Bayesian Adjustments for Misclassified Data

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Outline

- Statistical "trends" in medical journals
- Misclassification in analysis of diagnostic testing data
- User friendly software
- Misclassification in administrative database studies
- Extension to more complex situations (correlations, continuous data)
- Conclusion

Trends in Medical Journals

- "Recognition of a good idea"
  - Optional, but if you analyze data this way, reviewers generally will say it is a good idea

- "Commonplace"
  - If you do not analyze data this way, reviewers generally will ask you to do it

- What is considered as a "Good Idea" or is "Commonplace" changes over time.


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SUBMISSIONS
p > 0.05


Epi
editor
SUBMISSIONS
Confounding?


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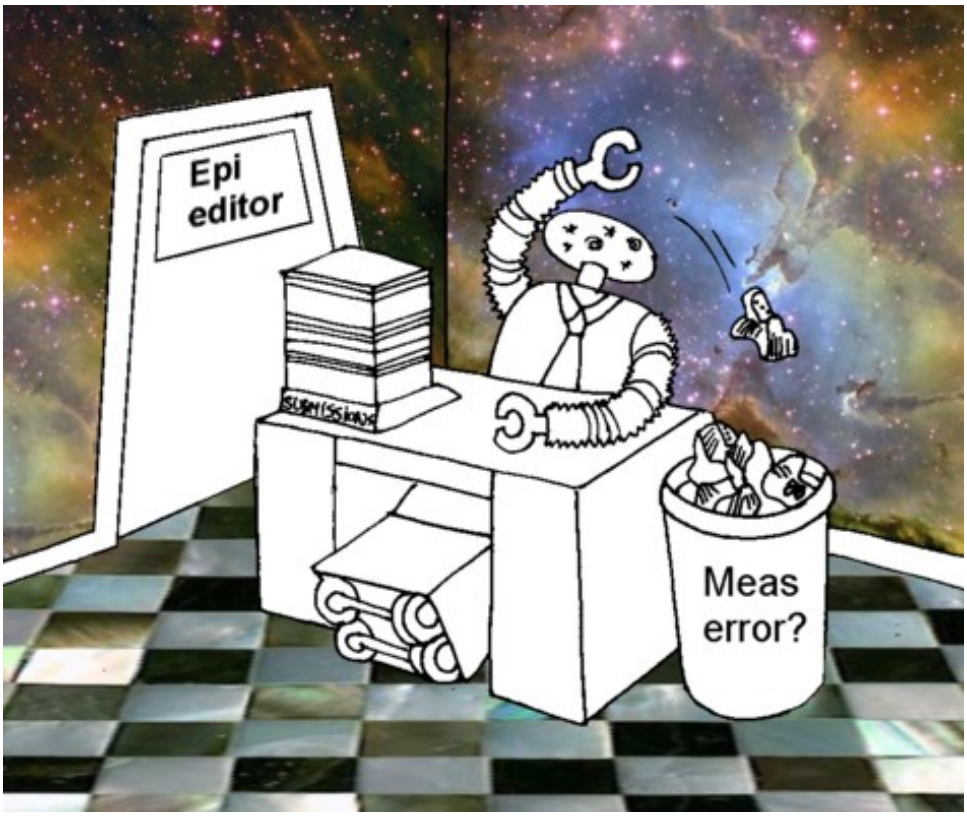
MAIL
No
hier
model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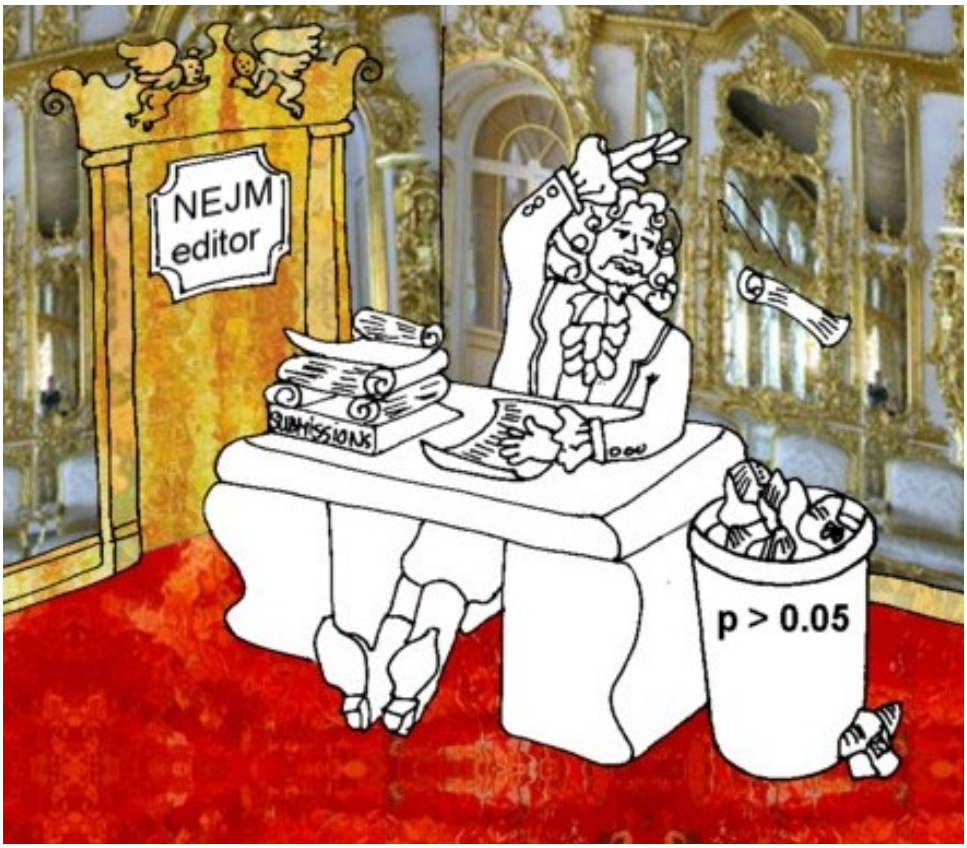
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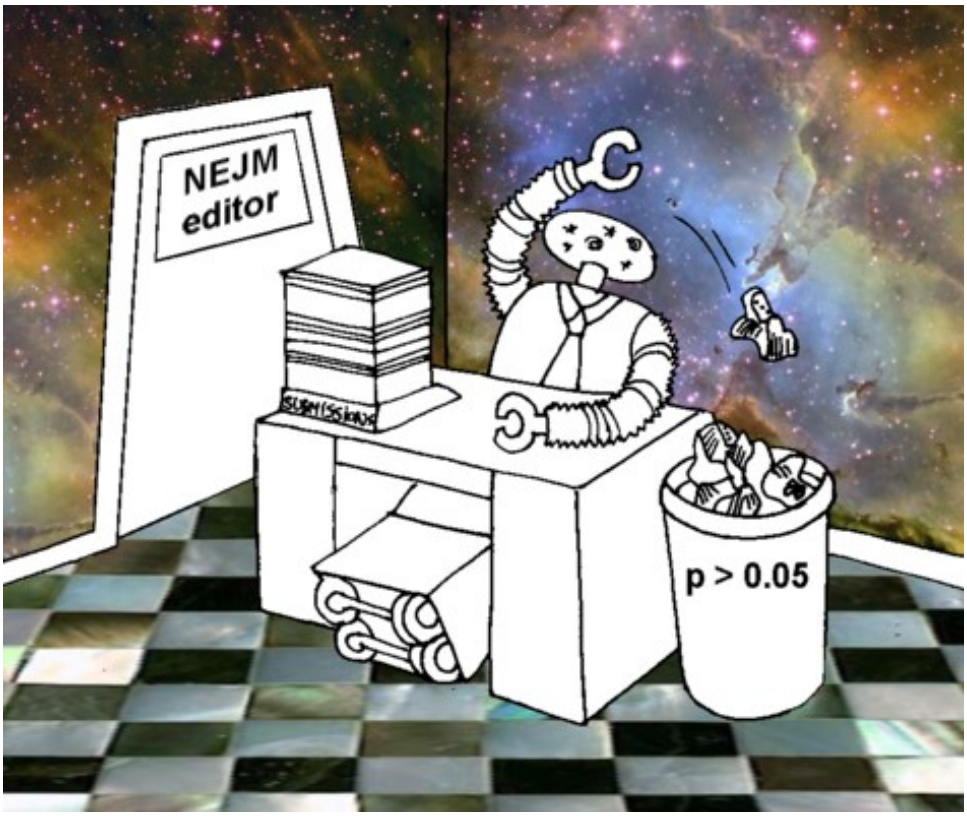
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Current Trends in Medical Journals (2007)

