

Abstract

The development of an appropriate model plays an important role for the estimation of unknown functional relations between medical, biological or epidemiological parameters. Such models can provide insight in the underlying mechanisms and be a basis during regulatory processes. However, the existing standard methods for analyzing the influence of a continuous predictor, such as analysis of variance or linear regression, exhibit numerous causes for criticism. The aim of this work is to examine linear splines for modeling dose-response relations in comparison to these standard methods, as well as to the more complex techniques of fractional polynomials and additive models. The methods are applied and compared to a dataset from an occupational study that examines the effects of exposure to polycyclic aromatic hydrocarbons in the workplace. In this context, the dose-response relation between exposure to phenanthrene and excretion of the urinary metabolites 1-, 2-+9-, 3- and 4-OH-phenanthrene is analyzed. Linear Splines, fractional polynomials and additive models are superior to the standard methods regarding the model fit. All three methods show a non-existent or weak relation between external and internal exposure in the low-dose range, while a clear influence becomes apparent in the high-dose range. Additionally, linear splines yield an estimate for the boundary between the two regions. Overall, the use of linear splines leads to a simple parametric model that is easy to communicate and present. Meanwhile it remains sufficiently flexible to fit complex shapes of dose-response curves. Linear splines represent a good compromise between standard methods and more complicated non-linear or non-parametric methods.