Bayesian Methods for Medical Device Safety Data

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Outline

- Background
  - Medical device safety data in clinical trials
- Bayesian Methods
  - Under hierarchical framework
- Application
- Simulation
- Conclusion

Objective

- Develop a unified Bayesian hierarchical framework for two-arm clinical trial (CT) data, with exposure information:
  - Parametric Bayesian models
  - Semi-parametric Bayesian model: Poisson + DPP
  - Semi-parametric Bayesian model: Zero-inflated Poisson (ZIP+DPP)
- R package to facilitate the utilization of the framework

Data Structure

AEs	Treatment group		Control Group	
	# of patients	Exposure time	# of patients	Exposure time
AE_1	X_{T1}	N_{T1}	X_{C1}	N_{C1}
…	…	…	…	…
AE_i	X_{Ti}	N_{Ti}	X_{Ci}	N_{Ci}
…	…	…	…	…
AE_I	X_{TI}	N_{TI}	X_{CI}	N_{CI}

Exposure time:

1. N_{ti} can be the total exposure time of all subjects in the treatment group, $N_{ti} = N_{ti'}$.
2. N_{ti} can be the total exposure time of subjects in the treatment group with AE_i , $N_{ti} \neq N_{ti'}$.
3. …

Exposure adjusted incidence rate (risk):

$\frac{X_{Ti}}{N_{Ti}}, \frac{X_{Ci}}{N_{Ci}}$ are the risk of AE_i for treatment group and cotnrol group respectively.

Frequentist method

1. Assumption: $X_{Ti} \sim \text{Pois}(\text{N}_{Ti}\ p_{Ti})$ and $X_{Ci} \sim \text{Pois}(\text{N}_{Ci}\ p_{Ci})$ for i=1,…,I;

   p_{Ti} and p_{Ci} are the parameter for incidence rates of AE_i from two groups.

2. Reparameterization of (p_{Ti}, p_{Ci}) to (δ_i, μ_i) is:

$$\delta_i = \log(p_{Ti}) - \log(p_{Ci}) = \log(p_{Ti} / p_{Ci})$$

$$\mu_i = \frac{1}{2}(\log(p_{Ti}) + \log(p_{Ci}))$$

where δ_i is the log relative risk and μ_i is the average risk

Parameter of interest

3. Frequentist method

MLE estimate of log relative risk: $\hat{\delta}_i = \log(\frac{X_{Ti}}{N_{Ti}}) - \log(\frac{X_{Ci}}{N_{Ci}})$; S.E. of $\hat{\delta}_i$: $\sqrt{\frac{1}{X_{Ti}} + \frac{1}{X_{Ci}}}$

a confidence interval of δ_i *is* : $\hat{\delta}_i \pm z_{\alpha/2}\sqrt{\frac{1}{X_{Ti}} + \frac{1}{X_{Ci}}}$

I: Parametric Hierarchical Bayesian Model

In a hierarchical Bayesian model, we propose the following priors:

$$\delta_i \mid \delta, \tau \sim^{iid} N(\delta, \tau^2)$$
$$\delta \sim \mathrm{U}(\mathrm{d}_0, \mathrm{e}_0)$$
$$\tau^2 \sim IG(a_0, b_0)$$
$$\mu_i \sim^{iid} N(0, c_0)$$

Given data $D(\underline{x}_{Ti}, \underline{x}_{Ci}) = \{(x_{Ti}, N_{Ti}), (x_{Ci}, N_{Ci})\}_{i=1}^{I}$, the likelihood function is:

$$L(p_{Ti}, p_{Ci} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci}) = \prod_{i=1}^{I} p(x_{Ti} \mid p_{Ti}) p(x_{Ci} \mid p_{Ci})$$
$$= \prod_{i=1}^{I} \left\{ \frac{\exp(-N_{Ti} p_{Ti})(N_{Ti} p_{Ti})^{x_{Ti}}}{x_{Ti}!} \frac{\exp(-N_{Ci} p_{Ci})(N_{Ci} p_{Ci})^{x_{Ci}}}{x_{Ci}!} \right\}$$
$$= \prod_{i=1}^{I} \left\{ \frac{\exp(-N_{Ti} \exp(\mu_i + 1/2\delta_i))(N_{Ti} \exp(\mu_i + 1/2\delta_i))^{x_{Ti}}}{x_{Ti}!} \frac{\exp(-N_{Ci} \exp(\mu_i - 1/2\delta_i))(N_{Ci} \exp(\mu_i - 1/2\delta_i))^{x_{Ci}}}{x_{Ci}!} \right\}$$