1. Bayesian analysis is "recognized as a good idea" but not required

2. Adjustment for measurement error is also "recognized as a good idea" but not required

3. Non-identifiability issues often means that $2 \Rightarrow 1$

4. Both ideas are increasing in popularity

Articles encouraging use of Bayesian methods in medicine

- Malakoff D. **Bayes offers a new way to make sense of numbers.** Science 1999;286:1460-1464. [Science review about the rise of Bayesian analysis]
- Dunson D. **Practical advantages of Bayesian analysis of epidemiologic data.** American Journal of Epidemiology 2001;153:1222-1226.
- Goodman S. **Of P-values and Bayes: A modest proposal.** Epidemiology. 2001;12:295-7. [Encourages use of Bayes Factors rather than p-values]
- Greenland S. **Multiple-bias modelling for analysis of observational data.** JRSSA 2005;168:267-306. [Encourages use of Bayesian methods for bias adjustments and measurement error/misclassification]

Quote from Greenland 2005

"**Conventional analytic results do not reflect any source of uncertainty other than random error**, and as a result readers must rely on informal judgments regarding the effect of possible biases. When standard errors are small these judgments often **fail to capture sources of uncertainty** and their interactions adequately. Multiple-bias models provide alternatives .... Typically, the **bias parameters** in the model are **not identified by** the analysis **data** and so the results depend completely on priors for those parameters. **A Bayesian analysis is then natural ...**"

Another quote from Greenland 2005

"Conventional analyses can be characterized as:

(a) **Employ frequentist statistical methods based on assumptions which may be grossly violated** and are not testable with the data under analysis:

(i) the study exposure is randomized within levels of controlled covariates

(ii) selection, participation and missing data are random

(iii) **there is no measurement error**

(b) **Address possible violations of assumptions with speculative discussions.** If they like the results, researchers argue that the biases are inconsequential. If they dislike the results they focus on possible biases."

Example: Diagnostic testing for Strongyloides infection

		Stool Examination		
		+	−	
Serology	+	38	87	125
	−	2	35	37
		40	122	162

- Prevalence $\approx 25\%$? Prevalence $\approx 75\%$?
- Sensitivity? Specificity?

Problem: Non-identifiability

- Table has 3 degrees of freedom

- There are five unknown parameters (prev + sens and spec from each test)

- Thus we have non-identifiability: There is an infinite number of solutions (estimates of the five parameters) that fit the data equally well

Frequentist Solution

- With 3 df, can only estimate 3 parameters at a time

- Solution: Pick any two parameters, and fix their values, use data to estimate other three

- Problems:
  - Which 2 to pick as "known"?
  - What if "known" values are inaccurate?
  - Even if exactly correct values selected for "known" parameters, confidence intervals are too narrow, as uncertainty in constrained values ignored.

