TB Vaccination

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Data creation

```r
library(data.table)
library(pomp)
library(ggplot2)
library(rstan)

rstan_options(auto_write = TRUE)
options(mc.cores = parallel::detectCores())

#everyone enters on jan 1
#results are for dec 31
newPeople <- data.table(id=1:1000,year=2000,age=1,timeNoVax=0,timeWithVax=0,vaccinated=0,ltbi=0,atbi=0,a

pomp::bake("data/peopleNoVax.RDS",{
  set.seed(4)
  peopleNoVax <- vector("list",length=17)
  peopleNoVax[[1]] <- newPeople[1,][-1,]
  for(i in 1:17){
    # NO VACCINATIONS
    if(i!=1) peopleNoVax[[i]] <- copy(peopleNoVax[[i-1]])
    peopleNoVax[[i]][,age:=age+1]
    peopleNoVax[[i]] <- rbind(peopleNoVax[[i]],newPeople)
    peopleNoVax[[i]][,year:=2000+i]

    N <- nrow(peopleNoVax[[i]])
    peopleNoVax[[i]][sample(1:N,size=round(N*0.050)),ltbi:=1]
    peopleNoVax[[i]][,timeNoVax:=timeNoVax+1]

    Nltbi <- sum(peopleNoVax[[i]]$ltbi)
    peopleNoVax[[i]][atbi==1,ltbi:=0]
    peopleNoVax[[i]][atbi==1,ageAtTB:=age]
    peopleNoVax[[i]][,atbi:=0] # people with ATBI go to the doctor and get cured last year
    peopleNoVax[[i]][sample(which(peopleNoVax[[i]]$ltbi==1),size=round(Nltbi*0.1)),atbi:=1]
  }
  peopleNoVax
}) -> peopleNoVax

pomp::bake("data/peopleWithVax.RDS",{
  set.seed(4)
  peopleWithVax <- vector("list",length=17)
  peopleWithVax[[1]] <- newPeople[1,][-1,]
  for(i in 1:17){
    # WITH VACCINATIONS, BUT STOPPING THEM AFTERWARDS
    if(i!=1) peopleWithVax[[i]] <- copy(peopleWithVax[[i-1]])
    peopleWithVax[[i]][,age:=age+1]
    peopleWithVax[[i]] <- rbind(peopleWithVax[[i]],newPeople)
```

```
    peopleWithVax[[i]][,year:=2000+i]
    N <- nrow(peopleWithVax[[i]])
    if(i>=10){
      peopleWithVax[[i]][sample(1:N,size=round(N*0.050)),ltbi:=1]
      peopleWithVax[[i]][,timeNoVax:=timeNoVax+1]
    } else {
      peopleWithVax[[i]][sample(1:N,size=round(N*0.050)),ltbi:=1]
      peopleWithVax[[i]][,timeWithVax:=timeWithVax+1]
    }

    Nltbi <- sum(peopleWithVax[[i]]$ltbi)
    peopleWithVax[[i]] <- peopleWithVax[[i]][atbi==0]
    peopleWithVax[[i]][atbi==1,ltbi:=0]
    peopleWithVax[[i]][atbi==1,ageAtTB:=age]
    peopleWithVax[[i]][,atbi:=0] # people with ATBI go to the doctor and get cured last year
    peopleWithVax[[i]][sample(which(peopleWithVax[[i]]$ltbi==1),size=round(Nltbi*0.1)),atbi:=1]
  }
  peopleWithVax
}) -> peopleWithVax
```

Detecting LTBI without vaccination

Lets try an easy model, detecting LTBI in unvaccinated people.

We have a Poisson binomial distribution, where the probability of person i not having LTBI is:

$$Pr(Y_i = 0|p, T_i) = (1 - p)^{T_i}$$

And the probability of person i having LTBI is:

