Hands-on training session 2

Hui-Walter models for diagnostic test evaluation

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Introduction

Overview

Date/time:

- 19th February 2020
- 16.00 - 17.00

Teachers:

- Matt Denwood (presenter)
- Giles Innocent

Recap

- Fitting models using MCMC is easy with JAGS / runjags

- But we must **never forget** to check convergence and effective sample size!

- More complex models become easy to implement
  - For example imperfect diagnostic tests
  - But remember to be realistic about what is possible with your data

Recap

- Fitting models using MCMC is easy with JAGS / runjags
- But we must **never forget** to check convergence and effective sample size!
- More complex models become easy to implement
    - For example imperfect diagnostic tests
    - But remember to be realistic about what is possible with your data

- So how do we extend these models to multiple diagnostic tests?

Session 2a: Hui-Walter models for 2 tests and 1 population

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

```
1  model{
2    Tally ~ dmulti(prob, TotalTests)
3
4    # Test1- Test2-
5      prob[1] <- (prev * ((1-se[1])*(1-se[2]))) + ((1-prev) *
       ↪  ((sp[1])*(sp[2])))
6
7    # Test1+ Test2-
8      prob[2] <- (prev * ((se[1])*(1-se[2]))) + ((1-prev) *
       ↪  ((1-sp[1])*(sp[2])))
9
10   # Test1- Test2+
11     prob[3] <- (prev * ((1-se[1])*(se[2]))) + ((1-prev) *
       ↪  ((sp[1])*(1-sp[2])))
```

```
1
2    # Test1+ Test2+
3      prob[4] <- (prev * ((se[1])*(se[2]))) + ((1-prev) *
     ↪  ((1-sp[1])*(1-sp[2])))
4
5    prev ~ dbeta(1, 1)
6    se[1] ~ dbeta(1, 1)
7    sp[1] ~ dbeta(1, 1)
8    se[2] ~ dbeta(1, 1)
9    sp[2] ~ dbeta(1, 1)
10
11   #data# Tally, TotalTests
12   #monitor# prev, prob, se, sp
13   #inits# prev, se, sp
14  }
```

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

```
1    ##      [,1] [,2]
2    ## [1,]   48    4
3    ## [2,]   12   36
```

```
1    library('runjags')
2
3    Tally <- as.numeric(twoXtwo)
4    TotalTests <- sum(Tally)
5
6    prev <- list(chain1=0.05, chain2=0.95)
7    se <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
8    sp <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
9
10   results <- run.jags('basic_hw.bug', n.chains=2)
```

[Remember to check convergence and effective sample size!]

	Lower95	Median	Upper95	SSeff	psrf
prev	0.308	0.440	0.570	4143	1.000
prob[1]	0.365	0.463	0.557	14078	1.000
prob[2]	0.075	0.132	0.201	13674	1.000
prob[3]	0.018	0.055	0.104	9283	1.001
prob[4]	0.252	0.343	0.434	12907	1.000
se[1]	0.819	0.932	1.000	5362	1.000
se[2]	0.693	0.846	1.000	3438	1.000
sp[1]	0.748	0.878	1.000	3522	1.000
sp[2]	0.861	0.948	1.000	5729	1.001

- Note the wide confidence intervals!

Practicalities

- These models need A LOT of data
  - And/or strong priors for one of the tests
- Convergence is more problematic than usual
- Be **very** vareful with the order of combinations in dmultinom!
- Check your results carefully to ensure they make sense!

Label Switching

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

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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 $>= 1$:

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

Or:

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

But not both!

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

Simulating data

Analysing simulated data is useful to check that we can recover
parameter values.

```
1  se1 <- 0.9; sp1 <- 0.95;
2  se2 <- 0.8; sp2 <- 0.99
3  prevalence <- 0.5; N <- 100
4
5  truestatus <- rbinom(N, 1, prevalence)
6  Test1 <- rbinom(N, 1, (truestatus * se1) + ((1-truestatus) *
   ↪  (1-sp1)))
7  Test2 <- rbinom(N, 1, (truestatus * se2) + ((1-truestatus) *
   ↪  (1-sp2)))
8
9  twoXtwo <- table(Test1, Test2)
10 Tally <- as.numeric(twoXtwo)
```

Can we recover these parameter values?

