Session 2

Basic Hui-Walter models

Matt Denwood 2021-06-28

Hui-Walter Model

- A particular model formulation that was originally designed for evaluating diagnostic tests in the absence of a gold standard
- Not necessarily (or originally) Bayesian but often implemented using Bayesian MCMC
- But evaluating an imperfect test against another imperfect test is a bit like pulling a rabbit out of a hat
 - If we don't know the true disease status, how can we estimate sensitivity or specificity for either test?

Model Specification

```
model{
  Tally ~ dmulti(prob, N)
  # Test1- Test2-
    prob[1] <- (prev * ((1-se[1])*(1-se[2]))) + ((1-prev) *
    \hookrightarrow ((sp[1])*(sp[2])))
  # Test1+ Test2-
    prob[2] <- (prev * ((se[1])*(1-se[2]))) + ((1-prev) *
    \hookrightarrow ((1-sp[1])*(sp[2])))
  # Test1- Test2+
    prob[3] <- (prev * ((1-se[1])*(se[2]))) + ((1-prev) *
    \hookrightarrow ((sp[1])*(1-sp[2])))
```

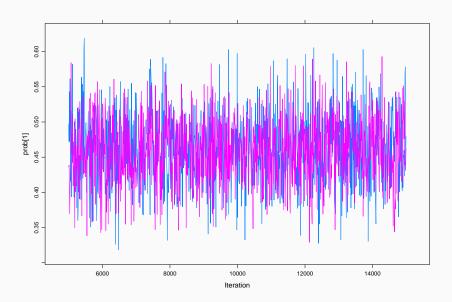
```
# Test1+ Test2+
  prob[4] <- (prev * ((se[1])*(se[2]))) + ((1-prev) *</pre>
  \hookrightarrow ((1-sp[1])*(1-sp[2])))
prev ~ dbeta(1, 1)
se[1] ~ dbeta(1, 1)
sp[1] ~ dbeta(1, 1)
se[2] ~ dbeta(1, 1)
sp[2] ~ dbeta(1, 1)
#data# Tally, N
#monitor# prev, prob, se, sp, deviance
#inits# prev, se, sp
```

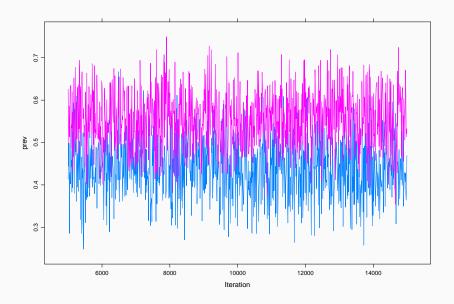
```
twoXtwo <- matrix(c(48, 12, 4, 36), ncol=2, nrow=2)
twoXtwo
## \[\(\int_{\cdot 1}\) \[\(\int_{\cdot 2}\)
## [1,] 48 4
## [2,] 12 36
library('runjags')
Tally <- as.numeric(twoXtwo)</pre>
N <- sum(Tally)
prev <- list(chain1=0.05, chain2=0.95)</pre>
se <- list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))
sp \leftarrow list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))
results <- run.jags('basic_hw.txt', n.chains=2)</pre>
```

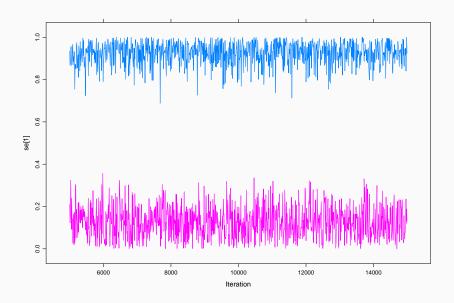
[Remember to check convergence and effective sample size!]

