Confidence intervals for proportions estimated by pooled testing based on Firth's bias correction

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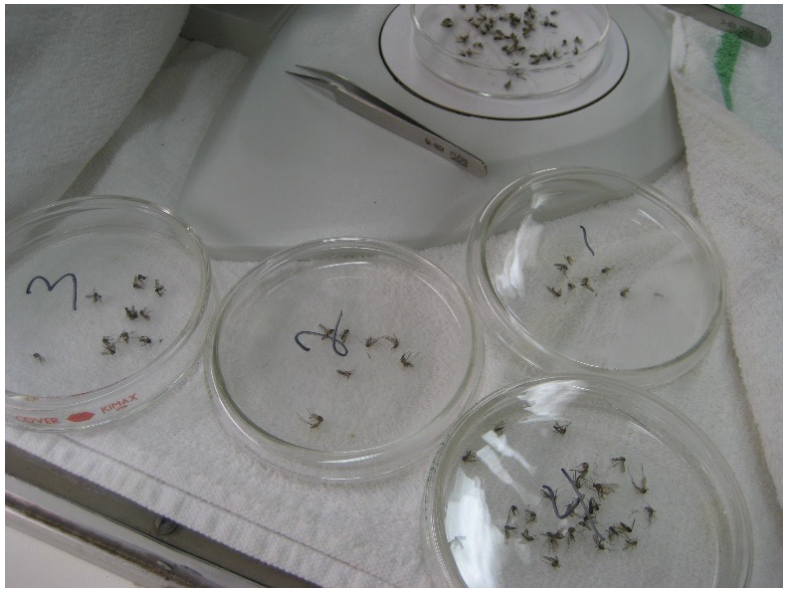
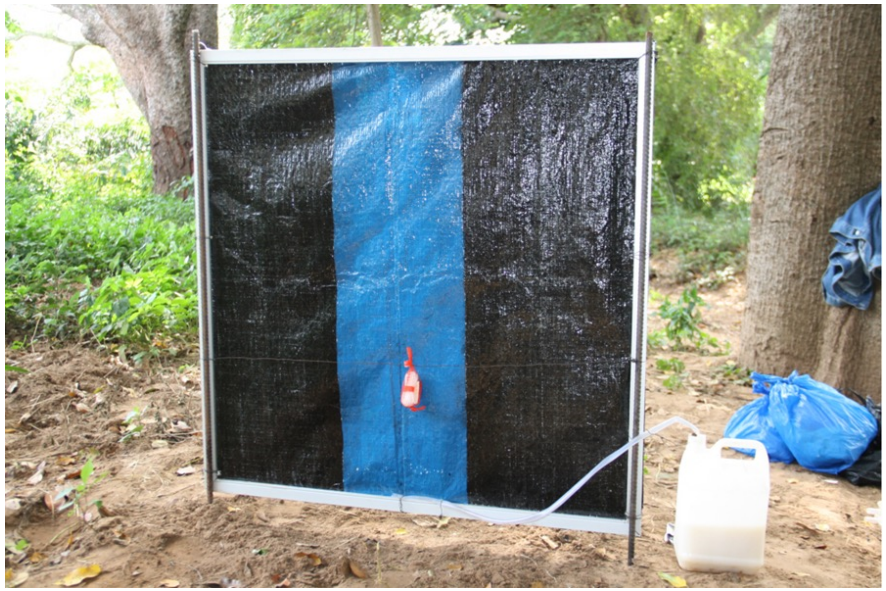
Testing pools (groups) of insects to estimate the prevalence p of a disease



