A confidence interval for the reaction index

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Abbreviations used:

CI: confidence interval

RI: reaction index
Introduction

In 1992, Brasch and Henseler (1) introduced the reaction index (RI) to assess the quality of patch test preparations. This index has been used by various researchers in the following, but no one, at least to our knowledge, comprehended the RI as a statistical estimate from a given sample which should have a measure of sampling variability with it. While Brasch and Henseler gave the rule of thumb not to use the index when having less than 100 non-negative test results, one would certainly prefer a mathematically derived confidence interval (CI) for the RI to assess statistical uncertainty. Only recently, our group had to resort to a computer-intensive bootstrap experiment to achieve CIs for the RI (2).

Methods

The reaction index relates the number of allergic reactions to the number of non-negative reactions by the formula

\[ \text{RI} = \frac{a - q - i}{a + q + i}, \]

with a the number of allergic, q the number of questionable, and i the number of irritant reactions.

As can be seen from the formula, the RI is not a true proportion with a range of values from 0 to 1, thus precluding the use of the standard confidence interval for a binomial proportion. In contrast, the RI can take values between -1 and 1.

However, writing \( \text{RI} = \frac{a}{a+q+i} - \frac{(q+i)}{(a+q+i)} \) one can perceive the RI as the difference of two true proportions X and Y with X:= \( \frac{a}{a+q+i} \) binomially distributed with success probability \( p := \frac{a}{a+q+i} \) and n := (a+q+i) and Y:= \( \frac{(q+i)}{(a+q+i)} \) binomially distributed with \( p' := \frac{(q+i)}{(a+q+i)} = 1 - \frac{a}{a+q+i} = 1 - p \) and n := (a+q+i), respectively. We note that the two binomial distributions X and Y can be interpreted...
as arising from a two-component multinomial distribution which gives their covariance
(3, p.7) as Cov(X,Y) = -n*p*p' = -n*p*(1-p). Using an elementary theorem from
probability theory (4, p.184) on the variance of the difference of random variables X,Y
we find
\[ \text{Var}(X - Y) = \text{Var}(X) + \text{Var}(Y) - 2 \text{Cov}(X, Y) = np(1 - p) + np'(1 - p') - 2(-np(1-p)) = 4np(1-p), \]
and thus the 95% confidence interval for RI, which is
\[ RI \pm 1.96 \frac{\sqrt{4np(1-p)}}{n} = RI \pm 1.96 \times 2 \times \frac{p(1-p)}{n}, \]
where 1.96 equals the corresponding two-sided 5% quantile from the standard
normal distribution. It is remarkable that the length of the confidence is exactly twice
the length of the simple CI for a binomial proportion. However, this becomes
intuitively clear by noting the range of values for the RI being twice the range for a
proportion.

In terms of the original terms this becomes
\[ RI \pm 1.96 \times 2 \times \sqrt{\frac{a(1-p)}{(a+q+i)^3}}, \]
In table 1 we give the RIs with 95% confidence intervals from the example of Brasch
and Henseler (1).

**Discussion**

To assess the sampling variability of the reaction index we derived a confidence
interval. This is simply to calculate and we encourage researchers to use it in their
future work.
References


Table 1: Reaction index values from the original paper of Brasch and Henseler (1) together with their 95%-confidence intervals

<table>
<thead>
<tr>
<th>Patch test preparation</th>
<th>a</th>
<th>q</th>
<th>i</th>
<th>RI</th>
<th>95%-CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nickel sulphate 2.5%</td>
<td>978</td>
<td>205</td>
<td>2</td>
<td>0.651</td>
<td>[0.607, 0.694]</td>
</tr>
<tr>
<td>Neomycin sulphate 20%</td>
<td>112</td>
<td>25</td>
<td>3</td>
<td>0.600</td>
<td>[0.467, 0.733]</td>
</tr>
<tr>
<td>Colophony 20%</td>
<td>156</td>
<td>44</td>
<td>1</td>
<td>0.552</td>
<td>[0.437, 0.667]</td>
</tr>
<tr>
<td>Balsam of Peru 25%</td>
<td>244</td>
<td>85</td>
<td>4</td>
<td>0.465</td>
<td>[0.370, 0.561]</td>
</tr>
<tr>
<td>Cobalt chloride 1%</td>
<td>263</td>
<td>105</td>
<td>1</td>
<td>0.425</td>
<td>[0.333, 0.518]</td>
</tr>
<tr>
<td>para-Phenylenediamine 1%</td>
<td>147</td>
<td>54</td>
<td>6</td>
<td>0.420</td>
<td>[0.297, 0.544]</td>
</tr>
<tr>
<td>Fragrance mix 8%</td>
<td>303</td>
<td>115</td>
<td>16</td>
<td>0.396</td>
<td>[0.310, 0.483]</td>
</tr>
<tr>
<td>Epoxy resin 1%</td>
<td>33</td>
<td>17</td>
<td>0</td>
<td>0.320</td>
<td>[0.057, 0.583]</td>
</tr>
<tr>
<td>Potassium dichromate 0.5%</td>
<td>129</td>
<td>86</td>
<td>4</td>
<td>0.178</td>
<td>[0.048, 0.308]</td>
</tr>
<tr>
<td>Formaldehyde 1%</td>
<td>83</td>
<td>47</td>
<td>42</td>
<td>-0.035</td>
<td>[-0.184, 0.114]</td>
</tr>
</tbody>
</table>

a = number of allergic reactions, q = number of questionable reactions, i = number of irritant reactions. The total number of tests w