Value in Health Volume 20, Issues 3 & 4

The following Editors' Choice articles will be included in the March & April 2017 issues (Volume 20; Issues 3 & 4) of *Value in Health*.

Summaries of selected Editors' Choice articles begin on page 27.

For all articles in these issues, and to see what services *Value in Health* provides for its authors see: http://www.ispor.org/valuehealth_index.asp.

MARCH 2017

ISPOR KNOWLEDGE PRODUCTS

Constrained Optimization Methods in Health Services Research — An Introduction: Report 1 of the ISPOR Optimization Methods Emerging Good Practices Task Force

Kalyan S. Pasupathy, William Crown, Nasuh Buyukkaramikli, Praveen Thokala, Alec Morton, Mustafa Sir, Deborah Marshall, Jon Tosh, William V. Padula, Maarten J. Ijzerman, Peter K. Wong

COMPARATIVE EFFECTIVENESS RESEARCH/HTA

Health Technology Assessment Case Studies: Factors Influencing Divergent HTA Reimbursement Recommendations in Australia, Canada, England, and Scotland

Sam Salek, Nicola Allen, Stuart Walker, Lawrence Liberti *(See summary on page 27)*

ECONOMIC EVALUATION

Costs for Childhood and Adolescent Cancer, 90 Days Pre-Diagnosis and 1-Year Post-Diagnosis: A Population-Based Study in Ontario, Canada

Karen Bremner, Claire de Oliveira, Ning Liu, Mark L Greenberg, Paul C. Nathan, Mary L. McBride, Murray D. Krahn *(See summary on page 27-28)*

HEALTH POLICY ANALYSIS

The Impact of China's National Essential Medicine Policy and Its Implications for Urban Outpatients: a Multivariate Difference-in-Differences Study

Jing Wu, Liman Ding

This article evaluates the effects of the National Essential Medicine Policy on outpatient service utilization and expenditure in Tianjin, China.

PATIENT-REPORTED OUTCOMES

A Review of Patient-Reported Outcome Labeling in the United States (2011-2015)

Ari Gnanasakthy, Carla DeMuro, Margaret Mordin, Emily Haydysch, Lynda Doward

The authors review new drug approvals (NDAs) by the Food and Drug Administration for 2006-2010 to show that 24.1% of new drugs had patient-reported outcome-related labeling. The authors review PRO-related labeling for NDAs for 2011-2015 and compare key findings reported previously.

PREFERENCE-BASED ASSESSMENTS

Preference Weighting of Health State Values: What Difference Does It Make, and Why?

Admassu Lamu, Thor Gamst-Klaussen, Jan Abel Olsen

This paper examines the extent to which preference-weighted value sets differ from unweighted values in the EQ-5D-5L and 15D instruments, based on a comprehensive dataset from 6 OECD countries, each with a representative healthy sample and 7 disease groups (N=7933).

POLICY PERSPECTIVE

Emerging Guidelines for Patient Engagement in Research

Susan Joan Bartlett, John Kirwan, Maarten de Wit, Lori Frank, Kirstie Haywood, Sam Salek, Samantha Brace-McDonnell, Anne Lyddiatt, Skye P. Barbic, Jordi Alonso, Francis Guillemin

In this article, the authors describe and discuss different experiences of integrating patients as full research partners in outcomes research from multiple perspectives (e.g., researcher, patient, and funder), drawing from 3 real-world examples.

SYSTEMATIC LITERATURE REVIEWS

The Estimation and Inclusion of Presenteeism Costs in Applied Economic Evaluation: A Systematic Review

Jesse Kigozi, Sue Jowett, Martyn Lewis, Pelham Barton, Joanna Coast *(See summary on page 28)*

BRIEF REPORTS

Health State Utilities Associated with Glucose-Monitoring Devices

Louis Matza, Katie Stewart, Evan Davies, Richard Hellmund, William Polonsky, David Kerr *(See summary on page 28)*

DECISION-MAKER COMMENTARY

Treacle and Smallpox: Two Tests for Multicriteria Decision Analysis Models in Health Technology Assessment

Alex Morton

In this commentary, the authors argue for 2 reasonable tests for MCDA models: the treacle test (can a winning intervention be incompletely ineffective?) and the smallpox test (can there be a winning intervention for a disease that no one suffers from?).

