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The Official News & Technical Journal Of The International Society For Pharmacoeconomics And Outcomes Research

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LETTER FROM THE EDITOR



All good things must come to an end and *ISPOR CONNECTIONS* is no exception to that rule. This marks the final issue of the 20-year run of our Society's "news and technical journal" (so hang on to this one, as it's destined to become a collector's item — hello, eBay!).

But fear not, faithful readers, as we're not trying to do anything to reduce your SF-36 mental health score — just the opposite, in fact. We wouldn't dare take away these pages you so carefully turn with anticipation without providing something to fill the void. Rather, we are engineering a makeover of the look and feel and content of *ISPOR CONNECTIONS* and — not to be outdone by the world's corporate giants — we are rebranding along the way. *ISPOR CONNECTIONS* is giving way to a new and improved publication, to be called Value & Outcomes Spotlight. You'll see what we're talking about in the New Year, when Vol. 1, No. 1 drops in your mailbox.

Until then, this final issue of *ISPOR CONNECTIONS* comes on the heels of the ISPOR 17th Annual European Congress, hosted by the 'colorful' city of Amsterdam (red lights, green leaves, William of Orange!), and we devote a full seven pages of this issue to various reflections, write-ups and photos from the meeting. The event drew nearly 5,000 attendees, who no doubt enjoyed the congress and with any luck found time to partake in the city's unique charms. It was another great meeting of our Society, with an informative scientific program, open forums for discussing our most pressing policy challenges, and excellent networking opportunities. It also represented a transition to ISPOR's new CEO and Executive Director, Nancy Berg (introduced on page 19).

We also have a variety of interesting articles worthy of this final issue of *ISPOR CONNECTIONS*, particularly two pieces from our Methodology section. The first focuses on meta-analyses of diagnostic test data and provides a nice summary of the pitfalls of pooling estimates of sensitivity and specificity separately, which ignores the correlation between these measures. Fortunately, rigorous methods have been developed to take account of this correlation in the estimation of pooled sensitivity and specificity as well as the receiver-operating-characteristic (ROC) curve.

The second methodology piece provides interesting insights on patient and caregiver experiences with electronic clinical outcomes assessments (eCOAs), such as patient-reported outcomes surveys, which in the current era are completed on tablets, smartphones, or other electronic devices much more frequently than on traditional hard-copy formats. The use of electronic devices facilitates measurement of the respondent experience, particularly as relates to the timing and duration of instrument completion (which can be done automatically by the device). The study findings debunk notions that eCOAs are overly burdensome to respondents, and the authors report some interesting excerpts from patient interviews that back up their findings. My personal favorite is the 12-year-old boy who said of his experience, "Um, I like how simple it was. It kind of reminded me of, like, the Nintendo DS."

It's a fitting metaphor for our current theme of out with the old and in with the new. We hope you'll react positively to *Value & Outcomes Spotlight* and can only dream that one day you'll enjoy it as much as a child does a handheld gaming device.

With best wishes for the holiday season.

David Thompson, PhD
Editor-in-Chief, *ISPOR CONNECTIONS*

Reflections from Amsterdam

Adrian Towse, MA, MPhil, 2014-2015 ISPOR President and Director, Office of Health Economics (OHE), London, UK



ISPOR's 17th Annual European Congress was a record-size of meeting for ISPOR and a great success. I am very grateful to the Co-Chairs Carin Uyl-de Groot and Finn Børllum Kristensen for all of their hard work, supported by many others including, once again, superb organisation by the ISPOR staff. I hope those of you who attended also got a little time to see the wonderful city of Amsterdam.

It was an opportunity to welcome Nancy Berg, the new CEO and Executive Director of ISPOR. Nancy joined ISPOR at the end of October of 2014. Nancy has run bigger member driven organisations than ISPOR and with a global span. (Yes they do exist – but not in the area of health outcomes research!) I am confident that she will work with ISPOR members and with the ISPOR staff to continue to ensure ISPOR has the organisation to support all of us.

I want to thank Bill Crown again for his leadership of the recruitment process during his Presidency. We look forward to working with you Nancy.

Nancy takes over an organisation that is in great shape as a result of Marilyn Dix Smith's leadership, and because of the hard work of many ISPOR members. ISPOR continues to grow, and to grow in all regions of the world.

As I said in my remarks in Montreal in an earlier issue of *ISPOR CONNECTIONS*, the priority for the organisation is to enable its members to contribute to improving the efficiency and effectiveness of health systems. We do this with one objective - to improve people's health. We make our contribution by developing the science of outcomes research and health economics to meet the diverse needs of decision makers. They have to address macro problems of making a health system deliver efficiently, as well as the micro level necessity of making informed decisions about the health technologies to use in that health system. Outcomes research can support both of these areas of decision making. ISPOR needs to help make that happen. One without the other is of limited value. We must tackle both.

ISPOR seeks to do this through our four key activities:

1. **Providing a global network for researchers and decision makers to come together.** Our global network now has two Regional Consortia (Asia Consortium and Latin America Consortium) and two regional networks, the Central and Eastern Europe Network and Arabic Network, and Africa Network as well as over 70 regional chapters, plus an extensive network of student chapters.

2. **Promoting research.** I want to draw attention to the 32% increase in *Value in Health's* impact factor, as well as ISPOR's plans to get the *Value in Health Regional Issues* listed on Medline/ PubMed. I also want to remind all ISPOR members of the ISPOR Scientific Presentations Database – much of the material presented at ISPOR's meetings is available on-line subject of course to authors / presenters consent. It is a huge resource, on line and free. In addition, the ISPOR Released Presentations page contains presentations available from specific meetings, also online and free.

3. **Promoting education.** Many ISPOR members attended short courses before the Amsterdam meeting. I also want to highlight the webinar series. The next two webinars you can register for are on Indirect Treatment Comparisons and on Performance Based Risk Sharing Arrangements.

