Validation of Some Functions in the exact2x2 R package
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Summary
This document details some of the checks that were done to ensure that the uncondExact2x2, boschloo and binomMeld.test functions were giving correct and reasonable results.

1 Introduction
Because some of the options in the functions uncondExact2x2 and boschloo produce tests and confidence intervals that are not available elsewhere, there is not necessarily an existing gold standard to check each option. Nevertheless, we do check some options for which there are functions available in other R packages (most notably, the Exact package) or other software (SAS and StatXact).

For the binomMeld.test function we create two different methods to calculate the p-values and confidence intervals and compare them. See Section 10 for those tests.

2 The Fast Algorithm
For some options, specifically, in the case when:

(parmtype=="difference") & (tmethod == "central") &
(gamma == 0) &
(method == "simple" | method=="user-fixed" | method=="FisherAdj")

Then the confidence intervals can be calculated using a faster algorithm, since we have monotonicity in the one-sided p-values. We test this by checking that the confidence intervals and p-values have unified inferences. Specifically, we calculate the 95% confidence interval, then check the p-value for the test with nullparm equal to one limit of the interval and see if the p-value is equal to 0.05. The check for method=="FisherAdj" is in \tests\testthat\test_FisherAdj.R.

3 FisherAdj: The Slow Algorithm
For parmtype="ratio" or parmtype="oddsratio" with method=="FisherAdj" we must use the slower algorithm. We checked method=="FisherAdj" for whether the confidence intervals and p-values have unified inferences in \tests\testthat\test_FisherAdj.R.

4 Boschloo Test
The Boschloo test is run with the boschloo function. There is a separate function because unlike most unconditional exact tests, the traditional way of calculating the alternative="less" option uses a different ordering function than calculating the alternative="greater" option. The boschloo uses the appropriate one-sided p-value from the Fisher’s exact test for ordering. We validate the p-values by testing them against the Exact R package and StatXact Version 11. They match for the data that we tested. The tests on the p-values are in \tests\testthat\test_Exact.R and \inst\slowTests\test_StatXact.R. Note that the default for alternative="two.sided" in our boschloo function is tmethod="central", but the traditional two-sided p-value for Boschloo’s test uses tmethod="minlike". Thus, we only tested the latter. There is no software of which we are aware that calculates the confidence intervals that match Boschloo’s test.
5 Confidence Intervals on Odds Ratios with method="score"

Agresti and Min (2002) discussed two ways of calculating the exact unconditional confidence intervals for the
odds ratio using the score statistic for ordering. The two ways correspond to the two options in tsmethod. But
the function `uncondExact2x2` with parmtype="oddsratio" and method="score" does not match the results in the
paper for either tsmethod, even though we used a more precise grid than the default (control$nPgrid=1000).
This could be due to using different algorithms for the calculation. Although Agresti and Min (2002) state
that "There is no assurance that an algorithm such as just described produces the correct interval", the same
can be said of the algorithms for `uncondExact2x2`. So it is not clear which software is closer to the true values.
The tests are in `\inst\slowTests\test_OddsRatioScore.R`.

6 The E+M Method

We check the E+M method of Lloyd (2008) by reproducing the some results on the example in Table 1 of
that paper. We reproduce the p-values using the Wald-pooled difference example (T rows: top is one-sided,
bottom is two-sided) and the E+M column (results are p=0.02518 [one-sided] and p=0.03681 [two-sided]).
This test is in `\inst\slowTests\test_EplusM.R`.

7 Berger and Boos Adjustment

Berger and Boos (1994) developed a method to adjust for nuisance parameters that tends to have better
power when applied to the 2x2 unconditional exact tests. We calculated their adjustment for the data
example in that paper, and the results agree between our `uncondExact2x2` and the `exact.test` from the Exact
R package. Both these functions differ by a small amount from the value given in the paper (in the paper,
p=0.037, while the functions give p=0.03781). The test is in `\tests\testthat\test_Exact.R`.

The `uncondExact2x2` results were fairly close for the examples we checked in StatXact 11 (difference in
log values within 0.02). See `\inst\slowTests\test_StatXact.R`.

8 Comparison with StatXact

We ran a comparison with StatXact version 11. The tests are in `\inst\slowTests\test_StatXact.R`. We
tested the parmtype="difference" and parmtype="ratio" with both tsmethod options with the method="score".
This is associated with either "invert two one-sided tests" (for tsmethod="central") or "invert a two-sided test"
(for tsmethod="square"). We found that in most cases with tsmethod="central" the agreement with "invert
two one-sided tests" was close. But we found some big differences when tsmethod="square" and "invert a
two-sided test".

We mention one case where we can show clearly that the StatXact 11 is wrong (in the other cases, it
is not as clear which software is more accurate). The case is x1/n1 = 0/7 and x2/n2 = 13/13. StatXact
11 using "invert a two-sided test" and Gamma=0 gives a 95% confidence interval on that difference as
(0.6088, 0.6101). This is wrong, because when θ1 = 0 and θ2 = 1 then the true differences is 1, and the
probability of observing x1/n1 = 0/7 and x2/n2 = 13/13 is also 1. So the actual coverage under that
assumption is 0, and the confidence interval is clearly not exact. For θ1 = ε and θ2 = 1 − ε with ε a very
small positive value, we would similarly get coverage close to 0. In contrast, the `uncondExact2x2` function
with parmtype="difference", tsmethod="square", and gamma=0 has the 95% confidence interval as (0.6088,1).
In this case the coverage is 100% (assuming the CI includes 1) when θ1 = 0 and θ2 = 1.

Comparison of Boschloo values has previously been mentioned in Section 4.

9 Comparison with SAS

We check some results and compared them with SAS version 9.4. Proc Freq has the Exact option, that
gives p-values for the Barnard test (uncondExact2x2 test of θ1 = θ2 with method="wald-pooled" and parm-
type="difference"). The Exact option also gives confidence intervals for the ratio and difference (uncondExact2x2 with method="score").

The methods agree, and the tests are in \inst\slowTests\test_SAS.R. The default control value for control$nPgrid option of the algorithm in uncondExact2x2 must be increased for a few of the values to match. This suggests that the default for SAS is more accurate than the default of control$nPgrid=100.

10 The binomMeld.test function

The option nmc in the binomMeld.test function allows calculation by Monte Carlo simulation. That provides a separate check for the numeric integration calculations. We compare the two calculation methods in \inst\slowTests\test_binomMeldtest.R.

References