APRIL 2017

COMPARATIVE-EFFECTIVENESS RESEARCH

HTA Policies for Use of Real-World Data in Health Technology Assessment: A Comparative Study of 6 HTA Agencies

Amr Makady, Renske ten Ham, Anthonius de Boer, Hans Hillege, Olaf Klungel, Wim Goettsch

This study aimed to review policies of 6 European HTA agencies on real-world data use in relative effectiveness assessments of drugs.

ECONOMIC EVALUATION

A Multigene Test Could Cost-Effectively Help Extend Life Expectancy for Women at Risk of Hereditary Breast Cancer

Yonghong Li, Andre Arellano, Lance Bare, Richard Bender, Charles Strom, James Devlin *(See summary on page 28)*

PATIENT-REPORTED OUTCOMES

Evaluation of Non-Completion Bias and Long-Term Adherence in a 10-Year Patient-Reported Outcome Monitoring Program in Clinical Routine

Eva Gamper, Virginie Nerich, Monika Sztankay, Caroline Martini, Johannes M. Giesinger, Lorenza Scarpa, Sabine Buxbaum, Martin Jeller, Bernhard Holzner, Irene Virgolini *(See summary on page 28-29)*

PREFERENCE-BASED ASSESSMENTS

R1 Instrument-Defined Estimates of the Minimally Important Difference for EQ-5D-5L Index Scores

Jeffrey A. Johnson, Nathan S. McClure, Fatima Al Sayah, Feng Xie, Nan Luo

In this article, the authors estimate the minimally important difference of EQ-5D-5L index score for available scoring algorithms including Canada, China, Spain, Japan, England, and Uruguay.

METHODOLOGY

Cost-Effectiveness Thresholds in Global Health: Taking a Multi-Sectoral Perspective

Michelle Remme, Melisa Martinez-Alvarez, Anna Vassall

The authors illustrate how current cost-effectiveness thresholds could result in health losses, particularly when considering health-producing interventions in other sectors or public health interventions with multi-sectoral outcomes.

SYSTEMATIC LITERATURE REVIEWS

Systematic Review of Health Economic Impact Evaluations of Risk Prediction Models: Stop Developing, Start Evaluating

Anoukh van Giessen, J. Peters, B. Wilcher, C.J. Hyde, K.G.M. Moons, G.A. de Wit, Erik Koffijberg *(See summary on page 29)*

Value in Health Editors' Choice Article Summaries

MARCH 2017

Health Technology Assessment (HTA) Case Studies: Factors Influencing Divergent HTA Reimbursement Recommendations in Australia, Canada, England, and Scotland (pp. 320-328)

This paper provides a comparison of national HTA recommendations from Australia, Canada, England, and Scotland and presents case studies to provide insights for factors leading to divergent outcomes. The scope and methodologies used to conduct HTA can vary greatly among agencies, because affordability and social and political factors are unique to each coverage population. The objectives of this study were to evaluate the national regulatory and HTA and reimbursement pathways for public health care in the four regions, and compare HTA recommendations to identify factors for differing national HTA recommendations. Information from the public domain was used to develop a regulatory and reimbursement process map for each jurisdiction. Published HTA agency recommendations from the Pharmaceutical Benefits Advisory Committee in Australia, the National Institute for Health and Care Excellence in England, the Common Drug Review in Canada, and the Scottish Medicines Consortium were identified and compared. Eighty-nine submissions met the study inclusion criteria, but only 26 were reviewed by all 4 agencies. Interestingly, the proportion of negative reimbursement recommendations decreased as the number of agencies that received a submission increased. The seven medicines that were reviewed by all HTA agencies (but only received a negative recommendation from one agency) were selected as case studies to evaluate the rationale for the initial recommendations and resubmissions. These case studies demonstrate examples in which new medicine indication pairs have been rejected because of uncertainties surrounding a range of factors including cost-effectiveness, comparator choice, clinical benefit, safety, trial design, and submission timing.