I: Parametric Hierarchical Bayesian Model

For the parameters $\underline{\theta} = \{\mu_1, ..., \mu_I; \delta_1, ..., \delta_I; \delta, \tau\}$, the joint prior distribution is:

$$\pi(\underline{\theta}) = \pi(\mu_1, ..., \mu_I; \delta_1, ..., \delta_I; \delta, \tau) = \{\prod_{i=1}^{I} \pi(\mu_i)\}\{\prod_{i=1}^{I} \pi(\delta_i \mid \delta, \tau)\}\pi(\delta)\pi(\tau)$$

The joint posterior distribution is:

$$\pi(\underline{\theta} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci}) \propto L(p_{Ti}, p_{Ci} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci})\pi(\underline{\theta})$$

$$\propto \{\prod_{i=1}^{I} p(x_{Ti} \mid p_{Ti}) p(x_{Ci} \mid p_{Ci})\}\{\prod_{i=1}^{I} \pi(\mu_i)\}\{\prod_{i=1}^{I} \pi(\delta_i \mid \delta, \tau)\}\pi(\delta)\pi(\tau)$$

The conditional posterior distribution can be calculated accordingly, specifically

$$\pi(\delta_i \mid \text{rest}) \propto p(\mathrm{x}_{Ci}, \mathrm{x}_{Ti} \mid \mu_i, \delta_i, \delta, \tau)\pi(\delta_i \mid \mu_i, \delta, \tau)$$

$$\propto \frac{\exp(-N_{Ti}\exp(\mu_i + 1/2\delta_i))(N_{Ti}\exp(\mu_i + 1/2\delta_i))^{x_{Ti}}}{x_{Ti}!} \frac{\exp(-N_{Ci}\exp(\mu_i - 1/2\delta_i))(N_{Ci}\exp(\mu_i - 1/2\delta_i))^{x_{Ci}}}{x_{Ci}!} \pi(\delta_i \mid \delta, \tau)$$

An equal-tailed credible interval of δ_i is $[\delta_{iL}, \delta_{iU}]$ with $P(\delta_i \le \delta_{iL}) = P(\delta_i > \delta_{iU}) = \alpha / 2$

II: Semi-parametric Model: Poisson + DPP

Dirichlet process prior (DPP) of δ_i: to allow a much rich class of distributions, to accommodate our lack of knowledge of the distributional structure of the relative risk.

Parametric prior of δ_i

$$\delta_i \mid \delta, \tau \sim^{iid} N(\delta, \tau^2)$$
$$\delta \sim \mathrm{U}(\mathrm{d}_0, \mathrm{e}_0)$$
$$\tau^2 \sim IG(a_0, b_0)$$
$$\mu_i \sim^{iid} N(0, c_0)$$

Non-parametric/Dirichlet prior of δ_i

$$\delta_i \sim DP(\alpha, \mathrm{G}_0)$$
$$\mathrm{G}_0 = N(\delta, \tau^2)$$
$$\delta \sim \mathrm{U}(\mathrm{d}_0, \mathrm{e}_0)$$
$$\tau^2 \sim \mathrm{I}G(\mathrm{a}_0, \mathrm{b}_0)$$
$$\alpha \sim \mathrm{U}(1, 10)$$
$$\mu_i \sim^{iid} N(0, \mathrm{c}_0)$$

Zero inflated Poisson (ZIP) Model

Zero-inflated Poisson (ZIP) model

$$X_{Ti} \sim \begin{cases} 0 & if\ \ Z_{Ti} = 1 \\ Pois(N_{Ti} p_{Ti}) & if\ \ Z_{Ti} = 0 \end{cases} ; Z_{Ti} \sim Bern(p_0)$$

$$X_{Ci} \sim \begin{cases} 0 & if\ \ Z_{Ci} = 1 \\ Pois(N_{Ci} p_{Ci}) & if\ \ Z_{Ci} = 0 \end{cases} ; Z_{Ci} \sim Bern(q_0)$$