4. **Providing resources.** I want to highlight three areas which demonstrate the increasing importance of partnering with other organisations when they have expertise that can help ISPOR deliver better resources to its members.

a. **Assessing the Evidence for Health Care**

Decision Makers

This is an interactive on-line questionnaire; a collaboration between ISPOR, the Academy of Managed Care Pharmacy (AMCP), and the National Pharmaceutical Council (NPC). It is

designed to assist health care professionals and/or decision makers in reviewing the evidence. It provides guidance on the effective use of the information in published and unpublished studies to determine if they are: a) relevant to the setting/decision in question, and b) credible.

b. **Tools for Patients**

ISPOR is collaborating with the European Patients' Academy on Therapeutic Innovation (EUPATI) as part of a European Commission / EFPIA Innovative Medicines Initiative (IMI).

c. **Good Practices for Outcomes Research**

This is one of three collaborative ISPOR/ AMCP/ NPC Good Practice Task Force reports that underpinned the evidence for decision makers' questionnaire I referred to earlier. I also want to draw attention to the earlier collaboration with the Society for Medical Care Decision Making (SMDM) for a series of very important Modelling Task Force Reports published in *Value in Health*.

Working with other organisations can be demanding, but although ISPOR is capable of doing many things on its own, there will be opportunities when we can achieve more in collaboration with other organisations and we will take them. In this context, it was a pleasure to welcome Carole Longson, the President of Health Technology Assessment International (HTAI) as a speaker in the Second Plenary Session in Amsterdam.

I want to end by revisiting one of many highlights of the Amsterdam Congress – the Avedis Donabedian Lifetime Achievement Award to Professor Bengt Jönsson. He is one of the true pioneers in the field – his 1976 doctoral thesis was on cost-benefit analysis in public health and medical care and since then he has published hundreds of papers, reports and book chapters worldwide.*

I recommend to ISPOR members a collection of essays published earlier this year commemorating Bengt's lifetime contribution to health economics. Edited by Tony Culyer and Gisela Kobelt, the book's list of contributors reads like a worldwide who's who of experts in the field, including Martin Buxton, Tony Culyer, Mike Drummond, Peter Zweifel, Bob Evans, Uwe Reinhardt, and Milt Weinstein. The 30 chapters address a range of topics including: health economics and politics; the theory underlying the design of health economic evaluation and its use in decision making; specific analytical techniques and approaches, e.g. QALYs; appropriate use of cost effectiveness analyses in health care decision making in general, in specific countries or to meet specific goals such as designing a benefits package; the health economics of particular diseases, e.g. diabetes and cancer; and chapters specifically on aspects of Bengt's contributions to the field.

*The book may be downloaded as a PDF from the website of the Swedish Institute of Health Economics. <http://www.ihe.se/portrait-of-a-health-economist.aspx>.

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Considerations When Meta-Analyzing Diagnostic Test Sensitivity and Specificity When an Adequate Reference Standard Exists



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KEY POINTS

- The assessment of the utility of a diagnostic test requires an understanding of two essential measures of a test performance; namely, sensitivity and specificity.
- Individual pooling of sensitivity and specificity estimates using traditional meta-analytic methods fails to account for the joint relationship between sensitivity and specificity.
- Current guidance suggest more complex (bivariate and hierarchical summary receiver operator curve) methods for pooling sensitivity and specificity be used preferentially.

The assessment of the utility of a diagnostic test requires an understanding of two essential measures of a test performance: sensitivity and specificity. Test sensitivity refers to the probability that the diagnostic test of interest will correctly identify a diseased person, while test specificity is defined as the probability its result will correctly identify a non diseased person. In order to calculate sensitivity and specificity, the binary (disease present or absent) results of a diagnostic test are compared to a reference standard test that is assumed to be 100% accurate at detecting presence or absence of disease. Using the 2x2 table depicted in Figure 1, sensitivity is calculated as $a/[a + c]$ and specificity as $d/[b + d]$.

Figure 1. Schematic for Calculating Sensitivity and Specificity of a Diagnostic Test.

TRUE STATE: Disease Presence via Reference Standard		
	Disease Present	Disease Absent
DIAGNOSTIC STATE: Index Test Result		
Positive	a	b
Negative	c	d
Total# Diseased & Non-Diseased	a+c	b+d

Table 1. Trade-Off between Sensitivity and Specificity of Detecting Acute Heart Failure with B-Type Natriuretic Peptide

BNP, pg/mL	Sensitivity, %	Specificity, %
50	97	62
80	93	74
100	90	76
125	87	79
150	85	83

Ideally, a test would have both near-perfect sensitivity and specificity (approaching 100%); however, in practice it is generally the case that as one of these measures increases, the other will decrease. This phenomenon is often an artifact of the need to re-categorize a continuous test result into a binary result (presence or absence of disease) for ease of interpretation. For example, a B-type (or brain) natriuretic peptide (BNP) level is a blood test often drawn to help rule out the presence of acute heart failure in the emergency setting. BNP levels are reported on a continuous scale, with a threshold of 100 pg/mL used for categorizing the results as positive or negative for having acute heart failure. (This threshold is called a “positivity threshold.”) Thus, patients with a score ≥ 100 are categorized as being positive for acute heart failure while patients with a score < 100 are categorized as not being in acute heart failure. Using this 100 pg/mL positivity threshold, BNP has a sensitivity of 90% and a specificity of 76% [1]. Some clinicians, however, have advocated for using a different positivity threshold. When different values are used (Table 1), we can see the expected trade-off between sensitivity and specificity often referred to as “threshold effect”.

META-ANALYSIS OF DIAGNOSTIC TESTS

Separate pooling of sensitivity and specificity estimates using traditional meta-analysis methods do not take into account the non-independent or joint relationship between sensitivity and specificity across diagnostic studies, as mentioned previously. Not accounting for this dependency can give suboptimal estimates of test performance. Consequently, more complex methods have been developed that account for the joint relationship between sensitivity and specificity across studies. These methods also account for between-study heterogeneity (variation) in sensitivity and specificity

estimates (that is, they account for heterogeneity of estimates between studies and hence use a random effects model).

