Session 2

Basic Hui-Walter models

Matt Denwood

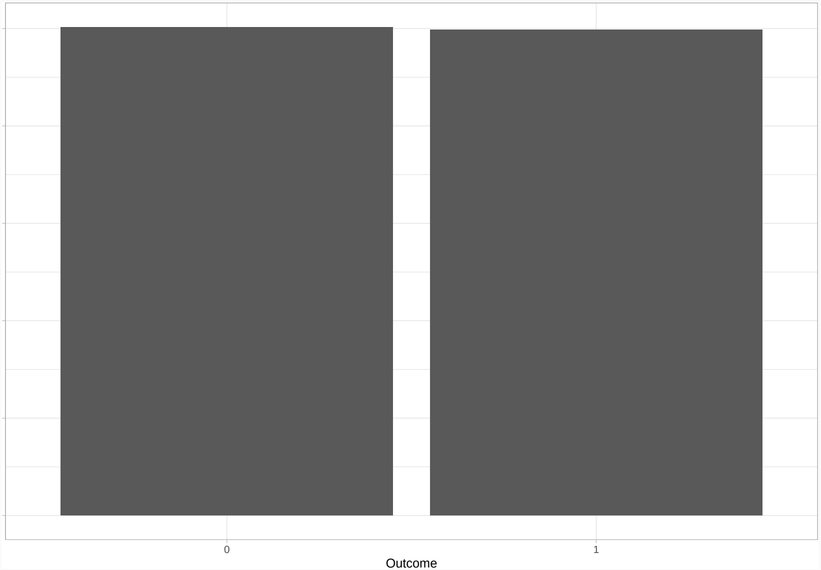
2021-06-28

Hui-Walter Model

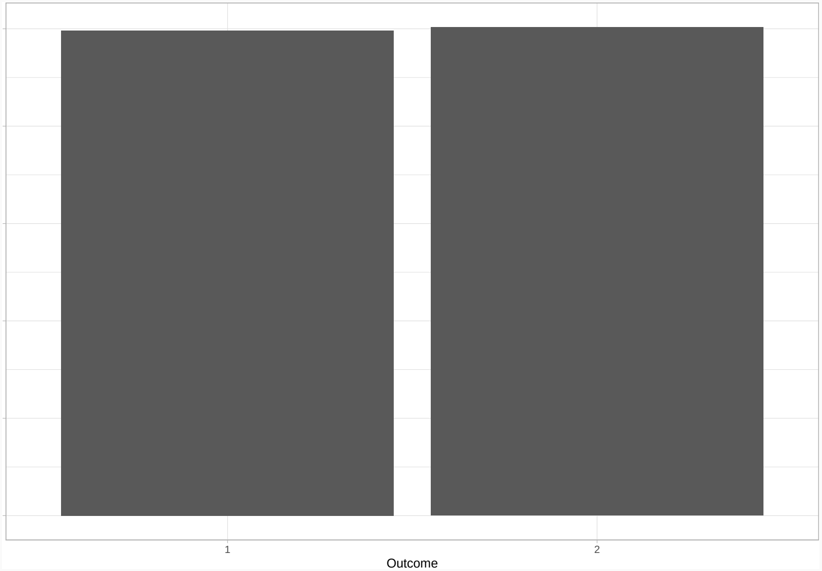
- A particular model formulation that was originally designed for evaluating diagnostic tests in the absence of a gold standard
- Not necessarily (or originally) Bayesian but often implemented using Bayesian MCMC
- But evaluating an imperfect test against another imperfect test is a bit like pulling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

