PooledInfRate

Brad J. Biggerstaff

2022-05-03

Introduction

Applications of *pooled* or *group testing* include two general aims: estimation of the population individual-level probability of positivity; and cost-efficient schemes of identification of positive individuals. The *PooledInfRate* package is concerned only with estimation applications. Functionality includes point and interval estimation of a proportion from binary (*positive* / *negative*) samples that have been pooled or grouped before assessment of positivity, which is determined only at the pool level. Estimation applications date back at least to Chiang and Reeves (1962), who developed asymptotic likelihood-based methods for pools of equal size in application to estimation of virus infection in mosquito collections. These authors also extended their analyses to two different pool sizes under a simplifying assumption to make the mathematical development tractable, but they were constrained from further extension by computational tools available at the time. The package name "PooledInfRate" is based on the use of "infection rate" in entomological applications and follows the author's development of the Microsoft Excel™ (Microsoft Corporation (n.d.)) add-in of the same name (https://www.cdc.gov/westnile/resourcepages/mosqSurvSoft.html).

The computational functionality of routines in this package for point estimation are the standard maximum likelihood estimate (MLE); the bias corrected estimate based on the methods of Gart (see Gart (1991)), as implemented by Hepworth (2005); the bias-reduced estimate based on Firth's correction (see Firth (1993) and Hepworth and Biggerstaff (2017)); and the traditional *minimum infection rate* (MIR) estimate used in entomology. Confidence intervals (CI) included are the score, skewness-corrected score, and bias-and-skewness-corrected score intervals following Gart (Gart (1991)) (see Hepworth 2005); the interval obtained by inverting the likelihood ratio test; the Wald interval; and an interval based on the MIR (see Hepworth (2005) and Biggerstaff (2008) for evaluations of these intervals). Also included are routines to compute point and CI estimates for the differences of proportions estimated from pooled samples, as detailed in Biggerstaff (2008).

To complement applications involving entomological surveillance for pathogens in disease vectors such as mosquitoes, the package provides routines to compute the *Vector Index* (Fauver et al. (2015)), a measure incorporating both population size or density and of vector infection prevalences ("infection rate"). Its computation is outlined below.

The methods mentioned so far assume that perfect tests or assays are used in testing the pools for "positivity." Extending this, functionality is included for point estimation when using an imperfect test with known sensitivity and specificity. Following Hepworth and Biggerstaff (2021), methods based both on Firth's correction (Firth (1993)) and on the standard MLE are included. There is currently a lack of theoretical work in this area for CI estimation in the case of imperfect tests, so none are presently included; future theoretical and corresponding package development in this area is anticipated.

Data structure

A variety of data structures may be used with estimation functions in *PooledInfRate*. As with R functionality in general, either individual `vector` objects or `data.frame` objects supply the data to the functions. The data must have at a minimum a recording of the number of positive pools, `x`, and the pool sizes, `m`, corresponding to those pools. A variable giving the number of pools, `n`, corresponding to those records may also be specified,

and when none is given, the values for `x` are assumed to be `0/1` and each `n` is assumed to be `1` by default. To carry out the same analyses for multiple groups at once, a grouping variable, either as a factor or a numeric vector that will be treated as a factor may be used. Illustrations for acceptable data formats are

```
x <- c(1,0,0,0)
m <- c(50,25,10,5)
```

and

```
ex1.dat <- data.frame(Pos = c(1,0,0,0), PoolSize = c(50,25,10,5))
ex1.dat
#>   Pos PoolSize
#> 1   1       50
#> 2   0       25
#> 3   0       10
#> 4   0        5
```

and

```
ex2.dat <- data.frame(Pos = c(2,1,0,1),
                      PoolSize = c(50,25,10,5),
                      NumPools = c(10,10,5,2),
                      Location = c("A","A","B","B"))
ex2.dat
#>   Pos PoolSize NumPools Location
#> 1   2       50       10        A
#> 2   1       25       10        A
#> 3   0       10        5        B
#> 4   1        5        2        B
```

and if there are different groups, say `Species`,

```
mosq.dat <- data.frame(Zone = c(1,1,2,2, 1,1,1,2,2, 1,1,2),
                       Species = rep(c("Culex pipiens","Culex tarsalis", "Culex quinquefaciatus"),
                                     c(4,5,3)),
                       Pos = c(1,0,0,1, 1,0,1,0,0, 0,1,0),
                       PoolSize = c(100,50,25,5, 200,100,50,25,10, 25,10,5),
                       Nights = c(5,5,3,3,5,5,5,3,3,5,5,3))
mosq.dat
#>    Zone               Species Pos PoolSize Nights
#> 1     1         Culex pipiens   1      100      5
#> 2     1         Culex pipiens   0       50      5
#> 3     2         Culex pipiens   0       25      3
#> 4     2         Culex pipiens   1        5      3
#> 5     1        Culex tarsalis   1      200      5
#> 6     1        Culex tarsalis   0      100      5
#> 7     1        Culex tarsalis   1       50      5
#> 8     2        Culex tarsalis   0       25      3
#> 9     2        Culex tarsalis   0       10      3
```

```
#> 10    1 Culex quinquefaciatus   0       25      5
#> 11    1 Culex quinquefaciatus   1       10      5
#> 12    2 Culex quinquefaciatus   0        5      3
```

Other data may naturally be included in data frames, and we will include these data sets and needed extensions of these data sets in certain examples below.

