A Bayesian synthesis of evidence for a dynamic transmission model: estimating HIV incidence among MSM

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Greek Stochastics, Lefkada

Outline

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1. Introduction
2. Prevalence model
3. Incidence model
4. Two-stage linear model
5. Two-stage transmission model
6. Combined prevalence & incidence model
7. Ongoing work

Motivation

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Human Immunodeficiency Virus

Estimates of HIV *prevalence* and *incidence* are essential for *understanding* and *monitoring* the epidemic, as well as for *assessing* the impact of public health interventions.

Challenges

- HIV has a long *asymptomatic* incubation period, so many infections *undiagnosed*
- Surveillance systems available only for certain *risk groups* and populations
- Surveillance and other survey/ad-hoc data subject to *biases*
- Data sometimes tell us only *indirectly* about the quantities of interest

Estimating HIV prevalence

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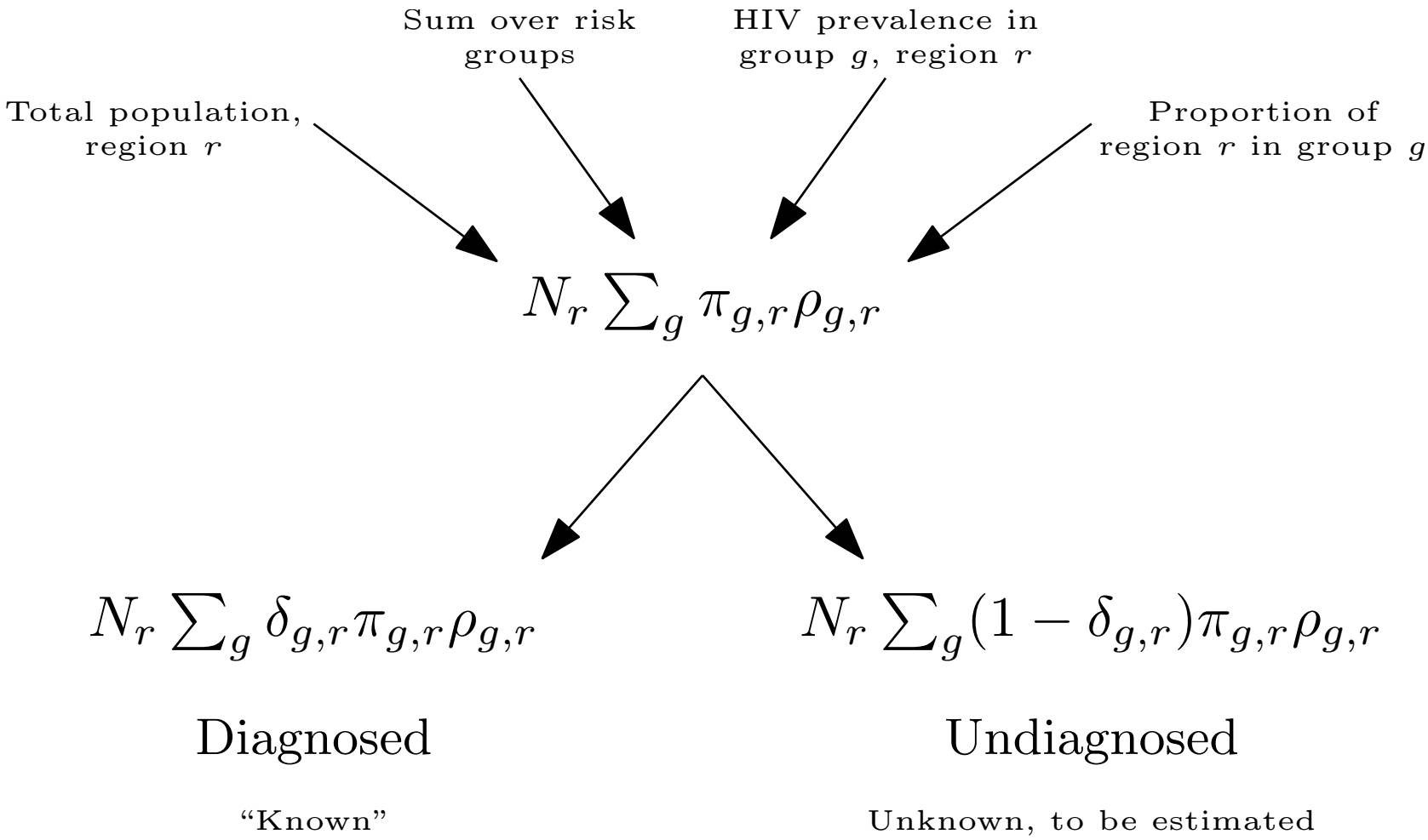

Estimate for each g and r:

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$\rho_{g,r}$ proportion of the population of r in g;

$\pi_{g,r}$ HIV prevalence;

$\delta_{g,r}$ proportion of infections which are diagnosed.

Then any function of these may be estimated.