Bayesian Solution

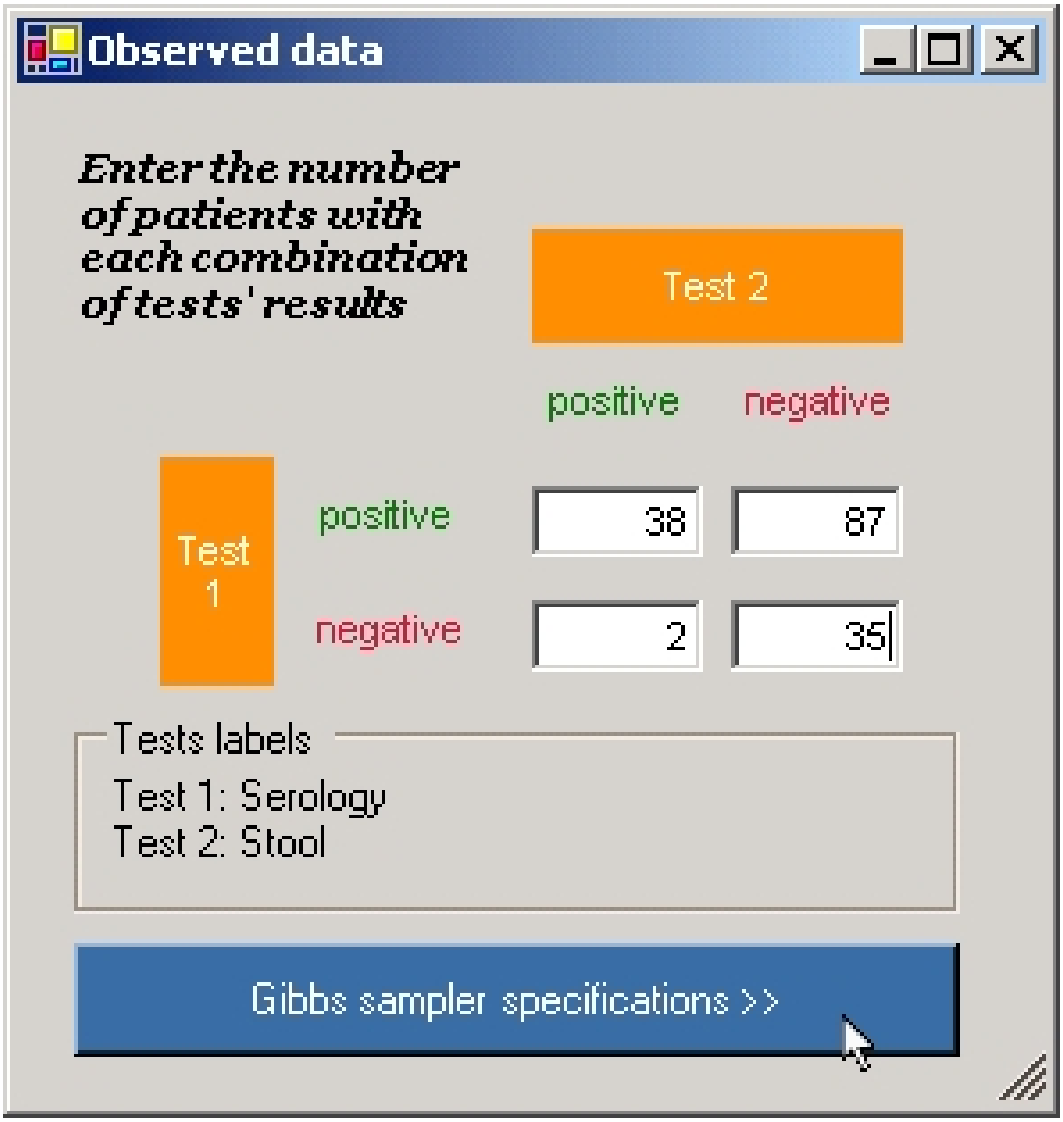
- Treat all five parameters as equal
- Place a prior distribution over each parameter
- At least two priors must be "informative", to get around identifiability problem
- Have priors, can write down likelihood, get posteriors for all parameters via Bayes Theorem
- Contains the frequentist solution as a special case, with point priors on two parameters and uniform priors on other three parameters . . . very unrealistic solution when looked at in this way