These newer methods for pooling sensitivity and specificity include random-effects bivariate [2] and hierarchical summary receiver operator curve [3] methods. In their simplest forms (no addition of covariates) these methods are mathematically equivalent and can be used to produce, among other metrics, average (mean) sensitivity and specificity estimates across studies (with an accompanying 95% confidence and prediction regions) and a summary curve representing the average receiver operating characteristic (ROC) curve (with sensitivity or the “true negative rate” on the vertical axis and one minus specificity or the “false positive rate” on the horizontal axis) for all studies. The more technical details of these models, and the impact of adding covariates into these models, are beyond the scope of this article but can be found elsewhere [2-5].

No firm guidance exists to aid investigators in whether summary points (one pair of pooled sensitivity and pooled specificity) or summary ROC (a series of pooled sensitivity and pooled specificity across different thresholds) is preferred for interpreting pooled results. Some researchers suggest that summary (mean) estimates may be more useful when sensitivity and specificity estimates do not vary widely across studies, whereas summary curves may be best positioned when the sensitivity and specificity of various studies included in the meta-analysis vary over a large range [4,5].

SOFTWARE IMPLEMENTATION

When performing separate pooling of sensitivity and specificity values, statistical software programs such as Meta-DiSc [6] or Review Manager [7] can

be used. The previously mentioned bivariate and hierarchical summary receiver operator curve methods, however, require more sophisticated statistical software programs. Both commercial and freeware programs are available to perform these more complex analyses (e.g., SAS, Stata, R with 'mada', WinBUGS, OpenBUGS), and these methods can be implemented using either a frequentist or Bayesian approach [5].

REAL-LIFE EXAMPLE

Coronary angiography (CAG) is an invasive method for detecting significant coronary artery narrowing, with >50% arterial stenosis indicative of coronary artery disease (CAD). Stress myocardial perfusion imaging (MPI) using positron emission tomography (PET) is a noninvasive diagnostic test for assessing the presence of CAD based upon visual interpretation and a validated (semi-quantitative) scoring approach of its results [8,9].

Nine prospective studies on diagnostic accuracy of PET MPI with CAG serving as a reference standard have been published (Table 2) [10].

For this example, we assume CAG is a perfect reference standard (100% diagnostic accuracy) and that PET MPI is unlikely to be associated with a threshold effect due to its standardized use (all studies used the same guidance-driven protocol

Table 2. Patient-Level Data for Included Positron Emission Tomography Studies
FN=false negative; FP=false positive; TN=true negative; TP=true positive

First Author, Year	a*(TP)	b*(FP)	c*(FN)	d* (TN)	Sensitivity	Specificity
Abramson, 2000	8	1	1	9	88.9	90.0
Chow, 2007	18	1	1	4	94.7	80.0
Go, 1990	142	11	10	39	93.4	78.0
Kajander, 2010	36	6	2	60	94.7	90.9
Marwick, 1992	43	1	3	3	93.5	75.0
Sampson, 2007	41	10	3	10	93.2	50.0
Santana, 2007	42	2	3	6	93.3	75.0
Stewart, 1991	50	3	10	18	83.3	85.7
Tamaki, 1988	47	0	1	3	97.9	100

**Corresponds to the lettering in Figure 1.*

for determining CAD) in the included studies [9]. Because we do not expect a threshold effect and sensitivity values did not vary over a wide range, summary estimates of sensitivity and specificity were deemed most desirable and a bivariate meta-analysis model was used. The bivariate model was fit in 'R' using the 'mada' package [11] and a summary estimates were obtained, along with summary curve plotted in the ROC space (Fig. 2).

The results of this analysis indicate PET MPI had a sensitivity of 91.3% [95% confidence interval (CI), 87.5-94.0%] and a specificity of 78.0% (95% CI, 66.4-86.4%). These values are at least as good as other noninvasive strategies for diagnosing CAD and, for this reason; the inclusion of PET MPI is common in clinicians' strategy to diagnosis CAD. The 95% confidence region or ellipse around the mean (summary) estimate of sensitivity and

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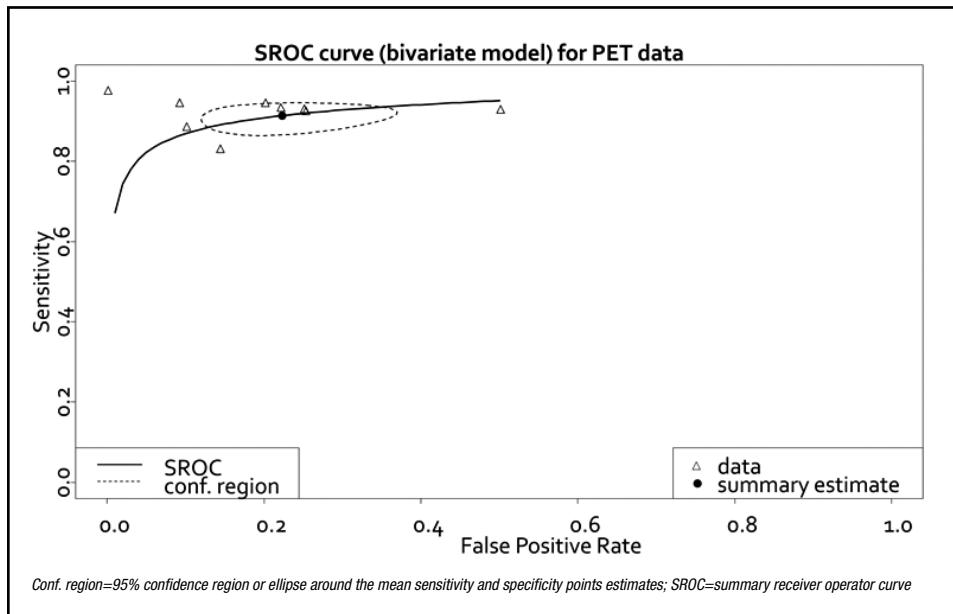


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Figure 2. Summary Point (with 95% Confidence Region) and Summary Curves Estimates Depicting the Results of the PET MPI Bivariate Meta-Analysis.



specificity in this figure can be used to show the region containing likely combinations of the mean values of sensitivity and specificity.