$$Pr(Y_i = 1|p, T_i) = 1 - Pr(Y_i = 0|p, T_i)$$

```
stanData <- copy(peopleNoVax[[17]])
stanData[ageAtTB>0,ltbi:=1]
stanData <- stanData[,.(R=.N),by=.(timeNoVax,timeWithVax,ltbi)]
data = list(N=nrow(stanData),
            R=stanData$R,
            y=stanData$ltbi*stanData$R,
            timeNoVax=stanData$timeNoVax)

stan_code = "
data {
  int<lower=0> N;
  int R[N];
  int y[N];
  vector[N] timeNoVax;
}
parameters {
  real<lower=0,upper=0.5> thetaNoVax;
}
model {
  thetaNoVax ~ beta(0.05, 1);
```

```
  for (n in 1:N){
    y[n] ~ binomial(R[n],1-((1-thetaNoVax)^timeNoVax[n]));
  }
}
"
pomp::bake("results/noVaxLTBI.RDS",{
  stan(model_code=stan_code,
               model_name="noVaxLTBI",
               data=data,
               iter=10000, chains=4, init=0, seed=4)
}) -> fit
summary(fit)$summary
```

```
##                      mean       se_mean          sd          2.5%
## thetaNoVax   4.955827e-02 7.385874e-06 0.0006438153   4.830014e-02
## lp__        -9.870137e+03 7.422981e-03 0.7257379087  -9.872220e+03
##                        25%           50%          75%         97.5%
## thetaNoVax   4.912818e-02     0.0495498 4.998994e-02   5.083482e-02
## lp__        -9.870297e+03 -9869.8573114 -9.869680e+03 -9.869630e+03
##                      n_eff       Rhat
## thetaNoVax 7598.342 1.001092
## lp__        9558.790 1.000284
```

Detecting LTBI with vaccination

Lets try a harder model, detecting LTBI when vaccination originally exists, and is then phased out.

We have a Poisson binomial distribution, where the probability of person not i having LTBI is:

$$Pr(Y_i = 0|p_w, p_n, TW_i, TN_i) = (1 - p_w)^{TW_i} \times (1 - p_n)^{TN_i}$$

And the probability of person i having LTBI is:

$$Pr(Y_i = 1|p_w, p_n, TW_i, TN_i) = 1 - Pr(Y_i = 0|p_w, p_n, TW_i, TN_i)$$

```
stanData <- copy(peopleWithVax[[17]])
stanData[ageAtTB>0,ltbi:=1]
stanData <- stanData[,.(R=.N),by=.(timeNoVax,timeWithVax,ltbi)]
data = list(N=nrow(stanData),
            R=stanData$R,
            y=stanData$ltbi*stanData$R,
            timeNoVax=stanData$timeNoVax,
            timeWithVax=stanData$timeWithVax
            )

stan_code = "
data {
  int<lower=0> N;
  int R[N];
  int y[N];
  vector[N] timeNoVax;
  vector[N] timeWithVax;
```

```
}
parameters {
  real<lower=0,upper=0.5> thetaNoVax;
  real<lower=0,upper=0.5> thetaWithVax;
}
model {
  thetaWithVax ~ beta(0.05, 1);
  thetaNoVax ~ beta(0.05, 1);

  for (n in 1:N){
    y[n] ~ binomial(R[n], 1-((1-thetaWithVax)^timeWithVax[n])*((1-thetaNoVax)^timeNoVax[n]));
  }
}
"

pomp::bake("results/withVaxLTBI.RDS",{
  stan(model_code=stan_code,
              model_name="withVaxLTBI",
              data=data,
              iter=10000, chains=4, init=0, seed=4)
}) -> fit
summary(fit)$summary
```

```
##                      mean      se_mean          sd          2.5%
## thetaNoVax    4.023537e-02 1.193584e-05 0.0009857973   3.830165e-02
## thetaWithVax  1.068818e-02 2.480706e-05 0.0020852201   6.601235e-03
## lp__         -7.533216e+03 1.260362e-02 1.0357132482 -7.535946e+03
##                      25%          50%          75%          97.5%
## thetaNoVax    3.957005e-02 4.023253e-02 4.089666e-02   4.218267e-02
## thetaWithVax  9.275577e-03 1.069942e-02 1.207870e-02   1.482700e-02
## lp__         -7.533628e+03 -7.532893e+03 -7.532477e+03 -7.532201e+03
##                   n_eff     Rhat
## thetaNoVax    6821.334 1.000376
## thetaWithVax 7065.667 1.000509
## lp__          6752.873 1.000107
```

Detecting ATBI without vaccination

Lets try a hard model, detecting ATBI in unvaccinated people. ATBI is incident TB and detected in the year that it occurs.