Risk groups in England & Wales

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Groups are further sub-divided by sex and current/past risk behaviour:

- MSM: Men who have sex with men
- IDUs: Injecting drug users (non-MSM)
- SSA-born: Heterosexual individuals born in Sub-Saharan Africa (non-IDUs)
- GUM: Heterosexual individuals (non-SSA), current GUM attendees
- LR: Lower risk heterosexual individuals (non-SSA, non-GUM)

Availability of data

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Risk group		N	ρ	π	δ	$\pi(1-\delta)$	$f(\rho, \pi, \delta)$
Men	MSM		NATSAL			UA GUM, GMSHS	SOPHID
	IDUs		HOCR, SEA	UA IDU	UA IDU		SOPHID
	SSA		Census, ONS births				SOPHID
	GUM		NATSAL			UA GUM	
	LR						
	ALL	ONS MYEs					SOPHID
Women	IDUs		HOCR, SEA	UA IDU	UA IDU		SOPHID
	SSA		Census, ONS births	UA PW	NSHPC, UA PW		SOPHID
	GUM		NATSAL			UA GUM	
	LR						
	non-SSA			UA PW	NSHPC, UA PW		
	ALL	ONS MYEs					SOPHID

Multi-parameter evidence synthesis

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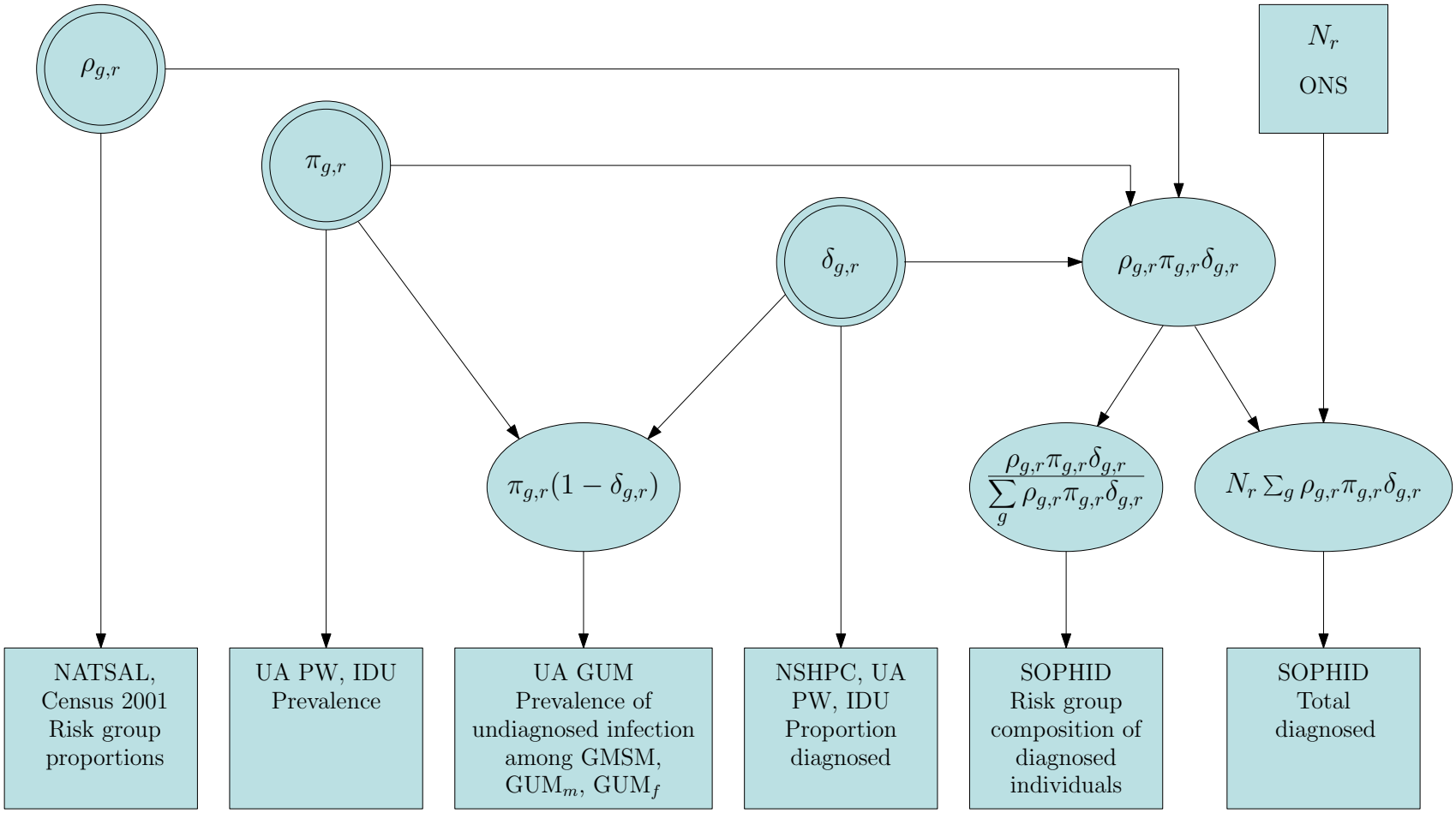
Aim

Synthesise evidence from *all* available sources to estimate parameters of interest

- evidence from potentially *different types* of studies
- *direct* evidence on parameters of interest
- *indirect* evidence on complex functions of parameters
- *Bayesian* setting:
  - Coherent and correct *propagation of uncertainty*
  - *Prior* information
  - Ease of model formulation to account both for *complex* relationships between data sources and for *biases*

Directed Acyclic Graph



Inference

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Priors

Unif(0,1) for basic parameters ρ, π, δ

Likelihood

- Poisson counts for total men and women diagnosed
- Remaining data available as proportions y/n

$$\begin{aligned} y &\sim \text{Binomial}(n, p) \\ p &= f(\rho, \pi, \delta) \end{aligned}$$

Hierarchy

We *borrow strength* across regions and risk groups in order to estimate parameters for (g, r) combinations where there is a lack of data.

