A multiple imputation approach to remove residual confounding through coarse data models

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Chen, Gilbert & Daling (1999)

- Maternal risk factors for Down's syndrome
- Smoking appears to be protective! OR=0.80 (95% CI 0.68-0.95)
- Then adjusted for age (dichotomised at 35) it is not significant but still on the protective side: OR=0.89 (95% CI 0.73-1.10)
- Finally, adjusted for the precise age in years, it disappears: OR=1.00 (95% CI 0.82-1.24)

Residual confounding

- Chen, Gilbert & Daling's 2nd analysis was residually confounded.
- Age was the confounder, and it was measured coarsely.
- We only know a region within which it might lie for each of the mothers in the study.
- Heitjan & Rubin investigated MLE methods for coarse data, but with covariates we generally don't care about the marginal distribution

Incomplete data

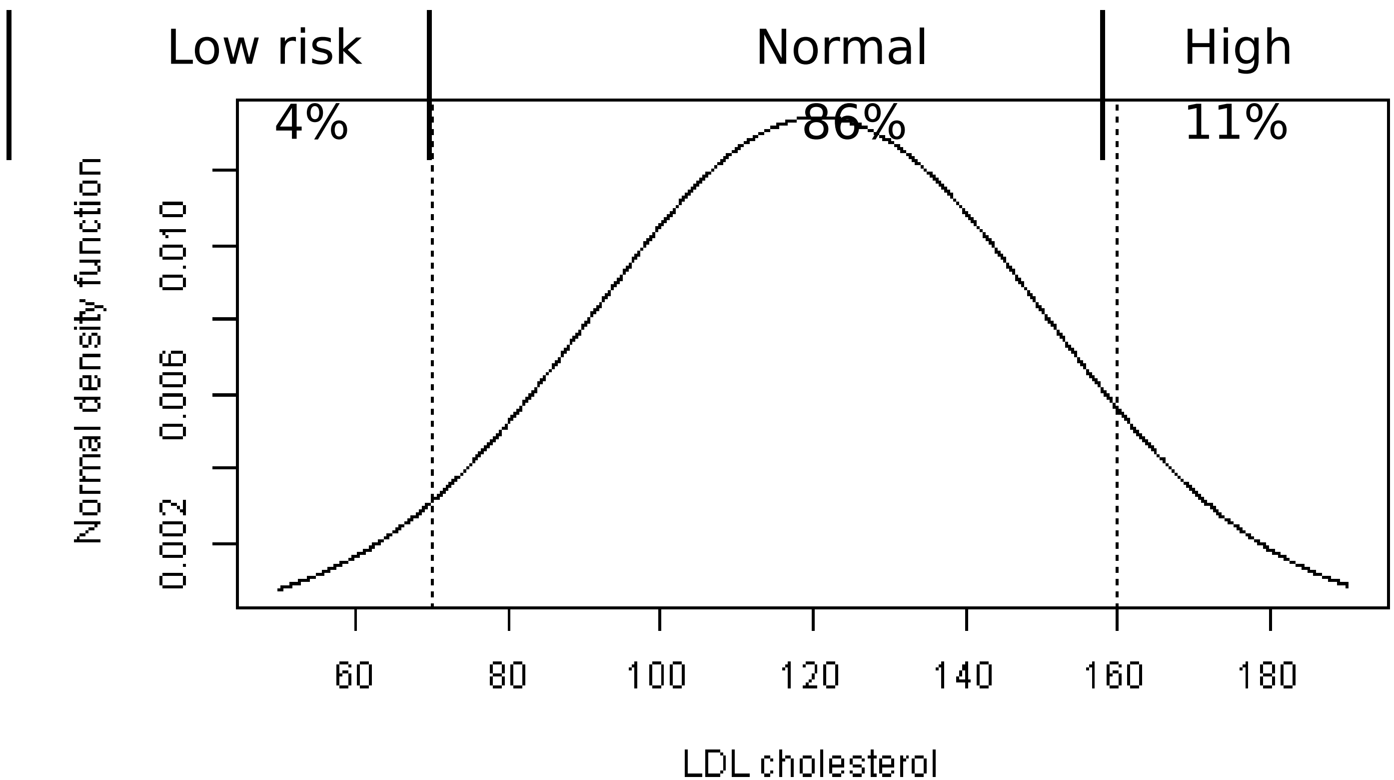
- This is a bit like missing data (note the presence of Don Rubin)
- In fact missing data is a special case of extreme coarseness.
- We can try some missing data methods on these confounding variables, but <u>we might not know which observations are coarsened</u>.
- For example, digit preference in number of cigarettes smoked per day.

