Marginal Regression Models for Multiple-Disease Group Testing Data

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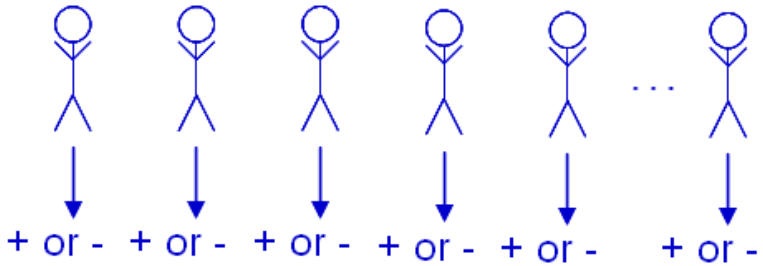
This research is supported in part by NIH grant R01AI067373

April 2, 2012

- Screen a large number of individuals for an infectious disease
- Individual testing



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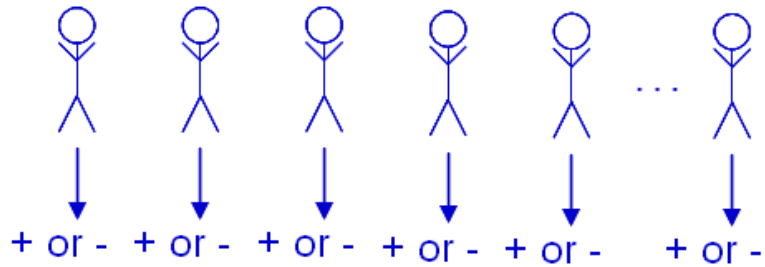
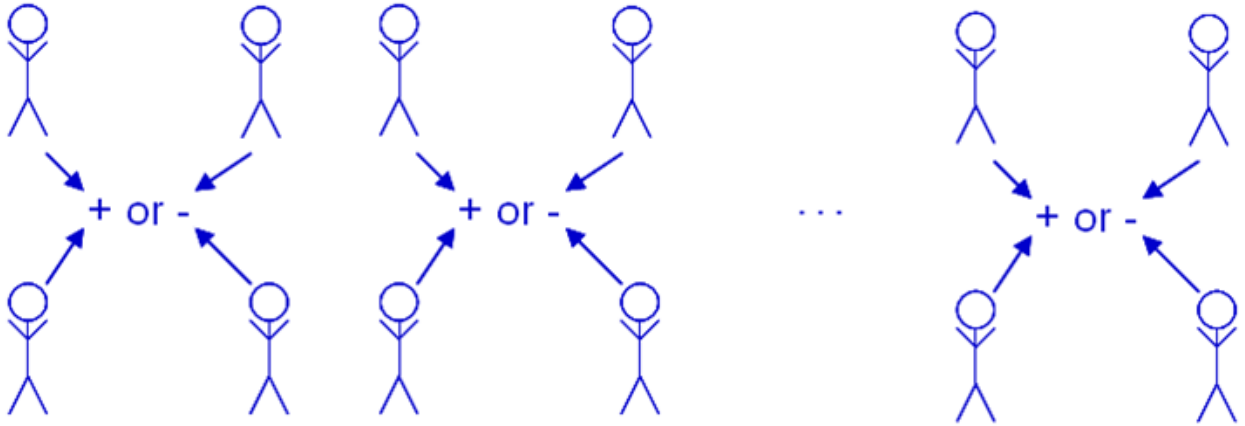


- May not feasible in high volume clinical specimen settings
  - Cost
  - Time

- Group testing (a.k.a., pooled testing)



