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Response to Editorial: Estimating Health-State Utility for Economic Models in Clinical Studies: An ISPOR Good Research Practices Task Force Report

This issue of *Value in Health* features an ISPOR Good Research Practices Task Force Report that makes recommendations for estimating health-state utility (HSU) for economic models in clinical studies, accompanied by an editorial by Professor Karen Kuntz. The Task Force Report states the consensus position of the ISPOR Task Force on Good Practices for Outcomes Research–Measurement of Health-State Utility Values for Economic Models in Clinical Studies. The report was developed under the ISPOR Vision 2020 initiative, which identified "Estimating health-state utilities for cost-effectiveness analysis" as one of the top two priorities for the development of good research practices guidance, as no such guidance existed.

The Task Force Report aims to provide helpful, practical advice for researchers planning the collection of health-utility data for economic modeling in clinical studies. Recommendations are made for the design of health-utility data collection in trials; the design of supplementary or alternative studies (including prospective and cross-sectional observational studies); and statistical analyses and reporting. Selection of utility measures and optimization of the timing of assessments to capture utility data for economic model health states and/or acute events (which have a short-term impact on quality of life) are discussed. Other issues considered include the mode of administration of the utility measure, special populations (e.g., patients who are unable to complete assessments), missing data, and generalizability of utility data collected in trials to economic model populations (i.e., patients expected to receive the intervention of interest in routine practice).

We welcome the editorial by Professor Kuntz, also published in this issue of *Value in Health*, which raises some important points and provides an opportunity for clarification of some of the recommendations made in the Good Research Practices Task Force Report.

Professor Kuntz states that "***The recommended measure for estimating health-state utilities is to use a generic preference-based indirect assessment, such as the EQ-5D, which is the preferred measure of many HTA [health technology assessment] authorities***". The Task Force Report does not recommend any particular measure or measures; rather it states that "***An instrument or instruments should be selected based on suitability for the disease or condition of interest, suitability for the population of respondents, and acceptability to the model's audience (e.g., the HTA authorities to which the model is expected to be submitted).***" These recommendations are consistent with selection of a generic preference-based measure, such as the EQ-5D, provided that the measure meets these criteria. Each of these criteria is important in selection of an instrument. Some HTA authorities have expressed a preference for a particular health-utility measure or measures, recognizing that different measurement methods produce different utility estimates, as well as the need for consistency in decision-making. However, it has also been recognized that the preferred measure may not be appropriate in all circumstances [1], and guidance is available on determining whether the preferred measure is appropriate and on selection of alternative measures [2]. If an alternative measure is used, some HTA authorities (e.g., the National Institute for Health and Care Excellence [NICE]) require empirical evidence demonstrating that their preferred measure lacks key dimensions of health and performs poorly on tests of construct validity and responsiveness in the population of interest [2]. The Task Force therefore recommends that "***If there is any doubt about the appropriateness of utility instruments for the condition of interest, this should be evaluated in terms of practicality, reliability, validity, and responsiveness based on empirical evidence*** [2] ***and using methods that take into consideration any requirements of the audience for the economic model (e.g., HTA agencies) for such evaluations***."

Professor Kuntz notes that "***Conducting a direct utility assessment with a standard gamble or time trade-off is essentially reserved as a last-resort option by the task force, despite the large body of literature that report health utilities based on direct assessment (both for hypothetical health states and a person's own health)…In fact, vignettes that are not based on validated HRQoL [health-related quality-of-life] measures do not meet the NICE Methods Guidance for alternatives to EQ-5D*** [2]. ***Though the task force report does not overtly place as high a bar on vignette descriptions, it seems to foreshadow a movement towards more rigorous requirements for vignette development than the traditional practice of developing vignettes based on expert opinion. This would add substantially to the already onerous task of direct utility assessment and the trade-offs between effort and return should be acknowledged and justified with appropriate evidence***." We note that while direct valuation of patients' own health state using time trade-off or standard gamble methods provides direct observations of health utility, there are technical, ethical, and practical obstacles to performing time trade-off and standard gamble experiments with patients. This approach is unlikely to be practical in the context of clinical studies, which are the focus of the Task Force Report. In addition, most HTA-type decision makers prefer the value of health to reflect the preferences or values of society. This cannot be achieved if patients are asked to rate their own health. Vignette studies are discussed only briefly as these are distinct from health-utility data collection in clinical studies (clinical trials and observational studies) which was the focus of the Task Force Report. We agree with Professor Kuntz's observation that vignettes that are not