For sake of comparison, if a traditional meta-analysis was performed for sensitivity separate from specificity using a simple random-effects approach, pooled estimates would have been 92.6% (95%CI, 89.8-94.8%) and 81.3% (95%CI, 74.9-86.6%), respectively. While these estimates do not differ dramatically from the corresponding estimate already given from the more advanced bivariate approach, this is not unexpected; as summary sensitivity and specificity estimates (and their standard errors) generated using simpler and more complex approaches are not expected to differ by much (often <5%) [12,13].

Ideally, a test would have both near-perfect sensitivity and specificity (approaching 100%); however, in practice it is generally the case that as one of these measures increases, the other will decrease.

Nevertheless, compared with traditional approaches with separate pooling of sensitivity and specificity, multivariate approaches may give (but not always give) more refined (closer to the true population value) and precise (lower standard errors) estimates of sensitivity and specificity, particularly if these metrics are strongly correlated (i.e., when a threshold effect exists) and when their results are not provided in all studies (missing data) [13]. There are other, more technical reasons for favoring the multivariate approach [13]. The more complex bivariate and hierarchical summary receiver

operator curve methods have been recommended in guidance documents from both the Agency for Healthcare Research and Quality (AHRQ) Evidence-Based Practice Center (EPC) [4,14] and the Cochrane Collaboration [5] because these approaches are more “theoretically motivated.”

RECOMMENDATIONS

- Current guidance documents suggest the more complex (bivariate and hierarchical summary ROC) methods for pooling sensitivity and specificity should be used preferentially, since traditional meta-analysis methods do not make allowances for the joint relationship between these metrics.
- The choice between reporting summary point and summary curve estimates when performing a diagnostic test meta-analysis should take into account the degree to which sensitivity and specificity estimates vary across studies.
- Summary estimates may be preferred when sensitivity and specificity estimates do not vary widely across studies, whereas summary curves may be preferred when they do.
- Performing these more complex analyses will require experience with more sophisticated computational algorithms, which could be implemented using programs such as SAS, Stata, R, or WinBUGS.
- Those whom wish to gain a better understanding of how to implement these advanced methods (including their use in more complex situations where covariates are entered into the model) may wish to start by reviewing the diagnostic test guides on meta-analysis from the Cochrane Collaboration and the Agency for Healthcare Research and Quality [4,5,14].

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Electronic Clinical Outcomes Assessments (eCOAs). How Long Do They Take to Complete and How Burdensome are They for Patients?

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KEY POINTS

- Respondent burden is often a concern when incorporating PROs and other COA instruments in trials.
- Retrospective data from three small qualitative studies demonstrated that completion times for eCOA instruments are shorter than typically estimated, and not burdensome to patients, even children/adolescents.
- There is no evidence that longer diaries result in more missing data.

WHAT ARE eCOAS?

Electronic clinical outcome assessments (eCOAs) include patient-reported outcomes (PRO), observer-reported outcomes (ObsRO), clinician reported outcomes, and performance related outcomes instruments, however, the term is mainly used with reference to PROs and ObsROs. eCOAs are completed on handheld PDAs, smartphones, or tablets and are increasingly used in clinical trials to replace traditional pen and paper methods of administration.

The advantages of electronic over paper administration include the avoidance of secondary data errors, more accurate and complete data, the ability to 'date and time stamp' precisely when respondents complete the instruments, and to record the time taken to complete upon each administration [1-5].

THE CONCERN ABOUT RESPONDER BURDEN

Regardless of mode of administration, there often remains a concern regarding the burden experienced by patients or caregivers when asked to complete a number of COA items, especially when COAs are completed daily or at multiple time points over a long period of time. Although relevant to all, these concerns are particularly critical in certain populations such as children, elderly patients, severely ill patients and patients with considerable physical, emotional or cognitive disability. The burden experienced can be affected by the number and format of questions, variability in response scales and the level of complication in the wording of items and instructions [1, 6]. Features of eCOA devices, such as skip patterns or 'branching logic' can decrease the time needed to complete instruments and therefore reduce the respondent burden, but despite these advantages, there is often still concern over the time it takes patients to complete instruments on an eCOA device.

WHAT CAN WE LEARN FROM SPECIFIC EXAMPLES OF ECOAS?

The aim of this research was to use retrospective

Figure 1. Overview of the Studies Included in Analyses.

Fibromyalgia	A women's health condition	Pediatric constipation (CC) and irritable bowel syndrome (IBS-C)
<p>Purpose and design</p> <ul style="list-style-type: none"> •Content validity testing of a daily diary assessing symptoms of fatigue in fibromyalgia, through pilot testing and cognitive debriefing. <p>Number of items</p> <ul style="list-style-type: none"> •23 items <p>Recall period</p> <ul style="list-style-type: none"> •24 hours <p>Population</p> <ul style="list-style-type: none"> •21 patients in the US were asked to complete the diary <p>Completion schedule</p> <ul style="list-style-type: none"> •Once a day, daily, for 4-10 days. The diary items were completed in the evening, between 5pm and midnight 	<p>Purpose and design</p> <ul style="list-style-type: none"> •Content validity testing of two daily symptom diaries and one weekly measure of the impact on health related quality of life. <p>Number of items</p> <ul style="list-style-type: none"> •Daily diary one initially comprised 10 items but was later increased to 13 items •Daily diary two comprised 4 items •Weekly diary comprised 31 items <p>Recall period</p> <ul style="list-style-type: none"> •The daily diaries both had a recall period of the past 24 hours, whereas the weekly questionnaire had a recall period of the past 7 days. <p>Population</p> <ul style="list-style-type: none"> •31 patients in the US (n=19) and in Germany (n=12) <p>Completion schedule</p> <ul style="list-style-type: none"> •Daily diaries once a day for 7-10 days and weekly diary once. 	<p>Purpose and design</p> <ul style="list-style-type: none"> •Content validity testing of child- and observer (parent) - completed eDiaries, developed to assess CC and IBS-C symptoms. <p>Number of items</p> <ul style="list-style-type: none"> •The child-completed diary comprised 36 items (or a minimum of 31 taking skip patterns into account) and the parent-completed diary comprised 39 items (or a minimum of 10 taking skip patterns into account). <p>Recall Period</p> <ul style="list-style-type: none"> •24 hours <p>Population</p> <ul style="list-style-type: none"> •36 Children aged 6-17 with CC or IBS-C and 30 parents of children aged 6-11 with CC or IBS-C at three locations in the US <p>Completion schedule</p> <ul style="list-style-type: none"> •Every day for 5-9 days.

qualitative and quantitative data from three qualitative pilot testing and cognitive debriefing studies to provide evidence regarding the time it actually takes patients and caregivers to complete eCOAs and how burdensome patients and caregivers really find eCOA completion.