The multinomial distribution

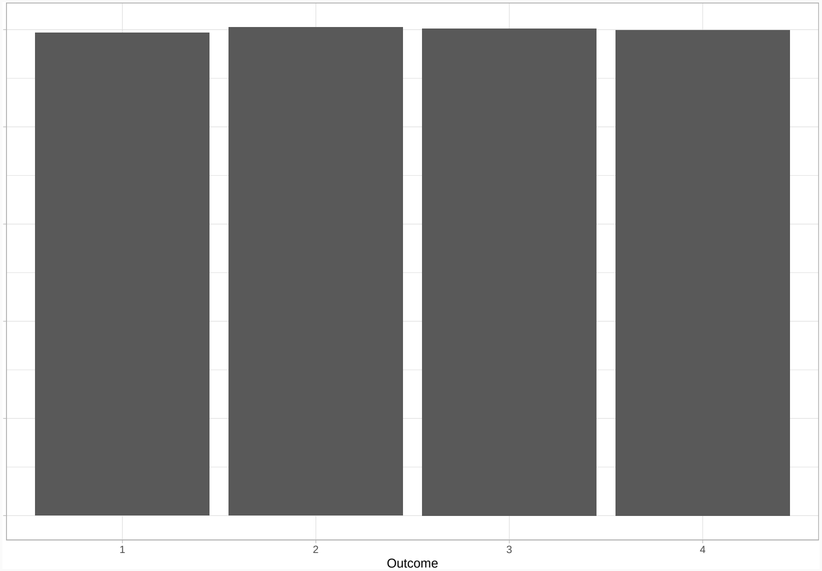
Binomial (always with two possible outcomes):



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
}
```

```r
twoXtwo <- matrix(c(48, 12, 4, 36), ncol=2, nrow=2)
twoXtwo
##      [,1] [,2]
## [1,]   48    4
## [2,]   12   36
```

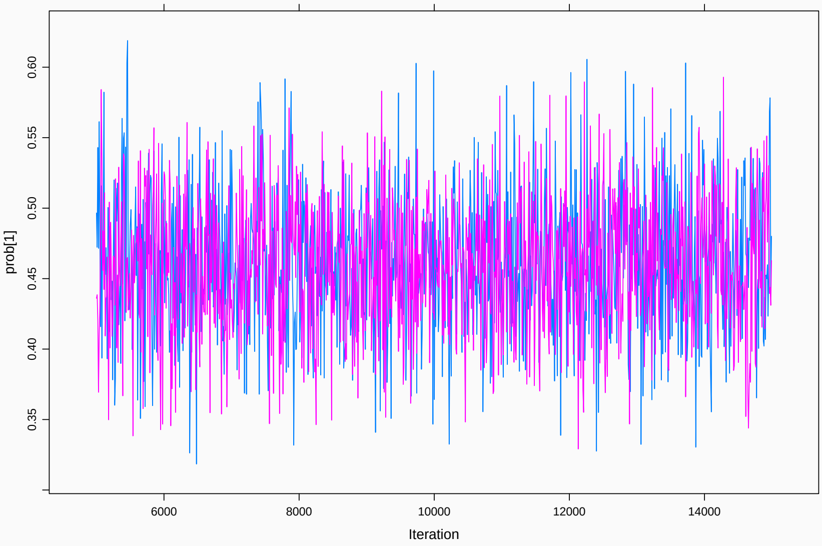
```r
library('runjags')

