MISSING DATA AND MEASUREMENT ERROR

September 22, 2019

Jon Fintzi

Biostatistics Research Branch National Institute of Allergy and Infectious Diseases National Institutes of Health

Overview

• Bayesian inference always starts with a model for the **joint distribution** of θ and y:.

$$\pi(\theta, y) = f(y|\theta)\pi(\theta) = \pi(\theta|y)m(y).$$

• Bayes rule yields the posterior distribution

$$\pi(\theta|y) = \frac{f(y,\theta)}{m(y)} = \frac{f(y|\theta)\pi(\theta)}{m(y)} \propto Likelihood \times Prior.$$

Last week we talked about hierarchical models, all we did was iterate on this ideas:

- Model expressed that people are self-similar, but also are similar to one another.
- Individuals are exchangeable in the prior reasonable to suppose that β_{Jon} and β_{Mike} come from the same distribution, but no prior information to differentiate Mike from Jon.
- We use the data to inform us about individuals and the population, individuals are no longer exchangeable in the posterior, i.e., $\pi(\beta_{Jon}|Y_{Jon},Y_{Mike}) \neq \pi(\beta_{Mike}|Y_{Jon},Y_{Mike})$.
- Different choices for model structure induce different features in the posterior, e.g., shrinkage with "mixed effects", horseshoe for inducing posterior sparsity.

Lecture 20 of Statistical Rethinking

Example: divorce rate vs. state population size.

• Treat true divorce rate as an unknown parameter:

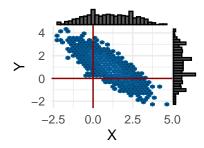
$$D_{obs,i} \sim N(D_{true,i}, D_{SE,i}^2)$$

 $D_{true,i} \sim \pi(\theta).$

- Effect is to shrink observed state divorce rates towards national average.
- If interested in divorce rate vs. population + marriage rate, can also model observed marriage as a noisy observation of the true marriage rate.
- Missing data is a form of measurement error.

Lecture 20 of Statistical Rethinking

- Common approaches to missing data:
 - o Complete case analysis (best case) introduce uncertainty, (worst case) introduce confounding.
 - Mean imputation, marginal imputation.



- Multiple imputation: simulate datasets from joint distribution, fit separately, and combine.
- Bayesian data augmentation: introduce missing data, Y_{miss} as latent variables. Target the joint posterior $\pi(Y_{miss}, \theta|Y_{obs})$.

Lecture 20 of Statistical Rethinking

- Different missingness mechanisms, MCAR, MAR, and MNAR, require different models.
- Imputation can improve precision for estimates of interest (shrinkage!).
- Bayesian inference always starts with a *joint* model for data, parameters, and covariates.

Plan for today

Two examples:

- Model BMI as a function of cholesterol and age.
 - o Data augmentation with brms (Burkner, 2019).
 - o Off-the-shelf, flexible, relatively straightforward syntax.
- Compartmental models for partially observed incidence data.
 - o Introduce true incidence as a latent variable.
 - o Ordinary differential equations describe the latent incidence.

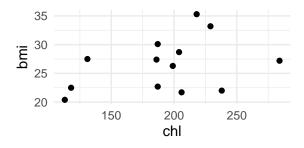
Data (nhanes from the mice package)

- 18 individuals, omit people missing both BMI and cholesterol.
- BMI (kg/m²)
- Total serum cholesterol (mg/dL)

```
## chl bmi
## 2 187 22.7
## 3 187 NA
## 5 113 20.4
## 6 184 NA
## 7 118 22.5
## 8 187 30.1
```

Key features:

- Missingness in cholesterol and BMI, we'll assume MAR so need to impute but not model missingness (see Statistical Rethinking lecture 20 for the explanation of this).
- Looks like higher BMI associated with slightly higher cholesterol.



Model:

$$BMI_{obs,i} \sim LogNormal(\mu_{bmi,i}, \sigma_{bmi}^{2})$$

$$BMI_{miss,i} \sim LogNormal(\mu_{bmi,i}, \sigma_{bmi}^{2})$$

$$\mu_{bmi,i} = \beta_{0} + \beta_{1}CHL_{i}$$

$$CHL_{obs,i} \sim Normal(\mu_{chl}, \sigma_{chl}^{2})$$

$$CHL_{miss,i} \sim Normal(\mu_{chl}, \sigma_{chl}^{2})$$

$$+ Priors...$$

- If MNAR, have to model probability of missing given latent value (Chapters 8 and 18 of Gelman et al., 2013).
- If we fit this in **Stan**, declare observed values as data and missing values as parameters, which we estimate just like any other parameters.