One-sample estimation (perfect test)

Function interfaces

The functions `pooledBin` ("pooled binary") provides the interface to both point and CI estimates, and there are both `default` and `formula` interfaces provided. The function `pIR` ("pooled infection rate") is a copy of `pooledBin` with a slightly different, and shorter name merely for convenience; in all the examples below, `pooledBin` and `pIR` can be used interchangeably. For single samples, the default methods are straightforward, with printed output being the point estimate and computed CI:

```
library(PooledInfRate)

pooledBin(x,m)
#>            P        Lower      Upper
#> 1 0.01257911 0.0007261606 0.07828496

with(ex2.dat, pooledBin(Pos, PoolSize, NumPools))
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295

with(mosq.dat, pIR(Pos, PoolSize))
#>            P       Lower      Upper
#> 1 0.01204838 0.004787647 0.02894633
```

When there is a grouping variable, as with the `mosq.dat` data set, an optional `group=` may be used to obtain individual results for each group:

```
pooledBin(Pos~PoolSize|Species,mosq.dat)
#>                 Species           P       Lower      Upper
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702
with(mosq.dat, pooledBin(Pos, PoolSize, group = Species))
#>                 Species           P       Lower      Upper
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702
```

The `formula` interface in R provides a convenient, generally consistent interface to modeling function expressions, and this interface has been adapted to ease use of the functions in `PooledInfRate`. As an example,

```
pooledBin(Pos ~ PoolSize, mosq.dat) # the second function argument is data=
#>            P       Lower      Upper
#> 1 0.01204838 0.004787647 0.02894633
```

Specification of a grouping variable is made using a vertical bar (`|`) in the formula:

```
pooledBin(Pos ~ PoolSize | Species, mosq.dat) # the second function argument is data=
#>                 Species           P       Lower      Upper
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702
```

This example data set `mosq.dat` does not have a "number of pools" variable, so the above evaluations do not need this specified, since by default this is a vector of `1`s. Use of formula interface to specify such a variable is required for the `ex2.dat` data set, however, and this is accommodated using "special" functions `m()` and `n()` (echoing the mathematical exposition in Hepworth and Biggerstaff (2017)). As an illustration, the following incorporates this variable:

```
pooledBin(Pos ~ m(PoolSize) + n(NumPools), ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
```

Because the pool size variable (`m()`) is *required* for any pooled estimation (and because it is easier when there is less typing), the `m()` specification is optional, so that

```
pooledBin(Pos ~ PoolSize + n(NumPools), ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
```

gives the same result. Further, since the `m()` and `n()` identifiers communicate to the fitting functions the roles of the variables, the order does not matter in the formula, so that the following all provide the same result:

```
pooledBin(Pos ~ m(PoolSize) + n(NumPools), ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
pooledBin(Pos ~   PoolSize  + n(NumPools), ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
pooledBin(Pos ~ n(NumPools) + m(PoolSize), ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
pooledBin(Pos ~ n(NumPools) +   PoolSize , ex2.dat)
#>             P       Lower      Upper
#> 1 0.005239825 0.001732855 0.01262295
```

Specification of the grouping variable is as above:

```
pooledBin(Pos ~ PoolSize + n(NumPools) | Location, ex2.dat)
#>   Location           P        Lower      Upper
#> 1        A 0.004242141 0.0011295580 0.01162209
#> 2        B 0.016119609 0.0009872462 0.07615332

# and use the (significant) 'digits' argument of print() to make for easier reading
print(pooledBin(Pos ~ PoolSize + n(NumPools) | Location, ex2.dat), digits = 3)
#>   Location       P    Lower  Upper
#> 1        A 0.00424 0.001130 0.0116
#> 2        B 0.01612 0.000987 0.0762
```

Access results

Beginning with package version 1.1, returned objects of class `pooledBin`/`pIR` can be accessed like data frames, using both `[.` and `$` extractor methods. Examples are

```
# original call
pooledBin(Pos ~ PoolSize | Zone, mosq.dat)
#>   Zone          P        Lower      Upper
#> 1    1 0.01115089 0.0039063581 0.03115368
#> 2    2 0.01294475 0.0008649086 0.06035809

# just Zone 2
pooledBin(Pos ~ PoolSize | Zone, mosq.dat)[2,]
#>   Zone          P        Lower      Upper
#> 1    2 0.01294475 0.0008649086 0.06035809

# just P
pooledBin(Pos ~ PoolSize | Zone, mosq.dat)[,"P"]
#> [1] 0.01115089 0.01294475
pooledBin(Pos ~ PoolSize | Zone, mosq.dat)$P
#> [1] 0.01115089 0.01294475

# assign and just CIs
pb.out <-  pooledBin(Pos ~ PoolSize | Zone, mosq.dat)
pb.out[,3:4]
#>          Lower      Upper
#> 1 0.0039063581 0.03115368
#> 2 0.0008649086 0.06035809
pb.out[c("Lower","Upper")]
#>          Lower      Upper
#> 1 0.0039063581 0.03115368
#> 2 0.0008649086 0.06035809
```