MSM

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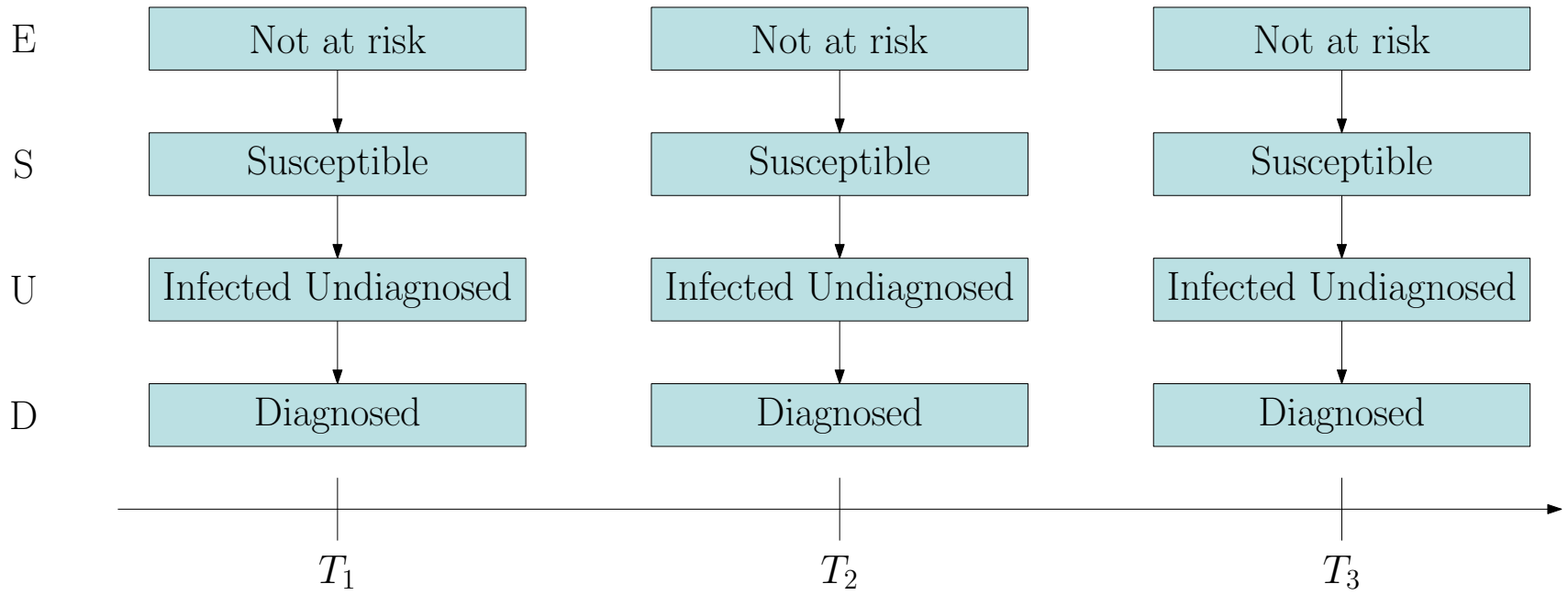
Year	2.5%	median	97.5%	Year	2.5%	median	97.5%
	$1-\rho(t)$				$(1-\delta(t))\pi(t)\rho(t)$		
2001	0.9611	0.9667	0.9718	2001	0.0004	0.0005	0.0007
2002	0.9611	0.9667	0.9716	2002	0.0005	0.0007	0.0011
2003	0.9610	0.9667	0.9720	2003	0.0005	0.0007	0.0010
2004	0.9609	0.9667	0.9722	2004	0.0005	0.0006	0.0009
2005	0.9607	0.9664	0.9713	2005	0.0004	0.0005	0.0007
2006	0.9608	0.9667	0.9719	2006	0.0005	0.0006	0.0008
2007	0.9608	0.9665	0.9718	2007	0.0004	0.0005	0.0007
	$(1-\pi(t))\rho(t)$				$\delta(t)\pi(t)\rho(t)$		
2001	0.0268	0.0318	0.0373	2001	0.0009	0.0009	0.0009
2002	0.0268	0.0316	0.0371	2002	0.0009	0.0009	0.0010
2003	0.0263	0.0316	0.0372	2003	0.0010	0.0010	0.0011
2004	0.0262	0.0315	0.0373	2004	0.0011	0.0011	0.0011
2005	0.0271	0.0319	0.0375	2005	0.0011	0.0012	0.0012
2006	0.0263	0.0315	0.0372	2006	0.0012	0.0013	0.0013
2007	0.0264	0.0316	0.0373	2007	0.0013	0.0013	0.0014

Table: Posterior mean and median estimates from stage 1 model of proportion of MSM in each compartment, with 95% credible intervals.

Incidence from prevalence



- Linear multi-state model, HIV incidence $\lambda(t)$ given flat prior
- Non-linear *dynamic transmission model*, $\lambda(t) = \beta(t)\pi(t)$, coefficient $\beta(t)$ is the *effective contact rate*. $\beta(t)$ may be further parameterised as the overall contact rate multiplied by the transmission rate following an infectious contact.