Where Z_{Ti}, Z_{Ci} are latent variables

p_0, q_0 are the zero-inflation parameters

Modified log relative risk:

$$RR_i = \log \frac{(1-p_0)p_{Ti}}{(1-q_0)p_{Ci}} = \log \frac{(1-p_0)}{(1-q_0)} + \delta_i$$

ZIP + DPP

$$\delta_i \sim DP(\alpha, \mathrm{G}_0)$$
$$\mathrm{G}_0 = N(\delta, \tau^2)$$
$$\delta \sim \mathrm{U}(\mathrm{d}_0, \mathrm{e}_0)$$
$$\tau^2 \sim \mathrm{IG}(\mathrm{a}_0, \mathrm{b}_0)$$
$$\alpha \sim \mathrm{U}(1,10)$$
$$\mu_i \sim^{iid} N(0, \mathrm{c}_0)$$
$$p_0 \sim \mathrm{beta}(\mathrm{f}_0, \mathrm{g}_0)$$
$$q_0 \sim \mathrm{beta}(\mathrm{f}_0, \mathrm{g}_0)$$

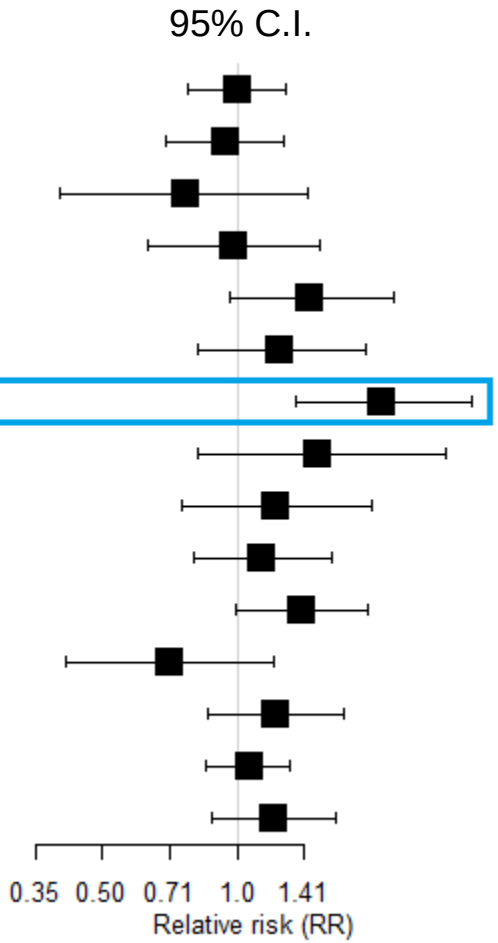
Alternative modeling: $Z_{Ti} \sim Bern(p_{0i}); Z_{Ci} \sim Bern(q_{0i}); p_{0i}, q_{0i}, \ldots$

