

Kolloquium „Statistische Methoden in der empirischen Forschung“

Wann: 20. November 2012, 17:00 – 18:30 Uhr

Wo: Landwirtschaftlich-Gärtnerische Fakultät der HU, Hörsaal 2, 2. Etage,
Invalidenstr. 42, 10115 Berlin

Joachim Röhmel (Bremen) mit Meinhard Kieser

Investigations on non-inferiority: the FDA draft guidance on treatments for nosocomial pneumonia - a case for exact tests for binomial proportions

This talk addresses statistical issues in non-inferiority trials where the primary outcome is a fatal event. The investigations are inspired by a recent FDA draft guideline on treatments for nosocomial pneumonia. The non-inferiority margin suggested in this guideline for the endpoint all-cause mortality is defined on different distance measures (rate difference and odds ratio) and is discontinuous. Furthermore, the margin enables considerable power for the statistical proof of non-inferiority at alternatives that might be regarded as clinically unacceptable, i.e., even if the experimental treatment is harmful as compared to the control.

We investigated the appropriateness of the proposed non-inferiority margin as well as the performance of possible test statistics to be used for the analysis. A continuous variant of the margin proposed in the FDA guideline together with the unconditional exact test according to Barnard showed favorable characteristics with respect to type I error rate control and power. To prevent from harmful new treatments being declared as non-inferior, it is proposed to add a 'second hurdle'. Examples are discussed and power characteristics when requiring both statistical significance and overcoming the second hurdle are explored.