THE STUDIES

In each of the three studies, patients or parent/caregivers were required to complete a daily diary on an eCOA device as part of 'mixed methods' pilot testing prior to cognitive interviews. These studies were conducted in patients with fibromyalgia, pediatric chronic constipation (CC), pediatric irritable bowel syndrome with constipation (IBS-C) and a women's health condition. The pediatric conditions were evaluated as part of the same study, and both included both a child completed PRO symptom diary and a parent/caregiver completed ObsRO diary, both completed daily.

For each study, participants first visited the research site for instruction on how to complete the diary and

use the eCOA device, then took the device home and completed it daily for a period of five to ten days. Participants were interviewed about their experience of completing instruments on the device during a second site visit. In all three studies the total time taken to complete the diary each day was recorded, and in two studies that did not involve branching logic, completion time per item was calculated. Number of days missed was captured in only two of the studies. In the cognitive interviews following the diary completion period, participants were asked about how long they thought it took to complete the diaries, and how burdensome they found the daily completion. An overview of the patient samples and study design for the studies is provided in Figure 1.

WHAT DID WE LOOK AT?

Analyses were performed using the eCOA data and any missing data to assess the following:

- Average completion times per questionnaire;
- Average completion times per item where there was no skip pattern/branching logic (women's

Figure 2. Average Completion Times Per Diary.

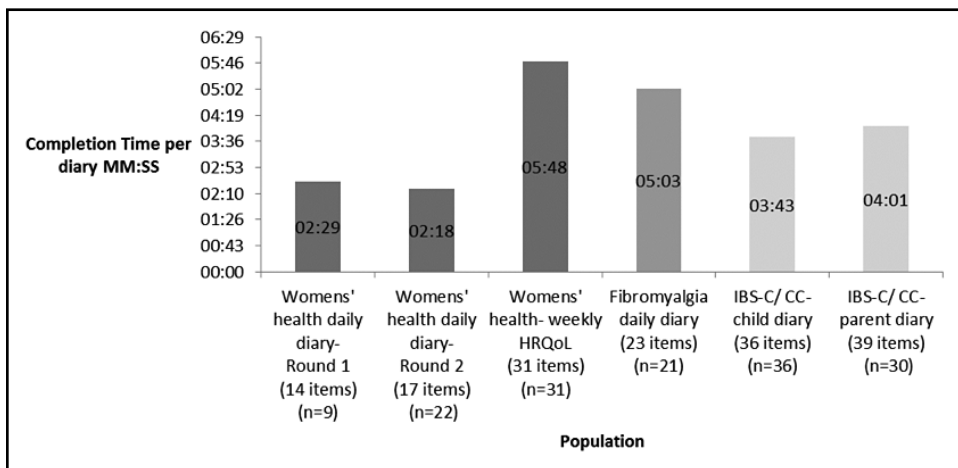
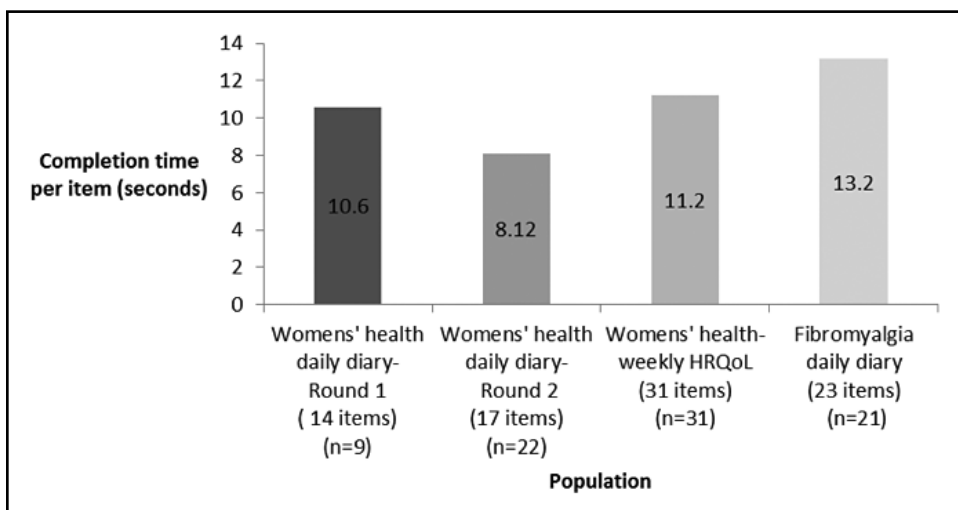


Figure 3. Average Completion Times Per Item.



health and fibromyalgia studies);

- Changes in completion times over the course of a seven-day period;
- Number of missed days throughout each study.

In addition, transcripts from cognitive debriefing interviews were transcribed verbatim and analysed in AtlasTi [6] using thematic analysis to identify patient quotes regarding ease/burden of diary completion.

WHAT DID WE LEARN ABOUT ECOA COMPLETION TIMES?

In all three studies, participants took a relatively short amount of time to complete the COA items, with average per-diary completion times for each disease area ranging from 2 minutes 18 seconds (17 items) to 5 minutes 48 seconds (31 items) (Fig. 2). This was highly variable with the shortest single diary completion being 31 seconds (39 items, parent CC/IBS-C) while the longest single completion time by an individual patient was 45 minutes 34 seconds (23 items, fibromyalgia). This was an outlier (the longest completion time excluding this diary administration being 14 minutes and 24 seconds) – it seems reasonable to believe that this longest time period involved the patient setting the diary aside

for a period of time during their diary completion.