Context

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- Literature on dynamic transmission models (see Isham (2005), Hethcote (2000) for reviews, Anderson & May (1991)):
  - Deterministic vs Stochastic
  - Individual vs population-level
  - Scenario-based sensitivity analyses
  - Cross-sectional prevalence data
  - Discrete/Continuous state space
  - Discrete/Continuous time
- Estimating incidence from prevalence *data*
  - e.g. Ades & Medley (1994), Gregson et al (1996), Hallett et al (2008)

Our work:

- Full probability model
- Estimate *both* prevalence and incidence
- Bayesian framework allows correct and complete propagation of uncertainty in data sources through to posterior estimates of prevalence and incidence

Multi-state model

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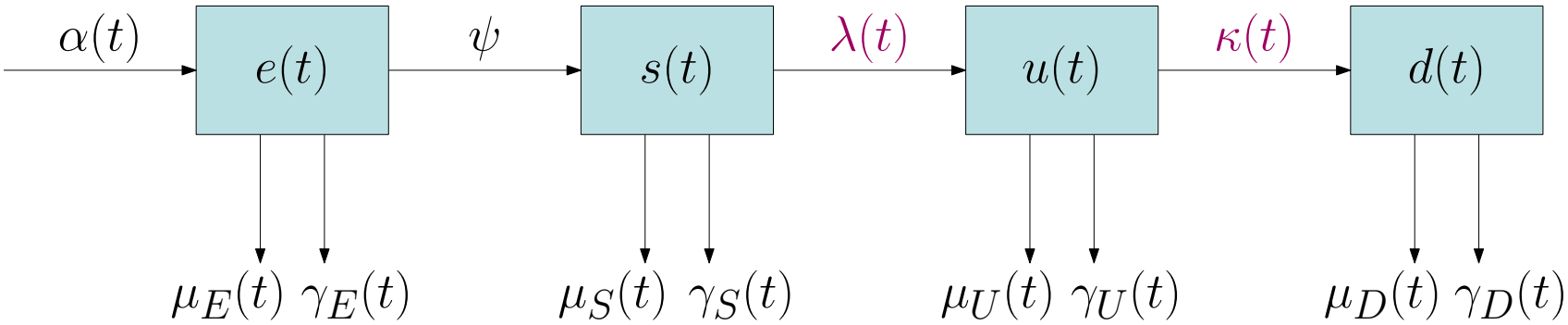
- $N(t)$ = total number of men aged 15-44 in England and Wales at time t
- $\rho(t) = s(t) + u(t) + d(t)$ = proportion of $N(t)$ who are men who have sex with men (MSM): Susceptible, Undiagnosed and Diagnosed respectively
- $1 - \rho(t) = e(t)$ = proportion of $N(t)$ who are *not* MSM



System of equations

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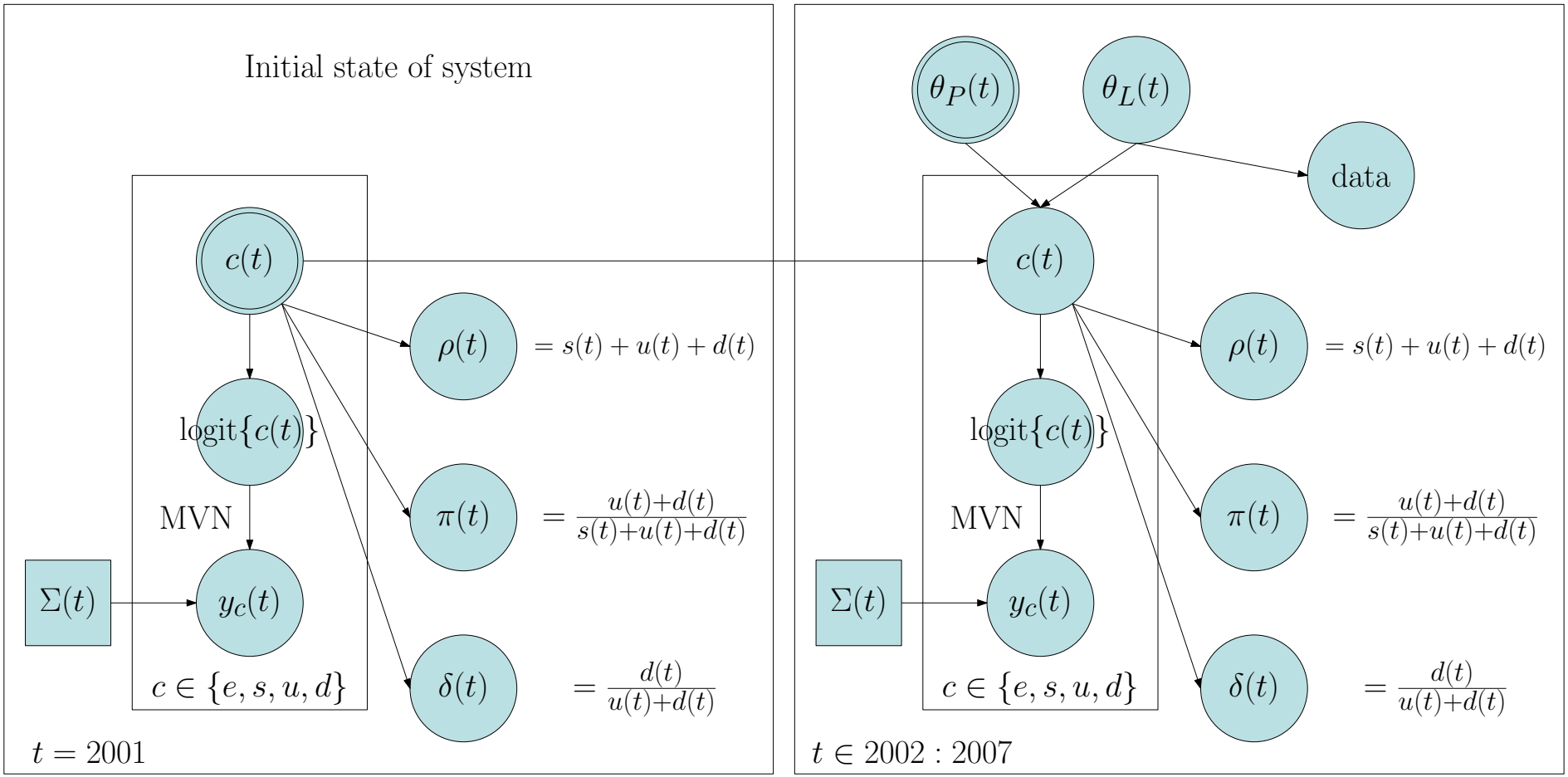
$$
\begin{aligned}
\frac{d}{dt}e(t) &= \frac{\alpha(t)}{N(t)} - (\mu_E(t) + \gamma_E(t) + \psi)e(t) - e(t)f(t) \\
\frac{d}{dt}s(t) &= \psi e(t) - (\lambda(t) + \mu_S(t) + \gamma_S(t))s(t) - s(t)f(t) \\
\frac{d}{dt}u(t) &= \lambda(t)s(t) - (\kappa(t) + \mu_U(t) + \gamma_U(t))u(t) - u(t)f(t) \\
\frac{d}{dt}d(t) &= \kappa(t)u(t) - (\mu_D(t) + \gamma_D(t))d(t) - d(t)f(t) \\
f(t) &= \Big[\frac{\alpha(t)}{N(t)} - (\mu_E(t) + \gamma_E(t))e(t) - (\mu_S(t) + \gamma_S(t))s(t) \\
&\quad -(\mu_U(t) + \gamma_U(t))u(t) - (\mu_D(t) + \gamma_D(t))d(t)\Big]
\end{aligned}
$$