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)
```

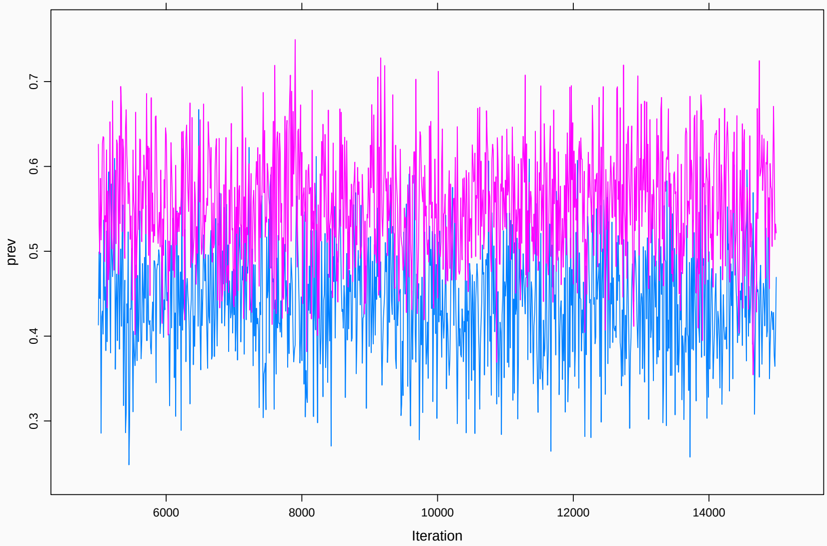
[Remember to check convergence and effective sample size!]

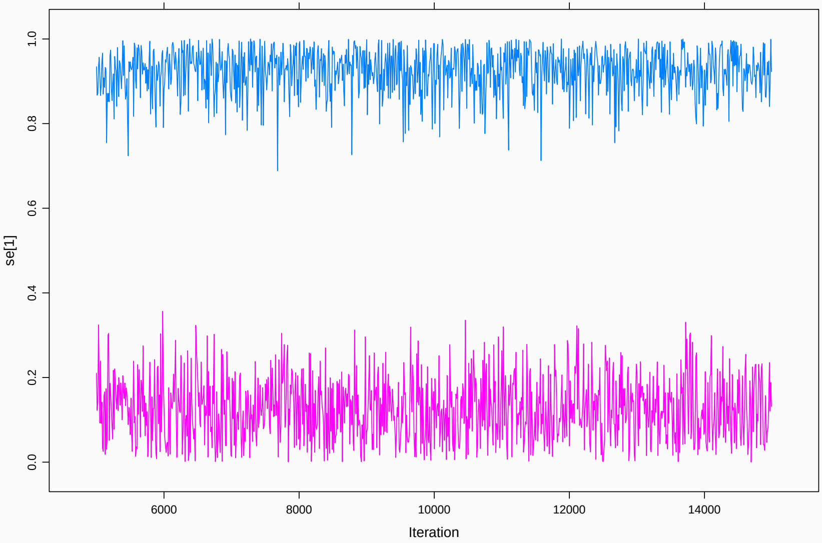
```
results
```

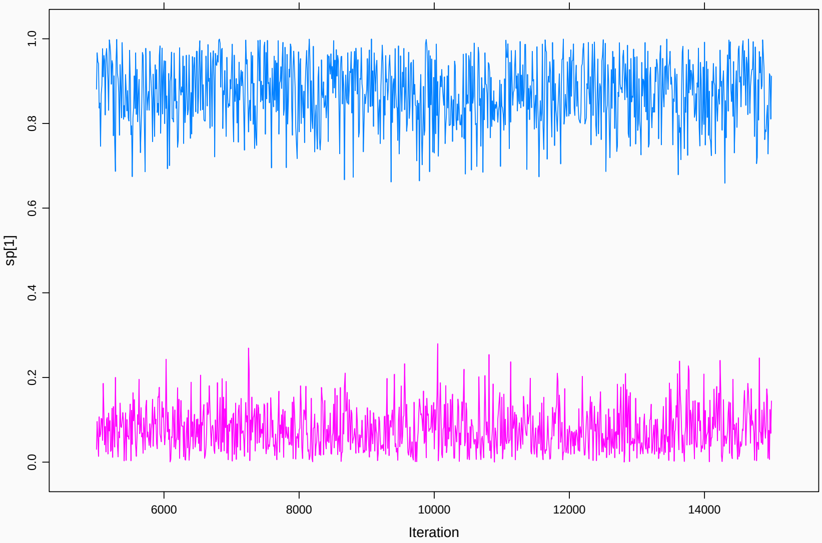
```
## Warning in c("plots", "vars", "mutate", "psrf.target",
## "normalise.mcmc", : 'length(x) = 21 > 1' in coercion to
## 'logical(1)'

## Warning in c("plots", "vars", "mutate", "psrf.target",
## "normalise.mcmc", : 'length(x) = 21 > 1' in coercion to
## 'logical(1)'

## Warning in c("plots", "vars", "mutate", "psrf.target",
## "normalise.mcmc", : 'length(x) = 21 > 1' in coercion to
## 'logical(1)'

## Warning in c("plots", "vars", "mutate", "psrf.target",
## "normalise.mcmc", : 'length(x) = 21 > 1' in coercion to
## 'logical(1)'