Application

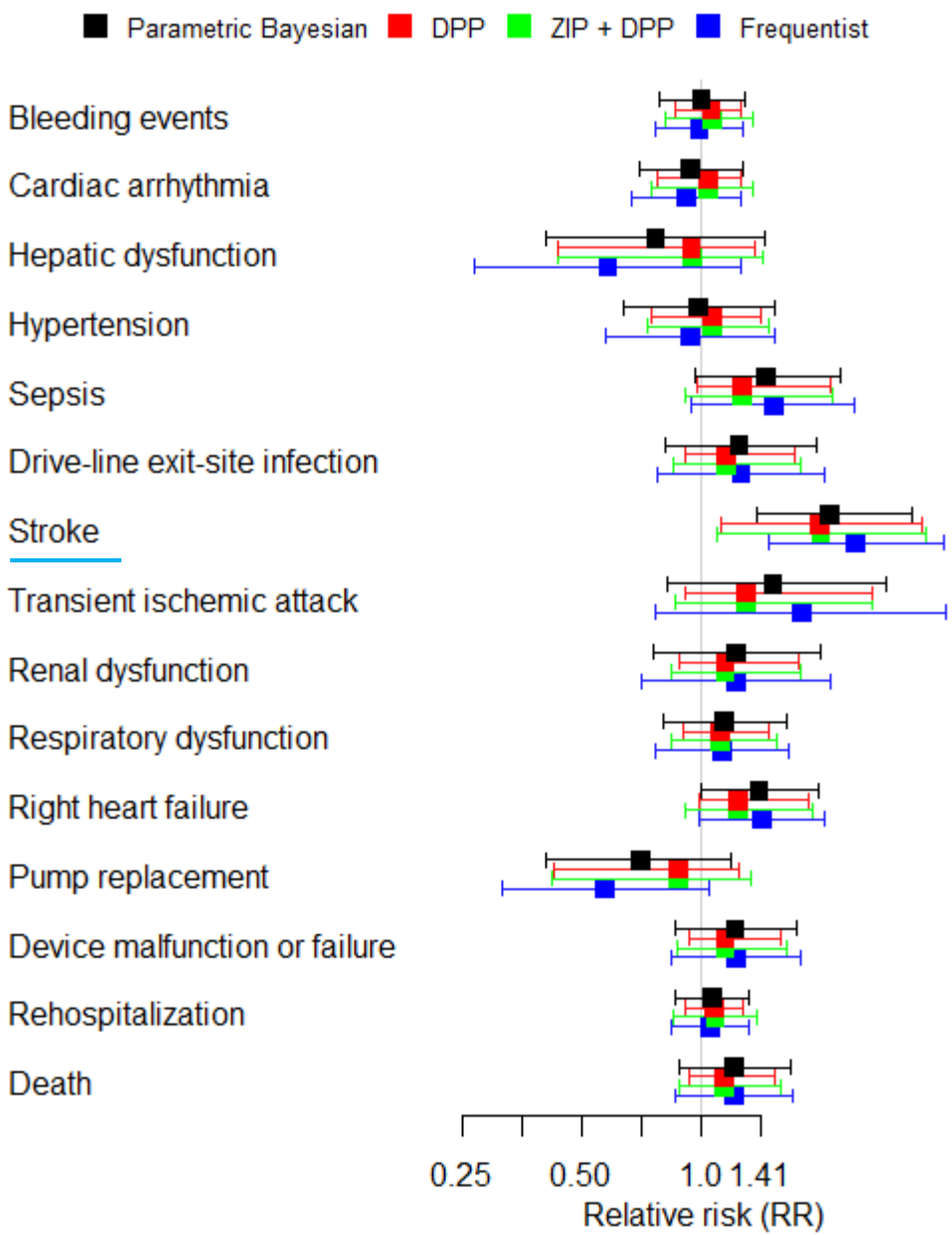
- Left ventricular assist device (LVAD) is a standard treatment for patients with advanced heart failure.
- A clinical study with patients randomized to two different designs of LVADs: Study device (HeartWare) vs. Control Device (HeartMate II)
- Objective: detect the safety signals when comparing HeartWare vs. Control Device(HeartMate II)
- Safety data published by Rogers et al.

Parametric Bayesian Hierarchical model

AE	HeartWare	HeartMate II	RR
Bleeding events	178	90	1
Cardiac arrhythmia	112	61	0.94
Hepatic dysfunction	14	12	0.77
Hypertension	47	25	0.98
Sepsis	70	23	1.45
Drive-line exit-site infection	58	23	1.24
Stroke	88	18	2.1
Transient ischemic attack	25	7	1.5
Renal dysfunction	44	18	1.21
Respiratory dysfunction	86	38	1.13
Right heart failure	114	40	1.39
Pump replacement	23	20	0.7
Device malfunction or failure	93	38	1.21
Rehospitalization	249	118	1.06
Death	116	48	1.2



***, Exposure of HearWare is 410 patient-year exposure of HeartMate II is 204 patient-year**



1. Left figure shows the forest plots with results from 4 methods.

2. All the methods detect the same safety signal, i.e., stroke.

3. DPP and ZIP + DPP results are very similar, with ZIP + DPP having slightly wider CI. The reasons could be:
   1) no zero inflation in the data;
   2) More uncertainly allowed in ZIP + DPP than in DPP