Directed acyclic graph



Likelihood

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$$L\Big(\mathbf{c}, \gamma, \mu_{\mathbf{D}}, \mu_{\mathbf{E}}, \kappa \quad | \quad \mathbf{y_c}, \mathbf{\Sigma}, \mathbf{y_{44}}, \mathbf{N}, \mathbf{y}_{\mu_{\mathbf{D}}}, \mathbf{D}, \mathbf{y}_{\text{deaths}}, \mathbf{y}_{\text{diagnoses}}\Big)$$

$$\propto \prod_{t=1}^{7} \Bigg\{ \exp\Big(-\frac{1}{2}(\mathbf{y_c(t)} - \text{logit}(\mathbf{c(t)}))^{\mathrm{T}} \Sigma^{-1}(t)(\mathbf{y_c(t)} - \text{logit}(\mathbf{c(t)}))\Big)$$

$$\times \quad \Big(\gamma(t)^{y_{44}(t)}(1-\gamma(t))^{T(t)-y_{44}(t)}\Big)$$

$$\times \quad \Big(\gamma_D(t)^{y^D_{44}(t)}(1-\gamma_D(t))^{D(t)-y^D_{44}(t)}\Big)$$

$$\times \quad \Big(\mu_D(t)^{y_{\mu_D}(t)}(1-\mu_D(t))^{D(t)-y_{\mu_D}(t)}\Big)$$

$$\times \quad \Big(\mu(t)^{y_{\text{deaths}}(t)}(1-\mu(t))^{T(t)-y_{\text{deaths}}(t)}\Big)$$

$$\times \quad \Big((\kappa(t)U(t))^{y_{\text{diagnoses}}}\exp(-\kappa(t)U(t))\Big) \Bigg\}$$

Priors

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$$
\begin{aligned}
\psi &\sim \text{Normal}(0.0049, 0.0006^2)I(0,) \\
\lambda(t) &\sim \text{Beta}(1,1) \\
\kappa(t) &\sim \text{Beta}(1,1) \\
\mathbf{c(2001)} &\sim \text{Dirichlet}(1,1,1,1)
\end{aligned}
$$

$$
\begin{aligned}
\mu_E(t) &\sim \text{Beta}(1,1) \\
\mu_D(t) &\sim \text{Beta}(1,1) \\
\gamma_E(t) &\sim \text{Beta}(1,1)
\end{aligned}
$$

Migration assumptions

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Model 1: As described above - includes data on proportions $\mathbf{c(t)}$, aging, mortality and diagnosis rates. Net migration assumed 0 in each state.

Model 2: As in 1, but allow for net outward migration of Diagnosed MSM (data from SOPHID - indistinguishable from loss to follow up).

Model 3: As in 2, but assume inward migration of men into E, outward migration from all 4 states (data from ONS).

Model 4: As in 3, but assume inward & outward migration occurs at equal rates in E, S and U; still assume only net outward migration/LTFU in D.

Model 5: As in 4, but assume MSM in S and U have higher migration rates than men in E (data from NATSAL).

