

Session 2

Introduction to Hui-Walter models

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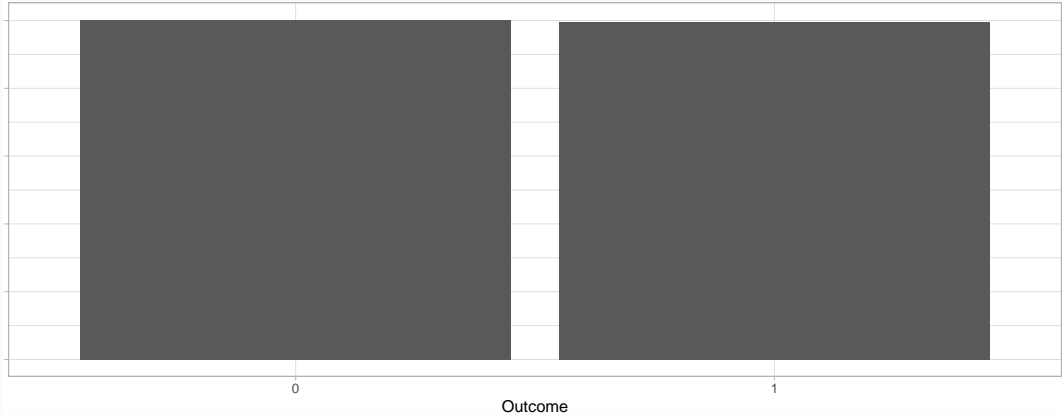
2022-09-12

Hui-Walter Model

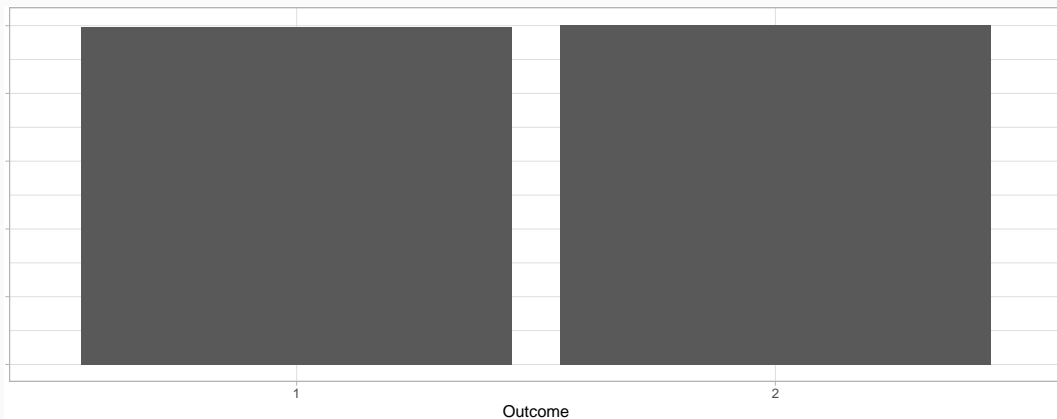
- A particular model formulation that was originally designed for evaluating diagnostic tests in the absence of a gold standard
- Not necessarily (or originally) Bayesian but often implemented using Bayesian MCMC
- But evaluating an imperfect test against another imperfect test is a bit like pulling 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?

The multinomial distribution

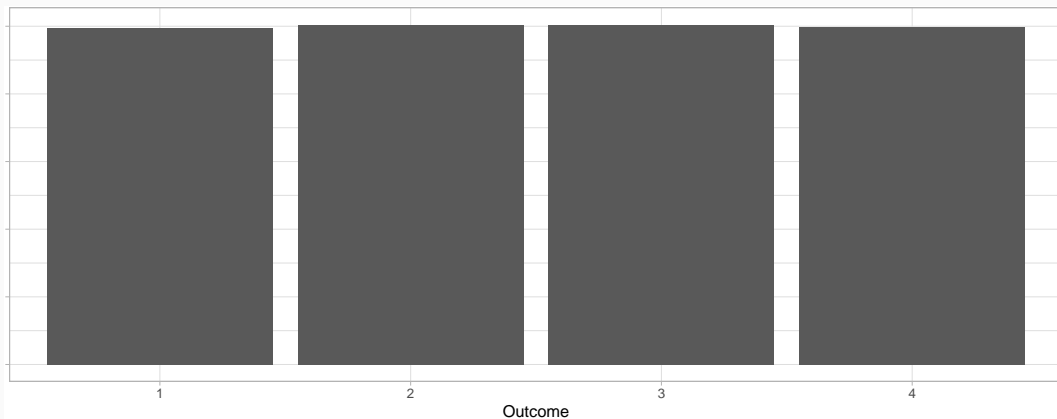
Binomial (always with two possible outcomes):