4. Parametric Bayesian result lies between frequentist method and DPP models.

Simulation Setting

Simulation steps:

1. Set up number of AEs in total (I = 50).
2. Generate exposure time for each AE and each arm from Poisson distribution, i.e., $N_{Ci}, N_{Ti} \sim Pois(mu.\text{exp}osure), mu.exposure = 50,100, \ldots 2000.$
3. Generate incidence rate in the control group for each AE from normal distribution truncated above 0.001, i.e., $p_{ci} \sim N(mu.pci, (mu.pci)^2), mu.pci = 0.05, 0.1..0.3$
4. Set up the relative risk for each AE, i.e., $\exp(\delta_i) = 1,1.5,2,5$, 1 for non-signals.
5. Calculate the incidence rate in the treatment group for each AE, i.e., $p_{Ti} = p_{Ci} * \exp(\delta_i)$
6. Generate the count data from independent Poisson distribution, i.e., $X_{Ti} \sim Pois(N_{Ti} p_{Ti})$ and $X_{Ci} \sim Pois(N_{Ci} p_{Ci})$ for i=1,…I
7. Generate 1,000 datasets for each scenario.
8. After Bayesian analysis, AEs with 95% credible interval not covering 0 are detected as signal.

Performance Characteristics:

$$Sensitivity = \frac{1}{N_{sim}} \sum_{l=1}^{l=N_{sim}} \frac{\text{\# of true signals detetected in the } l_{th} \text{ simulated data}}{\text{total \# of true signals in the } l_{th} \text{ simulated data}}$$

$$FDR = \frac{1}{N_{sim}} \sum_{l=1}^{l=N_{sim}} \frac{\text{\# of signals falsely detetected in the } l_{th} \text{ simulated data}}{\text{total \# of detected signals in the } l_{th} \text{ simulated data}}$$

Relative Risk

relative risk	Exposure time	Poisson + Normal		Poisson + DPP		Frequentist	
		Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR
1.5	100	0.04	0.1	0.01	0.03	0.12	0.56
	200	0.15	0.18	0.03	0.02	0.29	0.61
	500	0.45	0.28	0.1	0.03	0.57	0.54
	1000	0.79	0.31	0.31	0.03	0.85	0.45
	2000	0.98	0.33	0.69	0.02	0.98	0.43
2	100	0.22	0.09	0.08	0.03	0.4	0.5
	200	0.56	0.17	0.24	0.03	0.72	0.48
	500	0.93	0.22	0.66	0.02	0.96	0.42
	1000	1	0.28	0.95	0.02	1	0.41
	2000	1	0.34	1	0.01	1	0.43
5	100	0.98	0.09	0.95	0.02	0.99	0.33
	200	1	0.18	0.99	0.02	1	0.4
	500	1	0.27	1	0.01	1	0.41
	1000	1	0.34	1	0.01	1	0.42
	2000	1	0.38	1	0.01	1	0.43

Note: average incidence rate in the control group =0.1, one signal AE, in 50 AEs.

- For all 3 models, increasing the exposure time or the relative risk of the signal AE, can help increase the sensitivity. Frequentist method is the most sensitive, and Poisson +DPP is the most conservative and has FDR controlled in all scenarios.
- For a signal with relative risk =2, Poisson +DPP require 500 exposure time to achieve sensitivity over 0.6.

Ratio of Signals

Ratio of AE signals (50 total)	Exposure time	Poisson + Normal		Poisson + DPP		Frequentist	
		Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR
0.02(1 AE)	200	0.56	0.17	0.24	0.03	0.72	0.48
	500	0.93	0.22	0.66	0.02	0.96	0.42
	1000	1	0.28	0.95	0.02	1	0.41
0.06 (3 AE)	200	0.58	0.13	0.36	0.04	0.71	0.29
	500	0.94	0.14	0.79	0.02	0.97	0.23
	1000	1	0.18	0.98	0.01	1	0.23
0.1 (5 AEs)	200	0.62	0.1	0.44	0.05	0.71	0.2
	500	0.95	0.11	0.84	0.02	0.97	0.16
	1000	1	0.13	0.98	0.01	1	0.15
0.2 (10 AEs)	200	0.66	0.07	0.57	0.04	0.71	0.1
	500	0.96	0.08	0.89	0.02	0.97	0.08
	1000	1	0.08	0.99	0.01	1	0.08

Note: average incidence rate in the control group =0.1, relative risk =2, in 50 AEs.

