# Chapter 13: More estimators for $R_0$

Anna and Michael

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# Overview

Estimators based on ...

... final size data.

... age-structured data.

... a transmission experiment.

... intrinsic growth rate.

# Estimators based on age-structured data.

+ age-dependent estimation of force of infection and $R_0$
− indeterminacy of quantities, such as contact frequency matrix between age classes

# Next-generation operator

$$(K\phi)(a) = \int_0^\infty k(a,\alpha)\phi(\alpha)d\alpha \tag{1}$$

$$k(a,\alpha) = \int_0^\infty h(\tau,\alpha)c(a,\alpha+\tau)N(a)\frac{\mathcal{F}_d(\alpha+\tau)}{\mathcal{F}_d(\alpha)}d\tau \tag{2}$$

- $h(\tau,\alpha)$: measure of infectiousness
- $c(a,\alpha+\tau)$: quantification of age-dependent contact structure
- $N(a)$: steady-state population size
- $\frac{\mathcal{F}_d(\alpha+\tau)}{\mathcal{F}_d(\alpha)}$: ratio of survival functions

# Short-disease approximation

- combination of assumptions
- length of infectious period << average individual lifespan

$$\frac{\mathcal{F}_d(\alpha+\tau)}{\mathcal{F}_d(\alpha)} \approx 1$$

$$c(a, \alpha+\tau) \approx c(a, \alpha)$$

$$H(\alpha) = \int h(\tau, \alpha) d\tau$$

# Age-specific force of infection

$$\Lambda(a) = \int_0^\infty \int_0^\infty h(\tau, \alpha) c(a, \alpha + \tau) N(a) \Lambda(\alpha) \mathcal{F}_i(\alpha) \frac{\mathcal{F}_d(\alpha + \tau)}{\mathcal{F}_d(\alpha)} d\tau d\alpha \tag{3}$$

- $N(\alpha)$: steady-state population
- $\Lambda(\alpha)$: force of infection at age of infection $\alpha$
- $\mathcal{F}_i(\alpha)$: susceptibility survival function

# Separable mixing

$$c(a, \alpha) = f(a)g(a)$$

- assumption
- eigenvalue problem for $K$ becomes one-dimensional
- explicit expression for $R_0$ possible

# Approximation of $R_0$

- assumptions:
- 1) separable mixing
- 2) only one age class
- 3) $\mathcal{F}_i(a) = e^{-Qa}$
- 4) $g$ is constant
- 5) $h$ is independent of $\alpha$
- 6) $\mathcal{F}_d(a) = e^{-\mu a}$
- 7) $r \approx 0$

$$\hat{R}_0 = 1 + \frac{Q}{\mu + r} = \frac{L}{\bar{a}}$$

- $Q$: force of infection
- $\bar{a}$: mean age of infection
- $L$: life expectancy

# Estimator for age-specific $R_0$: Part I

$$R_0 = \int_0^{\infty} \psi(\alpha) f(\alpha) N(\alpha) d\alpha$$

$$\psi(\alpha) = \int_0^{\infty} h(\tau, \alpha) g(\alpha + \tau) \frac{\mathcal{F}_d(\alpha + \tau)}{\mathcal{F}_d(\alpha)} d\tau$$

# Estimator for age-specific $R_0$: Part II

- assumptions:
- 1) all individuals are susceptible at birth
- 2) natural mortality is independent of the force of infection
- $G(a)$: fraction of individuals of age a who will have antibodies to infection

$$G(a) = 1 - \mathcal{F}_i(a) = 1 - e^{-\int_0^a \Lambda(\alpha)d\alpha} \tag{4}$$

# Estimator for age-specific $R_0$: Part III

- another estimator for age-specific $R_0$:

$$\hat{R}_0 = \frac{\int_0^\infty I(a)\Lambda(a)\mathcal{F}_d(a)da}{\int_0^\infty I(a)\Lambda(a)\mathcal{F}_i(a)\mathcal{F}_d(a)da} \tag{5}$$

# Derivation of age-specific $R_0$

$$R_0 l(\alpha) = \int_0^\infty l(a)k(a,\alpha)da \tag{6}$$

$$R_0 \int_0^\infty \Lambda(\alpha)\mathcal{F}_i(\alpha)\mathcal{F}_d(\alpha)l(\alpha)d\alpha = \int_0^\infty \Lambda(\alpha)\mathcal{F}_i(\alpha)\mathcal{F}_d(\alpha) \tag{7}$$

$$\int_0^\infty l(a)k(a,\alpha)dad\alpha \tag{8}$$

$$\tag{9}$$

- switch the order of integration on the RHS
- insert $\frac{N(\alpha)N(a)}{N(\alpha)N(a)}$
- use $\Lambda(a) = \int \Lambda(\alpha)\mathcal{F}_i(\alpha)\frac{N(\alpha)}{N(a)}k(a,\alpha)d\alpha$
- population of constant size: $\frac{N(\alpha)}{N(a)} = \frac{\mathcal{F}_d(\alpha)}{\mathcal{F}_d(a)}$
- simplify RHS & substitute $a$ for $\alpha$ on LHS

# Estimator for age-specific $R_0$: Part IV

- impose additional assumption: separable mixing
- approximation for $R_0$

$$\hat{R}_0 = \frac{\int_0^\infty \Lambda^2(a) e^{-\mu a} da}{\int_0^\infty \Lambda^2(a) \mathcal{F}_i(a) e^{-\mu a} da} \tag{10}$$

- estimator of $R_0$ expressed by age-dependent force of infection $\Lambda(a)$
- estimate $\Lambda(a)$ for example via maximum-likelihood estimation

# Maximum likelihood estimation

- assumption: $\Lambda(a) = \Lambda_i$
- $n_i$: # of seronegative individuals at age interval $i$
- $m_i$: # of seropositive individuals at age interval $i$
- binomial likelihood: $\binom{n_i}{m_i}\ G_i^{m_i}(1-G_i)^{n_i-m_i}$
- $G_i = 1 - \exp(-\int_{a_i}^{a_{i+1}} \Lambda(a)da) = 1 - \exp(-\Lambda_i(a_{i+1} - a_i))$
- $L = \prod_{i=0}^{n-1}\ \binom{n_i}{m_i}\ G_i^{m_i}(1-G_i)^{n_i-m_i}$
- estimate of force of infection: $\hat{\Lambda}_i = \frac{-\ln(\frac{n_i - m_i}{n_i})}{a_{i+1} - a_i}$

Back to Michael.