Interlude: Algorithmic Implementation

```
Example - normal means problem with missing values: y_i \sim N(\mu, \sigma^2).
```

```
data {
  int<lower=0> N_obs; # number observed
  int<lower=0> N_mis; # number missing
  real y_obs[N_obs]; # vector of observed values
}
```

Interlude: Algorithmic Implementation

Example - normal means problem with missing values: $y_i \sim N(\mu, \sigma^2)$.

```
parameters {
  real mu;  # mean parameter
  real<lower=0> sigma; # standard deviation
  real y_mis[N_mis]; # missing values are parameters
}
```

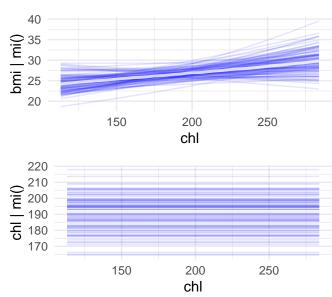
Interlude: Algorithmic Implementation

Example - normal means problem with missing values: $y_i \sim N(\mu, \sigma^2)$.

```
model {
    # joint distribution for observed and missing variables
    y_obs ~ normal(mu, sigma);
    y_mis ~ normal(mu, sigma);
}
```

Trivial to fit using **brms**:

Posterior is full of lines for BMI vs. cholesterol and values for cholesterol.



Interrogate the posterior predictive distribution to examine fit.

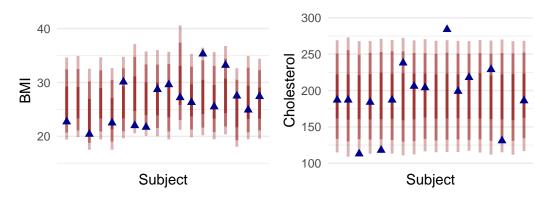
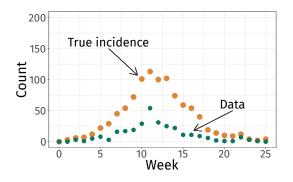


Figure 1: Posterior predicted BMI and cholesterol.

Parially observed incidence data:

- $N_{SI}(t_\ell)=$ Cumulative infections up to t_ℓ ,
- $Y_{\ell} =$ new cases seen in $(t_{\ell-1}, t_{\ell}]$,
- $Y_{\ell} \sim Neg.Binomial(\mu = \rho \times (N_{SI}(t_{\ell}) N_{SI}(t_{\ell-1})), \ \sigma^2 = \mu(1 + \mu/\phi)).$



Important:

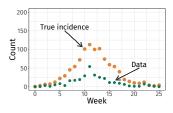
- Only observe a fraction of cases at discrete times.
- Data come from an outbreak that evolves *continuously* in time.

What do we want to learn?

- How many people were infected? How many people were infected?
- How to characterize the transmission dynamics of the outbreak?

What makes this difficult?

1. Under-reporting: epidemic process, \mathbf{X} , only partially observed.



- 2. Dependent happenings: \implies dependent data, $\mathbf{Y} = (\mathbf{Y_1}, \dots, \mathbf{Y_L})$.
 - o Observed data likelihood:

Relinood:
$$L(\mathbf{Y}|\boldsymbol{\theta}) = \prod_{\ell=1}^{\mathbf{L}} \pi(\mathbf{Y}_{\ell}|\mathbf{Y}_{1}, \dots, \mathbf{Y}_{\ell-1}, \boldsymbol{\theta}) \neq \prod_{\ell=1}^{\mathbf{L}} \pi(\mathbf{Y}_{\ell}|\boldsymbol{\theta}).$$

 \circ Intractable observed data likelihood State space of ${f N}$ is huge, even in small populations!

$$L(\mathbf{Y}|\boldsymbol{\theta}) = \int \prod_{\ell=1}^{L} \pi(\mathbf{Y}_{\ell}|\mathbf{Y}_{1}, \dots, \mathbf{Y}_{\ell-1}, \mathbf{N}, \boldsymbol{\theta}) \pi(\mathbf{N}|\boldsymbol{\theta}) d\mathbf{N}$$

Strategy:

- ullet Bayesian data augmentation introduce incident event processes, ${f N}=({f N_{SI}},{f N_{IR}})$, as latent variables in the model
- Target the joint posterior, $\pi(\mathbf{N}, \boldsymbol{\theta} | \mathbf{Y})$.

Challenge: Need a tractable representation for the transition density of $N(t_\ell)|N(t_{\ell-1}), heta$.

- ullet In large populations, not unreasonable to represent ${f N}$ with a deterministic system of ODEs.
- Classical tools in the disease modeling literature, see Allen (2008) and Blackwood (2018) for an overview.

Deterministic SIR model:

Incidence paths are solutions to systems of differential equations,

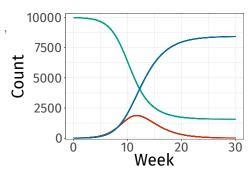
$$\frac{\mathrm{d}}{\mathrm{d}t} \begin{pmatrix} N_{SI} \\ N_{IR} \end{pmatrix} = \begin{pmatrix} \beta SI \\ \mu I \end{pmatrix},$$

$$= \begin{pmatrix} \beta(S_0 - N_{SI})(I_0 + N_{SI} - N_{IR}) \\ \mu(I_0 + N_{SI} - N_{IR}) \end{pmatrix},$$

subject to $X_0=(S_0,I_0,R_0),\ N_0=0.$

- β = per-contact infection rate.
- μ = recovery rate.
- Priors on $1/\mu$ = mean infectious period and $\mathcal{R}_0 = \beta N/\mu =$ basic reproduction number.