Increase the ratio/percentage of signals has 1) no effect on frequentist method, 2) can slightly increase the sensitivity of Poisson + Normal, 3) greatly help increase the sensitivity of Poisson + DPP

Incidence Rate

Average incidence rate of AE in control group	Exposure time	Poisson + Normal		Poisson + DPP		Frequentist	
		Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR
0.05	200	0.26	0.09	0.14	0.03	0.41	0.34
	500	0.71	0.12	0.47	0.03	0.81	0.25
	1000	0.96	0.14	0.82	0.02	0.98	0.23
0.1	200	0.58	0.13	0.36	0.04	0.71	0.29
	500	0.94	0.14	0.79	0.02	0.97	0.23
	1000	1	0.18	0.98	0.01	1	0.23
0.2	200	0.9	0.14	0.7	0.03	0.93	0.24
	500	1	0.17	0.98	0.01	1	0.22
	1000	1	0.2	1	0.01	1	0.23
0.3	200	0.97	0.15	0.87	0.02	0.99	0.24
	500	1	0.19	1	0.01	1	0.23
	1000	1	0.21	1	0.01	1	0.23

Note: Percentage of signal =0.06 (3 AE signals), relative risk =2, in 50 AEs.

Increasing the average incidence rate of AE has the similar effect of increasing the exposure time.

Zero-Inflation

Zero inflation parameter ($p_0 = q_0$)	Poisson + Normal		ZIP + Normal		Poisson + DPP		ZIP + DPP	
	Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR
1.00E-06	0.94	0.14	0.94	0.14	0.78	0.02	0.78	0.02
0.01	0.83	0.24	0.95	0.13	0.69	0.16	0.83	0.02
0.03	0.67	0.41	0.96	0.11	0.54	0.36	0.85	0.02
0.05	0.55	0.52	0.97	0.1	0.43	0.52	0.86	0.02
0.1	0.36	0.68	0.98	0.07	0.29	0.7	0.87	0.01
0.2	0.2	0.82	0.98	0.04	0.16	0.84	0.83	0.01
0.3	0.12	0.89	0.97	0.03	0.09	0.9	0.78	0.01
0.4	0.08	0.92	0.86	0.03	0.06	0.94	0.72	0.01
0.5	0.05	0.95	0.47	0.06	0.04	0.95	0.57	0.01

Note: Percentage of signal =0.06 (3 AE signals), relative risk =2, exposure time= 500, in 50 AEs.

1) When there is no zero-inflation (first row), Poisson and ZIP models behave similarly.
2) When the zero-inflation parameter is higher, the benefit of ZIP appears for both ZIP+ Normal and ZIP + DPP, with the latter one controlling FDR well while maintaining good sensitivity.

Zero-Inflation

Exposure -time	Poisson + Normal		ZIP + Normal		Poisson + DPP		ZIP + DPP		Frequentist	
	Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR	Sensitivity	FDR
50	0.08	0.09	0.07	0.05	0.04	0.06	0.04	0.02	0.17	0.29
100	0.25	0.24	0.24	0.11	0.13	0.19	0.14	0.05	0.38	0.44
200	0.54	0.27	0.61	0.11	0.3	0.27	0.4	0.04	0.64	0.38
300	0.7	0.26	0.8	0.12	0.46	0.22	0.59	0.03	0.75	0.34
400	0.79	0.24	0.9	0.12	0.6	0.18	0.74	0.03	0.82	0.32
500	0.84	0.25	0.96	0.12	0.68	0.17	0.82	0.02	0.85	0.31
600	0.86	0.25	0.97	0.14	0.76	0.15	0.89	0.02	0.86	0.31
700	0.88	0.25	0.99	0.13	0.79	0.14	0.91	0.02	0.88	0.29
800	0.87	0.27	0.99	0.15	0.82	0.15	0.94	0.02	0.87	0.31
900	0.89	0.27	1	0.15	0.85	0.13	0.96	0.01	0.89	0.31
1000	0.88	0.29	1	0.17	0.86	0.14	0.97	0.02	0.88	0.32
1500	0.88	0.29	1	0.18	0.87	0.12	0.99	0.01	0.88	0.31
2000	0.88	0.3	1	0.18	0.88	0.14	0.99	0.01	0.88	0.31

Note: Percentage of signal =0.06, zero inflation parameter=0.01, relative risk =2, in 50 AEs.

