

## **What Constitutes “Reliable Evidence”? – Rare Diseases and Clinical Trials –**

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This talk gets to the roots of what we, as statisticians, need to think carefully about. “Methodology” is the obvious territory for statisticians to get involved in, but often it merely scratches the surface of the fundamental problems.

We begin with a short story about Sasha, aged 3, who has cerebral palsy – and the desperate and total love shown to her by her parents. Sasha features a lot in the talk as we explore the constraints and over-simplification of the mantra that is “Evidence Based Medicine” (EBM). This is particularly pertinent when we are trying to study treatments for rare diseases (sometimes called “orphan drugs”) where it is often seemingly impossible to do properly powered randomised controlled trials. We look at inter-relationships between EBM and Bradford-Hill’s so-called “criteria” with respect to causality; we look at the dreadful success rates in drug development; we look at the critical importance of randomisation; we look at the disasters looming as a result of well-intentioned but short-sighted legislation and why Bayesian priors (though not necessarily the Bayesians themselves) might lead us down the wrong road. We conclude with suggestions on when to randomise, and when not.