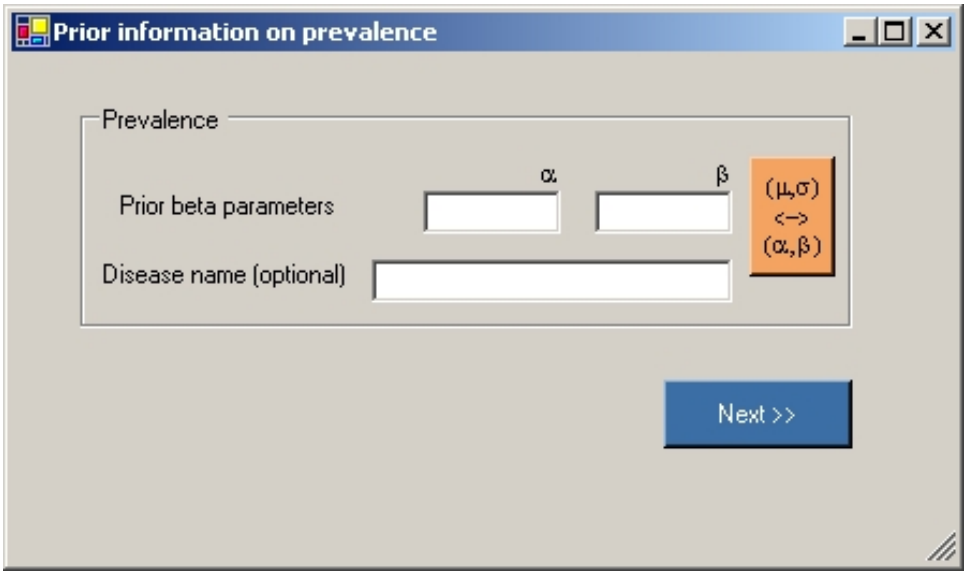
Bayesian Solution - Need For User Friendly Software

- Thousands of articles discussing new statistical methods are published every year
- Only a very small percentage of these find use in real applications
- An even smaller proportion of new methods find use by researchers other than the developers
- Reasons:
  - Too difficult for most non-statisticians to understand
  - Lack of recognition for applied work (not here!)
  - Even if understandable, lack of time to program
- Useful to provide user friendly software

Example: BayesDiagnosticTests Software

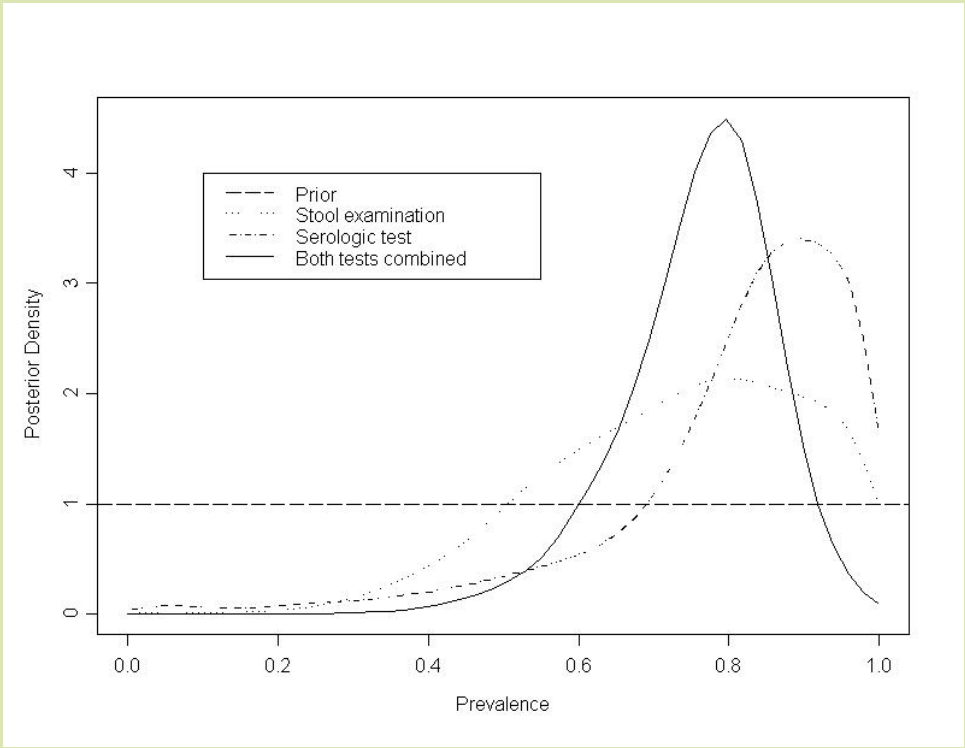
- Windows based exe file
- Input data + priors through user friendly "fill in the blanks" windows
- Runs a Gibbs sampler using WinBUGS by itself
- When ready (typically a few minutes) pops up posterior distributions + graphs
- Extensive manual, free help via email
- Let's look at the results from the Strongyloides example

