

Estimating local chlamydia incidence and prevalence using surveillance data: eAppendix 1

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June 8, 2016

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1 A model for chlamydia surveillance data

We propose a three-compartment model of chlamydia infection, testing and screening in a closed population, as illustrated below. Uninfected individuals (U) become infected with a constant incidence, and move to either the asymptomatic-infected (A) or symptomatic-infected (S) pool. Asymptomatic-infected individuals may leave A and return to U by spontaneous clearance of their infection or by detection and treatment under a screening programme. Symptomatic individuals too may clear their infection spontaneously or be screened, but will also seek treatment at a rate which is typically much higher than the rates of spontaneous clearance or screening.

```
In [1]: from IPython.display import Image
        Image(filename="figures/3_comp.png", width=500)
```

Out[1]: Out[1]:

This dynamic model has a steady-state solution which depends on the transition rates α_{UA} , α_{AU} , α_{US} and α_{SU} :

```
In [2]: import sympy as sym
        from sympy import *
        A, U, S = symbols("A U S")
        alpha_UA, alpha_AU, alpha_US, alpha_SU = symbols("alpha_UA alpha_AU alpha_US alpha_SU")

        model_dyn = [
            alpha_UA*U - alpha_AU*A,
            alpha_AU*A + alpha_SU*S - (alpha_UA + alpha_US)*U,
            alpha_US*U - alpha_SU*S,
            A + U + S - 1 # this equation sets the total population size to 1
        ]

        # steady-state solution
        sol_dyn = solve(model_dyn, A, U, S)

        # functions for calculating the proportion of the population in each compartment at
        # steady state, given transition rates between compartments
        dyn_fun = lambdify((alpha_UA, alpha_AU, alpha_US, alpha_SU), sol_dyn[A] + sol_dyn[S])
        U_fun = lambdify((alpha_UA, alpha_AU, alpha_US, alpha_SU), sol_dyn[U])
        A_fun = lambdify((alpha_UA, alpha_AU, alpha_US, alpha_SU), sol_dyn[A])
        S_fun = lambdify((alpha_UA, alpha_AU, alpha_US, alpha_SU), sol_dyn[S])

        sol_dyn

Out[2]: {S: alpha_AU*alpha_US/(alpha_AU*alpha_US + alpha_SU*(alpha_AU + alpha_UA)),
        U: alpha_AU*alpha_SU/(alpha_AU*alpha_US + alpha_SU*(alpha_AU + alpha_UA)),
        A: alpha_SU*alpha_UA/(alpha_AU*alpha_US + alpha_SU*(alpha_AU + alpha_UA))}
```

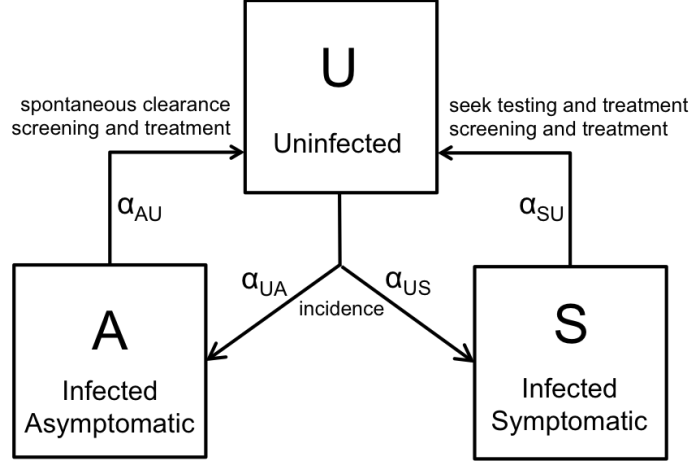


Figure 1: A model of chlamydia infection, clearance, testing and treatment.

The transition rates are functions of parameters describing behaviour and the natural history of infection:

$$\alpha_{UA} = \text{incidence} \times (1 - p_{\text{symptomatic}})$$

$$\alpha_{AU} = \text{rate of spontaneous clearance} + \text{rate of screening} \times p_{\text{truepositive}}$$

$$\alpha_{US} = \text{incidence} \times p_{\text{symptomatic}}$$

$$\alpha_{SU} = \text{rate of screening} \times p_{\text{truepositive}} + \text{rate of symptomatic testing} \times p_{\text{truepositive}}$$

Assuming all tests conducted are included in the surveillance data, the number of tests reported per unit time will be:

$$\text{rate of testing} = \text{rate of screening} + S \times \text{rate of symptomatic testing}$$