Summary and plot methods

To print out more detailed information on the estimation results, `summary` methods are provided. The resulting output contains details including the estimates themselves, estimation methods used, the total numbers of positive pools, the total number of individuals, and the total number of pools.

```
pir.combined.out <- pIR(Pos ~ PoolSize + n(NumPools), ex2.dat)
summary(pir.combined.out)
#>
#> Estimation of Binomial Proportion for Pooled Data
#>
#> Call: pIR(x = Pos ~ PoolSize + n(NumPools), data = ex2.dat)
#>
#> Point estimator        : Firth's Correction
#> CI method              : Skew-Corrected Score (Gart)
#> Confidence coefficient : 95%
#>
#>      PointEst       Lower      Upper Scale   N NumPools NumPosPools
#> 1 0.005239825 0.001732855 0.01262295     1 810       27           4

pir.location.out <- pIR(Pos ~ PoolSize + n(NumPools) | Location, ex2.dat)
summary(pir.location.out)
#>
#> Estimation of Binomial Proportion for Pooled Data
#>
#> Call: pIR(x = Pos ~ PoolSize + n(NumPools) | Location, data = ex2.dat)
#>
#> Point estimator        : Firth's Correction
#> CI method              : Skew-Corrected Score (Gart)
#> Confidence coefficient : 95%
#>
#>   Location    PointEst        Lower      Upper Scale   N NumPools NumPosPools
#> 1        A 0.004242141 0.0011295580 0.01162209     1 750       20           3
#> 2        B 0.016119609 0.0009872462 0.07615332     1  60        7           1

pir.mosq.out <- pIR(Pos ~ PoolSize | Species, mosq.dat)
print(summary(pir.mosq.out), digits=3)
#>
#> Estimation of Binomial Proportion for Pooled Data
#>
#> Call: pIR(x = Pos ~ PoolSize | Species, data = mosq.dat)
#>
#> Point estimator        : Firth's Correction
#> CI method              : Skew-Corrected Score (Gart)
#> Confidence coefficient : 95%
#>
#>                 Species    PointEst       Lower      Upper Scale   N NumPools
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548     1 180        4
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341     1 385        5
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702     1  40        3
#>   NumPosPools
#> 1           2
```

```
#> 2           2
#> 3           1
```

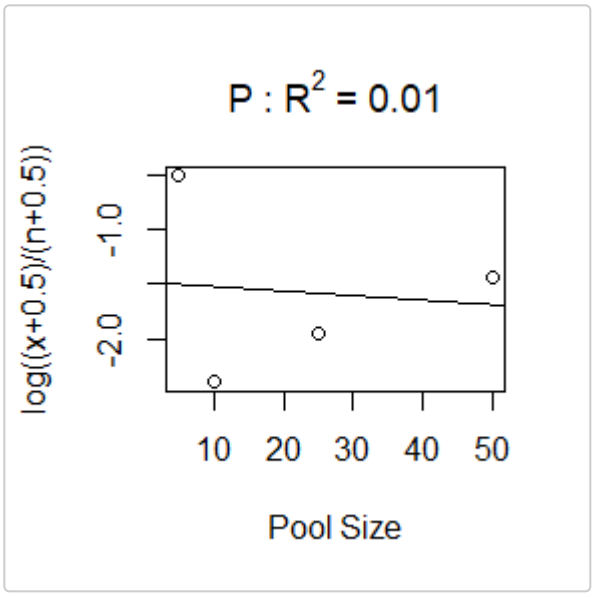
Further, the `summary` methods have an argument `simple` that can be used to return the detailed results as a data frame. To return the summary data frame, set `simple = TRUE` (default is `simple = FALSE`):

```
summary(pir.mosq.out)
#>
#> Estimation of Binomial Proportion for Pooled Data
#>
#> Call: pIR(x = Pos ~ PoolSize | Species, data = mosq.dat)
#>
#> Point estimator        : Firth's Correction
#> CI method              : Skew-Corrected Score (Gart)
#> Confidence coefficient : 95%
#>
#>                 Species    PointEst       Lower      Upper Scale   N NumPools
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548     1 180        4
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341     1 385        5
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702     1  40        3
#>   NumPosPools
#> 1           2
#> 2           2
#> 3           1

summary(pir.mosq.out, simple = TRUE)
#>                 Species    PointEst       Lower      Upper Scale   N NumPools
#> 1         Culex pipiens 0.013370328 0.002778929 0.05287548     1 180        4
#> 2        Culex tarsalis 0.006729853 0.001286999 0.02790341     1 385        5
#> 3 Culex quinquefaciatus 0.022851731 0.001595994 0.10915702     1  40        3
#>   NumPosPools
#> 1           2
#> 2           2
#> 3           1
```

A plot method of the diagnostic tool described by Chen and Swallow (1990) to evaluate the suitability of the binomial model is available.

```
plot(pir.combined.out)
```



and this also works when there are groups (though adjustment of the `layout` parameter may be required).

Missing data

Records with missing data on any of the variables used in the function calls are removed for estimation. For example,

```
x.na <- c(1,0,0,NA,1)
m.na <- c(10,50,25,10,10)

pooledBin(x.na, m.na)
#>            P       Lower      Upper
#> 1 0.01978085 0.004603328 0.06052267

summary(pooledBin(x.na,m.na))
#>
#> Estimation of Binomial Proportion for Pooled Data
#>
#> Call: pooledBin(x = x.na, m = m.na)
#>
#> Point estimator        : Firth's Correction
#> CI method              : Skew-Corrected Score (Gart)
#> Confidence coefficient : 95%
#>
#>     PointEst       Lower      Upper Scale  N NumPools NumPosPools
#> 1 0.01978085 0.004603328 0.06052267     1 95        4           2
```

and this is also true using the `formula` method interface.