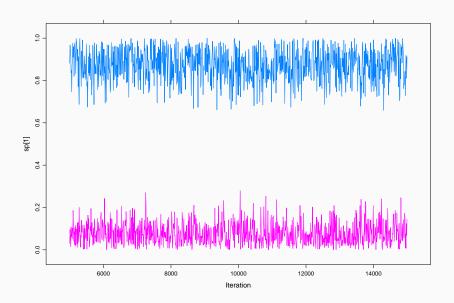
prev 0.328 0.499 0.668 4250 2.304 prob[1] 0.367 0.462 0.558 13858 1.000 prob[2] 0.072 0.132 0.202 14200 1.000 prob[3] 0.018 0.055 0.104 9602 1.000 prob[4] 0.255 0.343 0.438 13555 1.000 se[1] 0.028 0.570 1.000 4564 15.155 se[2] 0.000 0.385 0.965 4585 13.619 sp[1] 0.000 0.461 0.970 4527 15.261 sp[2] 0.036 0.581 1.000 4593 13.641						
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prob[2] 0.072 0.132 0.202 14200 1.000 prob[3] 0.018 0.055 0.104 9602 1.000 prob[4] 0.255 0.343 0.438 13555 1.000 se[1] 0.028 0.570 1.000 4564 15.155 se[2] 0.000 0.385 0.965 4585 13.619 sp[1] 0.000 0.461 0.970 4527 15.261 sp[2] 0.036 0.581 1.000 4593 13.641	prev	0.328	0.499	0.668	4250	2.304
prob[3] 0.018 0.055 0.104 9602 1.000 prob[4] 0.255 0.343 0.438 13555 1.000 se[1] 0.028 0.570 1.000 4564 15.155 se[2] 0.000 0.385 0.965 4585 13.619 sp[1] 0.000 0.461 0.970 4527 15.261 sp[2] 0.036 0.581 1.000 4593 13.641	prob[1]	0.367	0.462	0.558	13858	1.000
prob[4] 0.255 0.343 0.438 13555 1.000 se[1] 0.028 0.570 1.000 4564 15.155 se[2] 0.000 0.385 0.965 4585 13.619 sp[1] 0.000 0.461 0.970 4527 15.261 sp[2] 0.036 0.581 1.000 4593 13.641	prob[2]	0.072	0.132	0.202	14200	1.000
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	sp[1]	0.000	0.461	0.970	4527	15.261
deviance 12.304 15.134 21.447 8838 1.000	sp[2]	0.036	0.581	1.000	4593	13.641
	deviance	12.304	15.134	21.447	8838	1.000

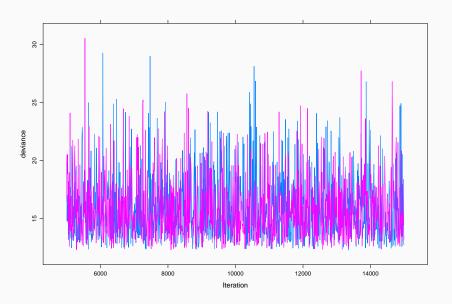
Does anybody spot a problem?

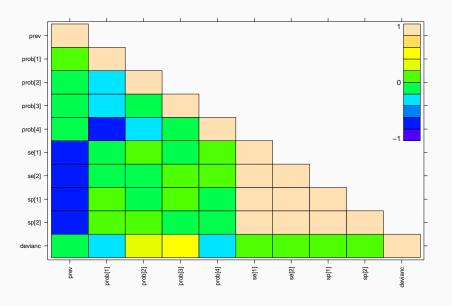












Label Switching

How to interpret a test with Se=0% and Sp=0%?

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• The test is perfect - we are just holding it upside down...

We can force se+sp >= 1:

```
se[1] ~ dbeta(1, 1)
sp[1] ~ dbeta(1, 1)T(1-se[1], )
```

Or:

```
se[1] ~ dbeta(1, 1)T(1-sp[1], )
sp[1] ~ dbeta(1, 1)
```

This allows the test to be useless, but not worse than useless.

Alternatively we can have the weakly informative priors:

```
se[1] ~ dbeta(2, 1)
sp[1] ~ dbeta(2, 1)
```

To give the model some information that we expect the test characteristics to be closer to 100% than 0%.

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```
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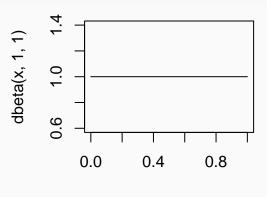
To give the model some information that we expect the test characteristics to be closer to 100% than 0%.

Or we can use stronger priors for one or both tests.

Priors

A quick way to see the distribution of a prior:

```
curve(dbeta(x, 1, 1), from=0, to=1)
```

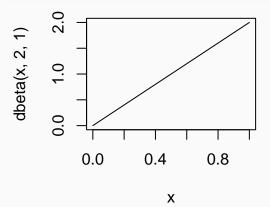


```
Χ
```

```
qbeta(c(0.025,0.975), shape1=1, shape2=1)
## [1] 0.025 0.975
```

This was minimally informative, but how does that compare to a weakly informative prior for e.g. sensitivity?

```
curve(dbeta(x, 2, 1), from=0, to=1)
```



```
qbeta(c(0.025,0.975), shape1=2, shape2=1)
## [1] 0.1581139 0.9874209
```

```
qbeta(c(0.025,0.975), shape1=2, shape2=1)
## [1] 0.1581139 0.9874209
```

Or more accurately:

```
library("TeachingDemos")
hpd(qbeta, shape1=2, shape2=1)
## [1] 0.2236068 1.0000000
```

```
qbeta(c(0.025,0.975), shape1=2, shape2=1)
## [1] 0.1581139 0.9874209
```

Or more accurately:

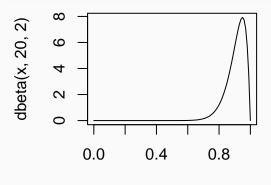
```
library("TeachingDemos")
hpd(qbeta, shape1=2, shape2=1)
## [1] 0.2236068 1.0000000
```

Credible vs confidence intervals:

- For MCMC these are usually calculated using highest posterior density (HPD) intervals
- Therefore there is a difference between:
 - qbeta(c(0.025,0.975), ...)
 - hpd(qbeta, ...)
- Technically HPD intervals are credible intervals. . .

