

Accepted Manuscript

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PII: S0021-9150(16)31437-X

DOI: [10.1016/j.atherosclerosis.2016.10.034](https://doi.org/10.1016/j.atherosclerosis.2016.10.034)

Reference: ATH 14846

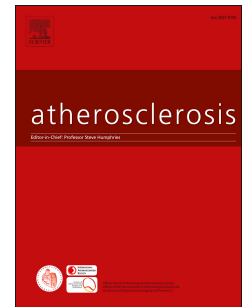
To appear in: *Atherosclerosis*

Received Date: 14 October 2016

Accepted Date: 19 October 2016

Please cite this article as: Trampisch HJ, Rudolf H, Lange S, Heterogeneity of therapeutic effects, *Atherosclerosis* (2016), doi: 10.1016/j.atherosclerosis.2016.10.034.

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Heterogeneity of therapeutic effects

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Keywords: heterogeneity, effect moderators, subgroup analysis, generalized linear model

About 10 years ago, Kramer et al. [1] stated: *“For the last half-century, randomized clinical trials (RCTs) have been the ‘gold standard’ of evaluating the efficacy or effectiveness of clinical interventions. Two concerns stand out: statistical vs. clinical significance and heterogeneity of effect sizes”*. While 20 years ago subgroup analyses were viewed rather critically (“Subgroups kill people” [2]), a change of paradigm appears to have taken place (“Not doing subgroup analyses has very probably killed more people” [3]), which can also be found in the requirements of organizations responsible for the assessment of drugs [4].

Heterogeneity of treatment effects and subgroup analysis

Heterogeneity of treatment effects (HTE) exists when not all patients respond to a treatment in a similar fashion [5]. A PubMed search for “RCT” in 2005 and 2015 gives 16.347 and 23.946 hits,

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