Options

Estimation methods

As described above, there are several point and CI methods available, and the choices are specified with the `pt.method` and `ci.method` parameters.

```
pIR(Pos ~ PoolSize, mosq.dat, pt.method = "firth", ci.method = "skew-score") # the defaults
#>            P       Lower      Upper
#> 1 0.01204838 0.004787647 0.02894633
pIR(Pos ~ PoolSize, mosq.dat, pt.method = "gart", ci.method = "score")
#>            P       Lower      Upper
#> 1 0.01177663 0.005035411 0.02742267
pIR(Pos ~ PoolSize, mosq.dat, pt.method = "mle", ci.method = "wald")
#>            P        Lower      Upper
#> 1 0.01349436 0.0003415766 0.02664713
# specification of "mir" for either sets the other to "mir"
pIR(Pos ~ PoolSize, mosq.dat, pt.method = "mir", ci.method = "mir")
#>             P       Lower      Upper
#> 1 0.008264463 0.001050471 0.01547845
```

Also, note that when all pool sizes are 1, then there is no pooling, so the standard Wilson score interval is returned, and `pt.method` is set to **"`mle`"** and `ci.method` is set to "score" in this case.

For users of the Microsoft Excel™ PooledInfRate add-in: *the default point estimation method for this R package is Firth's method, which is different than the one in Excel™, which is Gart's method.* This is because Firth's method was shown in Hepworth and Biggerstaff (2017) to perform generally better.

Scale

Estimated values for the prevalence are often very small in pooled testing applications, so a `scale` parameter is provided to facilitate reading output (`scale = 1000` is often used in entomological applications). Results are printed using the specified scale, both with the standard `print` and `summary` methods.

```
pIR(Pos ~ PoolSize, mosq.dat) # default scale = 1
#>            P       Lower      Upper
#> 1 0.01204838 0.004787647 0.02894633
pIR(Pos ~ PoolSize, mosq.dat, scale=1000)
#>          P    Lower    Upper Scale
#> 1 12.04838 4.787647 28.94633  1000
```

Confidence level and algorithm precision

To set the desired confidence level for CIs, the parameter `alpha`, with default `alpha = 0.05`, is used, with the confidence level equal to `100(1-alpha)%`.

The estimation methods used require iterative numerical computation, and the parameter `tol` (for "tolerance") is used to indicate how precisely estimation is required; the default is `.Machine$double.eps^0.5`.

Differences of proportions (two-sample)

The “equal” pair of functions `pooledBinDiff` / `pIRDiff` compute confidence intervals for differences of proportions, as detailed in Biggerstaff (2008). The interface for the default call is an expansion of the one-sample call: `pooledBin(x1,m1,x2,m2)`. For the formula interface, these functions are exactly the same as for the one-sample case, only a `group` variable is in this case *required*. Estimates of differences and CIs for all pairwise differences of the levels of the grouping variable are computed, and a `summary` method provides detail, including individual group estimates. Examples follow.

```
x1 <- c(1,0,0,0)
m1 <- c(100,50,25,10)
x2 <- c(1,1,0,0)
m2 <- c(50,40,30,20)
pooledBinDiff(x1,m1,x2,m2)
#>          Diff       Lower      Upper
#> 1 -0.01243859 -0.07141933 0.02351318

n1 <- c(10,20,30,40)
n2 <- rep(1,4)
pooledBinDiff(x1,m1,x2,m2,n1,n2)
#>         Diff       Lower        Upper
#> 1 -0.0182197 -0.07731165 -0.003005032

pooledBinDiff(Pos ~ PoolSize + n(NumPools) | Location, ex2.dat)
#>   Comparison        Diff       Lower       Upper
#> 1      A - B -0.01187747 -0.07192221 0.006954489

mdiff.out <- pIRDiff(Pos ~ PoolSize | Species, mosq.dat, scale=1000) # scale for easier
         interpretation

# Print fewer digits for easier reading
print(summary(mdiff.out), digits = 3)
#>
#> Estimation of Difference of Binomial Proportions for Pooled Data
#>
#> Call: pooledBinDiff(x = Pos ~ PoolSize | Species, data = mosq.dat, scale = 1000)
#>
#> Point estimator: Firth's Correction
#> CI method: Skew-Corrected Score (Gart)
#>
#>                               Comparison       Diff      Lower    Upper Scale
#> 1         Culex pipiens - Culex tarsalis   6.640475  -16.88456 45.69876  1000
#> 2  Culex pipiens - Culex quinquefaciatus  -9.481404  -94.13364 37.59940  1000
#> 3 Culex tarsalis - Culex quinquefaciatus -16.121878 -101.22793 16.10307  1000
#>
#> Group summaries:
#>
#>                 Species         P    Lower     Upper Scale Individuals Pools
#> 1         Culex pipiens 13.370328 2.778929  52.87548  1000         180     4
#> 2        Culex tarsalis  6.729853 1.286999  27.90341  1000         385     5
#> 3 Culex quinquefaciatus 22.851731 1.595994 109.15702  1000          40     3
#>   Positive Pools
#> 1              2
```

```
#> 2              2
#> 3              1

# as with the one-sample results, one can return the detailed summary as a data frame
summary(mdiff.out, simple = TRUE)
#>                 Species         P    Lower     Upper Scale Individuals Pools
#> 1         Culex pipiens 13.370328 2.778929  52.87548  1000         180     4
#> 2        Culex tarsalis  6.729853 1.286999  27.90341  1000         385     5
#> 3 Culex quinquefaciatus 22.851731 1.595994 109.15702  1000          40     3
#>   Positive Pools
#> 1              2
#> 2              2
#> 3              1
```