Modify the code in the Hui Walter model to force tests to be no worse than useless

Simulate data and recover parameters for:

- N=10
- N=100
- N=1000

Optional Exercise

Compare results with the following priors for test 1:

- Sensitivity = 0.9 (95% CI: 0.85 - 0.95)
- Specificity = 0.95 (95%CI: 0.92-0.97)

[These are the same as in session 1]

Session 2b: Hui-Walter models for 2 tests and N populations

Hui-Walter models with multiple populations

- Basically an extension of the single-population model
- Works best with multiple populations each with differing prevalences
  - Including an unexposed population works well
  - BUT be wary of assumptions regarding constant sensitivity/specificity across populations with very different types of infections

Independent intercepts for populations

```
1  model{
2    for(p in 1:Populations){
3      Tally[1:4, p] ~ dmulti(prob[1:4, p], TotalTests[p])
4      # Test1- Test2- Pop1
5        prob[1, p] <- (prev[p] * ((1-se[1])*(1-se[2]))) +
   ↪  ((1-prev[p]) * ((sp[1])*(sp[2])))
6      ## etc ##
7      prev[p] ~ dbeta(1, 1)
8    }
9
10   se[1] ~ dbeta(HPSe[1,1], HPSe[1,2])T(1-sp[1], )
11   sp[1] ~ dbeta(HPSp[1,1], HPSp[1,2])
12   se[2] ~ dbeta(HPSe[2,1], HPSe[2,2])T(1-sp[2], )
13   sp[2] ~ dbeta(HPSp[2,1], HPSp[2,2])
14
15   #data# Tally, TotalTests, Populations, HPSe, HPSp
16   #monitor# prev, prob, se, sp
17   #inits# prev, se, sp
18  }
```

Auto Hui-Walter

We would usually start with individual-level data in a dataframe:

```r
1  se1 <- 0.9; se2 <- 0.8; sp1 <- 0.95; sp2 <- 0.99
2  prevalences <- c(0.1, 0.5, 0.9)
3  N <- 100
4
5  simdata <- data.frame(Population = sample(seq_along(prevalences),
   ↪  N, replace=TRUE))
6  simdata$probability <- prevalences[simdata$Population]
7  simdata$truestatus <- rbinom(N, 1, simdata$probability)
8  simdata$Test1 <- rbinom(N, 1, (simdata$truestatus * se1) +
   ↪  ((1-simdata$truestatus) * (1-sp1)))
9  simdata$Test2 <- rbinom(N, 1, (simdata$truestatus * se2) +
   ↪  ((1-simdata$truestatus) * (1-sp2)))
```

```
1   head(simdata)
```

```
1   ##    Population probability truestatus Test1 Test2
2   ## 1          2         0.5          0     0     0
3   ## 2          3         0.9          1     1     1
4   ## 3          1         0.1          0     0     0
5   ## 4          2         0.5          1     1     1
6   ## 5          3         0.9          1     0     1
7   ## 6          2         0.5          0     0     0
```

[Except that probability and truestatus would not normally be known!]

The model code and data format for an arbitrary number of populations (and tests) can be determined automatically

There is a function (provided in the GitHub repo) that can do this for us:

```r
simdata$Population <- factor(simdata$Population,
  levels=seq_along(prevalences), labels=paste0('Pop_',
  seq_along(prevalences)))

source("autohuiwalter.R")
auto_huiwalter(simdata[,c('Population','Test1','Test2')],
  outfile='autohw.bug')
```

This generates self-contained model/data/initial values etc (ignore covse and covsp for now):

```
1   model{
2
3       ## Observation layer:
4
5       # Complete observations (N=100):
6       for(p in 1:Populations){
7           Tally_RR[1:4,p] ~ dmulti(prob_RR[1:4,p], N_RR[p])
8
9           prob_RR[1:4,p] <- se_prob[1:4,p] + sp_prob[1:4,p]
10      }
11
12
13      ## Observation probabilities:
14
15      for(p in 1:Populations){
16
17          # Probability of observing Test1- Test2- from a true
            ↪  positive::
18          se_prob[1,p] <- prev[p] * ((1-se[1])*(1-se[2]) +covse12)
19          # Probability of observing Test1- Test2- from a true
```

