EDITORIAL

Expectation and (un)predictability

Clinical and scientific expectation and prediction, in a context of uncertainty, are basic concepts for developing, designing, and performing clinical research. This is reflected in formulating appropriate and promising research hypotheses while also facing the ethical dilemmas related to required equipoise, in estimating prior probabilities, in designing adequate procedures for decision making during studies, and in defining the framework for correctly interpreting the results. Moreover, for the implementation of results in clinical practice, more individualized predictions would be welcome [1]. Given the context of uncertainty, which is in fact the justification of doing the research, these are not easy tasks, and we can always learn from one another’s experiences from clinical trials, and etiologic, diagnostic, and prognostic research.

In this issue, the importance of expectation and prediction is highlighted in various ways. First, Giard evaluates a Dutch trial that yielded results that were quite contrary to expectations [2], with a special focus on the problem of timely detection of adverse events (AEs) and the role of data monitoring and safety committees. In a related article, Knottnerus and Spigt elaborate on the question of when an interim analysis should be unblinded to the data monitoring committee and present a general decision structure for this purpose as a help, not as an imperative, as individual situations may vary and are often complex. Besselink et al. respond to both these commentaries from the perspective of their study [2] and revisit the 2005 DAMOCLES guidelines, emphasizing that statistical criteria such as stopping rules should be agreed on in advance and regarded as guidelines for recommending stopping rather than compelling rules [3]. The interesting question here is how the balance should be found between applying general guidelines and dealing with individual situations.

In dealing with uncertainty of treatment effects, also in relation to planning and interpreting studies, Bayesian analysis of prior probability distributions is increasingly common. In connection to this, Johnson and coworkers performed an important systematic review on methods to elicit beliefs for Bayesian priors. Until comparative studies are performed, based on their results, these authors recommend strategies to reduce the effects of bias on the elicitation. Further in this issue, in a cross-sectional study among clinicians, the same group reports on the feasibility and performance of a specific belief elicitation method to assess prognosis.

Appropriate clinical prediction is also a central topic in observational research. For example, in triage systems of emergency departments, optimal prediction by assessment of prognosis is very important in determining the clinical priority of patients based on their presented features. In a theoretical—conceptual approach, Moll presents the methodological challenges in triage research and makes a plea for shifting from a focus on consensus to the validation of decision rules and for viewing triage as diagnostics research. Other examples of observational prediction research are the systematic review by Muir et al. showing that balance impairment is a predictor of fall risk; the study by Moore et al. on the predictive value of claims-based outpatient urticaria diagnosis codes to identify potential vaccine-related adverse effects and the analysis by Smith et al. on the predictive ability of a broad range of physical, mental, health service/care utilization, and health behavior variables on self-rated health across socioeconomic groups.

Moreover, in this issue, methodological challenges in studying drug utilization have also been addressed. In an original study using a large drug-dispensing database, Gardarsdottir et al. report that different methods to construct antidepressant treatment episodes influence the estimated episode length. This may have important implications for studies that focus on drug exposure—outcome relationships and for epidemiological analysis. Pit and Byles studied the agreement between two methods of measuring medication use in older people: self-report by phone and home visits. Their finding that this agreement is generally high suggests that researchers may consider using the relatively inexpensive phone method in future studies.

Also the results reported by Middleton et al. may make community-based research among older people more feasible, as proxy-reported physical activity in people with symptoms of cognitive impairment appear to be a valid estimate. On the other hand, as presented by Cook et al., in community-based mammography screening difficulty may occur in women with clinical factors, as the latter had a greater chance for a false-positive evaluation by the radiologist. But in a prospective study on laboratory diagnostic testing in low disease probability situations, Houben et al. showed in contrast to common expectations that cascade effects (false-positive test results evoking additional diagnostic investigations or referrals to specialists) were rare.

Shiels et al. shed light on a nasty methodological problem in prospective observational studies, in comparing
three methods to deal with competing risks in studying the specific effect of highly active antiretroviral therapy (HAART) on health outcome (acquired immunodeficiency syndrome—defining cancers).

Finally, in connection to an earlier article in the Journal of Clinical Epidemiology [4], in an interesting discussion between Berger & Do and Foley & Speechley, another nasty methodological problem is addressed: the generally poor reporting of allocation concealment in published trials [5].

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References