Costs for Childhood and Adolescent Cancer, 90 Days Prediagnosis and 1 Year Post Diagnosis: A Population-Based Study in Ontario, Canada (pp. 345-356)

This paper provides estimates of the costs of cancer care for children (≤14 years old) and adolescents (15-19 years old) in the 90-day period prediagnosis and the 1-year period after diagnosis. Patients who were diagnosed with cancer from 1995 to 2009 in Ontario, Canada were identified in population-based cancer registries and each was matched to 3 non-cancer controls. Patients and controls were linked to administrative health care data to obtain estimates of total costs of care for children and adolescents for the 3 most common diagnostic groups (leukemia, lymphoma, and central nervous system tumors), and a fourth category for "other" cancers. Net costs were defined as the cost difference between patients with cancer and controls. All costs were from the public payer perspective and expressed in 2012 Canadian dollars. There were 4,396 children diagnosed with cancer during our analysis period; 36% >

had leukemia, 21% central nervous system tumors, 10% lymphoma, and 33% other cancers. Adolescents numbered 2,329; the majority were diagnosed with lymphoma (29%). Bone and soft tissue sarcoma, germ cell tumor, and thyroid carcinoma each comprised 12% to 13%. Mean net prediagnosis costs were $5,810 and $1,127, while mean net postdiagnosis costs were $136,413 and $62,326 for children and adolescents, respectively. The highest cost postdiagnosis was for leukemia ($157,764 for children and $172,034 for adolescents). Inpatient hospitalization costs comprised 69% to 74% of postdiagnosis costs. Costs were higher for patients who died within 1 year of diagnosis; this finding held for both patient cohorts. Costs of caring for children are higher than those for adolescents and adults. Substantial survival gains in children mean that treatment may still be very cost-effective. These estimates are essential to assess the cost-effectiveness of cancer care for children, adolescents, and measure health system performance.

The Estimation and Inclusion of Presenteeism Costs in Applied Economic Evaluation: A Systematic Review (pp. 496-506)

This paper explores the important but rarely addressed concept of presenteeism in health economic evaluations. Productivity costs in relation to paid work broadly consist of productivity loss to society because of absence from work (absenteeism) or working with limitations due to illness (presenteeism). The evidence is that presenteeism generates a significantly higher cost than absenteeism, but is rarely considered in economic evaluations. Exclusion of these costs could significantly underestimate the value of interventions that reduce limitations at work due to illness. This research aimed to explore the extent to which presenteeism has been considered in economic evaluation and cost-of-illness studies. The paper identified studies that have included presenteeism, and examined how valuation was performed, and the degree of impact on total costs. This review highlights the limited role of presenteeism in economic evaluations and the impact of its exclusion. While acknowledging that further research is required to improve methods for capturing and valuing presenteeism, it is clear that economic studies in health care should prioritize the inclusion of presenteeism alongside absenteeism in estimating productivity loss.

Health State Utilities Associated with Glucose-Monitoring Devices (pp. 507-511)

A growing body of evidence suggests that health-state utilities may be influenced not only by health status and treatment outcomes, but also by the process of receiving care. These process utilities quantify the impact of treatment process attributes, such as mode of administration and dose frequency. Small utility differences associated with treatment process could affect results of a cost-utility analysis and therefore have important implications for subsequent decision making. For patients with diabetes who are treated with insulin, an important aspect of the treatment process is self-monitoring of glucose levels. Conventional glucose monitoring requires a blood sample, typically obtained by pricking the finger. In contrast, a recently developed glucose-monitoring system does not require routine finger pricks. Instead, patients wear a sensor on the back of the upper arm and scan the sensor with a touch-screen device to obtain glucose levels. Differences in the process of glucose monitoring could have an impact on a patient's quality of life. If this impact were quantified in terms of health-state utility, it could be useful for economic modeling. Therefore, the purpose of this study was to estimate the utilities associated with the conventional and newer glucose-monitoring devices. Overall, current findings indicate that there is a measurable difference in preference between different glucose-monitoring strategies. Results provide potentially useful utility values that may be used in cost-utility models focusing on treatment and management of diabetes. In addition, this study adds to previously published research on treatment-process utility. Whereas previous studies have identified utilities associated with a range of treatment-process attributes, such as mode of administration and dose frequency, the current study is the first to quantify the utility impact associated with the ongoing use of medical devices.