We have a Poisson binomial distribution, where the probability of person i not having ATBI is:

$$Pr(ATBI_i = 0|p_{\text{atbi}}, p_{\text{ltbi}}, T_i) = Pr(LTBI_i = 0|p_{\text{atbi}}, p_{\text{ltbi}}, T_i) + Pr(LTBI_i = 1 \text{ without activation}|p_{\text{atbi}}, p_{\text{ltbi}}, T_i)$$

$$= (1 - p_{\text{ltbi}})^{T_i} + \Sigma_{t=1}^{t=T_i} Pr(\text{Incident LTBI infection at time } t, \text{ no activation})$$

$$= (1 - p_{\text{ltbi}})^{T_i} + \Sigma_{t=1}^{t=T_i}(1 - p_{\text{ltbi}})^{t-1} \times p_{\text{ltbi}} \times (1 - p_{\text{atbi}})^{T_i - t + 1}$$

And the probability of person i having LTBI is:

$$Pr(ATBI_i = 1|p_{\text{atbi}}, p_{\text{ltbi}}, T_i) = 1 - Pr(ATBI_i = 0|p_{\text{atbi}}, p_{\text{ltbi}}, T_i)$$

```r
cases <- list()
for(i in 1:14){
  cases[[i]] <- peopleNoVax[[i]][atbi==1]
}
cases <- rbindlist(cases)
controls <- peopleNoVax[[17]][atbi==0 & ageAtTB==0]
cases
```

```
##         id year age timeNoVax timeWithVax vaccinated ltbi atbi ageAtTB
##    1: 496 2001   1         1           0          0    1    1       0
##    2: 850 2001   1         1           0          0    1    1       0
##    3: 860 2001   1         1           0          0    1    1       0
##    4: 865 2001   1         1           0          0    1    1       0
##    5: 942 2001   1         1           0          0    1    1       0
##   ---
## 1929: 803 2014   2         2           0          0    1    1       0
## 1930: 903 2014   2         2           0          0    1    1       0
## 1931: 983 2014   2         2           0          0    1    1       0
## 1932: 692 2014   1         1           0          0    1    1       0
## 1933: 719 2014   1         1           0          0    1    1       0
```

```r
cases[,ageAtTB:=0]
controls[,ageAtTB:=0]

stanData <- rbind(controls[,.(R=.N),by=.(timeNoVax,timeWithVax,atbi)],cases[,.(R=.N),by=.(timeNoVax,time
data = list(N=nrow(stanData),
            R=stanData$R,
            y=stanData$atbi*stanData$R,
            timeNoVax=stanData$timeNoVax)

stan_code = "
data {
  int<lower=0> N;
  int timeNoVax[N];
  int R[N];
  int y[N];
}
parameters {
  real<lower=0,upper=0.5> ltbiNoVax;
  real<lower=0,upper=0.5> atbiNoVax;
}
model {
real ps;
  ltbiNoVax ~ beta(0.05, 1);
  atbiNoVax ~ beta(0.05, 1);

  {
    int replicates;
    int personTime;
    real prob_ltbi_no_tb;

    for (n in 1:N){
      prob_ltbi_no_tb = (1-ltbiNoVax)^timeNoVax[n];
      personTime = timeNoVax[n];
```

```
      replicates = R[n];

      for(t in 1:personTime){
         prob_ltbi_no_tb = prob_ltbi_no_tb + ((1-ltbiNoVax)^(t-1))*ltbiNoVax*((1-atbiNoVax)^(personTime-
      }

      y[n] ~ binomial(R[n], 1-prob_ltbi_no_tb);
    }
  }
}

"

pomp::bake("results/noVaxATBI.RDS",{
  stan(model_code=stan_code,
            model_name="noVaxATBI",
            data=data,
            iter=10000, chains=4, init=0, seed=4)
}) -> fit
summary(fit)$summary
```

```
##                   mean     se_mean        sd          2.5%          25%
## ltbiNoVax    0.1377507 0.14723672 0.2082359  1.680510e-02  1.735962e-02
## atbiNoVax    0.3782281 0.14725045 0.2082572  1.703154e-02  3.665443e-01
## lp__      -6737.5267238 0.01304701 1.0621821 -6.740365e+03 -6.737951e+03
##                    50%          75%          97.5%         n_eff        Rhat
## ltbiNoVax    0.0176942    0.1357622      0.4998091      2.000225  262.854545
## atbiNoVax    0.4982943    0.4993698      0.4999491      2.000262  166.143214
## lp__     -6737.1952609 -6736.7598293 -6736.4833275   6627.899108   1.000793
```