TITLE: The application of a Poisson difference model under the Skellam distribution assumption for the analysis of the change in count measurements in a random effects repeated measures model

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ABSTRACT:

Background:
Count data are routinely collected in clinical trials to evaluate medical treatments in patients. A variety of statistical methods have been adequately or inadequately employed, ranging from Analysis of Covariance to analyse the change from baseline counts, non-parametric methods and basic Poisson models to analyse the post baseline count measurements. In this presentation we show the use of Bayesian longitudinal models to analyse count measurements collected over time and have extended the Skellam distribution to a longitudinal setting to analyse the difference between postbaseline and baseline counts. We illustrate the methods on clinical trial data (number of incontinence periods) of patients with an overactive bladder.

Methods:
A variety of Bayesian fixed and random effects models have been employed to analyse repeated counts at the end of the treatment period. We focus here on longitudinal counts assuming a Skellam's distribution to analyse the difference in counts in the motivating dataset. We analyzed the difference between active and placebo in the change in incontinence episodes after 12 weeks of treatment compared to baseline. The models included age gender and geographic region as covariates. Additionally, a multivariate Skellam distribution was built in order to account for measures of consecutive weeks. Goodness of fit techniques were used to evaluate the models.

Results:
The Skellam distribution is not a classical distribution to analyse repeated count data. The model has some interesting features such as removing unknown individual extreme effects and reducing variation. . We interpret the results as the expected change in the differences compared to placebo, which is different from previously published frequentist results. Goodness of fit tests showed that the Poisson difference model was superior to the previously applied random effects model in this population. It is also allowed for an intuitive interpretation of patient improvement when the change from baseline count is used as measurement of interest.

Conclusions:
The Skellam distribution applied to the difference in count data allows for a statistical evaluation of patient improvement that is more in line with clinical evaluation.