How to make a medical scare story

Smith & Ebrahim. Int J Epidemiol (2001); 30: 1-11.

Can we say anything about the true values?

LDL cholesterol:



Artificial data based on statistics of Oda & Kawai. Diab Care (2009); 32(9): e113.

Consider two “current smokers”

Ingredients

- Assumption about form of the conditional distribution of confounder's true values (hopefully informed by evidence)
- Any other correlates in the data, leading to conditional distribution
- Assumption about coarsening mechanism (hopefully informed by evidence)

Procedure

- Find the parameters of the conditional distribution of the true confounder, and if necessary the coarsening mechanism
- Plug these into the conditional distribution of the true values given all known data
  - (under your assumptions...)
- Multiply impute from this
  - or do it all in one by MCMC / HMC
- Analyse the substantive model as normal and combine by Rubin's rules

Heitjan-Rubin and its extension

$$
\begin{aligned}
L(\boldsymbol{\theta}, \boldsymbol{\gamma} \mid X^*) = f(X^* \mid \boldsymbol{\theta}, \boldsymbol{\gamma}) &= \int_X f(X, X^* \mid \boldsymbol{\theta}, \boldsymbol{\gamma})\, dX \\
&= \int_X f(X^* \mid X, \boldsymbol{\gamma}) f(X \mid \boldsymbol{\theta})\, dX \qquad (1)
\end{aligned}
$$

$$
f(C \mid C^*, X, Y, \boldsymbol{\alpha}, \boldsymbol{\gamma}) = \frac{f(C^* \mid C, X, Y, \boldsymbol{\gamma}) f(C \mid X, Y, \boldsymbol{\alpha})}{\int_C f(C^* \mid C, X, Y, \boldsymbol{\gamma}) f(C \mid X, Y, \boldsymbol{\alpha})\, dC} \qquad (2)
$$

Example: Heaped Poisson

$$f(C \mid X, Y, \boldsymbol{\alpha}) = \frac{(e^{-\lambda_i} \lambda_i^{c_i})}{c_i!} \quad \text{, where} \quad \lambda_i = e^{\alpha_0 + \alpha_1 x_i + \alpha_2 y_i}$$

$$f(C^* \mid C, X, Y, \boldsymbol{\gamma}) = \pi_i^{g_i I(c_i^* = 5\lfloor c_i/5 \rfloor)} (1 - \pi_i)^{(1-g_i) I(c_i^* = c_i)}$$