APRIL 2017

A Multigene Test Could Cost-Effectively Help Extend Life Expectancy for Women at Risk of Hereditary Breast Cancer (pp. 547-555)

Multigene panel testing is increasingly being used to assess risk for hereditary cancer because multiple pathogenic variants in multiple genes confer risk for cancer. This study investigated whether in patients at risk of hereditary breast cancer, testing with a panel of 7 breast cancer associated genes is cost effective compared with only testing the 2 BRCA1/2 genes, which harbor the most common pathogenic variants. The additional genes in the 7-gene panel would result in an increased average life expectancy if those who tested positive followed the risk reduction recommended by the National Comprehensive Cancer Network guidelines. The cost of these life-year gains were assessed in a decision-analytic model that compared the 7-gene to the BRCA1/2 testing scenarios. The model estimated life expectancies and total health care costs from a payers' perspective, which included costs for genetic testing, genetic consultation, and cancer treatment, as well as the guideline-recommended risk-reduction strategies: prophylactic surgery, MRI surveillance, and mammography. The model predicted that 7-gene testing would increase quality-adjusted life years at a cost of $48,000 for patients aged 40 years and $70,000 for patients aged 50 years. Life expectancy would increase at a cost of $24,000 per year for patients aged 40 years and $42,000 per year for patients aged 50 years. Furthermore, the authors found that the more frequently the pathogenic variants are detected, the more cost effective multigene panel testing becomes. Thus, as more pathogenic variants are found in each gene and as new breast cancer-associated genes are added to panels, multigene panel testing should become even more cost effective in the clinical management of patients at risk of hereditary breast cancer.

Evaluation of Non-Completion Bias and Long-Term Adherence in a 10-Year Patient-Reported Outcome Monitoring Program in Clinical Routine (pp. 610-617)

This paper represents a case study on the investigation of a patient-reported outcome (PRO) monitoring program in clinical oncological routine. The focus was on the sustainability of routine PRO measurement outside a controlled study setting and on the representativeness of collected data for the population of interest. The potential risk of not completing a PRO questionnaire and of poor adherence with routine PRO assessment because of patient characteristics was assessed. Furthermore, we were interested in the impact of the mode of PRO assessment on completion rates and compared paper-pencil and electronic data collection with regard to the number of missing questionnaires. Data from 1,484 eligible patients who were admitted to the department to receive nuclear therapy or for follow-up visits were used for analyses. The rate of patients who never completed PRO questionnaires was clearly higher when using paper-pencil assessment (odds ratios [OR] between 2.72 and 4.31) as was the rate of patients with poor adherence with routine PRO assessment (OR 2.23). Furthermore, male patients had a higher risk of poor adherence (OR 1.69), independent of mode of assessment. While most patients completed a PRO questionnaire at least once, there were high percentages (60.1% to 76.9%) of poor long-term adherence (defined as >20%

missing questionnaires across observed period) within both electronic and paper-pencil assessments. Our results indicate that a potential completion bias regarding certain patient characteristics requires consideration when aiming at using routine PRO data for retrospective group level analyses. In general, electronic PRO assessment increased the usability our clinical routine PRO data by clearly increasing overall completion and long-term adherence rates.

Systematic Review of Health Economic Impact Evaluations of Risk Prediction Models: Stop Developing, Start Evaluating (pp. 711-719)
In the past decades, a huge number of risk prediction models (PMs) have been developed with the purpose to aid in medical decision making. The application of a PM, especially if it includes (new and expensive) test results, may be regarded as a medical intervention. However, whereas medical interventions are evaluated increasingly on their impact in terms of (long-term) health effects and costs, evaluation of PMs is often limited to assessment of statistical performance. In this paper, we evaluated the current state of health economic evaluation (HEE) of PMs by performing a comprehensive systematic review. After searching four large databases for HEEs of PM-based strategies and compiling an extensive checklist, we scored items focusing on general characteristics, model characteristics, and quality of HEEs of PMs. We found that despite the many PMs in the medical literature, HEE of PMs remains rare. If performed, such evaluations commonly are not conducted in collaboration with the PM developers nor based on the original individual patient data, possibly limiting modeling possibilities. In addition, we observed great variety in the quality and methodology of the HEEs, which may complicate interpretation of HEE results and implementation of PMs in practice. Because specific guidance on performing HEE of PMs is currently lacking, we evaluated and discussed the specific challenges in performing HEEs of PMs, based on the results of our review, and provided recommendations on these challenges. ■