Access results

Beginning with package version 1.1, returned objects of class `pooledBinDiff`/`pIRDiff` can be accessed like data frames, using both `[.` and `$` extractor methods. Examples are

```
# original call
pooledBinDiff(Pos ~ PoolSize | Species, mosq.dat)
#>                              Comparison         Diff       Lower      Upper
#> 1         Culex pipiens - Culex tarsalis  0.006640475 -0.01688456 0.04569876
#> 2  Culex pipiens - Culex quinquefaciatus -0.009481404 -0.09413364 0.03759940
#> 3 Culex tarsalis - Culex quinquefaciatus -0.016121878 -0.10122793 0.01610307

# just the Culex pipiens - Culex quinquefaciatus comparison
pooledBinDiff(Pos ~ PoolSize | Species, mosq.dat)[2,]
#>                              Comparison         Diff       Lower     Upper
#> 1 Culex pipiens - Culex quinquefaciatus -0.009481404 -0.09413364 0.0375994

# just the differences
pooledBinDiff(Pos ~ PoolSize | Species, mosq.dat)[,"Diff"]
#> [1]  0.006640475 -0.009481404 -0.016121878
pooledBinDiff(Pos ~ PoolSize | Species, mosq.dat)$Diff
#> [1]  0.006640475 -0.009481404 -0.016121878

# assign and just CIs
pbd.out <-  pooledBinDiff(Pos ~ PoolSize | Species, mosq.dat)
pbd.out[,3:4]
#>         Lower      Upper
#> 1 -0.01688456 0.04569876
#> 2 -0.09413364 0.03759940
#> 3 -0.10122793 0.01610307
pbd.out[c("Lower","Upper")]
#>         Lower      Upper
#> 1 -0.01688456 0.04569876
#> 2 -0.09413364 0.03759940
#> 3 -0.10122793 0.01610307
```

Missing data

As with the one-sample functions, records with missing data on any of the variables used in the function calls are removed for estimation.

Options

Options `scale`, `alpha`, and `tol` are the same as for the one-sample functions.

Vector Index

In mosquito-borne disease surveillance, the *Vector Index* (*VI*) is a measure used in evaluating risk of infection in a human population, often to aid decisions on community interventions, such as area-wide vector mosquito abatement (see, e.g., Fauver et al. (2015)). Primarily used in mosquito-borne disease surveillance, the *VI* is the sum of the products of a measure of population "size" and the infection rate over vector species. Because this definition requires the specification of "vector species" over which to perform these computations, an additional variable is needed beyond those specified in the `pooledBin` / `pIR` functions above. This is accommodated in the default and formula interfaces as follows.

Field collections of mosquitoes used for such surveillance can result in a wide range of data configurations, and the individuals that contribute to the population size measures may not be the same as those used in estimating the infection rate (prevalence).

All and only individuals in pools contribute to population size measure

The most straightforward data situation is when all individuals in the collection are used in both components, the population measure and the infection rate estimate. Data in this case may be formatted as above, say with the example `mosq.dat` data set and the example just shown.

For the default interface, a `vector` parameter is used, so using the `mosq.dat` example data set above,

```
vi.out <- with(mosq.dat, vectorIndex(Pos,PoolSize,vector=Species)) # or use VI()
vi.out
#>         VI
#> 1 1.424553
```

and there is a `summary` method available to provide detail:

```
summary(vi.out)
#>
#> Call:  VI(x = Pos, m = PoolSize, vector = Species)
#>
#> Prevalence estimate method : firth
#> Use non-tested individuals in abundance estimate : FALSE
#> Use tested pools' pool sizes in abundance estimate : TRUE
#>
#>         VI
#> 1 1.424553
```

```
#>
#> Detail by group and vector:
#>
#>                  Species    Avg N           P (Avg N) * P
#> 1         Culex pipiens 45.00000 0.013370328   0.6016647
#> 2        Culex tarsalis 77.00000 0.006729853   0.5181987
#> 3 Culex quinquefaciatus 13.33333 0.022851731   0.3046898
```

Using the formula interface, the vector species variable is specified after a forward slash symbol (`/`), written after the main part of the formula:

```
vectorIndex(Pos ~ PoolSize / Species, mosq.dat)
#>         VI
#> 1 1.424553
```

Computing the *VI* by groups is available using the same interface as groups for the one- and two-sample functions. Note, however, that using the `formula` interface, the group variable **must** come before the slash (`/`) indicating the vector species variable. Examples using the `mosq.dat` data set are

```
with(mosq.dat, vectorIndex(Pos, PoolSize, vector=Species, group=Zone))
#>   Zone        VI
#> 1    1 1.8732123
#> 2    2 0.3963581

VI(Pos ~ PoolSize | Zone / Species, mosq.dat)
#>   Zone        VI
#> 1    1 1.8732123
#> 2    2 0.3963581
```