Mean item-level completion times were calculated by dividing the daily completion time by the number of items. As this could not be calculated in diaries involving skip patterns/branching logic, the data is only available from the fibromyalgia daily diary, and the women's health daily and weekly diaries. Mean per-item completion times ranged from 8.12 seconds to 13.2 seconds (Fig. 3).

Notably, the longest single per-item completion time was 2 minutes 5 seconds (however, this is likely to be an anomaly where the patient was distracted and put the diary down during diary completion) and the shortest was 1.6 seconds (both from the 17 item diary completed by the women's health sample). For all three studies the average completion time per day decreased from day 1 to day 7, suggesting a decreasing burden placed on participants over the course of a study (Fig. 4).

WERE COMPLETION TIMES DIFFERENT IN PEDIATRIC SAMPLES?

To further investigate completion times in a pediatric sample, the per-diary completion times for the CC/IBS-C child-completed daily diaries were compared

among the following age groups: 6-8 years, 9-11 years, 12-14 years, and 15-17 years. We found that completion time was slightly longer for younger children in the 6-8 and 9-11 age groups than for children aged 12-17. Notably however, average completion times were still short across all age groups, ranging from just 2 minutes 19 seconds (15-17 year olds) to 4 minutes 14 seconds (6-8 year olds) (Fig. 5).

DO RESPONDENTS SIMPLY STOP COMPLETING THE eCOAS?

Two studies collected the number of days a diary was not completed. In one of these studies no participant missed more than one day, and in the second only two participants or 12% missed more than one diary completion. Reasons given during the cognitive interview for missing a diary completion included forgetting to complete, reminder alarms not going off, leaving the diary at home, or device malfunction. As the devices used in these studies did not typically allow participants to skip items, it was not possible to calculate item-level missing data. However, in the rare instances where patients stopped completing the diary mid-way through there was no pattern of patients stopping on a particular question or after a particular number of questions. Thus, the findings did not suggest a specific item or number of items was particularly problematic.

WHAT DID THE RESPONDENTS THEMSELVES SAY?

During the cognitive interviews most participants reported that the diary was quick and easy to fit into their daily routine and wasn't a burden to incorporate into their daily lives:

"Um, it's fast, it's convenient. You know, you can jot down how you're feeling and the pain symptoms that you have for that day." (33 year old female describing the women's health diary)

"I would do it for two weeks, yeah. It wasn't big – it's not a big imposition, it really isn't, it's right there; it's fairly easy to do. It's not invasive." (50 year old female referring to the fibromyalgia diary)

"Um I - I thought - I thought it was simple and didn't - wasn't a challenge and it didn't interfere with our day or anything" (Parent of an 11 year old from the CC study)

"It's just nice. It's high tech. It's - it's, you know - it's easy to, um - to see and to - to control with your finger. It's - it's convenient, you know. You don't have to write it down, you know. I like the, um, just touch your answer and, um, move on to the next question. It's - it's nice." (40 year old female referring to the women's health diary)

The participants also reported finding an alarm feature helpful to remind them to complete the diary:

Figure 4. Per Diary Completion Times by Day.

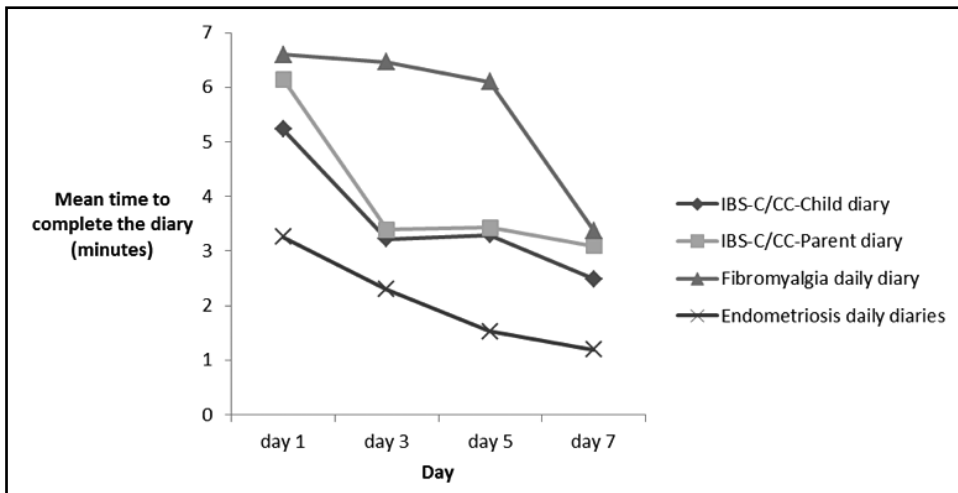
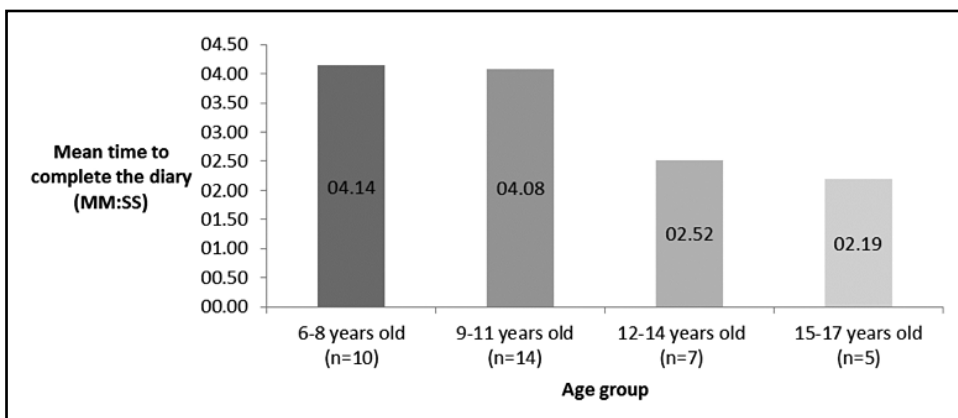


Figure 5. Average Time to Complete Diary by Age Group.