Posterior incidence & diagnosis rates

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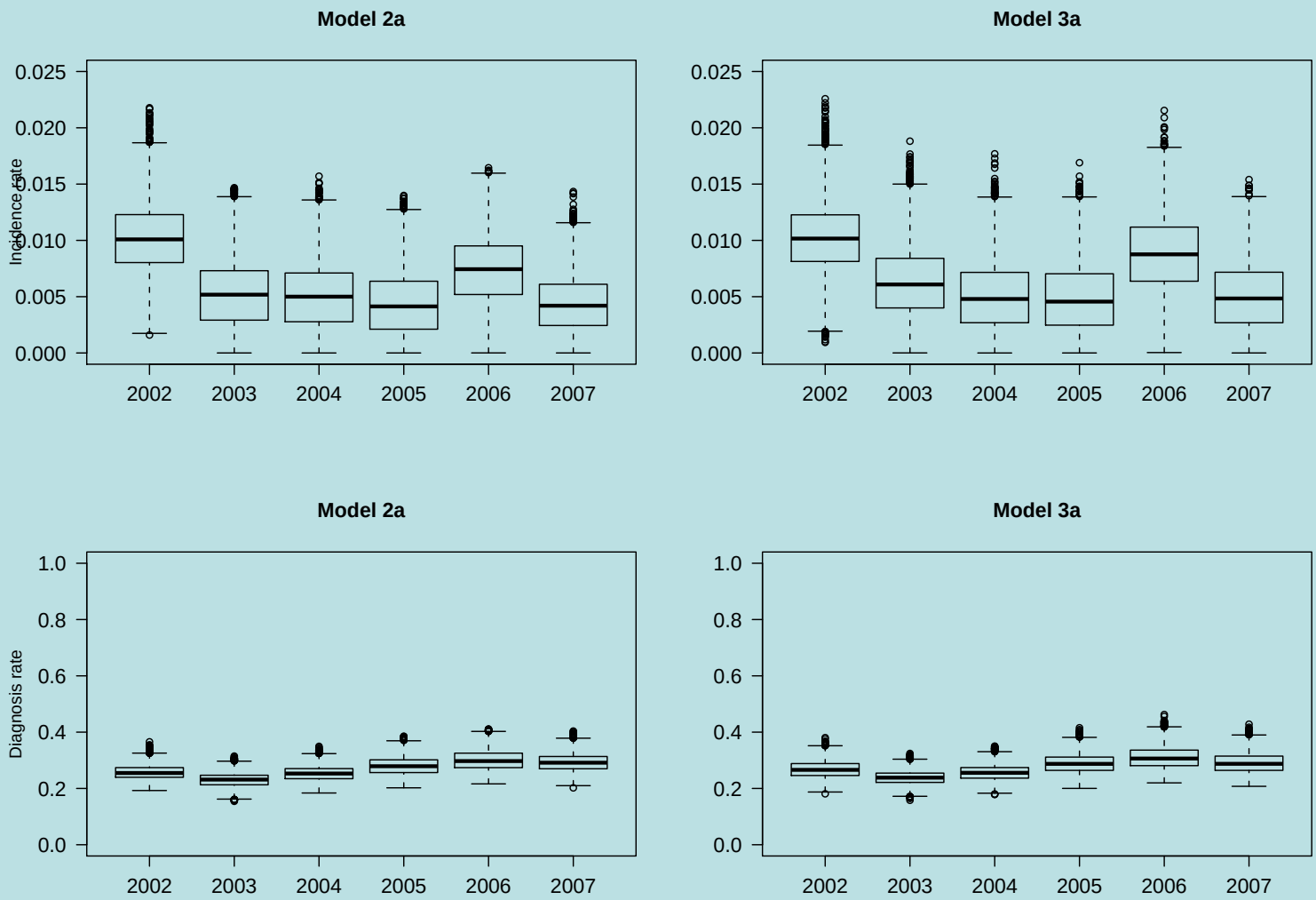

Dynamic transmission modelling

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Homogeneous mixing ("mass action")

$$\lambda(t) = \beta(t)\pi(t)$$

The effective contact rate, $\beta(t)$ is the average number of contacts per unit time a susceptible individual makes which would be *sufficient for transmission* if the contact is infectious. The assumption of *homogeneous mixing* is not particularly realistic for HIV and other STIs.

Different contact groups

$$\lambda(t) = \chi_U(t)\tau_U(1-\delta(t))\pi(t) + \chi_D(t)\tau_D\delta(t)\pi(t)$$

$\chi_U(t)$ is the per-susceptible contact rate with *undiagnosed* individuals, $\chi_D(t)$ with *diagnosed* individuals. The τ are transmission rates given an infectious contact, also assumed to differ between diagnosed/undiagnosed contacts. Homogeneous mixing assumed within groups.

Further stratification

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Homogeneous mixing within risk groups, no contact across groups

$$\lambda_g(t) = \chi_g^U(t)\tau_U(1-\delta_g(t))\pi_g(t) + \chi_g^D(t)\tau_D\delta_g(t)\pi_g(t)$$

Mixing matrix describing contact across groups

$$\lambda_g(t) = \sum_i \phi_{gi}^U(t)\chi_g^U(t)\tau_U(1-\delta_i(t))\pi_i(t) + \sum_i \phi_{gi}^D(t)\chi_g^D(t)\tau_D\delta_i(t)\pi_i(t)$$

The ϕ are matrices of probabilities of an individual in group g choosing a contact from group i, ranging from *fully assortative* to *homogeneous* mixing. The χ still represent the rates of contact.

Priors

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Different contact groups

$$
\begin{aligned}
\lambda(t) &= \chi_U(t)\tau_U(1-\delta(t))\pi(t) + \chi_D(t)\tau_D\delta(t)\pi(t) \\
\tau_U &\sim \text{Unif}(0, 0.3) \\
\tau_D &\sim \text{Unif}(0, \tau_U) \\
\chi_U(t) &\sim \text{Gamma}(1, 4) \\
\chi_D(t) &\sim \text{Unif}(0, \chi_D(t))
\end{aligned}
$$