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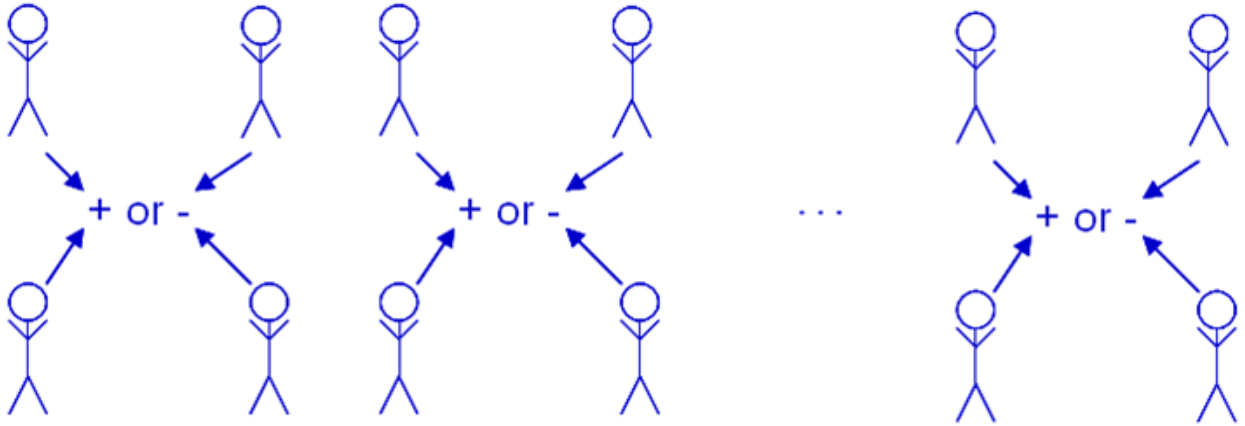

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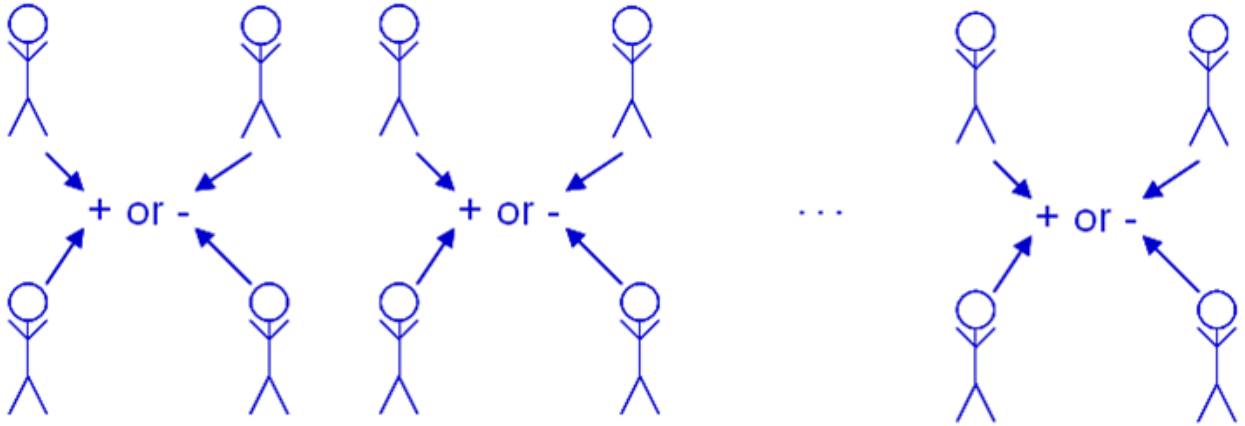

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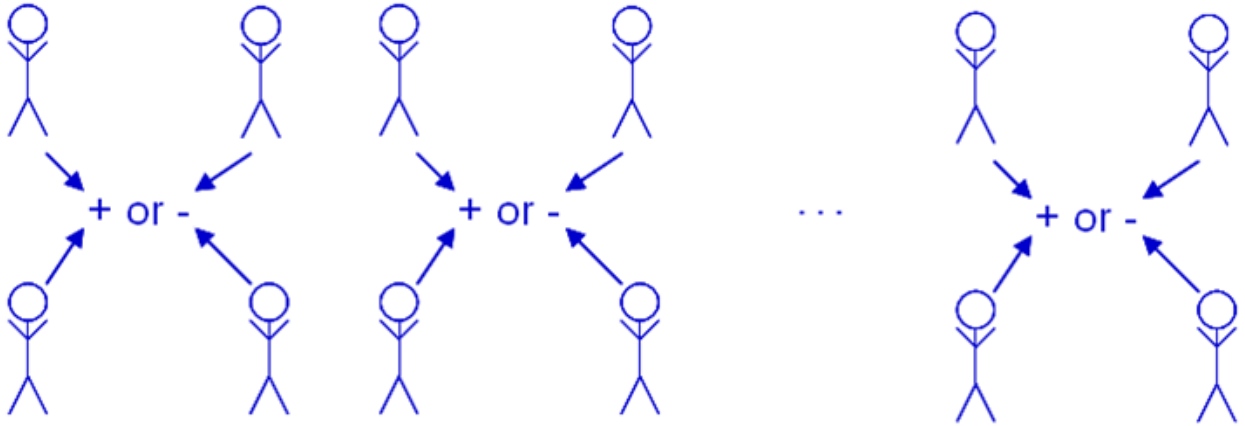