$$\pi_i = \text{expit}(\gamma_0 + \gamma_1 x_i + \gamma_2 y_i)$$

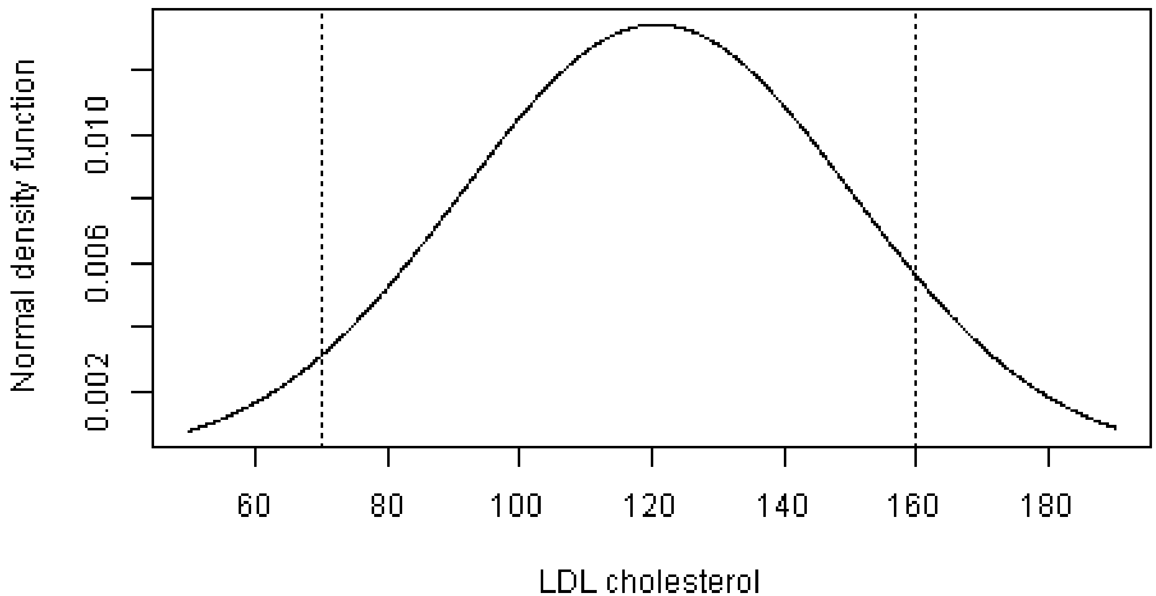
$$\frac{\frac{e^{-\lambda_i} \lambda_i^{c_i}}{c_i!} \pi_i^{g_i I(c_i^* = 5\lfloor c_i/5 \rfloor)} (1 - \pi_i)^{(1-g_i) I(c_i^* = c_i)}}{\left(\pi_i \sum_{j=0}^{4} \frac{e^{-\lambda_i} \lambda_i^{(c_i^* + j)}}{(c_i^* + j)!} \right)^{g_i} \left(\frac{e^{-\lambda_i} \lambda_i^{c_i^*}}{c_i^*!} (1 - \pi_i) \right)^{(1-g_i)}}$$

Example: Heaped Poisson

```
program define resconf_poisson
    version 11
    args lnfj loglambda logitpi
    tempvar pi
    tempvar lambda
    qui gen double `lambda'=exp(`loglambda')
    qui gen double `pi'=exp(`logitpi')/(1+exp(`logitpi'))
    qui replace `lnfj'=((1-g)*((-1*`lambda') + (cstar*`loglambda') + ln(1-`pi') - lnfactorial(cstar))) + ///
                    (g*((-1*`lambda')+ln(((`lambda'^(cstar+1))/round(exp(lnfactorial(cstar+1))) * `pi') + ///
                                          ((`lambda'^(cstar+2))/round(exp(lnfactorial(cstar+2))) * `pi') + ///
                                          ((`lambda'^(cstar+3))/round(exp(lnfactorial(cstar+3))) * `pi') + ///
                                          ((`lambda'^(cstar+4))/round(exp(lnfactorial(cstar+4))) * `pi'))))
end
```