The above calculations assume that collection effort is constant (i.e., represents the same time in the environment for collection) across traps. Mosquito trapping effort, often expressed “per trap night” to reflect the duration between retrievals of specimens, may differ by trap, however, and when pools are trap-specific or contain individuals caught in traps using the same effort, a trapping effort variable provided to specify this. For the `default` interface, a `trap.time` variable is specified, while for the `formula` interface the variable is included *after* the `Vector` variable, separated by a colon (`:`). Examples using the `mosq.dat` data set are

```
with(mosq.dat, vectorIndex(Pos, PoolSize, vector=Species, trap.time = Nights, group=Zone))
#>   Zone        VI
#> 1    1 0.3746425
#> 2    2 0.1321194

VI(Pos ~ PoolSize | Zone / Species:Nights, mosq.dat)
#>   Zone        VI
#> 1    1 0.3746425
#> 2    2 0.1321194
```

An external data set (only) is used to provide the population size measure

It may be that field collections used for computing the measure of population size differ, or that individual mosquitoes are pooled from different traps possibly representing different collection efforts. If the counts of mosquitoes caught are aggregated separately by collection effort, and otherwise some or all of them are pooled for testing and infection rate estimation, these pieces of data may be combined in computing the *VI* by formatting the data using missing values (`NA`) for the `response` data to be used in computing the population size measure. This is possible in both the `default` and `formula` interfaces by correct specification of the `n.use.traps` and `n.use.na` parameter options, which indicate what subsets of the data are to be used to compute the population measure (reflected in the "`n.use.`" in the parameter names).

As an example data set, the document *West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control* of the US Centers for Disease Control and Prevention, Division of Vector-Borne Diseases, contains this example data set in Appendix 2 (written here in aggregated form):

```
pools.dat <- data.frame(Species=c("Cx. tarsalis","Cx. pipiens"),
                        Pos=c(1,1),
                        PoolSize=c(50,50),
                        NumPools=c(6,5))
pools.dat
#>        Species Pos PoolSize NumPools
#> 1 Cx. tarsalis   1       50        6
#> 2  Cx. pipiens   1       50        5
```

In addition to the pool testing data, the total number of *Cx. tarsalis* caught for 6 traps was 442, and the total number of *Cx. pipiens* caught for 6 traps was 233. To include this information in the `pools.dat` data set, (1) enter missing values (`NA`) for the "number positive" variable (`x`); (2) treat the "pool size" variable (`m`) as the collection count; and augment "number of pools" variable (`n`) as `1`.

```
traps.dat <- data.frame(Species = c("Cx. tarsalis","Cx. pipiens"),
                        Pos = c(NA,NA),
                        PoolSize=c(442, 233),
                        NumPools=c(1,1)) # note NumPools should be 1 for each entry
vi.dat <- rbind(pools.dat, traps.dat)
vi.dat
#>        Species Pos PoolSize NumPools
#> 1 Cx. tarsalis   1       50        6
#> 2  Cx. pipiens   1       50        5
#> 3 Cx. tarsalis  NA      442        1
#> 4  Cx. pipiens  NA      233        1

VI(Pos ~ PoolSize + n(NumPools) / Species, vi.dat, n.use.traps = FALSE, n.use.na = TRUE)
#>         VI
#> 1 2.411893
summary(VI(Pos ~ PoolSize + n(NumPools) / Species, vi.dat, n.use.traps = FALSE, n.use.na = TRUE))
#>
#> Call:  VI(x = Pos ~ PoolSize + n(NumPools)/Species, data = vi.dat, n.use.traps = FALSE, n.use.na =
         TRUE)
#>
#> Prevalence estimate method : firth
#> Use non-tested individuals in abundance estimate : TRUE
#> Use tested pools' pool sizes in abundance estimate : FALSE
#>
```

```
#>         VI
#> 1 2.411893
#>
#> Detail by group and vector:
#>
#>        Species Avg N           P (Avg N) * P
#> 1 Cx. tarsalis   442 0.003341092   1.4767625
#> 2  Cx. pipiens   233 0.004013436   0.9351305
```

Finally, to account for trapping effort, recall that these vector mosquito counts are from 6 traps (assumed to be for 1 night each). Augment the `vi.dat` data set as

```
# put 1s in for the pool data for later; use values for trap nights in application
vi.dat$TrapNights <- c(1,1,6,6)
vi.dat
#>        Species Pos PoolSize NumPools TrapNights
#> 1 Cx. tarsalis   1       50        6          1
#> 2  Cx. pipiens   1       50        5          1
#> 3 Cx. tarsalis  NA      442        1          6
#> 4  Cx. pipiens  NA      233        1          6

VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat,
                                    n.use.traps = FALSE, n.use.na = TRUE)
#>          VI
#> 1 0.4019822
summary(VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat,
                                    n.use.traps = FALSE, n.use.na = TRUE))
#>
#> Call:  VI(x = Pos ~ PoolSize + n(NumPools)/Species:TrapNights, data = vi.dat, n.use.traps = FALSE,
         n.use.na = TRUE)
#>
#> Prevalence estimate method : firth
#> Use non-tested individuals in abundance estimate : TRUE
#> Use tested pools' pool sizes in abundance estimate : FALSE
#>
#>          VI
#> 1 0.4019822
#>
#> Detail by group and vector:
#>
#>        Species    Avg N           P (Avg N) * P
#> 1 Cx. tarsalis 73.66667 0.003341092   0.2461271
#> 2  Cx. pipiens 38.83333 0.004013436   0.1558551
```