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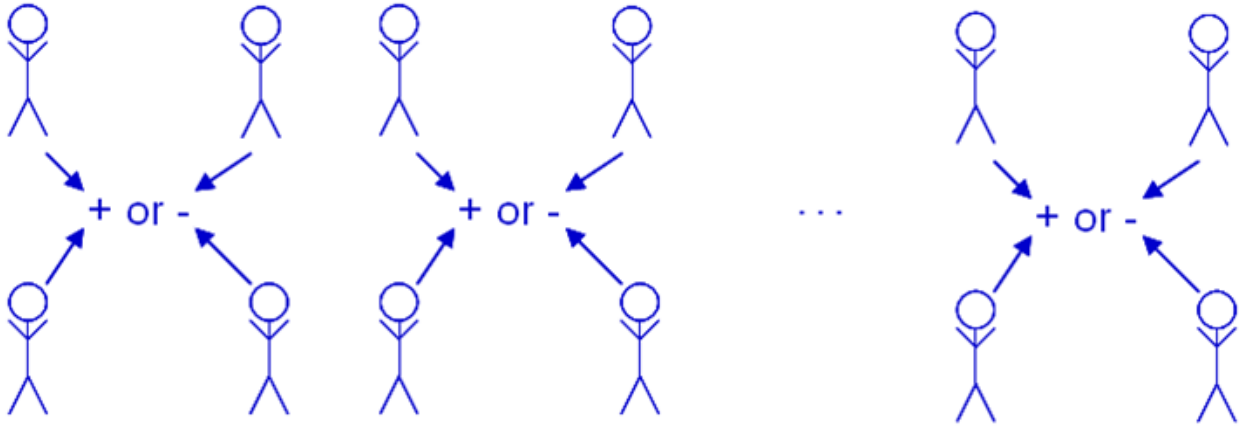

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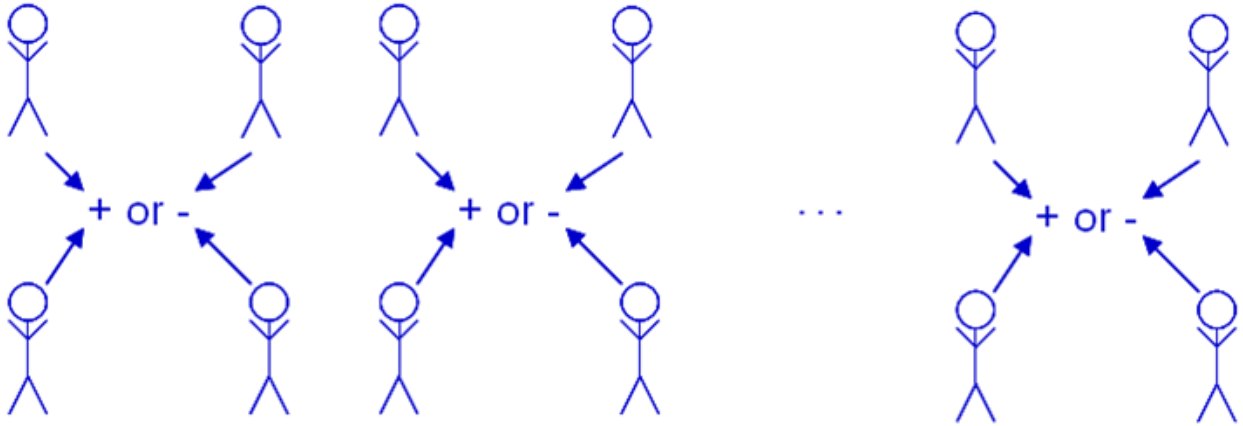

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- Classification vs. estimation

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- Only Hughes-Oliver and Rosenberger (2000) address multiple-disease problem in group testing
  - Estimate overall prevalence
  - Perfect diagnostic tests

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  - Probability of positivity dependent on covariates
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  - Correlated binary data problem
    - Disease responses are unobserved for each individual

- Individual responses
  - $\tilde{Y}_{ijk}$ = true unknown individual status of disease j for the ith individual in kth
    - $i = 1, \ldots, I_k$
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  - Likely correlated across $j = 1, \ldots, J$
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- Model: $\text{logit}(\tilde{p}_{ijk}) = \beta_{0j} + \beta_{1j} x_{1ik} + \cdots + \beta_{p-1,j} x_{p-1,ik}$
- Problem: $\tilde{Y}_{ijk}$ are not observed in group testing when no retests are performed