CDC testing mosquitoes



Trapping black flies in Africa

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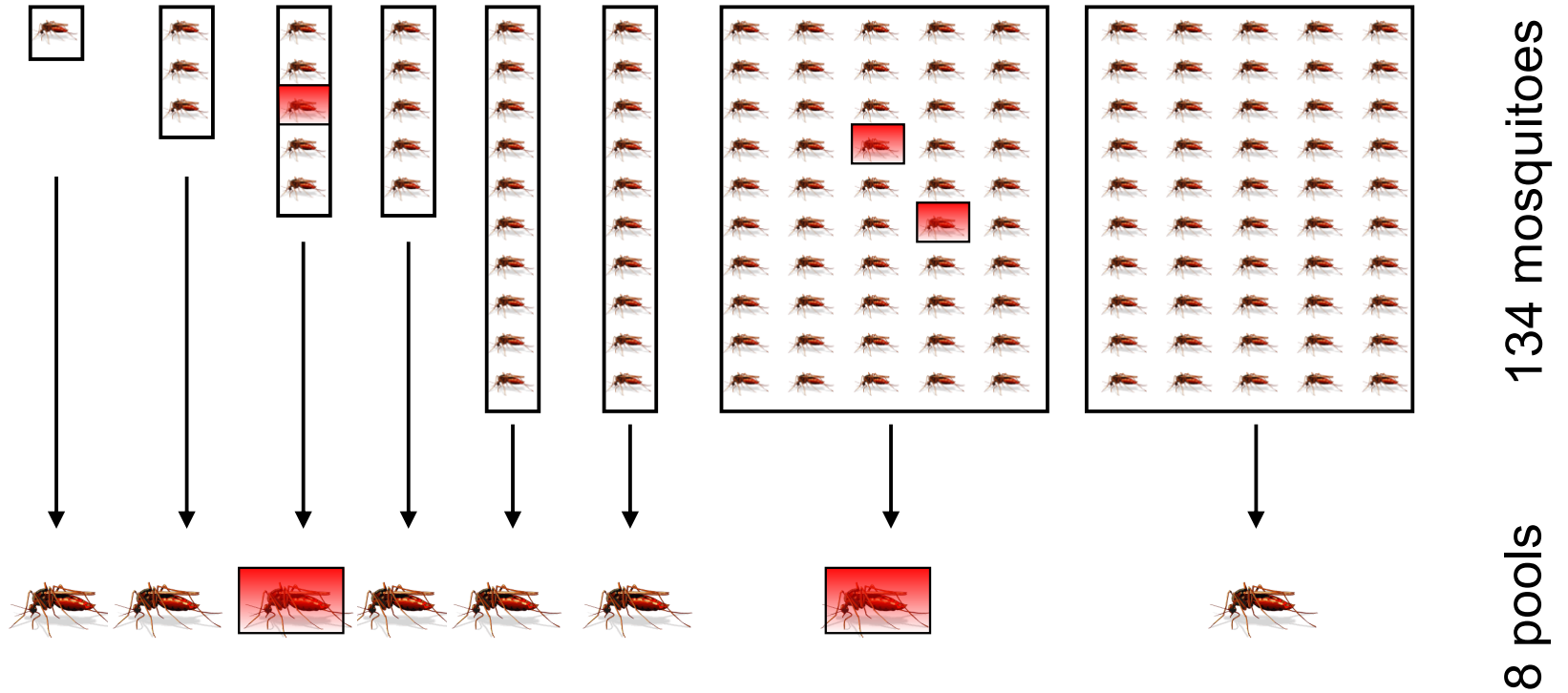
Pooled testing of mosquitoes



MLE: found by iteration, and positively biased.

Inference on *p*

Point estimation:

- "MIR" (*minimum infection rate*, biased low)
- MLE (biased high)
- Gart bias correction
- **Firth's bias correction**

Interval estimation:

- Standard likelihood-based CIs
- **Score interval with skewness correction**

Applying Firth's score adjustment

Considered point estimation

- Problem: MLE is biased
- Solution
  - Bias in MLE due to $E[S(p)] = 0$ at true p; curvature of $S(p)$
  - Introduce "small bias into the score function" $S(p)$