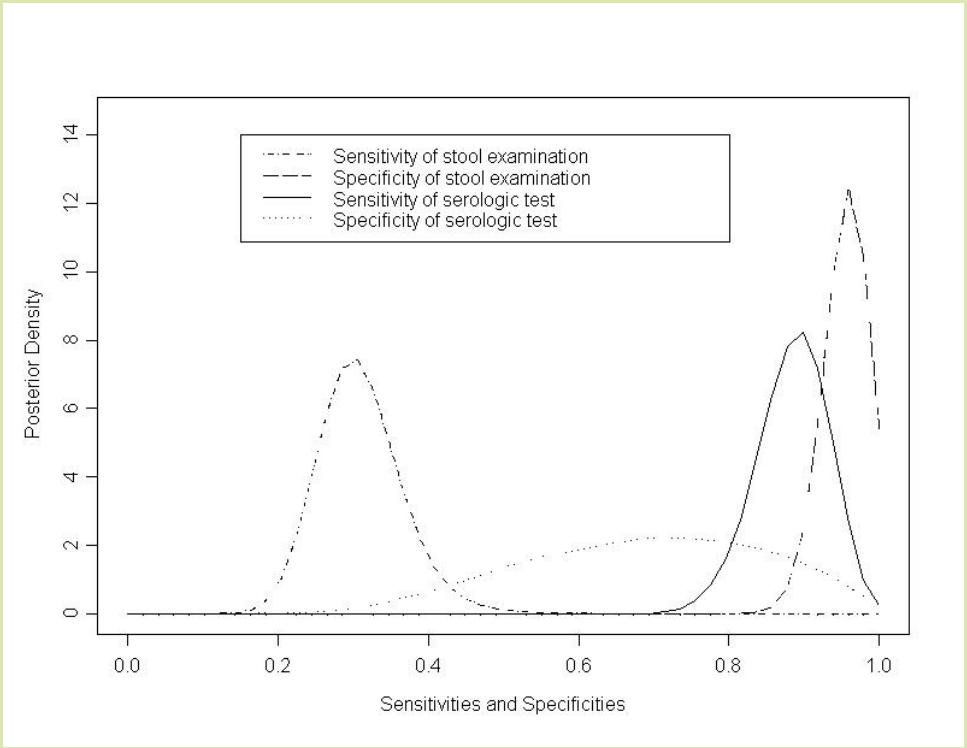

Observed data
Enter the number of patients with each combination of tests' results
Test 2
positive
negative
Test 1
positive
negative
38
87
2
35
Tests labels
Test 1: Serology
Test 2: Stool
Gibbs sampler specifications >>


Prior information on prevalence
Prevalence
α
β
Prior beta parameters
(μ,σ)
<–>
(α,β)
Disease name (optional)
Next >>

Results: Strongyloides Example

		Stool Examination		Serology	
	Prev	Sens	Spec	Sens	Spec
Prior Information	0.50 0.03 – 0.98	0.24 0.07 – 0.47	0.95 0.89 – 0.99	0.81 0.63 – 0.92	0.72 0.31 – 0.96
Stool Examination Alone	0.74 0.41 – 0.98	0.30 0.21 – 0.47	0.95 0.88 – 0.99		
Serology Alone	0.80 0.23 – 0.99			0.83 0.73 – 0.92	0.58 0.22 – 0.94
Both Tests Combined	0.76 0.52 – 0.91	0.31 0.22 – 0.44	0.96 0.91 – 0.99	0.89 0.80 – 0.95	0.67 0.36 – 0.95


Prior
Stool examination
Serologic test
Both tests combined
Posterior Density
0
1
2
3
4
0.0
0.2
0.4
0.6
0.8
1.0
Prevalence


Sensitivity of stool examination
Specificity of stool examination
Sensitivity of serologic test
Specificity of serologic test
Posterior Density
0
2
4
6
8
10
12
14
0.0
0.2
0.4
0.6
0.8
1.0
Sensitivities and Specificities

Application to Administrative Database Research

- Primary data collection can be expensive

- Researchers are increasingly using information collected in administrative databases (e.g. RAMQ)

- Such databases typically contain substantial proportions of misclassification errors (e.g. diagnoses).