Posterior rates

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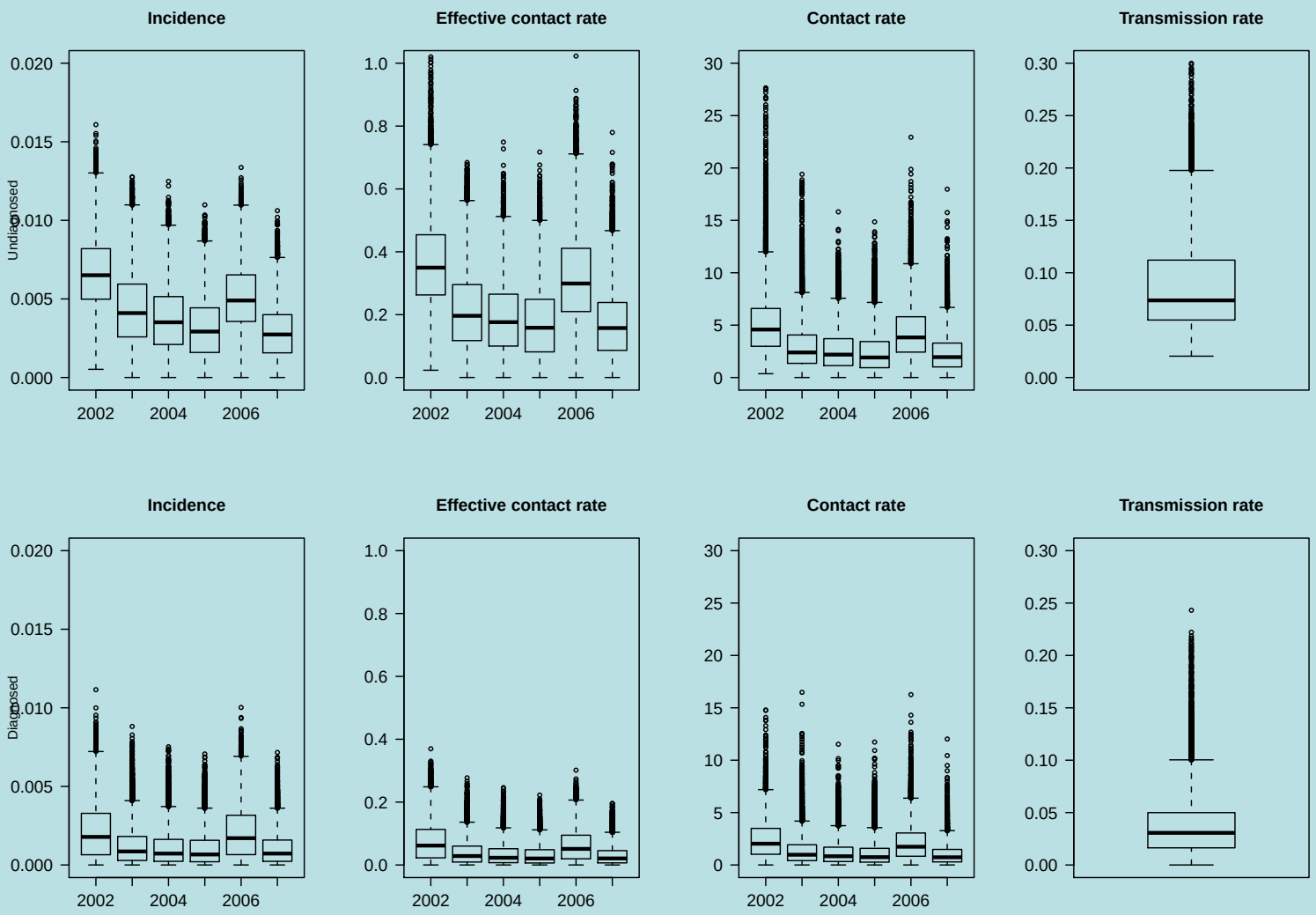