Expected information

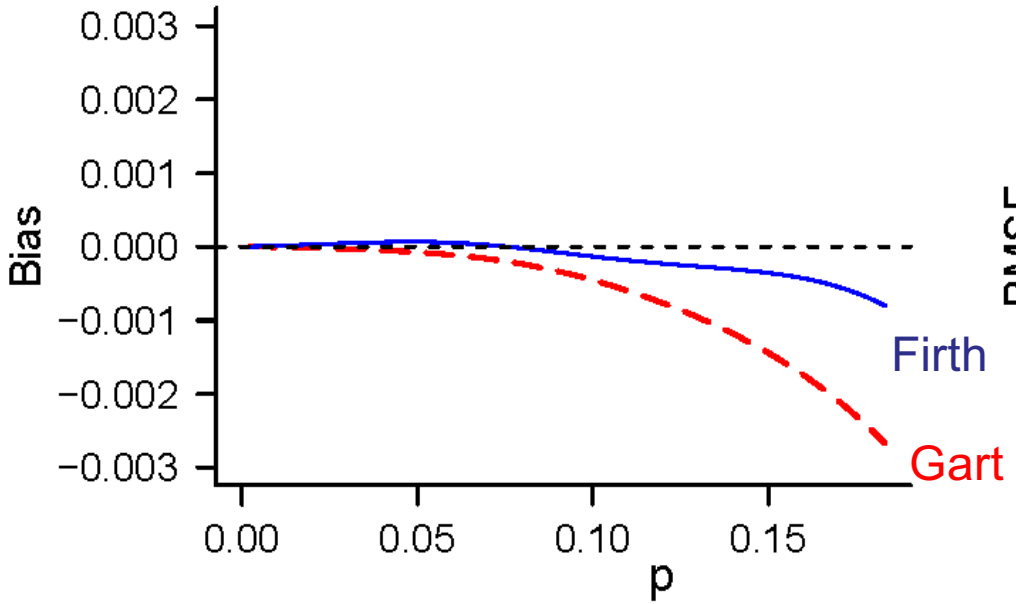
$$\breve{S}(p) = S(p) - I(p)b(p)$$

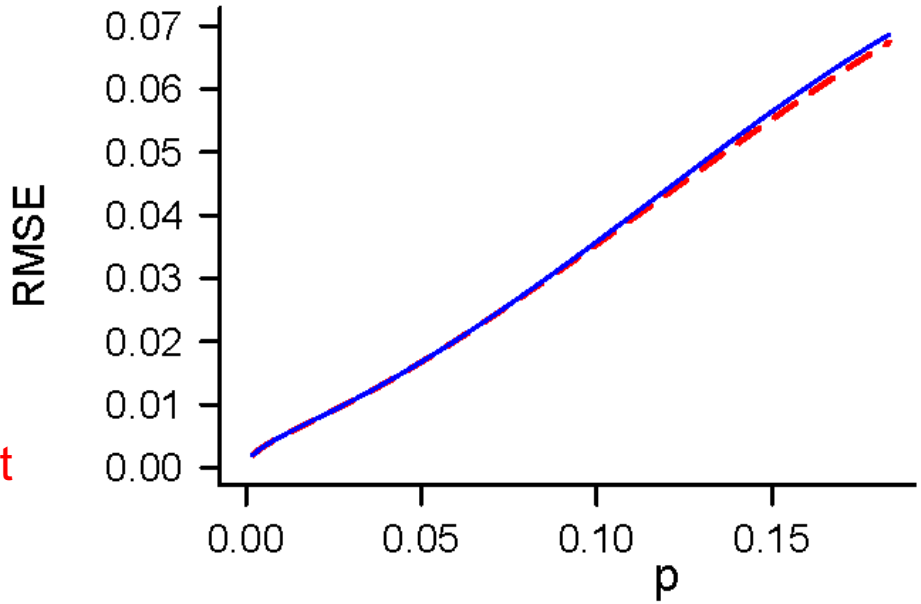
Observed information

$$\acute{S}(p) = S(p) - i(p)b(p)$$

Bias of estimators: 500 individuals in 5 pools of 5, 5 pools of 10, 5 pools of 25, 6 pools of 50