And the number of diagnoses per unit time will be:

$$\begin{aligned} \text{rate of new diagnoses} = & (A + S) \times (\text{rate of screening} \times p_{\text{truepositive}}) \\ & + (U \times \text{rate of screening} \times p_{\text{falsepositive}}) \\ & + (S \times \text{rate of symptomatic testing} \times p_{\text{truepositive}}) \end{aligned}$$

Let's assume that:

- 51.0% of incident infections are asymptomatic.
- Infections (whether symptomatic or not) clear spontaneously or through background antibiotic use at a rate 0.47 per year.
- Symptomatic cases seek and obtain testing and treatment at a rate 14.4 per year.
- 97.1% of tests in infected individuals return a positive result.
- 0.314% of tests in uninfected individuals return a positive result.

```

In [3]: p_asymp = 0.510
        sc = 0.47
        att_symp = 14.4
        p_true_pos = 0.971
        p_false_pos = 0.00314

```

It is then possible to calculate the steady-state proportion of the population in each compartment given the rate of screening and incidence, and from these proportions to calculate the total prevalence, and the rates of new tests and diagnoses.

```

In [4]: %matplotlib inline
        from numpy import *
        import matplotlib.pyplot as plt

        inc = linspace(0, 0.5, 101) # incidence
        scr = linspace(0, 0.5, 101) # screening
        inc,scr = meshgrid(inc, scr)

        # proportion of population in each compartment
        ZU = U_fun(inc*p_asymp, sc + scr*p_true_pos, inc*(1-p_asymp), scr*p_true_pos + att_symp*p_true_pos)
        ZA = A_fun(inc*p_asymp, sc + scr*p_true_pos, inc*(1-p_asymp), scr*p_true_pos + att_symp*p_true_pos)
        ZS = S_fun(inc*p_asymp, sc + scr*p_true_pos, inc*(1-p_asymp), scr*p_true_pos + att_symp*p_true_pos)

        Zprev = 1 - ZU
        Ztest = scr + ZS*att_symp
        Zdiag = (ZA+ZS)*scr*p_true_pos + ZU*scr*p_false_pos + ZS*att_symp*p_true_pos

In [5]: fig = plt.figure(figsize = (12, 7))

        ax1 = fig.add_subplot(231)
        p = ax1.pcolor(inc,scr, ZU)
        c = ax1.contour(inc,scr, ZU, [0.6,0.7,0.8,0.9], colors=['k','k','k','k'])
        plt.clabel(c, manual = [(0.1,0.05), (0.2,0.05), (0.4,0.05)], fmt='%1.1f')
        cb = fig.colorbar(p, ax=ax1)
        #ax1.set_xlabel('Incidence')
        ax1.set_ylabel('Screening Rate (years  $^{-1}$ )')
        t = ax1.text(0.25, 0.45, 'Uninfected', ha='center', size='large')
        t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
        ax1.set_ylim(0, 0.5)
        ax1.set_xlim(0, 0.5)

        ax2 = fig.add_subplot(232)
        p = ax2.pcolor(inc,scr, ZS)
        c = ax2.contour(inc,scr, ZS, (0.003,0.006,0.009,0.012), colors='k', manual=True)
        plt.clabel(c, manual = [(0.1,0.35), (0.2,0.35), (0.35,0.35), (0.45,0.35)])
        cb = fig.colorbar(p, ax=ax2)
        t = ax2.text(0.25, 0.45, 'Infected, Symptomatic', ha='center', size='large')
        t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
        ax2.set_ylim(0, 0.5)
        ax2.set_xlim(0, 0.5)

        ax3 = fig.add_subplot(233)
        p = ax3.pcolor(inc,scr, ZA)
        c = ax3.contour(inc,scr, ZA, (0.1,0.2,0.3), colors='k')
        plt.clabel(c, manual = [(0.1,0.1), (0.2,0.1), (0.4,0.1)], fmt='%1.1f')
        cb = fig.colorbar(p, ax=ax3)
        t = ax3.text(0.25, 0.45, 'Infected, Asymptomatic', ha='center', size='large')
        t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
        ax3.set_ylim(0, 0.5)
        ax3.set_xlim(0, 0.5)

        ax4 = fig.add_subplot(234)
        p = ax4.pcolor(inc,scr, Zprev)
        c = ax4.contour(inc,scr, Zprev, (0.1,0.2,0.3), colors='k')
        plt.clabel(c, manual = [(0.1,0.1), (0.2,0.1), (0.4,0.1)], fmt='%1.1f')
        cb = fig.colorbar(p, ax=ax4)
        ax4.set_xlabel('Incidence (years  $^{-1}$ )')
        ax4.set_ylabel('Screening Rate (years  $^{-1}$ )')
        t = ax4.text(0.25, 0.45, 'Prevalence', ha='center', size='large')
        t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
        ax4.set_ylim(0, 0.5)
        ax4.set_xlim(0, 0.5)

        ax5 = fig.add_subplot(235)
        p = ax5.pcolor(inc,scr, Ztest)
        c = ax5.contour(inc,scr, Ztest, (0.2,0.4,0.6), colors='k')
        plt.clabel(c, manual = [(0.45,0.05), (0.45,0.25), (0.45,0.45)], fmt='%1.1f')
        cb = fig.colorbar(p, ax=ax5)
        ax5.set_xlabel('Incidence (years  $^{-1}$ )')

