TB Vaccination

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Data creation

We construct three datasets: `peopleNoVax`, `peopleWithVax`, and `peopleTB`.

`peopleNoVax` is a dataset that spans 17 years. Each year, 10000 people are added to it. Each year, a person has a 5% annual risk of being infected with LTBI. Once a person is infected with LTBI, they have a 2.5% annual risk of being infected with ATBI.

`peopleWithVax` is a dataset that spans 17 years. Each year, 10000 people are added to it. For the first 10 years, a person has a 5% annual risk of being infected with LTBI. Subsequently they have a 2.5% annual risk of being infected with LTBI. Once a person is infected with LTBI, they have a 2.5% annual risk of being infected with ATBI.

`peopleTB` is a dataset that spans 17 years. Each year, 10000 people are added to it. Each year, a person has a 5% annual risk of being infected with ATBI.

```
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=1:10000,year=2000,age=1,timeNoVax=0,timeWithVax=0,vaccinated=0,ltbi=0,atbi=0

if(FALSE){
  file.remove("data/peopleNoVax.RDS")
  file.remove("data/peopleWithVax.RDS")
  file.remove("data/peopleTB.RDS")
  file.remove("results/noVaxLTBI.RDS")
  file.remove("results/withVaxLTBI.RDS")
  file.remove("results/ATBI.RDS")
  file.remove("results/noVaxATBI.RDS")
}

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]

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

    Nltbi <- sum(peopleWithVax[[i]]$ltbi==1 & peopleWithVax[[i]]$ageAtTB==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]]$ltbi==1 & peopleWithVax[[i]]$ageAtTB==0),size=rou
  }
  peopleWithVax
}) -> peopleWithVax

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

    peopleTB[[i]][,timeNoVax:=timeNoVax+1]

    peopleTB[[i]][,atbi:=0] # people with ATBI go to the doctor and get cured last year
```

```
    N <- sum(peopleTB[[i]]$ageAtTB==0)
    peopleTB[[i]][sample(which(peopleTB[[i]]$ageAtTB==0),size=round(N*0.05)),atbi:=1]
    peopleTB[[i]][atbi==1,ageAtTB:=age]
  }
  peopleTB
}) -> peopleTB
```

Detecting LTBI without vaccination

We will try to model the annual risk of LTBI in the dataset `peopleNoVax`, where LTBI is only measured at the end of the dataset (i.e. after 17 years).

For a person i, who has spent T_i years at risk, their probability of not having LTBI is:

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

And their corresponding probability of having LTBI is:

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

```
stanData <- copy(peopleNoVax[[17]])
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  4.996660e-02 2.324218e-06 0.0002020466  4.957123e-02
## lp__       -9.904536e+04 8.661057e-03 0.7103202531 -9.904734e+04
##                      25%           50%           75%         97.5%
## thetaNoVax  4.982977e-02  4.996657e-02  5.010166e-02  5.036368e-02
## lp__       -9.904552e+04 -9.904509e+04 -9.904492e+04 -9.904487e+04
##                 n_eff     Rhat
## thetaNoVax 7556.996 1.000427
## lp__       6726.151 1.000013
```

Detecting LTBI with vaccination

We will try to model the annual risk of LTBI in the dataset `peopleWithVax`, where LTBI is only measured at the end of the dataset (i.e. after 17 years), however, the risk of LTBI has changed due to the cessation of vaccination.

For a person i, who has spent TW_i years at risk when vaccinations were occurring, and TN_i years at risk when no vaccinations were occuring, their probability of not 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 <- 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    5.010210e-02 4.030704e-06 0.0003370411  4.944198e-02
## thetaWithVax  2.529498e-02 8.147072e-06 0.0006895297  2.394224e-02
## lp__         -9.863473e+04 1.153416e-02 1.0014517034 -9.863745e+04
##                         25%           50%           75%         97.5%
## thetaNoVax    4.987414e-02  5.010327e-02  5.032944e-02  5.076345e-02
## thetaWithVax  2.482474e-02  2.530020e-02  2.576694e-02  2.662851e-02
## lp__         -9.863512e+04 -9.863443e+04 -9.863402e+04 -9.863375e+04
##                   n_eff     Rhat
## thetaNoVax   6992.041 1.000197
## thetaWithVax 7163.130 1.000373
## lp__         7538.559 1.000411
```

Detecting straight ATBI without vaccination

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

cases <- cases[,.(R=.N),by=.(timeNoVax,timeWithVax,atbi)]
controls <- controls[,.(R=.N),by=.(timeNoVax,timeWithVax,atbi)]

stanData <- rbind(controls,cases)
#stanData <- cases
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> atbiNoVax;
}
model {
  atbiNoVax ~ beta(0.05, 1);

  {
    int replicates;
    int personTime;
    real prob_no_atbi;
    real prob_atbi_in_year;

    for (n in 1:N){
      prob_no_atbi = (1-atbiNoVax)^timeNoVax[n];
      prob_atbi_in_year = (1-atbiNoVax)^(timeNoVax[n]-1)*atbiNoVax;
      replicates = R[n];

      if( y[n]==0 ){
        target += R[n]*log(prob_no_atbi);
      } else {
        target += binomial_lpmf(y[n] | R[n], prob_atbi_in_year);
      }

    }
  }
}

"

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