Discussion

1. The framework can handle exposure time via Poisson model
2. Some AEs could be correlated (not shown in simulation). The natural clustering property of the DPP is potential helpful in ascertaining clusters of AEs that have similar relative risks.
3. Parametric Bayesian model can not control FDR well. However, semi-parametric Bayesian model with DPP is relatively more conservative with FDR well controlled.
4. Regularized measure of relative risk in ZIP model can adjust the zero inflation scenario.
5. Bayesian model, especially semi-parametric DPP model is much more time consuming

Future Work

- Implement the framework in a R package with the functions of
  - Parametric $\longrightarrow$ Semi-parametric $\longrightarrow$ Zero-inflation
  - Poisson model with adoption of exposure
  - Binomial model without exposure information
  - With options of prior selections
  - Automatically write WinBugs model file
  - Run the model file in R environment with R2JAGS

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APPENDIX

II: Semi-parametric Model: Poisson + DPP

DPP property: if $\delta_1 ..., \delta_I \sim DP(\alpha, \mathrm{G}_0)$, then $\delta_1 ..., \delta_I$ are exchangeable, therefore

$$\pi(\delta_i \mid \text{rest}) \propto p(\mathrm{x}_{Ci}, \mathrm{x}_{Ti} \mid \mu_i, \delta_i, \delta_1, ...\delta_{i-1}, \delta_{i+1}, ..., \delta_I, \mathrm{G}_0)\pi(\delta_i \mid \mu_i, \delta_1, ...\delta_{i-1}, \delta_{i+1}, ..., \delta_I, \mathrm{G}_0)$$

$$\propto \frac{\exp(-N_{Ti}\exp(\mu_i + 1/2\delta_i))(N_{Ti}\exp(\mu_i + 1/2\delta_i))^{x_{Ti}}}{x_{Ti}!} \frac{\exp(-N_{Ci}\exp(\mu_i - 1/2\delta_i))(N_{Ci}\exp(\mu_i - 1/2\delta_i))^{x_{Ci}}}{x_{Ci}!}$$

$$*\pi(\delta_i \mid \delta_1, ...\delta_{i-1}, \delta_{i+1}, ..., \delta_I, \mathrm{G}_0)$$

where $\pi(\delta_i \mid \delta_1, ...\delta_{i-1}, \delta_{i+1}, ..., \delta_I, \mathrm{G}_0) \propto \frac{\alpha}{\alpha + I - 1} dG_0 + \frac{1}{\alpha + I - 1}\sum_{j \neq i}^{I} I(\delta_j = \delta_i), dG_0 \sim N(\delta, \tau^2)$

Implementation of DPP (stick-breaking process):

1. generate a set of iid. atoms $\delta_l^* \sim G_0$
2. generate a set of weights w, $w_1 = v_1$ and $w_l = v_l \prod_{j<l}(1 - v_j)$ for $l > 1$, where v_j are iid with $v_j \sim beta(1, \alpha)$ for $j = 1, ..., \infty$
3. $\delta_i \sim DP(\alpha, \mathrm{G}_0) = \sum_{l=1}^{\infty} w_l I(\delta_i = \delta_l^*)$, where $I(\delta_i = \delta_l^*)$ is a point mass at δ_l^*.
4. In practice, one can truncate the sum of the preceding mixture at some finite number L, i.e., $DP(\alpha, \mathrm{G}_0) = \sum_{l=1}^{L} w_l I(\delta_i = \delta_l^*)$ as an approximation. $L = \sqrt{I}$ for large I and $L = I$ for small I.