"It was easy, because the alarm went off and it reminded me." (Parent of a 4 year old from the CC study)

The children who completed the CC/IBS-C diary reported that the diary was 'fun' and compared using it to a hand-held video game:

"Um, I like how simple it was. It kind of reminded me of like the Nintendo DS" (12 year old male from the IBS-C study)

"I liked watching my daughter do it. She reminded me, Mom, it's time to go do that thing. It's time to go - she enjoyed doing it." (Parent of an 8 year old female from the IBS-C study)

Without it being a focus of the interview, some participants also spontaneously commented that they preferred using an ePRO device to pen and paper:

"To me since it was all electronic, I knew that, OK, I only have to spend five minutes every night, five to ten minutes every night instead of getting out a piece of paper and filling out something. To me I would much rather prefer to use something like that than filling out a survey on a piece of paper." (Parent of a 6 months old male from the CC study)

WHAT CAN WE CONCLUDE?

Combined data from three, relatively small, qualitative studies provides evidence that completing eCOA instruments, even those with a relatively large number of items (up to 40 included here) on a daily basis, is not burdensome to participants and that the daily diaries can be completed surprisingly quickly. In addition there is no evidence that longer diaries result in more missing data: very few diary completions were missed across all three studies. The consistency across studies, regardless of total questionnaire length, shows that per-item completion times are not substantially impacted by the length of the instrument. The findings also provide evidence that children find electronic diary completion easy and quick. Although the younger children included (aged 6-8) did take slightly longer to complete the diaries, the time taken to complete was still relatively short.

These findings suggest that concerns regarding patient burden associated with electronic PRO and ObsRO completion are largely unfounded, even in child/adolescent populations. Given the general advantages of using eCOA over paper COA, this study provides further support for the use of eCOA in clinical trials. If eCOAs are carefully designed, using reminder alarms, skip-patterns and event

driven items, completion burden can be reduced even further. These findings not only relate to daily diaries where the patients take the device home, but also could apply in cases where patients complete instruments on their own device (mPRO) or on site a scheduled visit. In these data it was not possible to evaluate differences for older participants or for other specific groups. Further work is warranted in populations where patient burden is of particular concern (e.g. elderly patients, severely ill patients and patients with considerable physical, emotional or cognitive disability).

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DISCLOSURE

The 3 studies in this article were projects in which Adelphi were paid consultants on the development of the diaries, there was no payment for the development of the article. The DFS-Fibro study was funded by Pfizer. 

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The Value of Oncology Therapies and Emerging Access Hurdles: Germany, Canada, and the United States



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KEY POINTS

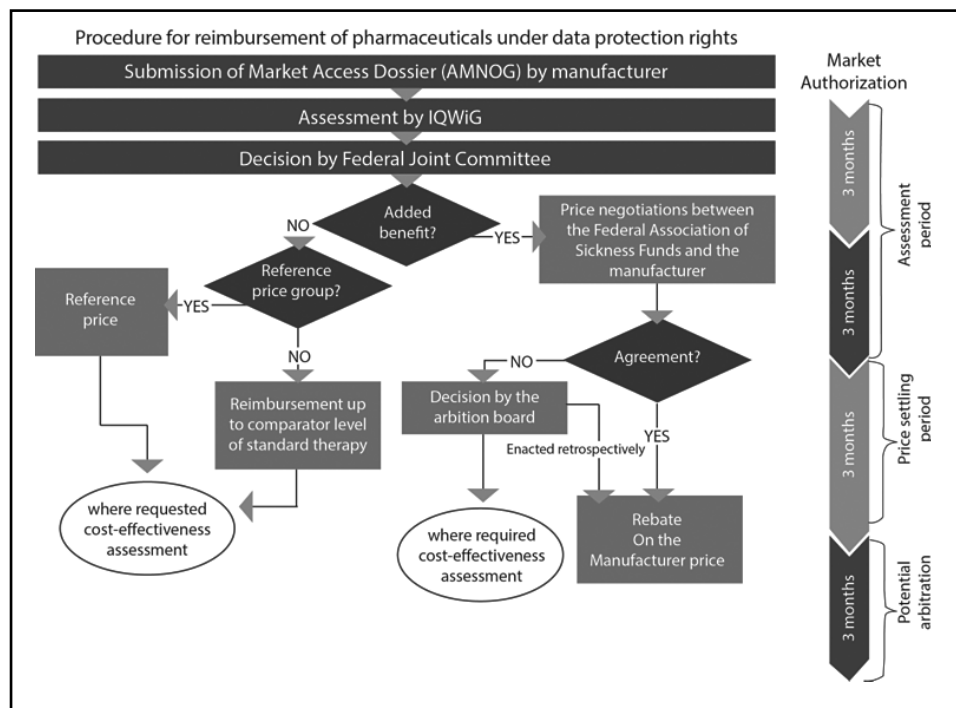
- The tug of war between product manufacturers and payers often originates from the price setting of the product in relation to its perceived quality—or more specifically, the assumed benefits (in terms of health outcomes) that patients and the society can reap from the product.
- Early planning for HEOR activities in a drug’s development process would be even more important in the future in order to align trial design, particularly in regard to choice of comparator; identify study populations or subpopulations in line with comparator therapy according to label indication.
- By closely monitoring the trends around market access opportunities and challenges in key revenue potential markets, manufacturers must balance the requirements and practices of many different markets in designing a global trial program, selecting endpoints, and implementing post-marketing real-world studies.

Today’s priority around market access and reimbursement activities for oncology therapies boils down to a single question: how to demonstrate the “value” of a therapy in an environment that is constantly evolving over time and considerably variable across multiple countries.

The tug of war between product manufacturers and payers often originates from the price setting of the product in relation to its perceived quality—or more specifically, the assumed benefits (in terms of health outcomes) that patients or society can reap from the product. In contrast to other medicines, cancer drugs often hold specialized and licensed indications, often specific to one or more factors: tumor sites, chemotherapy regimen, and sequence of treatment. Thus, the value equation is even more complex in oncology.

This overview describes recent paradigm shifts and emerging market access and reimbursement hurdles in oncology in three key countries—Germany, Canada, and the US—and identify what can be learned from the evolving landscape for developing access strategies and value propositions for innovative oncology therapies.