## Warning in c("plots", "vars", "mutate", "psrf.target",
## "normalise.mcmc", : 'length(x) = 21 > 1' in coercion to
## 'logical(1)'
```

	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

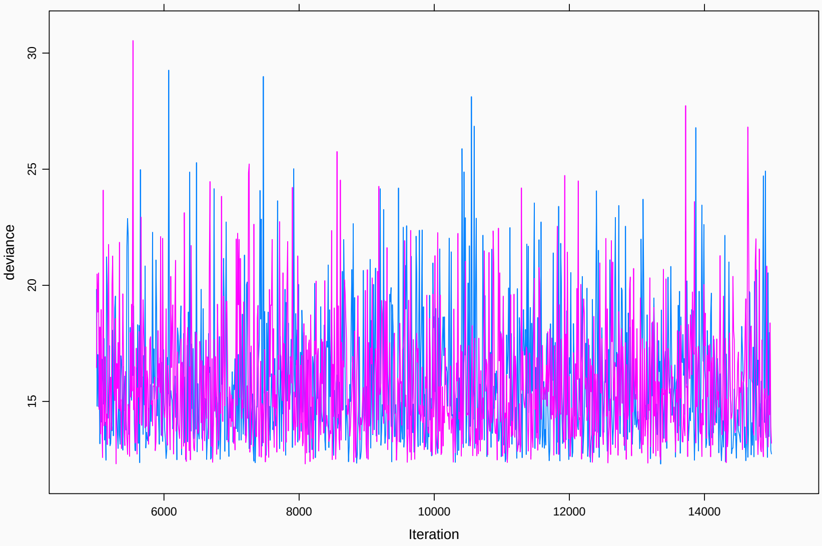

prob[1]
0.35
0.40
0.45
0.50
0.55
0.60
6000
8000
10000
12000
14000
Iteration

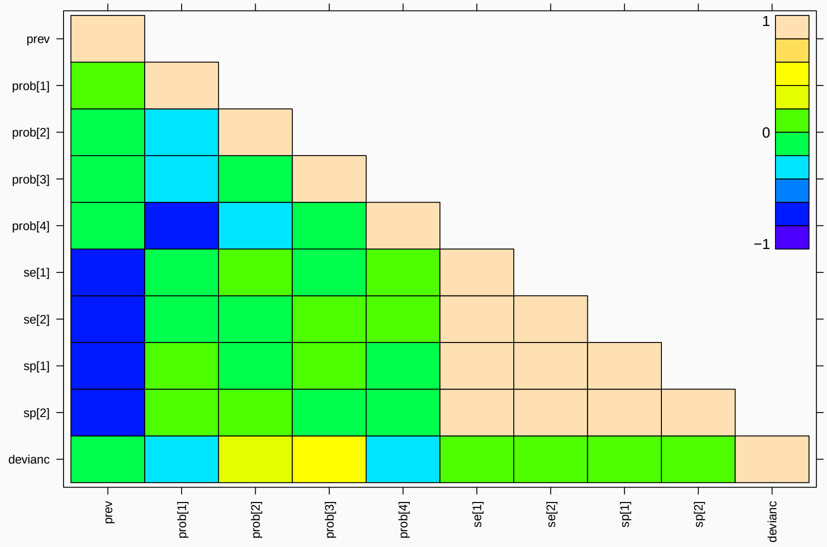

prev
0.3
0.4
0.5
0.6
0.7
Iteration
6000
8000
10000
12000
14000


se[1]
Iteration
0.0
0.2
0.4
0.6
0.8
1.0
6000
8000
10000
12000
14000



sp[1]
1.0
0.8
0.6
0.4
0.2
0.0
6000
8000
10000
12000
14000
Iteration


deviance
30
25
20
15
6000
8000
10000
12000
14000
Iteration


prev
prob[1]
prob[2]
prob[3]
prob[4]
se[1]
se[2]
sp[1]
sp[2]
devianc
1
0
−1

Label Switching

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

Label Switching

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

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

Label Switching

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

- 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%.

Alternatively we can have the weakly informative priors:

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

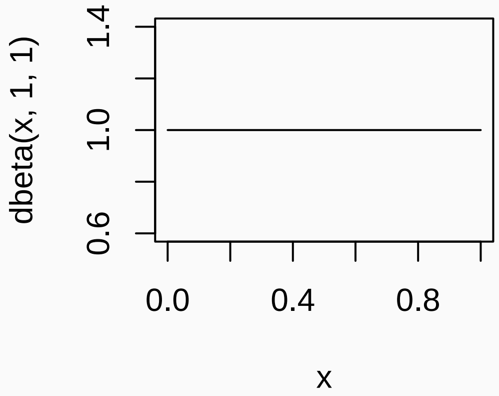
To give the model some information that we expect the test characteristics to be closer to 100% than 0%.

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

Priors

A quick way to see the distribution of a prior:

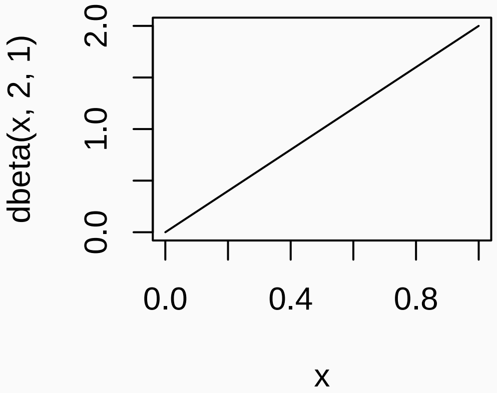
```
curve(dbeta(x, 1, 1), from=0, to=1)
```