III: Semi-parametric Model: ZIP + DPP

1. The joint prior distribution is:

$$\pi(\underline{\theta}) = \pi(\underline{z}_{Ti}, \underline{z}_{Ci}; p_0, q_0; \mu_1, ..., \mu_I; \delta_1, ..., \delta_I; \delta, \tau) = \{\prod_{i=1}^{I} \pi(\underline{z}_{Ti} \mid \mathrm{p}_0)\}\pi(\mathrm{p}_0)\{\prod_{i=1}^{I} \pi(\underline{z}_{Ci} \mid \mathrm{q}_0)\}\pi(\mathrm{q}_0)\{\prod_{i=1}^{I} \pi(\mu_i)\}\{\prod_{i=1}^{I} \pi(\delta_i \mid \delta, \tau)\}\pi(\delta)\pi(\tau)$$

2. The joint posterior distribution is:

$$\pi(\underline{\theta} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci}) \propto L(p_{Ti}, p_{Ci} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci})\pi(\underline{\theta})$$

$$\propto \{\prod_{i=1}^{I} p(x_{Ti} \mid \mathrm{z}_{Ci}, p_{Ci})p(x_{Ci} \mid \mathrm{z}_{Ci}, p_{Ci})\}\{\prod_{i=1}^{I} \pi(\mathrm{z}_{Ti} \mid \mathrm{p}_0)\}\pi(\mathrm{p}_0)\{\prod_{i=1}^{I} \pi(\mathrm{z}_{Ci} \mid \mathrm{q}_0)\}\pi(\mathrm{q}_0)\{\prod_{i=1}^{I} \pi(\mu_i)\}\{\prod_{i=1}^{I} \pi(\delta_i \mid \delta, \tau)\}\pi(\delta)\pi(\tau)$$

3. Given data $D(\underline{x}_{Ti}, \underline{x}_{Ci}) = \{(x_{Ti}, N_{Ti}), (x_{Ci}, N_{Ci})\}_{i=1}^{I}$), the complete likelihood function of ZIP model is:

$$L(p_{Ti}, p_{Ci} \mid D(\underline{x}_{Ti}, \underline{x}_{Ci}, \underline{z}_{Ti}, \underline{z}_{Ci},) = \prod_{i=1}^{I} p(x_{Ti}, \mathrm{z}_{Ti} \mid \mathrm{p}_0, p_{Ti})p(x_{Ci}, \mathrm{z}_{Ci} \mid \mathrm{q}_0, p_{Ci})$$

$$= \prod_{i=1}^{I} \left\{ p_0^{\,z_{Ti}} (1-\mathrm{p}_0)^{(1-\mathrm{z}_{Ti})} \left(\frac{\exp(-N_{Ti}\, p_{Ti})(N_{Ti}\, p_{Ti})^{x_{Ti}}}{x_{Ti}\,!}\right)^{(1-\mathrm{z}_{Ti})} q_0^{\,z_{Ci}} (1-q_0)^{1-z_{Ci}} \left(\frac{\exp(-N_{Ci}\, p_{Ci})(N_{Ci}\, p_{Ci})^{x_{Ci}}}{x_{Ci}\,!}\right)^{(1-z_{Ci})} \right\}$$

...

4. Specifically, the conditional posterior distribution of Z_{Ti}, Z_{Ci} as:

$$Z_{Ti} \mid \mathrm{x}_{Ti} = 0, rest \sim Bern\left(\frac{p_o}{p_0 + (1-\mathrm{p}_0)\exp(-N_{Ti}\exp(\mu_i + 1/2\delta_i))}\right); Z_{Ci} \mid \mathrm{x}_{Ti} = 0, rest \sim Bern\left(\frac{q_o}{q_0 + (1-q_0)\exp(-N_{Ci}\exp(\mu_i + 1/2\delta_i))}\right)$$

And

$$\mathrm{p}_0 \mid \mathrm{z}_{Ti}, rest \sim Beta(\mathrm{f}_0 + \sum_{i=1}^{I} z_{Ti}, g_0 + I - \sum_{i=1}^{I} z_{Ti}); q_0 \mid \mathrm{z}_{Ci}, rest \sim Beta(\mathrm{f}_0 + \sum_{i=1}^{I} z_{Ci}, g_0 + I - \sum_{i=1}^{I} z_{Ci})$$