```

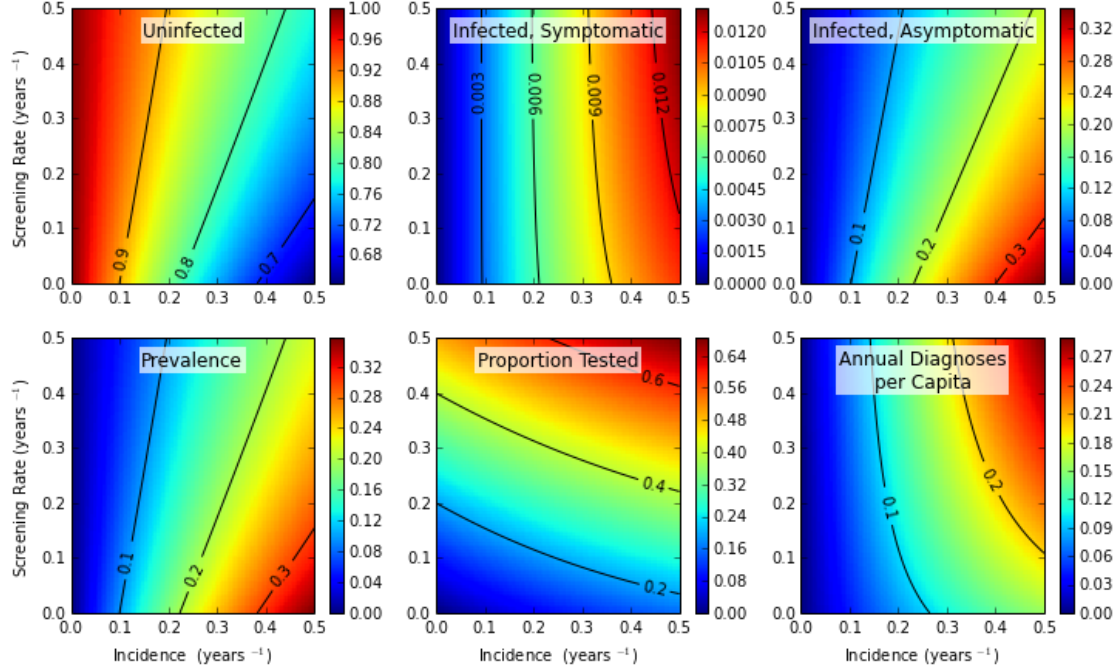


Figure 2: Upper row: the effects of incidence and screening rate on the proportion of individuals who are uninfected, infected-symptomatic and infected-asymptomatic in the model at steady state. Lower row: prevalence, testing and diagnosis rates corresponding to each combination of incidence and screening rate.

```

t = ax5.text(0.25, 0.45, 'Proportion Tested', ha='center', size='large')
t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
ax5.set_ylim(0, 0.5)
ax5.set_xlim(0, 0.5)

ax6 = fig.add_subplot(236)
p = ax6.pcolor(inc,scr, Zdiag)
c = ax6.contour(inc,scr, Zdiag, (0.1,0.2), colors='k')
plt.clabel(c, manual = [(0.2,0.2), (0.4,0.25)], fmt='%1.1f')
cb = fig.colorbar(p, ax=ax6)
ax6.set_xlabel('Incidence (years  $^{-1}$ )')
t = ax6.text(0.25, 0.412, 'Annual Diagnoses\per Capita', ha='center', size='large')
t.set_bbox(dict(facecolor='white', alpha=0.7, edgecolor='None'))
ax6.set_ylim(0, 0.5)
ax6.set_xlim(0, 0.5)

plt.show()

```

From the figures, it is clear that a particular pair of observed testing and diagnosis rates corresponds to a single point in the (incidence, screening rate) plane, which in turn corresponds to a particular prevalence. Note, however, that this mapping depends on the parameter values which have been assumed.