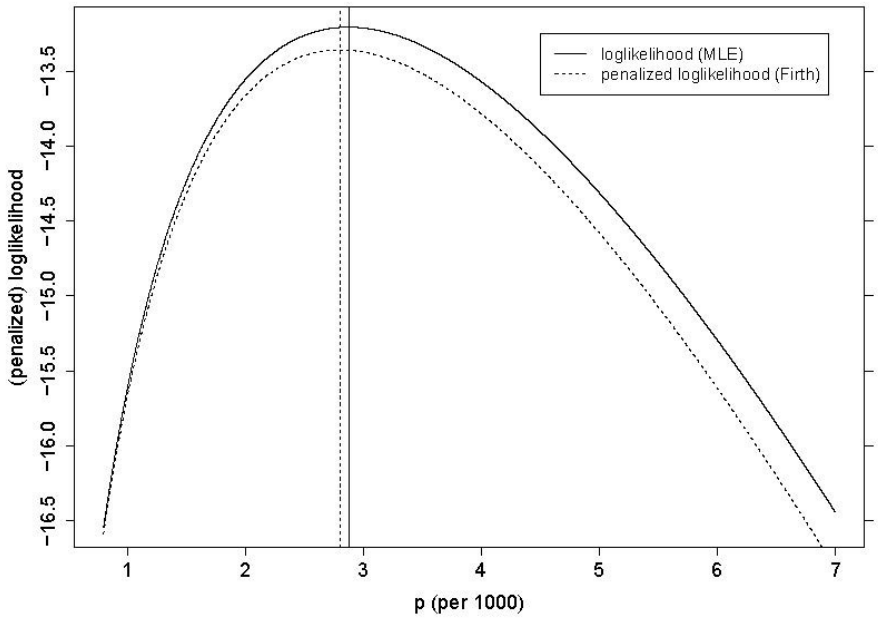
$500: 5^5\ 10^5\ 25^5\ 50^6$





Motivation

- With the improved performance for point estimation using Firth's correction, we sought to develop CIs based on Firth's corrected score function.
- Shifts and "squeezes" the standard log-likelihood.
- Natural to view in the framework of penalized likelihood inference.



What we found

- Firth-based penalized CIs with expected information are computationally the same as standard score-based intervals.
- Penalized likelihood is a consistent inferential framework for point and interval estimation, unifying existing recommended methods.
- Using observed information made a small difference in most situations. The difference was greater for “unlikely” outcomes (more positives in smaller pools than in larger pools).

Example: Fort Collins West Nile virus

- City of Fort Collins, Colorado, collects and tests mosquitoes for West Nile virus weekly throughout the transmission season
- Decisions on mosquito abatement measures are based, in part, on estimates of WNV infection rates
- Data from one city quadrant in week 35 of 2016: 108 mosquitoes
- 14 pools, 2 positive pools (one of size 1, one of size 5)
- $108 : 1_1^2\ 2_0^1\ 4_0^1\ 5_1^1\ 6_0^2\ 10_0^1\ 11_0^1\ 12_0^4\ 14_0^1$

Example: Fort Collins WNV CIs

WNV prevalence estimates (per 1,000 mosquitoes)

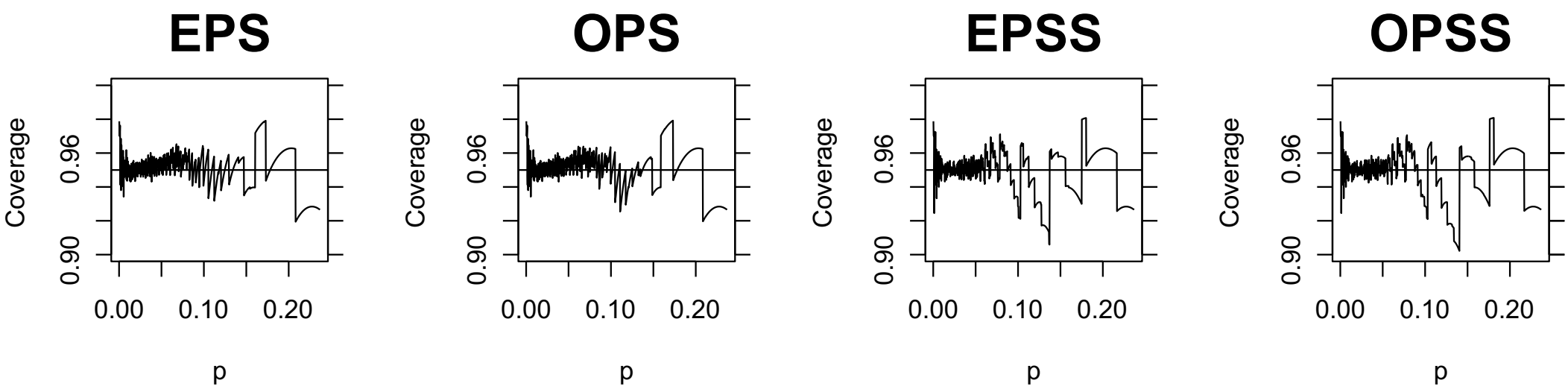
Method	Information	p	Lower	Upper
Score	Expected	18.090	5.207	57.752
Score	Observed	18.000	5.199	57.452
Skew-corrected Score	Expected	18.090	3.457	56.871
Skew-corrected Score	Observed	18.000	3.453	56.577