Multinomial with two possible outcomes:



Multinomial with four possible outcomes:



Model Specification

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

```

# Test1+ Test2+
  prob[4] <- (prev * ((se[1])*(se[2]))) + ((1-prev) * ((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
##      [,1] [,2]
## [1,]  48   4
## [2,]  12  36
```

```
library('runjags')
```

```
Tally <- as.numeric(twoXtwo)
N <- sum(Tally)
```

```
prev <- list(chain1=0.05, chain2=0.95)
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))
```

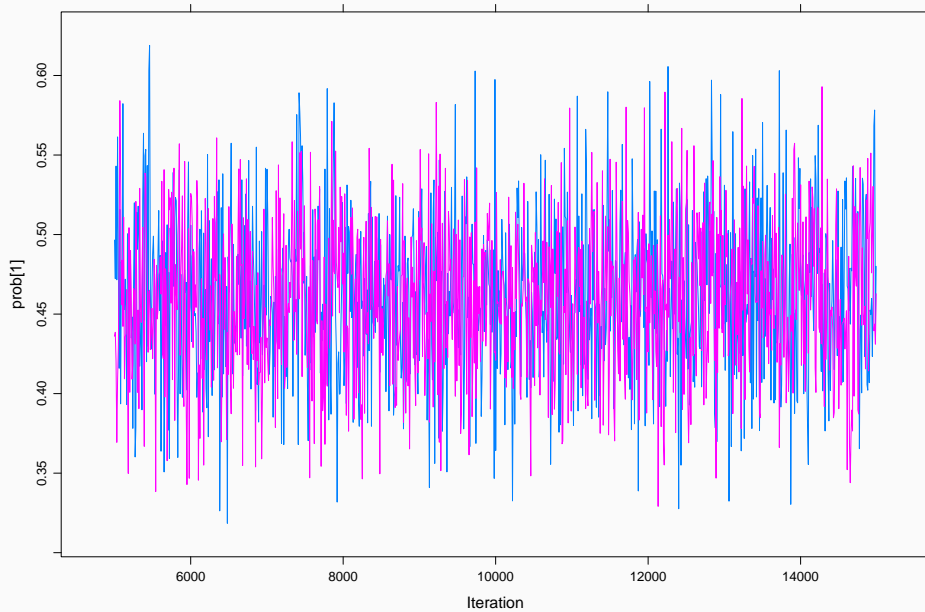
```
results <- run.jags('basic_hw.txt', n.chains=2)
```

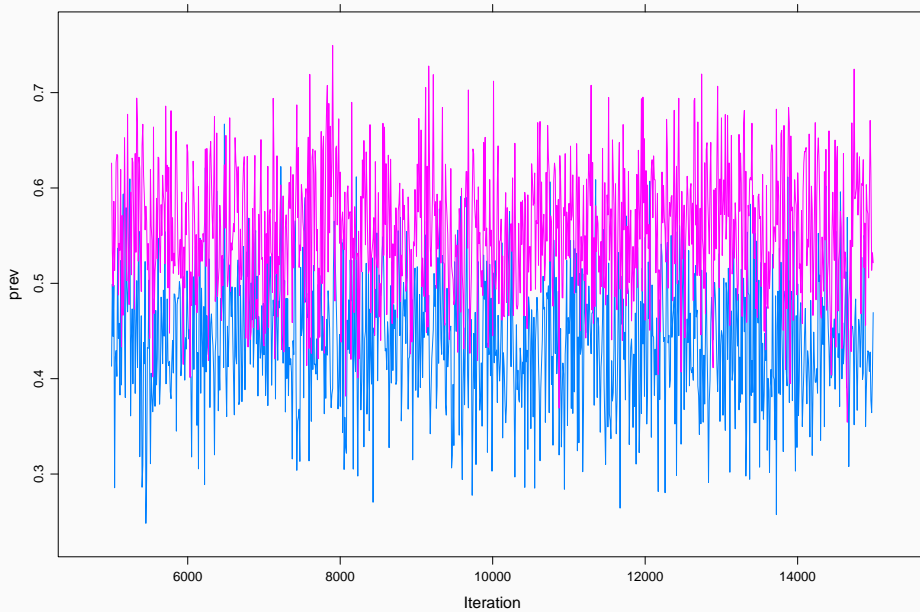
[Remember to check convergence and effective sample size!]