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- Testing error
  - $\tilde{Z}_{jk}$ = true group response
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- Relationship between individual and groups:

$$\begin{aligned} \theta_{jk} &= \eta_j P(\tilde{Z}_{jk} = 1) + (1 - \delta_j) P(\tilde{Z}_{jk} = 0) \\ &= \eta_j + (1 - \delta_j - \eta_j) \prod_{i=1}^{I_k} (1 - \tilde{p}_{ijk}) \end{aligned}$$

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- S-step – solve for vector of parameters $\boldsymbol{\beta}$ in

$$\Psi^{obs}(\boldsymbol{\beta}, \boldsymbol{\alpha}) = \sum_k \sum_i \mathbf{D}'_{ik} \mathbf{V}'_{ik} (\boldsymbol{\omega}_{ik} - \tilde{\mathbf{p}}_{ik}) = \mathbf{0}$$

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- Iterate between E and S-steps until convergence

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  - One can show that

$$
\begin{aligned}
Cov(Z_{jk}, Z_{j'k}) \quad = \quad & (\delta_j + \eta_j - 1)(\delta_{j'} + \eta_{j'} - 1) \times \\
& \left[\prod_{i=1}^{I_k} \left\{ \alpha_{jj'} \sqrt{Var(\tilde{Y}_{ijk}) Var(\tilde{Y}_{ij'k})} + (1 - \tilde{p}_{ijk})(1 - \tilde{p}_{ij'k}) \right\} - \right. \\
& \left. \prod_{i=1}^{I_k} (1 - \tilde{p}_{ijk})(1 - \tilde{p}_{ij'k}) \right]
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$$

- Provides way to estimate $\alpha_{jj'}$
  - Use method of moment estimator
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- Simpler form of estimator for $\alpha_{jj'}$
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  - $\beta_{01} = -6, \beta_{02} = -7, \beta_{11} = 0, \beta_{12} = 1, \beta_{21} = 0.1, \beta_{22} = 0.1$
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- $B = 1000$ simulated data sets

- Mean row:
  $\beta_{01} = -6, \beta_{02} = -7, \beta_{11} = 0, \beta_{12} = 1, \beta_{21} = 0.1, \beta_{22} = 0.1$
- SE/SD row: $B^{-1} \sum_{b=1}^{B} \sqrt{\widehat{Var}(\hat{\beta}_{rj})} / \sqrt{(B-1)^{-1} \sum_{b=1}^{B} (\hat{\beta}_{rjb} - \bar{\hat{\beta}}_{rj})^2}$
- Coverage row: 95% confidence level

α	K	I_k	Measure	$\hat{\beta}_{01}$	$\hat{\beta}_{02}$	$\hat{\beta}_{11}$	$\hat{\beta}_{12}$	$\hat{\beta}_{21}$	$\hat{\beta}_{22}$
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0.6	2000	5	Mean	-6.01	-7.04	0.02	1.05	0.10	0.10
			SE/SD	1.01	0.98	0.97	0.98	1.02	0.97

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			Coverage	0.96	0.94	0.94	0.95	0.96	0.94

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0.6	1000	10	Mean						
			SE/SD						
			Coverage						
0.2	2000	5	Mean						
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    - Chlamydia: Sensitivity $= \eta_2 = 0.928$, Specificity $= \delta_2 = 0.960$
  - Artificially form groups of size 5 by testing date
    - $Z_{jk} = 1$ if any positives in group, $Z_{jk} = 0$ otherwise
    - No "best" way to obtain group responses

- Estimation (continued)
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    - All covariates are binary except for age

- Estimate model with linear terms only
  - $\text{logit}(\tilde{p}_{ijk}) = \beta_{0j} + \beta_{1j}\text{Age}_{ik} + \cdots + \beta_{p-1,j}(\text{Contact STD})_{ik}$

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  - Fit model to individual responses for comparison
    - Use standard GEE methodology with no testing error
    - Non-convergence when incorporating testing error via methods in Neuhaus (2002)

- OMITTED BIG TABLE

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    - Restriction: Same individuals are always pooled together

Marginal Regression Models for Multiple-Disease Group Testing Data

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This research is supported in part by NIH grant R01AI067373

April 2, 2012