And can be run directly from R:

```
1  results <- run.jags('autohw.bug')
2  results
```

	Lower95	Median	Upper95	SSeff	psrf
se[1]	0.752	0.864	0.957	9578	1.000
se[2]	0.769	0.892	1.000	6664	1.001
sp[1]	0.764	0.870	0.965	8251	1.000
sp[2]	0.926	0.983	1.000	3987	1.000
prev[1]	0.000	0.057	0.165	6384	1.000
prev[2]	0.259	0.427	0.592	11556	1.000
prev[3]	0.698	0.853	0.977	7340	1.000
covse12	0.000	0.000	0.000	NA	NA
covsp12	0.000	0.000	0.000	NA	NA

- Modifying priors must still be done directly in the model file
- The model needs to be re-generated if the data changes
    - But remember that your modified priors will be reset
- There must be a single column for the population (as a factor), and all of the other columns (either factor, logical or numeric) are interpreted as being test results
- The function will soon be included in the runjags package
    - Feedback welcome!

Observation-level model specification

```
1   model{
2
3     for(i in 1:N){
4       Status[i] ~ dcat(prob[i, ])
5
6         prob[i,1] <- (prev[i] * ((1-se[1])*(1-se[2]))) +
7                      ((1-prev[i]) * ((sp[1])*(sp[2])))
8         prob[i,2] <- (prev[i] * ((se[1])*(1-se[2]))) +
9                      ((1-prev[i]) * ((1-sp[1])*(sp[2])))
10        prob[i,3] <- (prev[i] * ((1-se[1])*(se[2]))) +
11                     ((1-prev[i]) * ((sp[1])*(1-sp[2])))
12        prob[i,4] <- (prev[i] * ((se[1])*(se[2]))) +
13                     ((1-prev[i]) * ((1-sp[1])*(1-sp[2])))
14
15        logit(prev[i]) <- intercept +
          ↪ population_effect[Population[i]]
16    }
```

```
1
2    intercept ~ dnorm(0, 0.33)
3    population_effect[1] <- 0
4    for(p in 2:Pops){
5      population_effect[p] ~ dnorm(0, 0.1)
6    }
7    se[1] ~ dbeta(1, 1)T(1-sp[1], )
8    sp[1] ~ dbeta(1, 1)
9    se[2] ~ dbeta(1, 1)T(1-sp[2], )
10   sp[2] ~ dbeta(1, 1)
11
12   #data# Status, N, Population, Pops
13   #monitor# intercept, population_effect, se, sp
14   #inits# intercept, population_effect, se, sp
15 }
```

- The main difference is the prior for prevalence in each population
- We also need to give initial values for `intercept` and `population_effect` rather than `prev`, and tell `run.jags` the data frame from which to extract the data (except `N` and `Pops`):

```
1  intercept <- list(chain1=-1, chain2=1)
2  population_effect <- list(chain1=c(NA, 1, -1), chain2=c(NA, -1,
   ↪  1))
3  se <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
4  sp <- list(chain1=c(0.5,0.99), chain2=c(0.99,0.5))
5
6  simdata$Status <- with(simdata, factor(interaction(Test1, Test2),
   ↪  levels=c('0.0','1.0','0.1','1.1')))
7  N <- nrow(simdata)
8  Pops <- length(levels(simdata$Population))
9  glm_results <- run.jags('glm_hw.bug', n.chains=2, data=simdata)
```

Also like in session 1, the estimates for se/sp should be similar, although this model runs more slowly.

Note: this model could be used as the basis for adding covariates

For a handy way to generate a GLM model see runjags::template.jags

- Look out for integration with autohuiwalter in the near (ish) future. . .

Exercise

Play around with the autohuiwalter function

Notice the model and data and initial values are in a self contained file

Ignore the covse and covsp for now

[There is no particular solution to this exercise!]

Summary

- Estimating sensitivity and specificity is like pulling a rabbit out of a hat
- Multiple populations helps **a lot**
- Strong priors for one of the tests helps even more!
- Make sure you tabulate the data correctly . . . or use the automated model generator!