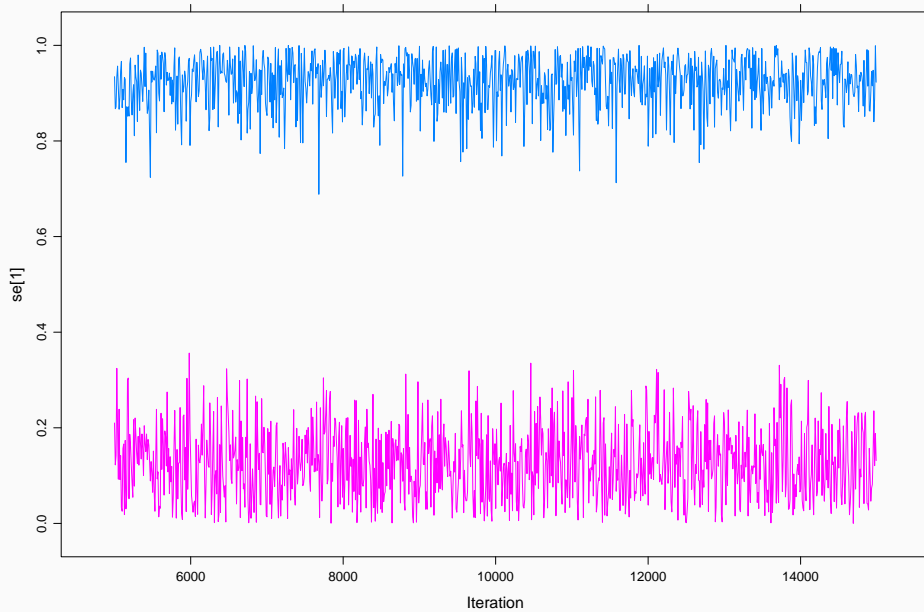
results

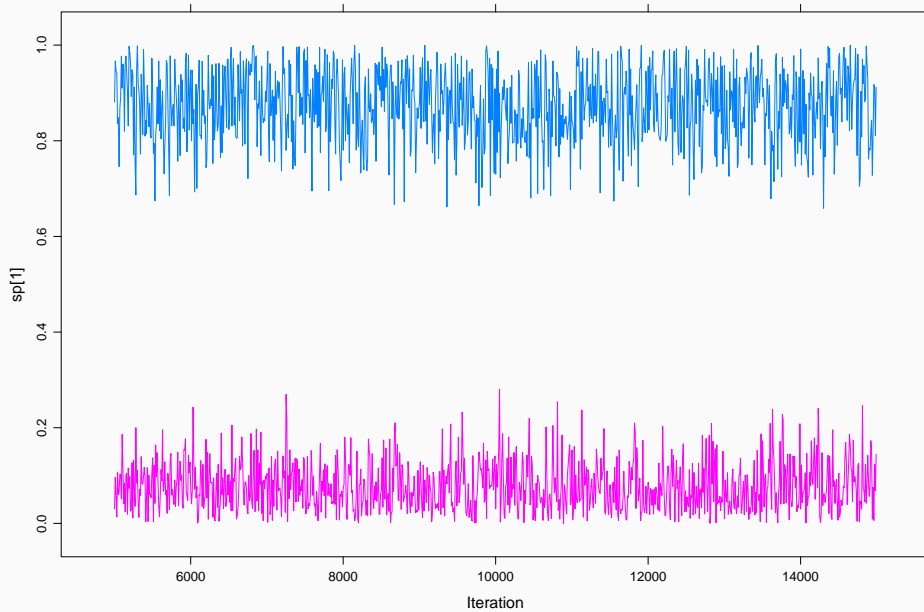
| | Lower95 | Median | Upper95 | SSeff | psrf |
|----------|---------|--------|---------|-------|--------|
| prev | 0.328 | 0.499 | 0.668 | 4250 | 2.288 |
| prob[1] | 0.367 | 0.462 | 0.558 | 13858 | 1.000 |
| prob[2] | 0.072 | 0.132 | 0.202 | 14200 | 1.000 |
| prob[3] | 0.018 | 0.055 | 0.104 | 9602 | 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 |
| deviance | 12.304 | 15.134 | 21.447 | 8838 | 1.000 |