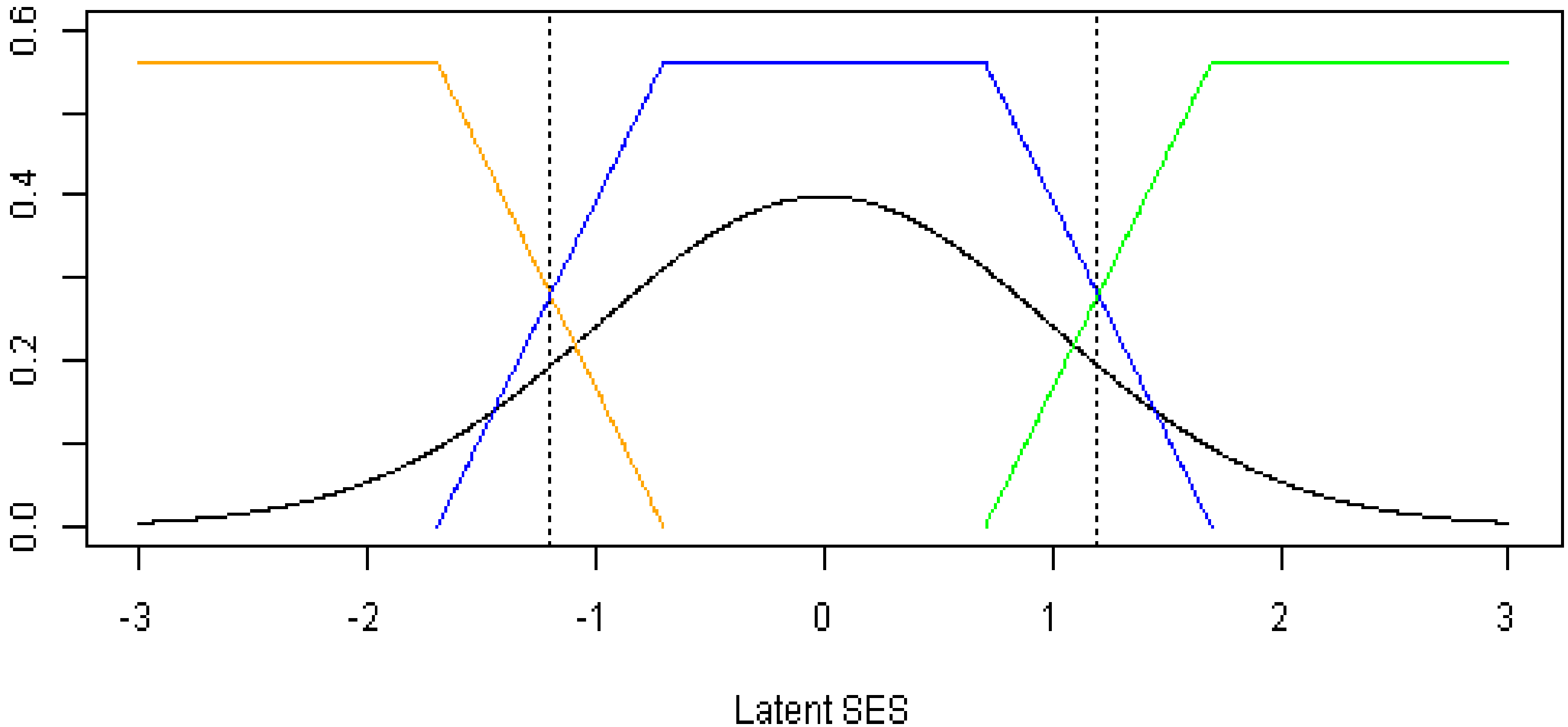
Interval-censored normal

- A special case because most stats software has Tobit-esque regressions for this kind of data
- Get the predicted value and the SE
- Impute truncated normal by rejection sampling



Interval-censored with overlap...

- Useful sensitivity analysis
- Allows some misclassification
- Linear overlap makes integration simpler



Whitehall II attrition

- Real-life example based on Mein et al (2012)
- Gender difference in non-response at phase 2 of the study, adjusted for age
- Occupational grade (3 levels) is confounder – a coarse proxy for socio-economic status
- Looks like grade and sex are more strongly correlated than SES (including other predictors)

Model	**Beta**	**95% CI**
Confounded	0.262	0.161 to 0.362
Residually confounded	-0.012	-0.127 to 0.102
Imputed x80 (intreg)	0.028	-0.086 to 0.143

What's next?

- Robustness to mispecification
- Collection of likelihood functions for various common coarsening mechanisms and forms of conditional distribution
- Application to clustered coarsening such as coding habits of data collectors

References

- Chen, Gilbert & Daling “Maternal smoking and Down syndrome: the confounding effect of maternal age” Am J Epidemiol (1999); 149(5):442-446
- Heitjan & Rubin “Ignorability and coarse data” Ann Stat (1991); 19(4):2244-2253.
- Mein et al “Predictors of two forms of attrition in a longitudinal health study involving ageing participants: An analysis based on the Whitehall II study” BMC Med Res Meth (2012); 12:164.