```
##                    mean      se_mean           sd          2.5%
## atbiNoVax  5.000067e-02 2.451507e-06 0.0002021065  4.960702e-02
## lp__      -2.360101e+05 8.109510e-03 0.7305285894 -2.360122e+05
##                     25%           50%           75%         97.5%    n_eff
## atbiNoVax  4.986375e-02  4.999907e-02  5.013366e-02  5.040290e-02 6796.637
## lp__      -2.360103e+05 -2.360098e+05 -2.360097e+05 -2.360096e+05 8114.938
##                Rhat
## atbiNoVax 1.000848
## lp__      1.000348
```

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:

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

```
pl <- 0.05
pa <- 0.05
TS <- ts <- 17
t <- 1:ts

s1 <- (1-pl)^ts # NO LTBI IN FIRST 10 YRS
s2 <- ((1-pl)^t)*pl*((1-pa)^(ts-t+1)) # LTBI + NO ATBI IN FIRST 10 YRS
sum(s1)+sum(s2)
```

```
## [1] 0.7557525
```

```
f <- c() # ATBI IN FIRST 10 YRS
for(i in 1:TS){
  ts <- i
  t <- 1:ts
  f[i] <- sum(((1-pl)^t)*pl*((1-pa)^(ts-t))*pa)
}
sum(f)
```

```
## [1] 0.2151535
```

```
sum(s1)+sum(s2)
```

```
## [1] 0.7557525
```

```
sum(f)+sum(s1)+sum(s2)
```

```
## [1] 0.970906
```

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

cases <- cases[,.(R=.N),by=.(timeNoVax,timeWithVax,atbi)]
controls <- controls[,.(R=.N),by=.(timeNoVax,timeWithVax,atbi)]

stanData <- rbind(controls,cases)
stanData[timeNoVax==1]
```

```
##    timeNoVax timeWithVax atbi    R
## 1:         1           0    0 9987
## 2:         1           0    1  193
```

```r
#stanData <- cases
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_no_atbi;
    real prob_atbi_in_year;
    real survival;

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

      personTime = timeNoVax[n];
      replicates = R[n];
      if( y[n]>0 ){
        prob_atbi_in_year = 0;
        for(t in 1:personTime){
           prob_atbi_in_year = prob_atbi_in_year + ((1-ltbiNoVax)^(t-1))*ltbiNoVax*((1-atbiNoVax)^(pers
        }
        target += R[n]*log(prob_atbi_in_year);
      } else {
        survival=0;
        for(q in 1:personTime){
          prob_atbi_in_year = 0;
          for(t in 1:q){
             prob_atbi_in_year = prob_atbi_in_year + ((1-ltbiNoVax)^(t-1))*ltbiNoVax*((1-atbiNoVax)^(q-
          }
          survival=survival+prob_atbi_in_year;
        }
        target += R[n]*log(1-survival);
      }
    }
  }
```

```
}

"

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%
## ltbiNoVax  3.642509e-02 0.0002101232 0.01052668  2.152884e-02
## atbiNoVax  3.695687e-02 0.0002106053 0.01058756  2.154914e-02
## lp__      -5.365239e+04 0.0116597673 0.85470352 -5.365478e+04
##                     25%           50%           75%         97.5%    n_eff
## ltbiNoVax  2.771922e-02  3.466684e-02  4.405016e-02  5.885932e-02 2509.777
## atbiNoVax  2.807275e-02  3.541144e-02  4.460931e-02  5.902365e-02 2527.278
## lp__      -5.365267e+04 -5.365209e+04 -5.365180e+04 -5.365168e+04 5373.425
##                Rhat
## ltbiNoVax 1.000399
## atbiNoVax 1.000206
## lp__      1.000301
```