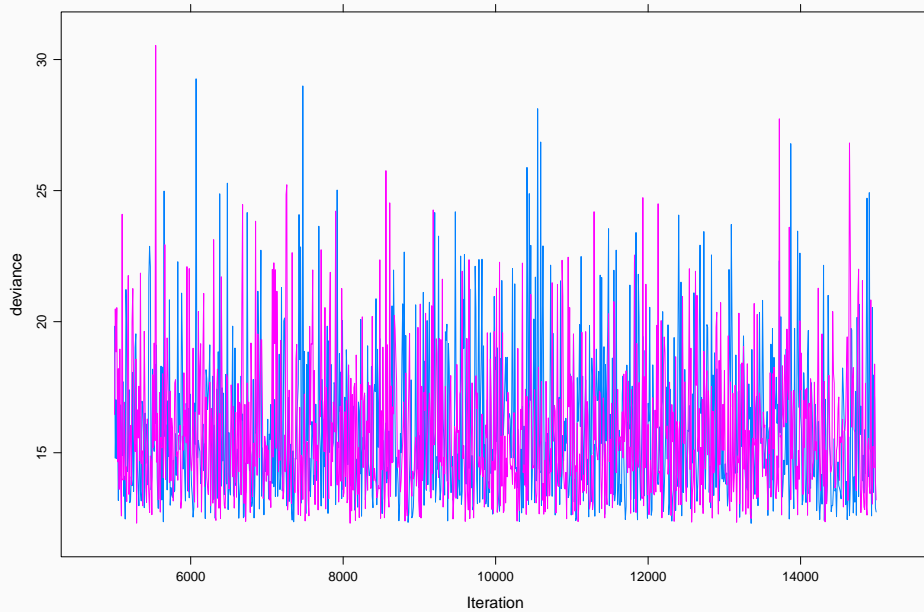
- Does anybody spot a problem?

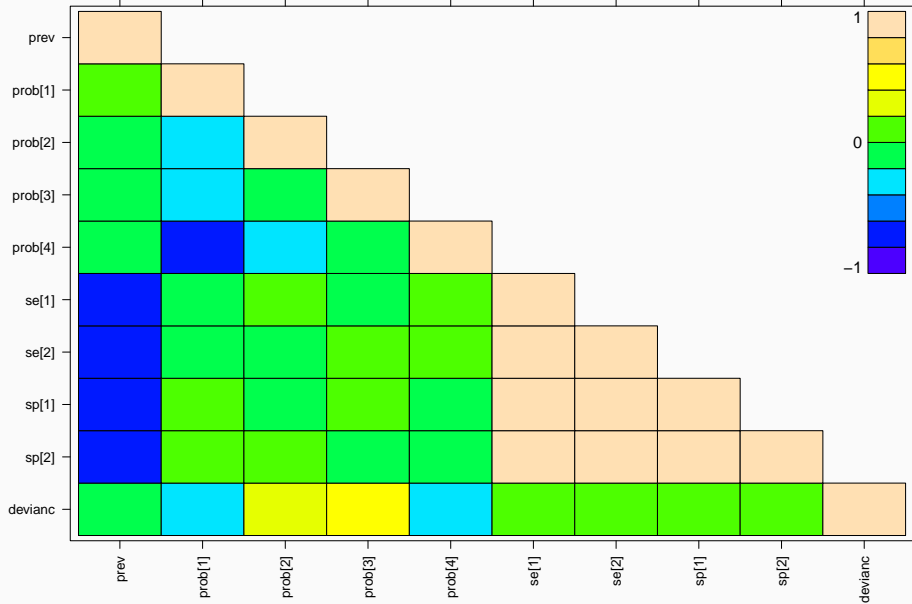












Label Switching

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

We can force $se+sp \geq 1$:

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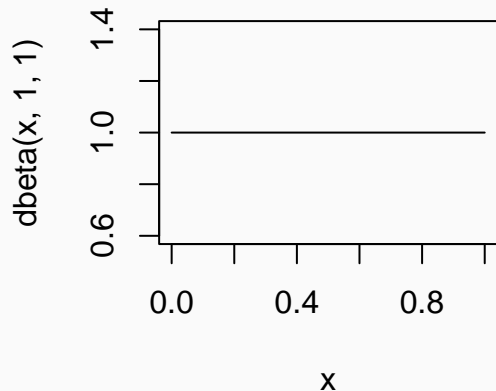
To give the model some information that we expect the test characteristics to be closer to 100% than 0%.

