

# Heroin Model Summary

## Original

$$\begin{aligned}
 \frac{dS}{dt} &= \beta E - \alpha S - \underbrace{S(\sigma + \xi(I + H))}_{\text{to resistant}} - \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{to opioid addiction}} - \underbrace{S(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} \\
 &\quad + \underbrace{rR}_{\text{resist loss}} - g d_S S + (1 - g)(d_S(E + R) + d_I I + d_H H) \\
 \frac{dE}{dt} &= -\beta E + \alpha S - \underbrace{E(\sigma + \xi(I + H))}_{\text{to resistant}} - \underbrace{E(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} - \underbrace{\epsilon E}_{\text{to I}} - d_S E \\
 \frac{dI}{dt} &= \underbrace{\epsilon E}_{\text{from E}} + \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{from S}} - \underbrace{\gamma(H)I}_{\text{to H}} - \underbrace{iI}_{\text{to R}} - d_I I \\
 \frac{dH}{dt} &= \underbrace{\gamma(H)I}_{\text{from I}} + \underbrace{(S + E)(\mu_1 + \mu_2 H)}_{\text{from S and E}} - \underbrace{hH}_{\text{to R}} - d_H H \\
 \frac{dR}{dt} &= \underbrace{(S + E)(\sigma + \xi(I + H))}_{\text{from S and E}} + \underbrace{iI}_{\text{from I}} + \underbrace{hH}_{\text{from H}} - \underbrace{rR}_{\text{resist loss}} - (1 - g)d_S R \\
 &\quad + g(d_S(S + E) + d_I I + d_H H) \\
 \gamma(H) &= \gamma_0(\mu_1 + \mu_2 H)
 \end{aligned}$$

We assume that  $0 \leq \delta_1 \leq \delta_2 \leq 1$ ,  $\mu_1 < \mu_2$ , and  $d_r$  includes both natural death and backsliding from drug resistant to susceptible. If  $g = 0$  you get back the June version of the discrete-time dynamical system.

**Results at equilibrium using the default parameters** put the resistant population quite high, at around 0.77 of the total population. Susceptibles are around 0.2, and the total number of opioid and heroin addicts are 6,827,303 and 410,016 respectively. The opioid number is likely a bit high and the heroin number low, since according to the American Society of Addiction Medicine, of the 20.5 million Americans 12 or older that had a substance use disorder in 2015, 2 million had a substance use disorder involving prescription pain relievers and 591,000 had a substance use disorder involving heroin.

## I and H feeds S

$$\begin{aligned}
\frac{dS}{dt} &= \beta E - \alpha S - \underbrace{S(\sigma + \xi(I + H))}_{\text{to resistant}} - \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{to opioid addiction}} - \underbrace{S(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} \\
&\quad + \underbrace{iI}_{\text{from I}} + \underbrace{hH}_{\text{from H}} + \underbrace{rR}_{\text{resist loss}} - g d_S S + (1 - g)(d_S(E + R) + d_I I + d_H H) \\
\frac{dE}{dt} &= -\beta E + \alpha S - \underbrace{E(\sigma + \xi(I + H))}_{\text{to resistant}} - \underbrace{E(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} - \underbrace{\epsilon E}_{\text{to I}} - d_S E \\
\frac{dI}{dt} &= \underbrace{\epsilon E}_{\text{from E}} + \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{from S}} - \underbrace{\gamma(H)I}_{\text{to H}} - \underbrace{(i + d_I)I}_{\text{to S, rec. \& death}} \\
\frac{dH}{dt} &= \underbrace{\gamma(H)I}_{\text{from I}} + \underbrace{(S + E)(\mu_1 + \mu_2 H)}_{\text{from S and E}} - \underbrace{(h + d_H)H}_{\text{to S, rec. \& death}} \\
\frac{dR}{dt} &= \underbrace{(S + E)(\sigma + \xi(I + H))}_{\text{from S and E}} - \underbrace{rR}_{\text{resist loss}} - (1 - g)d_S R \\
&\quad + g(d_S(S + E) + d_I I + d_H H) \\
\gamma(H) &= \gamma_0(\mu_1 + \mu_2 H)
\end{aligned}$$

**Results at equilibrium using the default parameters** lower the number of resistant people considerably, to 0.45 of the total population. Susceptibles rise in a corresponding manner, to 0.4. There are significantly more opioid addicts (21,084,408) and more heroin addicts (1,585,819).

## No R

$$\begin{aligned}
\frac{dS}{dt} &= \beta E - \alpha S - \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{to opioid addiction}} - \underbrace{S(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} + \underbrace{iI}_{\text{from I}} + \underbrace{hH}_{\text{from H}} + d_I I + d_H H + d_S E \\
\frac{dE}{dt} &= -\beta E + \alpha S - \underbrace{E(\mu_1 + \mu_2 H)}_{\text{to heroin addiction}} - \underbrace{\epsilon E}_{\text{to I}} - d_S E \\
\frac{dI}{dt} &= \underbrace{\epsilon E}_{\text{from E}} + \underbrace{S(\delta_1 E + \delta_2 I)}_{\text{from S}} - \underbrace{\gamma(H)I}_{\text{to H}} - \underbrace{(i + d_I)I}_{\text{to S, rec. \& death}} \\
\frac{dH}{dt} &= \underbrace{\gamma(H)I}_{\text{from I}} + \underbrace{(S + E)(\mu_1 + \mu_2 H)}_{\text{from S and E}} - \underbrace{(h + d_H)H}_{\text{to S, rec. \& death}} \\
\gamma(H) &= \gamma_0(\mu_1 + \mu_2 H)
\end{aligned}$$

**Leaving off a resistant population** does not force everyone to heroin. As might be expected, the numbers of both opioid addicts and heroin addicts do increase (37,428,464 and 4,344,805), but this could likely be controlled for using different parameter values.

### Sensitivity analysis notes

Information about parameter sensitivity for each of these models was obtained using the Sobol method and omitted the death rates  $d_S$ ,  $d_I$ , and  $d_H$ , holding them constant (see `heroin_model.py` for the values). Sensitivity was measured with respect to the model steady state as measured by the value of  $S$ ,  $E$ ,  $I$ ,  $H$ , and  $R$  at the end of a 1000 year long simulation. Variance of the model of the last 50 years of the 1000 year simulation was also calculated for use as a possible indication of oscillations. Sensitivity to second-order interactions among the parameters was also calculated.

Saltelli's extension of the Sobol sequence was used to generate  $N(2D+2)$  model inputs for sampling, where  $D$  is the dimension of the parameter space (14 in our case) and  $N$  was chosen to be 10000 and 50000 in separate trials. Parameter sensitivity with respect to independent variable steady states did not vary between these trials, suggesting a sufficient number of samples. Sensitivity with respect to variance did vary, but in all cases the maximum variance recorded in any model was on the order of  $10^{-5}$ , suggesting that oscillations likely do not play a significant role in the parameter space of interest, if they are present at all.