The `Avg N` values reported in the `summary` result match the CDC result. To match the *VI* result exactly, note that the CDC computation used the MIR as the estimate of the infection rate, so compute this using

```
VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat, n.use.traps = FALSE, n.use.na = TRUE,
         pt.method="mir")
#>          VI
#> 1 0.4008889
```

```
summary(VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat, n.use.traps = FALSE, n.use.na =
        TRUE, pt.method="mir"))
#>
#> Call:  VI(x = Pos ~ PoolSize + n(NumPools)/Species:TrapNights, data = vi.dat, n.use.traps = FALSE,
        n.use.na = TRUE,
#>
#> Prevalence estimate method : mir
#> Use non-tested individuals in abundance estimate : TRUE
#> Use tested pools' pool sizes in abundance estimate : FALSE
#>
#>          VI
#> 1 0.4008889
#>
#> Detail by group and vector:
#>
#>        Species    Avg N           P (Avg N) * P
#> 1 Cx. tarsalis 73.66667 0.003333333   0.2455556
#> 2  Cx. pipiens 38.83333 0.004000000   0.1553333
```

An external data set together with the pooled data sizes (counts) are used to provide the population size measure

Finally, if the individuals in the pools are not also counted in the "not-tested" data set (since doing so would over-count the collected number of individuals), these counts can be included in the computation of the population size measure, making sure that the collection effort variable (`trap.time`; `TrapNights` in the example) is correct for all the individuals in the pools. To include these in the computation, simply set the `n.use.traps` variable to `TRUE`:

```
# not trying to match the CDC guidelines report here, since in the example more individuals are
# included in the population size (mosquito density) measure
VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat,
                                    n.use.traps = TRUE, n.use.na = TRUE)
#>          VI
#> 1 0.6310828
summary(VI(Pos ~ PoolSize + n(NumPools) / Species:TrapNights, vi.dat,
                                    n.use.traps = TRUE, n.use.na = TRUE))
#>
#> Call:  VI(x = Pos ~ PoolSize + n(NumPools)/Species:TrapNights, data = vi.dat, n.use.traps = TRUE,
        n.use.na = TRUE)
#>
#> Prevalence estimate method : firth
#> Use non-tested individuals in abundance estimate : TRUE
#> Use tested pools' pool sizes in abundance estimate : TRUE
#>
#>          VI
#> 1 0.6310828
#>
#> Detail by group and vector:
#>
#>        Species Avg N           P (Avg N) * P
```

```
#> 1 Cx. tarsalis   106 0.003341092   0.3541557
#> 2  Cx. pipiens    69 0.004013436   0.2769271
```

Access results

Beginning with package version 1.1, returned objects of class `vectorIndex`/`VI` can be accessed like data frames, using both `[.` and `$` extractor methods. Examples are

```
# original call
VI(Pos ~ PoolSize | Zone / Species, mosq.dat)
#>   Zone        VI
#> 1    1 1.8732123
#> 2    2 0.3963581

# just Zone 2
VI(Pos ~ PoolSize | Zone / Species, mosq.dat)[2,]
#>   Zone        VI
#> 1    2 0.3963581

# just the VIs
VI(Pos ~ PoolSize | Zone / Species, mosq.dat)[["VI"]]
#> [1] 1.8732123 0.3963581
VI(Pos ~ PoolSize | Zone / Species, mosq.dat)$VI
#> [1] 1.8732123 0.3963581
```

Options

Other options to the `vectorIndex` / `VI` functions are the same as those for `pooledBin`, so that the user may specify the method for point estimation.

Confidence interval for *VI*

The *VI* is a measure used for evaluation of infection risk of some human pathogen, but in principle it is not estimating a population quantity, though it is expected to be proportional to the number of infected individual vectors. Because of this, at this time functionality is not included to compute CIs (which are inferential beasts, after all) to accompany *VI* computations. Inclusion of CI computations to provide some measure of "uncertainty" or "variability" of the *VI* computed is being evaluated, and this would be straightforward conditional on the collection counts. A more complete measure of such variability would include uncertainty in the counts, too, and this is not presently available (but is being evaluated).

Imperfect test

The methods used for point estimation of population individual-level prevalence using `pooledBin` assume that the test used to assess the "positivity" of a pool are perfect. Hepworth and Biggerstaff (2021) extend the

methods of Hepworth and Biggerstaff (2017) to include imperfect tests, quantified through known values for test *sensitivity* and *specificity*. This functionality is available via the function `ipooledBin`; there is not at present a corresponding `ipIR`, as further development will see this extension incorporated directly into `pooledBin`.