based on validated HRQoL measures do not meet the NICE requirements for alternatives to EQ-5D [1] and the Task Force Report recognizes the conclusions of the NICE Decision Support Unit that, no matter how good the qualitative work, vignettes will not be able to fully reflect the varied distribution of symptoms, physical functioning, pain, and feelings of well-being among patients in a given health state [2]. We recognize that these methods may have a limited role where it is not possible to collect data from patients directly [2], and we cite published guidelines for their application. But most decision makers prefer health status to be reported by patients themselves and then valued using societal weights. Given the importance of health-utility estimates for HTA decisions in determining patients' and physicians' access to treatments, product price, and manufacturers' return on investment, we believe that if vignettes are to be used, the incremental investment in developing high-quality vignettes is warranted. We also believe that it is important for Good Research Practice guidelines to make recommendations that reflect best practice.

Professor Kuntz raises an important point that early research activities recommended by the Task Force in parallel with phase 1 trials may not end up being useful if the product is not approved. We would like to clarify that these early activities need not be extensive or time consuming and may be tailored according to the product and health condition; the main purpose being to provide enough background information to determine whether there is a need for research in parallel with phase 2 studies. For example, if there is uncertainty regarding whether a health-utility measure is able to detect changes in HRQoL in the condition of interest, qualitative and/or quantitative research may be needed to investigate the appropriateness of the measure before including it in a phase 3 trial. In some cases, collection of data to allow development of a mapping algorithm may be needed, or utility estimates for long-term disease progression may be needed that may not be measurable within the period of follow-up of phase 3 trials. These studies take time, and phase 2 trials may provide an opportunity to conduct some of this research. Lastly, from a pragmatic standpoint of designing randomized trials, this early planning provides health economists an opportunity to engage with the trial development team to assess resources and constraints of including health-utility measures in the planned trials or to explore other opportunities to collect these data outside of the trials. Therefore, when one or more of these situations apply, initial planning as early as the end of phase 1 may be valuable.

Professor Kuntz noted that the early research steps should be more explicit about what is entailed for the model conceptualization process, referring the reader to the ISPOR-SMDM Modeling Good Research Practices Task Force Report on conceptualizing a decision-analytic model. She also commented, ***"The task force report only applies to the collection of health-state utilities for economic models in clinical studies and is not focused on CEAs [cost-effectiveness analyses] alongside clinical trials using statistical comparisons…What's missing is a broader discussion of factors that should be considered when deciding if a model should be used or not in the first place."*** The scope of the report was defined during the early discussions among the Task Force leadership group. Details concerning the model conceptualization process and the choice of whether to use a model versus an analysis alongside a trial are not within the scope of the Task Force Report. These considerations are extensive topics in their own right, and guidelines are already in existence. We anticipate that the reader will refer to appropriate best practice guidelines, including those developed by ISPOR, and any requirements of the model's audience (e.g., HTA authorities) in this respect.

We thank Professor Kuntz for her thoughtful editorial and for providing an opportunity for clarification of these aspects of the Task Force Report. We hope that the guideline will be helpful for health economics and outcomes researchers in designing health-utility data collection in clinical trials, optimizing methods, and planning any additional studies needed to supplement trial data, to meet the needs of economic models for HSU estimates.

ISPOR Estimating Health-State Utility for Economic Models in Clinical Studies Task Force

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