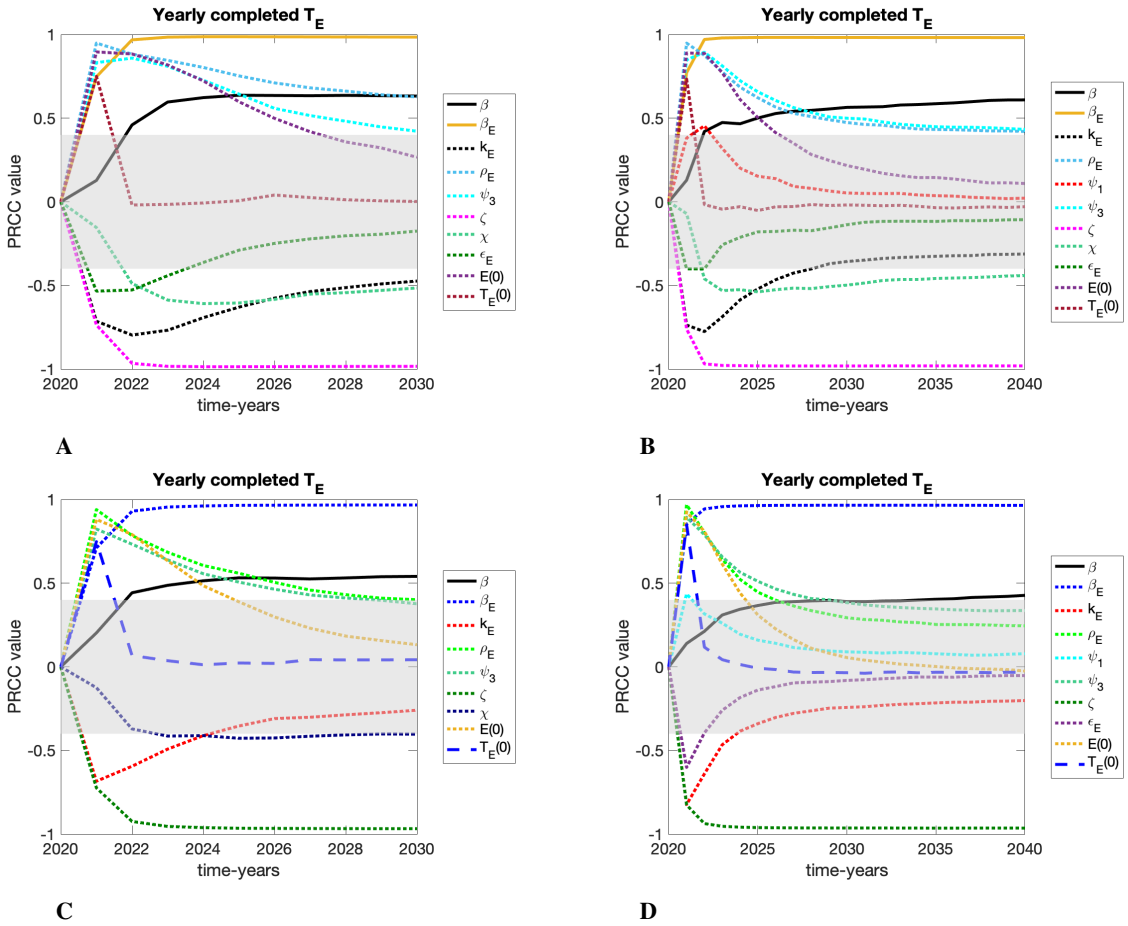

Figure S.30. Illicit Opioids: PRCC Results over Time for the Number of Individuals Who Successfully Completed Treatment from the T_E Class, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.8. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.

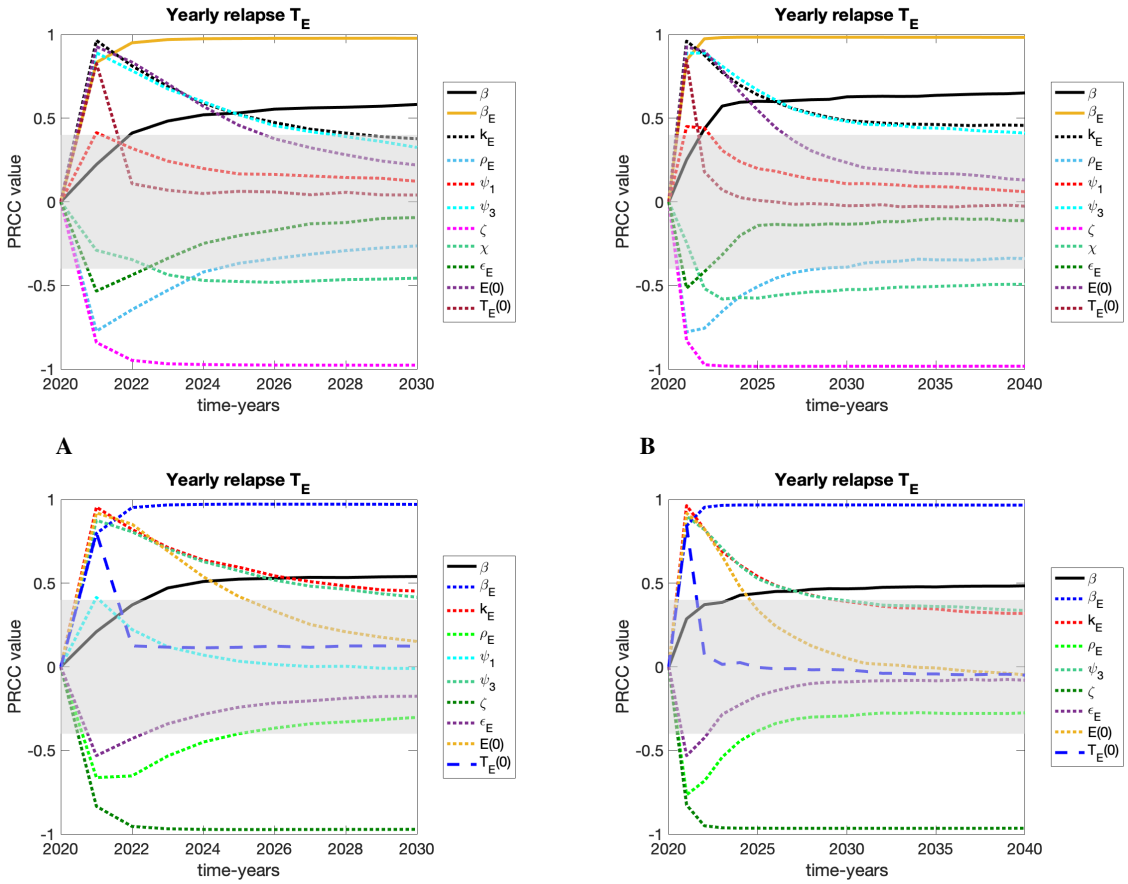

Figure S.31. Illicit Opioids: PRCC Results over Time for Those Who Are Entering I for the First Time, with Greyed Region Denoting a Lack of Significance. These Results Are Summarized in the Text and in Table S.8. The Left Figures Have a Final Time of 2030 Whereas the Right Figures Have a Final Time of 2040. The Top Figures Keep δ and δ_E Constant at Their 2020 Values Whereas the Bottom Figures Use the Extrapolation Functions for δ and δ_E.