```
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?

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



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

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

Or more accurately:

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

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

Or more accurately:

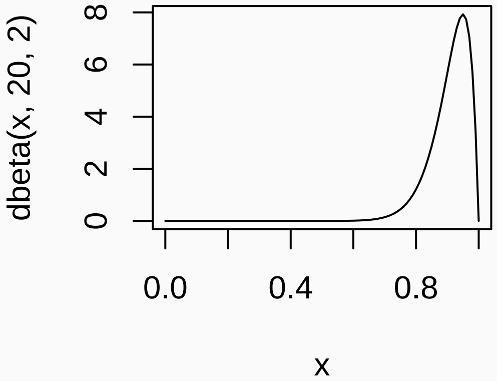
```r
library("TeachingDemos")
hpd(qbeta, shape1=2, shape2=1)
## [1] 0.2236068 1.0000000
```

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
```

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

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"

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.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
```

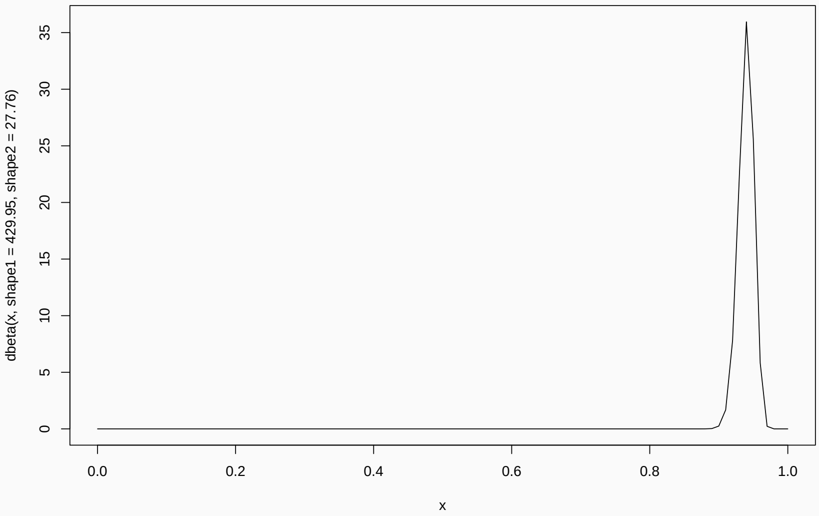
The PriorGen package

“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
```

Note: `themedian` could also be `themean`

```r
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))
```

Initial values

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

```r
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))
```

Let's change these to:

```r
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)

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)
```

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)

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)
```

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!