Confidence interval evaluation

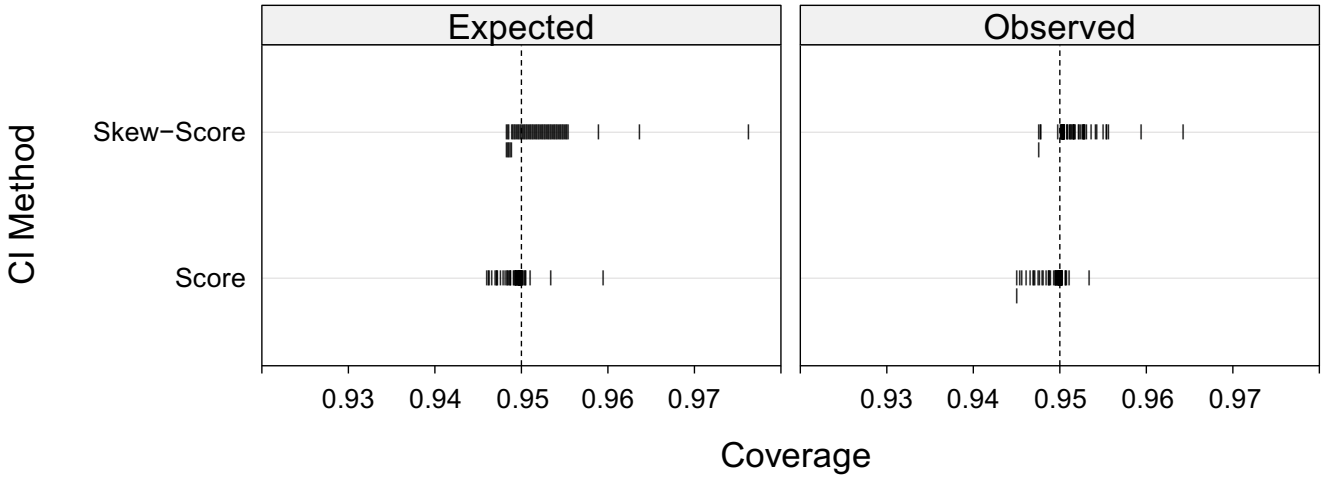
- 59 pooling configurations
- 1000 values of p in $(0, \psi)$
  $\psi = p$ such that Pr(all pools positive) = 0.05
- Coverage (exact)
- Expected length
- Directional non-coverage

CI evaluation: example coverage

$2500: 5^{10}\ 50^{49}$



CI evaluation: overall coverages



CI evaluation: overall results

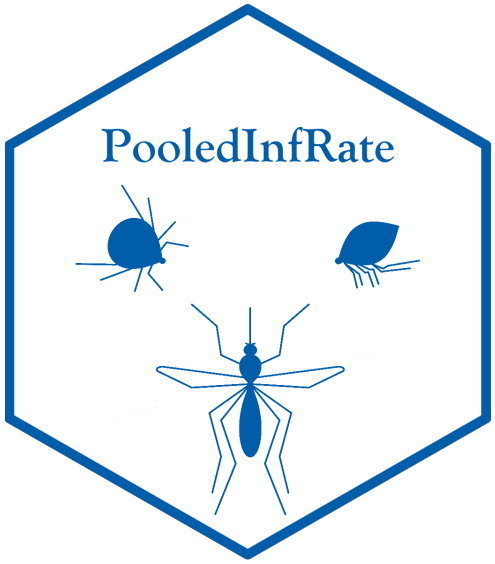
Method	Information	Coverage	Exp Length	Left NC	Right NC	Cov Symm
Score	Expected	94.93	5.546	2.856	2.207	12.82
Score	Observed	94.92	5.529	2.884	2.193	13.62
Skew	Expected	95.21	5.815	2.292	2.495	-4.23
Skew	Observed	95.21	5.801	2.290	2.496	-4.30

Coverage Symmetry = difference in percent non-coverage
= 100(Left NC – Right NC)/(Left NC + Right NC)

CI evaluation: summary

- Skewness correction works as expected (and seen previously)
  - Improves coverage
  - Symmetrizes non-coverage
- Expected and observed information are almost the same
  - This is an overall “averaging” result
  - Not surprising, since E[$i(p)$] = $I(p)$
  - Observed information does better for unlikely outcomes

PooledInfRate R Package



Other R pacakges: binGroup2, binGroup

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References

G. Hepworth & B.J. Biggerstaff (2017). Bias correction in estimating proportions by pooled testing. *JABES* 22:602–614.

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B.J. Biggerstaff & G. Hepworth. Confidence intervals for a proportion estimated from pooled samples based on Firth's corrected score. Submitted to *Biometrical Journal*.

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