Directed acyclic graph

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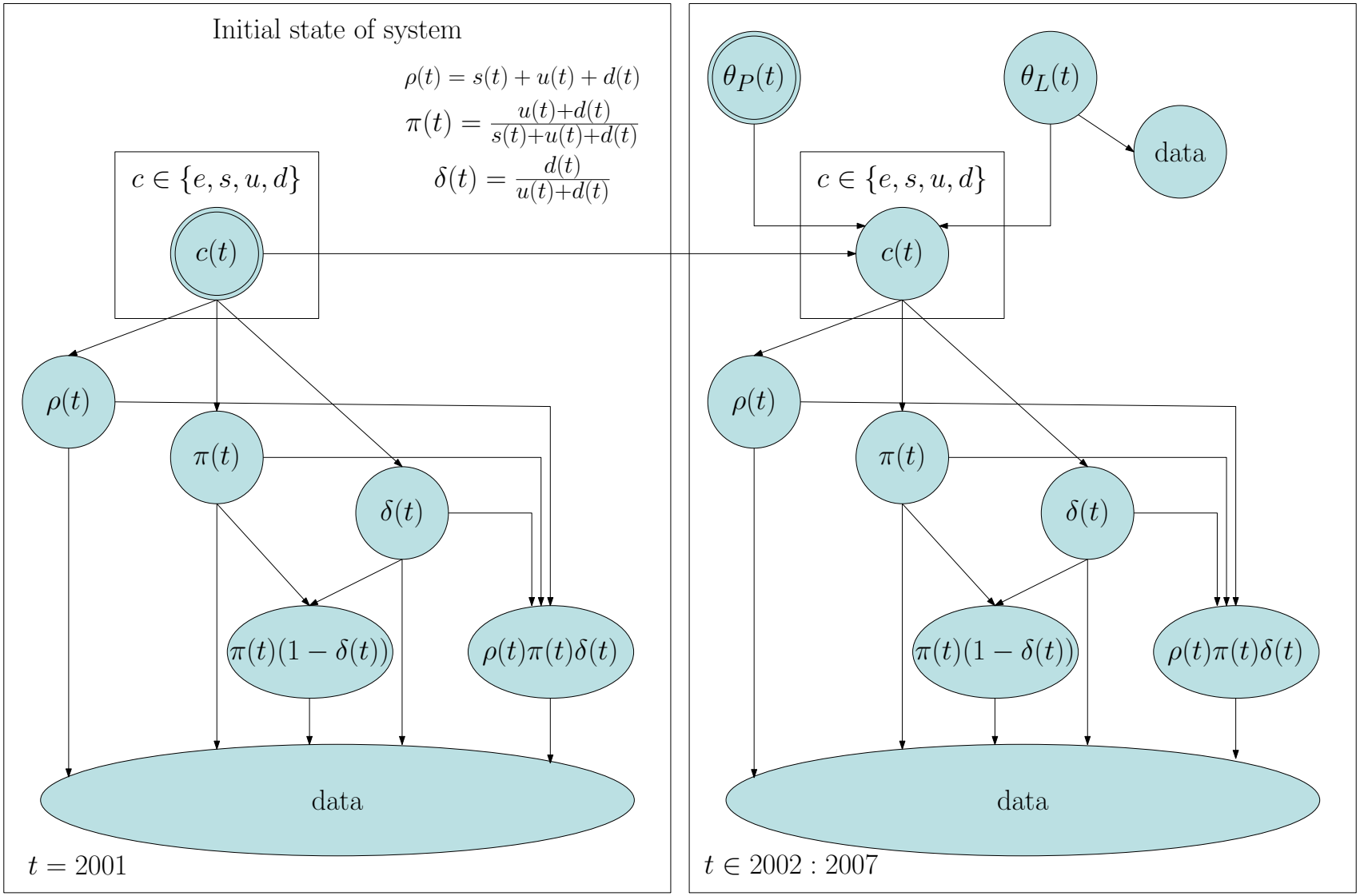
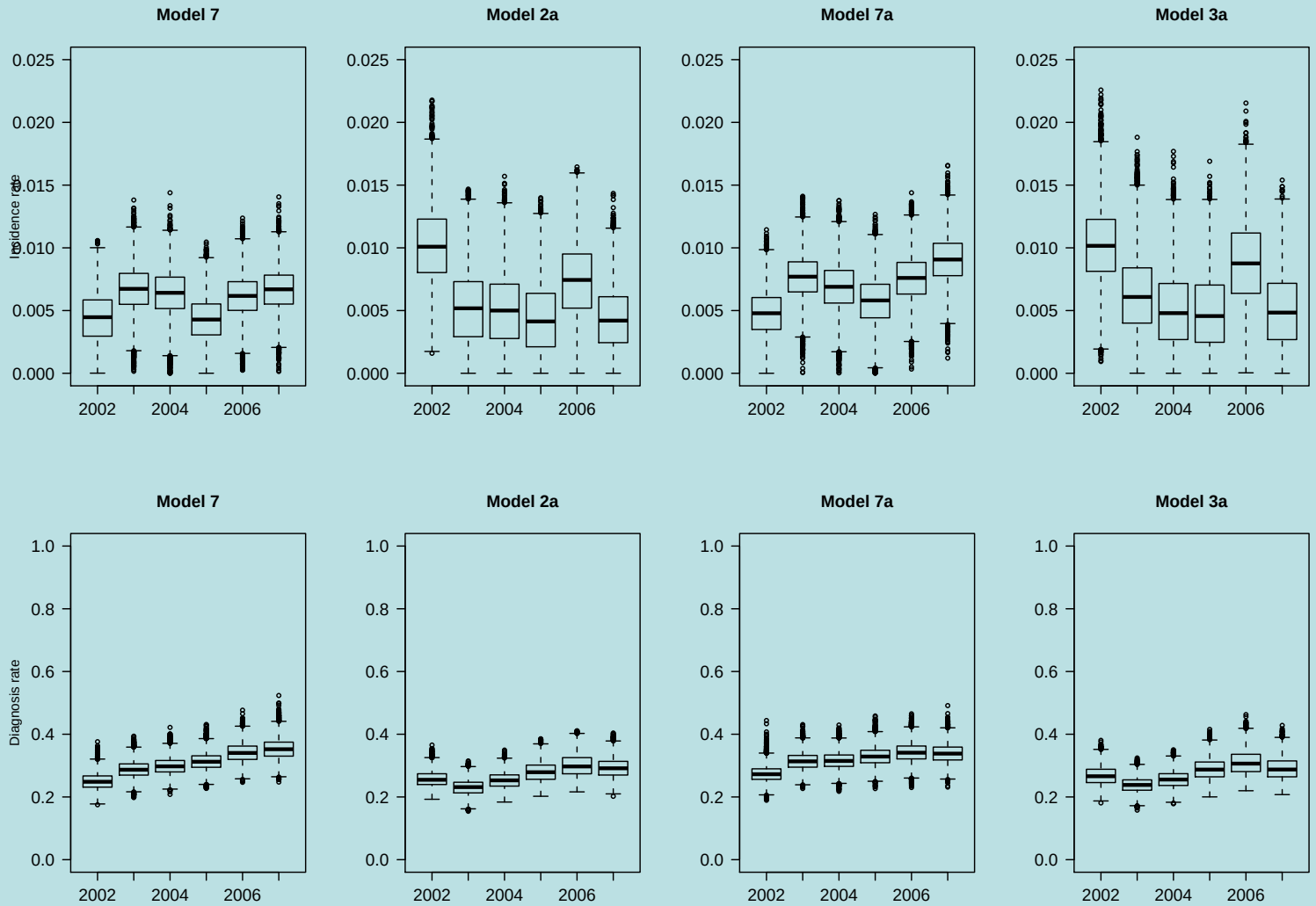


Posterior estimates



Ongoing work

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- Combined prevalence, incidence & transmission model.
- Incorporate data on resistance to inform transmission from Diagnosed individuals.
- Split MSM into further risk groups by current/past practice, STI clinic attendance and age, incorporate contact/transmission between the groups.
- Expand to other risk groups.

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