For various reasons, it is important that clinical research and practice match as much as possible [1]. First, clinical research questions should address problems that are or will be encountered in clinical practice. Second, to produce both convincing and useful results, and as a favorable start of implementation processes, research designs and methods should integrate real practice data, experiences, and challenges as much as possible. And third, given the fast development of new clinical fields to be explored and new interventions to be tested with limited research resources and patient recruitment opportunities, designing new studies for every piece of the knowledge mosaic separately is not a sustainable strategy for the future: research designs should as much as possible converge with practice, serving both internal and external validity. An additional advantage would be that care quality could more directly benefit from better standardization of procedures and observations.

As to the first two of these issues — clinical relevance of research questions and the match between research methods and clinical practice — the Variance and Dissent series on ‘the comprehensive diagnostic study,’ presents important experiences, ideas, and insights. The series starts with an original article by Donner-Banzhof et al., who propose the comprehensive diagnostic study to deal better with clinical presentations where a large number of diagnostic tests or even diagnostic strategies should be evaluated in relation to several diseases or disease categories, as is often the case in primary care research. This is followed by a discussion between these authors and Van den Bruel and Perera. The latter put forward that, while the importance of symptom-based presentations and dealing with several disease outcomes has earlier been recognized, with many studies already having been published, a number of difficulties have not yet been solved, such as: too few data in very specific subgroups, dealing with rare but severe diseases, defining appropriate reference standards, and problems such as model overfitting and lack of appropriate precision estimates. Donner-Banzhof et al. further discuss these issues, and emphasize that we should move away from the need of “one study being conducted for each disease of relevance in a defined clinical situation.” Indeed, more comprehensive studies may help to develop research strategies beyond conducting separate studies for every new mosaic piece of knowledge. Together with both teams of discussants, we would welcome more work and progress on this topic.

An important practice-relevant addition to the already quite long and lively international publication record of clinical epidemiological research on diagnostic tests is the work being done on using tests to study disease development over time and to monitor patients with chronic diseases. In this context, Bell et al. describe how evidence from trials and cohort studies may be used to guide choice of tests for monitoring purposes. They propose four specific criteria that can support evidence-based decision making on which tests to use, and illustrate this with clinical examples.

Not only diagnostic but also treatment choices are often more complex than simple yes-no decisions. It is therefore interesting to see how the reporting of mixed treatment comparisons (MTCs) in published systematic reviews is developing over time. In a narrative review of systematic reviews, Lee shows that such publications have increased rapidly in recent years. However, as such reports are difficult to identify with current search methods, the authors make a plea for indexing MTCs in databases and for consensus on standards for conducting and reporting them.

Sustainability, not only of mosaic-piece—specific clinical research, but also of health care services, is a matter of growing concern internationally. In this connection, the work by Haines et al. on developing a feasible research design to evaluate disinvestment in health technologies of uncertain (or even absent) effectiveness or cost-effectiveness is very relevant. They discuss related methodological options, with special attention for potentials and limitations of the stepped-wedged, roll-in cluster randomized trial design.

For efficient epidemiological and health care research, cause-of-death registers and the possibility to link these to other data sources are essential, and continuously evaluating and promoting the validity of such approaches is important. Klijs et al. investigated to what extent underlying and multiple causes of death data represent end-of-life hospital morbidity data in individuals and at population level. There was poor agreement at individual level but reasonable agreement at population level. The implications of these findings are discussed.

For scientific, practical, and budgetary reasons, efficient recruitment of participants is paramount, and knowledge on factors that influence this process is very helpful. Based on data from a large randomized trial of low back pain in primary care, Williams and co-authors found that a higher socio-economic status of the area, a prompt follow-up after the initial study training of GPs, and a higher number of
face-to-face visits were associated with a higher recruitment rate. While the ability to predict recruitment based on GP characteristics seems limited, these insights can be helpful to improve recruitment procedures. The latter was also the aim of the study of Drummond et al., who evaluated two monetary incentives (“bird in the hand cash” and “prize draws”) in increasing the response rates to postal questionnaires from primary care physicians. From a 3-arm randomized trial, also including a no-incentive group, it was concluded that both incentives worked, but the (modest) cash incentive was most effective and cost-effective.

Van Kempen and co-workers focused on improving the identification of frail older people in primary care, and tested a 2-step tool they developed for this purpose among patients 70 years of age or older. They concluded that their instrument, the EASY-Care Two-step Older Persons Screening, correlated well with physical and social measures, and that the tool can identify patients with a wide spectrum of interacting problems.

Valid and efficient sampling is a classic topic in clinical epidemiology. But, as van Rein and co-authors emphasize, with regard to (in)appropriate subject selection in case-control studies, there has been much less attention paid to case than to control sampling. Using a case-control study on the effect of statins on major bleedings during treatment with vitamin K antagonists as an example, they describe how to detect survivor bias and how to deal with it in order to check for over-optimistic results.

In the evaluation of screening for colorectal cancer, a common approach is to compare observed numbers of colorectal cancer (CRC) deaths in screening participants with expected numbers derived from general population data. Using the cancer registry data, Brenner et al. illustrate that this approach can lead to substantial overestimation of expected CRC deaths in screening cohorts. They make recommendations for deriving valid screening effect estimates.

In the study of life course epidemiology, the analysis of longitudinal observational data is often necessary to infer on the plausibility and consistency of causal models. La Bastide-van Gemert et al. exemplify a statistical tool using directed acyclic graphs (DAGs) for exploring causal inference, based on data from the Prevention of Renal and Vascular Endstage Disease study. They recommend that search algorithms and causal diagrams should be used in addition to more traditional approaches. Another application of directed acyclic graphs is presented by Röhrig and her team, to examine the association between electrocardiographic findings and disability status in older adults. They demonstrated that associations found in unadjusted analysis and in age- and sex-adjusted logistic models were no longer significant when adjusting for other possible confounders identified by the DAG method. The authors stress the importance of adequately identifying confounding.

Developing and testing subjective well-being measures for adults have already received much attention from the clinical research community, but for children this has not been the case. Therefore, Ravens-Sieberer and her group worked to conceptualize children’s subjective well-being (SWB) and to produce appropriate item pools to be used in computerized adaptive testings (CATs), based on interviews with experts, children, and parents. They demonstrate that children and adolescents were able to comprehend and respond to questions about happiness, meaningful life, optimism, and goal orientation, and formulate further steps for research.

In economic evaluations, the quality weight to assess the number of QALYs can be gained from appropriate preference-based measures. Wong et al. compared the internal and external responsiveness of 3 preference-based SF-6D indices in patients with CRC. Based on their results, they conclude that the use of a preference-based index mapped from a condition-specific measure improved responsiveness in patients with CRC.

Many years after the introduction of the ‘numbers needed to treat’ method, there is still discussion on how it should be best applied and interpreted. Girerd and colleagues react to a previous article on this subject, highlighting differences between a risk difference (RD) and an incidence rate difference (IRD) approach [2], and Bender and colleagues respond. An informative correspondence is also conducted between McGregor and Guyatt et al., on the limitations and advantages of weak recommendations in the context of the GRADE guidelines [3,4] and on the evidence base to support GRADE formatting recommendations.

The submissions to the Journal of Clinical Epidemiology have substantially increased in recent years, a development also observed by many other journals. Submitting a scientific paper is indeed a very frequent intervention in the career of researchers. We, therefore, recommend the new 1-pager by Kotz and Cals on effective writing and publishing scientific papers, this time dealing with submitting a paper.

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