Joint model, $\pi(\mathbf{Y}, \mathbf{N}, \boldsymbol{\theta})$, where \mathbf{N} has the *Markov* property.

- ullet Data, ${f Y}$, are conditionally independent given ${f N}$.
- Simplified complete data likelihood:

$$L(\mathbf{Y}, \mathbf{N}|\boldsymbol{\theta}) = \pi(\mathbf{N}(\mathbf{t_0})|\boldsymbol{\theta}) \prod_{\ell=1}^{L} \pi(\mathbf{Y}_{\ell}|\mathbf{N}(\mathbf{t}_{\ell}), \boldsymbol{\theta}) \pi(\mathbf{N}(\mathbf{t}_{\ell})|\mathbf{N}(\mathbf{t}_{\ell-1}), \boldsymbol{\theta}).$$

- $\circ \pi(Y_{\ell}|\mathbf{N}(\mathbf{t}_{\ell}),\boldsymbol{\theta})$ sampling model, negative binomial.
- $\circ \pi(\mathbf{N}(\mathbf{t}_{\ell})|\mathbf{N}(\mathbf{t}_{\ell-1}), \theta)$ transition density for latent epidemic, SIR
- ullet Here, $oldsymbol{ heta}$ maps 1:1 onto ${f N}$ so no need to sample ${f N}$ explicitly.
- ullet Stochastic representations of ${f N}$ require sampling latent paths. Tradeoff realism and computational tractability.

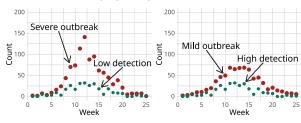
Key point: true incidence is missing data. In the Bayesian paradigm we estimate it like any other parameter by including it in our joint model and targeting the posterior!

Goal: Infer $\pi(\theta, \mathbf{N}|\mathbf{Y}) \propto \mathbf{L}(\mathbf{Y}|\mathbf{N}, \theta)\pi(\mathbf{N}|\theta)\pi(\theta)$.

ullet Outbreak dynamics: $\pi(\mathbf{N}|oldsymbol{ heta})$



• Observation model: $L(Y|N, \theta)$

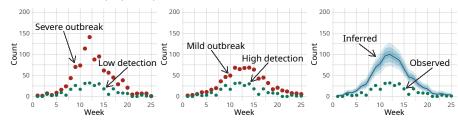


Goal: Infer $\pi(\theta, \mathbf{N}|\mathbf{Y}) \propto \mathbf{L}(\mathbf{Y}|\mathbf{N}, \theta)\pi(\mathbf{N}|\theta)\pi(\theta)$.

ullet Outbreak dynamics: $\pi(\mathbf{N}|oldsymbol{ heta})$



• Observation model: $L(\mathbf{Y}|\mathbf{N}, \boldsymbol{\theta})$

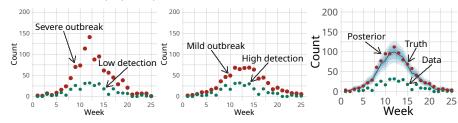


Goal: Infer $\pi(\theta, \mathbf{N}|\mathbf{Y}) \propto \mathbf{L}(\mathbf{Y}|\mathbf{N}, \theta)\pi(\mathbf{N}|\theta)\pi(\theta)$.

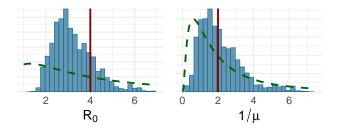
ullet Outbreak dynamics: $\pi(\mathbf{N}|oldsymbol{ heta})$



• Observation model: $L(\mathbf{Y}|\mathbf{N}, \boldsymbol{\theta})$



Posterior distributions of model parameters:



Wrapping up

- Quantify two kinds of uncertainty, epistemic, which reflects subjective ignorance, and aleatory, which is uncertainty due to chance.
- A Bayesian model always defines a joint distribution for data and parameters.
- Some simple examples, PREVAIL II and linear regression; some complex hierarchical models and missing data.
- Failure modes of misspecified priors under poorly chosen scales, weakly informative priors as a reasonable strategy.
- Good workflow is like going to the dentist.
- Various computational tools.

References

Allen, Linda JS. "An introduction to stochastic epidemic models." Mathematical epidemiology. Springer, Berlin, Heidelberg, 2008. 81-130.

Blackwood, Julie C., and Lauren M. Childs. "An introduction to compartmental modeling for the budding infectious disease modeler." *Letters in Biomathematics* 5.1 (2018): 195-221.

P. Burkner. "Handle Missing Values with brms."

https://cran.r-project.org/web/packages/brms/vignettes/brms_missings.html (2019).

Gelman, Andrew, et al. Bayesian data analysis. Chapman and Hall/CRC, 2013.