What about a more informative prior?

```
curve(dbeta(x, 20, 2), from=0, to=1)
```



```
qbeta(c(0.025,0.975), shape1=20, shape2=2)
## [1] 0.7618401 0.9882507
hpd(qbeta, shape1=20, shape2=2)
## [1] 0.7919691 0.9973994
```

Х

Choosing a prior

What we want is e.g. Beta(20,1)

But typically we have median and 95% confidence intervals from a paper, e.g.:

"The median (95% CI) estimates of the sensitivity and specificity of the shiny new test were 94% (92-96%) and 99% (97-100%) respectively"

Choosing a prior

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But typically we have median and 95% confidence intervals from a paper, e.g.:

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How can we generate a Beta(,) prior from this?

The PriorGen package

"The median (95% CI) estimates of the sensitivity and specificity of the shiny new test were 94% (92-96%) and 99% (97-100%)"

```
library("PriorGen")

## Loading required package: rootSolve
findbeta(themedian = 0.94, percentile=0.95, percentile.value = 0.92)

## [1] "The desired Beta distribution that satisfies the specified

→ conditions is: Beta( 429.95 27.76 )"

## [1] "Here is a plot of the specified distribution."

## [1] "Descriptive statistics for this distribution are:"

## Min. 1st Qu. Median Mean 3rd Qu. Max.

## 0.8910 0.9322 0.9399 0.9393 0.9473 0.9749

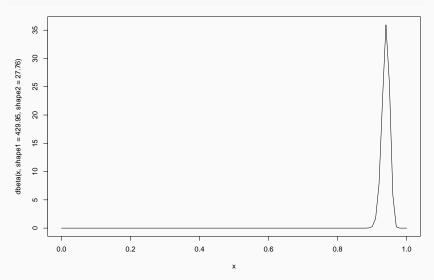
## [1] "Verification: The percentile value 0.92 corresponds to the 0.05

→ th percentile"

hpd(qbeta, shape1=429.95, shape2=27.76)

## [1] 0.917172 0.960435
```

curve(dbeta(x, shape1=429.95, shape2=27.76))



Initial values

Part of the problem before was also that we were specifying extreme initial values:

```
se <- list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))
sp <- list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))</pre>
```

Initial values

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se <- list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))
sp <- list(chain1=c(0.01,0.99), chain2=c(0.99,0.01))</pre>
```

Let's change these to:

```
se <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
sp <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
```

Analysing simulated data

This is useful to check that we can recover parameter values!

```
# Set a random seed so that the data are reproducible:
set.seed(2021-06-28)
se \leftarrow c(0.9, 0.6)
sp \leftarrow c(0.95, 0.9)
N < -1000
prevalence <- 0.5
data <- tibble(Status = rbinom(N, 1, prevalence)) %>%
  mutate(Test1 = rbinom(N, 1, se[1]*Status + (1-sp[1])*(1-Status))) %%
  mutate(Test2 = rbinom(N, 1, se[2]*Status + (1-sp[2])*(1-Status)))
twoXtwo <- with(data, table(Test1, Test2))
Tally <- as.numeric(twoXtwo)</pre>
```

Analysing simulated data

This is useful to check that we can recover parameter values!

```
# Set a random seed so that the data are reproducible:
set.seed(2021-06-28)
se < -c(0.9, 0.6)
sp \leftarrow c(0.95, 0.9)
N < -1000
prevalence <- 0.5
data <- tibble(Status = rbinom(N, 1, prevalence)) %>%
  mutate(Test1 = rbinom(N, 1, se[1]*Status + (1-sp[1])*(1-Status))) %%
  mutate(Test2 = rbinom(N, 1, se[2]*Status + (1-sp[2])*(1-Status)))
twoXtwo <- with(data, table(Test1, Test2))
Tally <- as.numeric(twoXtwo)</pre>
```

We know that e.g. the first test has Sensitivity of 90% and Specificity of 95% - so the model *should* be able to tell us that...

Practical Session 2

Points to consider

- 1. What is the typical autocorrelation (and therefore effective sample size) of Hui-Walter models compared to the simpler models we were running earlier? Is there any practical consequence of this?
- 2. How does changing the prior distributions for the se and sp of one test affect the inference for the other test parameters?

Summary

- Hui-Walter models can do magical things, but:
 - They typically exhibit high autocorrelation
 - They may not converge
 - Need a larger sample for the same effective sample size
- More informative priors for one test will
 - Improve identifiability of the model
 - Impact the inference for all other parameters in the model!