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

Priors

A quick way to see the distribution of a prior:

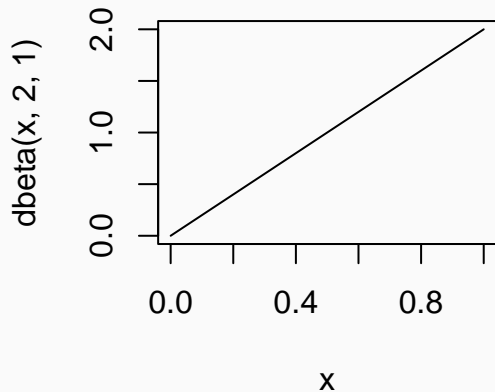
```
curve(dbeta(x, 1, 1), from=0, to=1)
```



```
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
```

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Or more accurately:

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

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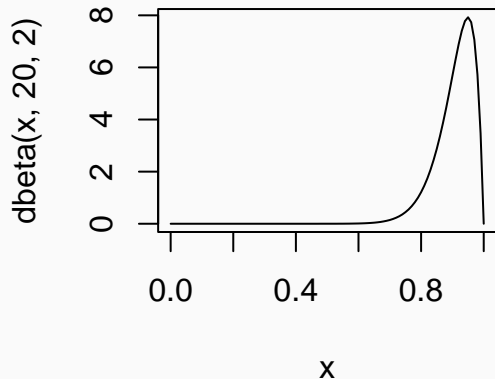
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```

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
```

Choosing a prior

What we want is e.g. $\text{Beta}(20,1)$

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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How can we generate a $\text{Beta}(,)$ 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.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.  
## 0.8906 0.9322 0.9401 0.9395 0.9474 0.9721  
## [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
```

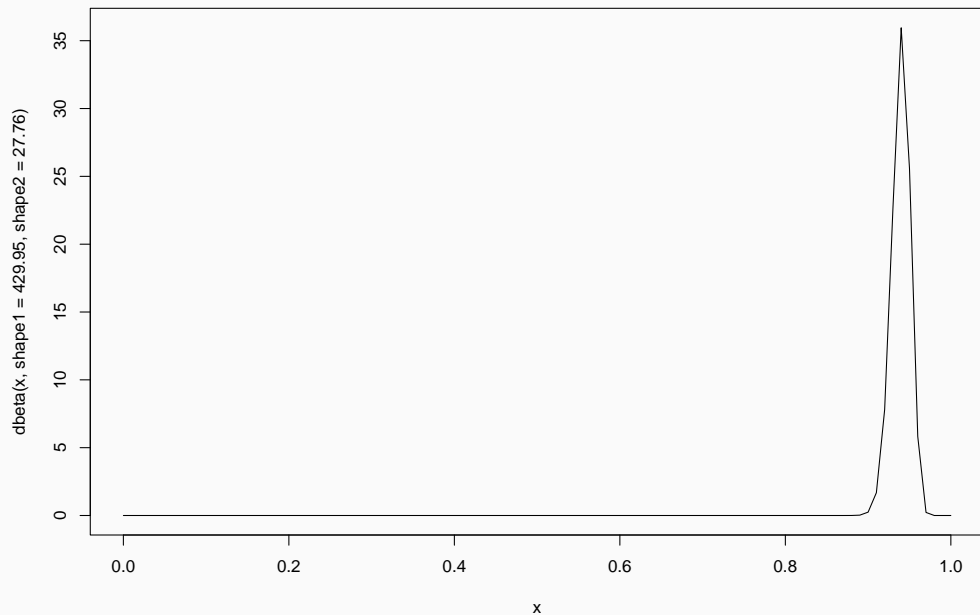
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```

Note: themedian could also be themean

```
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))
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```

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(2022-09-12)
```

```
sensitivity <- c(0.9, 0.6)
```

```
specificity <- c(0.95, 0.9)
```

```
N <- 1000
```

```
prevalence <- 0.5
```

```
data <- tibble(Status = rbinom(N, 1, prevalence)) %>%
```

```
  mutate(Test1 = rbinom(N, 1, sensitivity[1]*Status + (1-specificity[1])*(1-Status))) %>%
```

```
  mutate(Test2 = rbinom(N, 1, sensitivity[2]*Status + (1-specificity[2])*(1-Status)))
```

```
twoXtwo <- with(data, table(Test1, Test2))
```

```
Tally <- as.numeric(twoXtwo)
```

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twoXtwo <- with(data, table(Test1, Test2))
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Tally <- as.numeric(twoXtwo)
```

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 are seemingly magical, but:
 - They typically exhibit high autocorrelation
 - They may not converge, particularly with 1 population (see later!)
 - Need a larger sample for the same effective sample size
- More informative priors for one test will
 - Improve identifiability of the model
 - Affect the posterior inference for the other test!