The principle difference between `pooledBin` and `ipooledBin` is the specification of the parameters `sens` and `spec`, which both default to `1`, a default perfect test. Using the `mosq.dat` data set from above:

```
ipooledBin(Pos ~ PoolSize | Species, mosq.dat, sens=0.9, spec=0.95)
#>                 Species           P
#> 1         Culex pipiens 0.009979804
#> 2        Culex tarsalis 0.006631455
#> 3 Culex quinquefaciatus 0.019706390
summary(ipooledBin(Pos ~ PoolSize | Species, mosq.dat, sens=0.9, spec=0.95))
#>
#> Estimation of Binomial Proportion for Pooled Data using an Imperfect Test
#>
#> Call: ipooledBin(x = Pos ~ PoolSize | Species, data = mosq.dat, sens = 0.9, spec = 0.95)
#>
#> Sensitivity :  0.9
#> Specificity :  0.95
#> Point estimator : firth
#>
#>                 Species    PointEst   N NumPools NumPosPools Scale
#> 1         Culex pipiens 0.009979804 180        4           2     1
#> 2        Culex tarsalis 0.006631455 385        5           2     1
#> 3 Culex quinquefaciatus 0.019706390  40        3           1     1
```

Estimates based on the uncorrected MLE for imperfect tests are also available by setting the `pt.method` parameter:

```
ipooledBin(Pos ~ PoolSize | Species, mosq.dat, sens=0.9, spec=0.95, pt.method="mle")
#>                 Species           P
#> 1         Culex pipiens 0.015051887
#> 2        Culex tarsalis 0.009239927
#> 3 Culex quinquefaciatus 0.028026274
summary(ipooledBin(Pos ~ PoolSize | Species, mosq.dat, sens=0.9, spec=0.95, pt.method="mle"))
#>
#> Estimation of Binomial Proportion for Pooled Data using an Imperfect Test
#>
#> Call: ipooledBin(x = Pos ~ PoolSize | Species, data = mosq.dat, pt.method = "mle", sens = 0.9,
#>        spec = 0.95)
#>
#> Sensitivity :  0.9
#> Specificity :  0.95
#> Point estimator : mle
#>
#>                 Species    PointEst   N NumPools NumPosPools Scale
#> 1         Culex pipiens 0.015051887 180        4           2     1
#> 2        Culex tarsalis 0.009239927 385        5           2     1
#> 3 Culex quinquefaciatus 0.028026274  40        3           1     1
```

Compared to `pooledBin`, the additional parameter `p.start` gives the user the options of specifying a starting starting value for the numerical algorithm (Newton-Raphson) used in estimation; there is a default value set for this when `p.start = NULL`, as is the default.

Confidence intervals are not included as a option for `ipooledBin`, because at present there is not a theoretically recommended method. (This is why this functionally has not yet been incorporated into the base `pooledBin` function.)

Finally, a word of caution: as noted in Hepworth and Biggerstaff (2021), convergence of the computational algorithm in the presence of an imperfect test is not assured (either computationally or theoretically) for every value of sensitivity and specificity for a given data set, as some data are simply incompatible with some test performance specifications. Should the user encounter convergence issues using specified values for `sens` and `spec`, the recommendation is to evaluate estimates for a variety of these parameter specifications, perhaps beginning by assuming a perfect test, to see how estimates are impacted by such specifications.

Biggerstaff, BJ. 2008. “Confidence Intervals for the Difference of Two Proportions Estimated from Pooled Samples.” *Journal of Agricultural, Biological, and Environmental Statistics* 13 (4): 478–96.

Chen, CL, and WH Swallow. 1990. “Using Group Testing to Estimate a Proportion, and to Test the Binomial Model.” *Biometrics* 46 (4): 1035–46.

Chiang, CL, and WC Reeves. 1962. “Statistical Estimation of Virus Infection Rates in Mosquito Vector Populations.” *American Journal of Hygiene* 75 (3): 377–91.

Fauver, JR, L Pecher, JA Schurich, BG Bolling, M Calhoon, ND Grubaugh, KL Burkhalter, et al. 2015. “Temporal and Spatial Variability of Entomological Risk Indices for West Nile Virus Infection in Northern Colorado: 2006–2013.” *Journal of Medical Entomology* 53 (2): 425–34. https://doi.org/10.1093/jme/tjv234.

Firth, D. 1993. “Bias Reduction of Maximum Likelihood Estimates.” *Biometrika* 80: 27–38.

Gart, JJ. 1991. “An Application of Score Methodology: Confidence Intervals and Tests of Fit for One-Hit Curves.” In *Handbook of Statistics*, 8:395–406. Elsevier Science Publishers.

Hepworth, G. 2005. “Confidence Intervals for Proportions Estimated by Group Testing with Groups of Unequal Size.” *Journal of Agricultural Biological and Environmental Statistics* 10 (4): 478–97.

Hepworth, G, and BJ Biggerstaff. 2017. “Bias Correction in Estimating Proportions by Pooled Testing.” *Journal of Agricultural, Biological and Environmental Statistics* 22 (4): 602–14. https://doi.org/10.1007/s13253-017-0297-2.

———. 2021. “Bias Correction in Estimating Proportions by Imperfect Pooled Testing.” *Journal of Agricultural, Biological and Environmental Statistics* 26 (1): 90–104. https://doi.org/10.1007/s13253-020-00411-5.

Microsoft Corporation. n.d. *Microsoft Excel*. https://office.microsoft.com/excel.