Example: Prevalence of OA in 65+ from RAMQ data

Three imperfect clues about OA are available:

- ICD-9 diagnostic code for OA
- At least one prescription for acetaminophen or an NSAID, but not methotrexate or plaquenil
- Received injection common in OA, an arthroplasty or a tibial osteotomy

Methods

- Similar to case with two tests, but can use data from one, two, or all three tests (7 combinations in all)

- Priors not needed if all three tests are used

- Idea is to compare results from a variety of models, to check robustness of prevalence estimates

OA data from RAMQ data base

Test 1 Phys. Diagnosis	Test 2 Medication	Test 3 Medical Acts	Number of individuals observed
+	+	+	11,816
+	+	-	57,222
+	-	+	3,320
+	-	-	25,651
-	+	+	9,610
-	+	-	260,923
-	-	+	5,002
-	-	-	595,415

- Test 1 +ve = 11,816+ 57,222 +3,320 +25,651 = 98,009
- N = 968,959

Results with no Misclassification Adjustment

- Naive estimate using physician diagnosis error is 10.1%, 95% Credible Interval (CrI) 10.1-10.2

- Very narrow interval, but accounts only for uncertainty due to random variation, not for extra variability due to misclassification

- How much confidence can we place in this seemingly very accurate estimate?

Results with Misclassification Adjustment

	Prev	Sens 1	Sens 2	Sens 3	Spec 1	Spec 2	Spec 2
Prior distribution	**50.0**	75.0	75.0	25.0	95.0	60.0	95.0
	0.0-100	70.0-80.0	70.0-80.0	20.0-30.0	90.0-100	55.0-65.0	90.0-100
One Test							
Physician diagnosis alone	**11.5**	72.8			95.4		
	4.5-14.2	63.2-82.4			92.8-99.9		
Prescribed medication alone	**9.5**		72.3			71.1	
	3.3-22.0		62.5-81.9			66.3-75.6	
Medical procedure alone	**10.6**			22.1			99.2
	5.2-18.6			14.7-33.8			97.9-99.9
Two Tests							
Combination of physician diagnosis and prescribed medication	**11.8**	75.1	76.1		98.9	70.5	
	8.6-14.8	68.4-81.4	73.9-78.4		98.1-99.1	70.1-71.3	
Combination of physician diagnosis and medical acts	**9.8**	74.1		23.5	96.7		99.2
	6.4-13.7	63.2-83.2		15.9-31.1	94.3-99.6		98.6-99.3
Combination of prescribed medication and medical acts	**10.0**		77.6	24.0		70.6	99.6
	6.8-16.4		72.2-83.3	18.2-38.2		68.2-72.5	99.3-99.9
Three Tests							
3 tests using non-informative priors	**14.8**	58.2	78.3	18.2	98.1	72.4	99.5
	14.5-15.1	57.0-59.0	77.6-79.0	17.8-18.5	98.0-98.3	72.3-72.6	99.5-99.5

Comparison of Estimates

- Usual estimate: 10.1% (10.1-10.2), width = 0.1
- Adj estimate (3 tests): 14.8% (14.5-15.1), width = 0.6
- Bias $\approx$ 50%, CrI width grows by a factor of 6
- Other plausible estimates range from 3.3% to 22%
- Must admit true answer not really known
- All estimates depend on unverifiable assumptions
- Problems carry over to regressions based on risk factors for OA, etc.

Extensions

- Different numbers of tests
- Correlations among dichotomous tests
- Continuous diagnostic test results (Para + Non-Para)
- Combinations of continuous and dichotomous tests
- Correlations among continuous tests
- Hierarchical models for diagnostic test data

Conclusions

- Important to consider measurement/misclassification error in Epi (coming trend?)

- For real impact:
  - not enough to develop methods
  - need user friendly software

- Beware of unadjusted results from Administrative Database research

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