Graph 1. Benefit Assessment—AMNOG.



of IQWiG (the Institute for Quality and Efficiency in Healthcare), a health technology assessment (HTA) body in Germany that conducts an evaluation of the drug’s additional benefit, which serves as a basis for a final resolution by the G-BA.

This benefit can be at 1 of 4 positive levels: major, considerable, minor, or unquantifiable added benefit. If any positive level of added benefit is found, for any patient subpopulation, the drug can go forward to the next step of price negotiation with the payers, the Federal Association of Sickness Funds (GKV). If “no benefit” is found for all patient groups, the drug

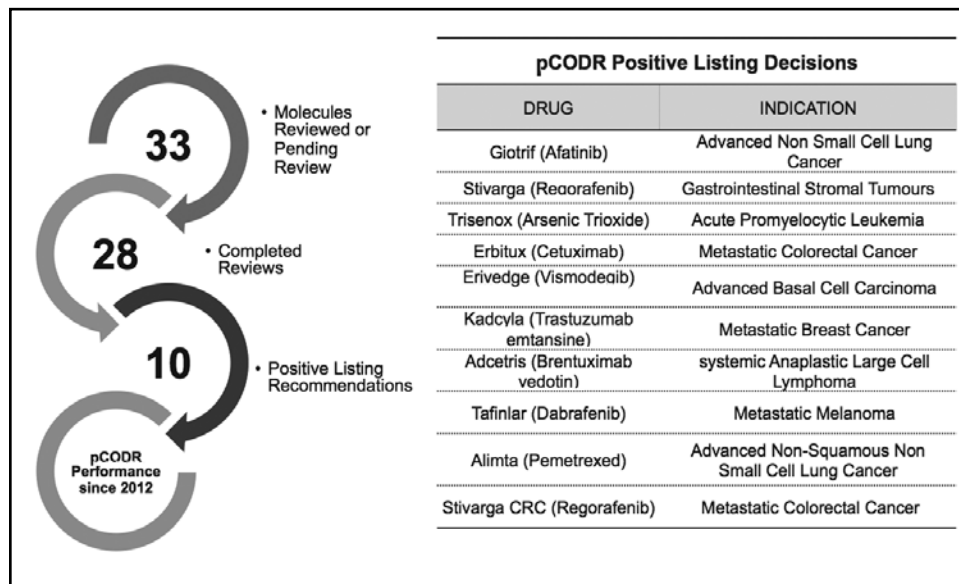
is relegated to the reference pricing system for the reimbursement price or is reimbursed at same price as the comparator if there are fewer than three therapeutic alternatives.

HOW DID ONCOLOGY DRUGS IN THE LAST 3 YEARS FARE IN GERMANY?

Thus far under AMNOG, the majority of products undergoing review have achieved access in Germany; for these products, average discount after benefit assessment in relation to ex-factory price was approximately 20% for cancer treatments, similar to

the average discount level seen in other indications. Although the general rule may be that higher added benefit, with stronger evidence, would be associated with a lower discount, the relationship between added benefit level and percentage price discount to date has not been so clear cut, inferring additional complexities involved in the negotiation phase.

Graph 2. pCODR Statistics (since 2012).



EVIDENCE-BASED RECOMMENDATIONS FOR CANCER TREATMENTS BY PAN-CANADIAN ONCOLOGY DRUG REVIEW (PCODR) IN CANADA

The Canadian Agency for Drugs and Technologies in Health (CADTH), Canada's national HTA agency for public payers, recently assumed responsibility for a national review process dedicated to cancer. The pan-Canadian Oncology Drug Review (pCODR) was created in 2011 but is, in fact, a broadening of the Joint Oncology Drug Review (JODR) program that was initiated by the collaboration of several provinces in 2007. Thus far, pCODR has reviewed 33 molecules (Graph 2), while JODR managed an additional 38 reviews during its 4-year mandate.

Partnering with the provincial cancer agencies, the Canadian Partnership Against Cancer, and CADTH, pCODR assesses cancer drugs and makes recommendations to the provinces and territories (with the exception of Quebec) to guide their drug-funding decisions. Based on a deliberative framework that includes clinical benefit, economic evaluation, adoption feasibility, and patient-based values, the pCODR Expert Review Committee (pERC) can: 1) recommend funding; 2) recommend not funding; or 3) recommend payers consider only if certain conditions are met.

PCODR STATISTICS SINCE 2012 AND MOVING FORWARD

Historically, Canada's public drug plans cover, on average 57%, of cancer drugs; compared to

an average of 79.9% for 31 other Organisation for Economic Co-operation and Development (OECD) countries [1]. Gaining a favorable listing recommendation remains challenging in Canada; only 10 of 33 molecules have received a positive recommendation to list (Graph 2).

Oncology is a political and emotionally charged therapeutic area. Thus, it has been somewhat shielded from rigorous cost-containment measures in the US. Prices of cancer drugs, however, are coming under more scrutiny by US private payers. Among specialty therapeutic categories, cancer drug costs constitute the highest per-member-per-month spend, accounting for nearly 11% of a private payer's total spend [2].

NEW PAYER MODELS HAVE EMERGED FOR ONCOLOGY TREATMENTS IN THE US

In addition to rising drug costs, current oncology practices such as the "buying and billing" of drugs, lack of transparency in outcomes data and standardized frameworks for tracking quality, has led payers to seek payment reform. In 2012, 16% of health insurers had already adopted new payment and contracting arrangements such as outcomes-based payments, risk-sharing agreements, cost-sharing with patients, evidence-based clinical pathways, shared savings, and medical homes bundled payments. Of those that have not, 37% expect to adopt them within the next three years [3]. Almost all of these new payment models are designed both to transfer financial risk to providers and patients and to promote value-based payment (Graph 3).

Reimbursement rejections occurred mainly because of insufficient cost-effectiveness or excessive cost, while at times the committee could not determine the value for money of the drugs from several of the submitted pharmacoeconomic analyses. Even when drugs were recommended, the majority carried specific clinical criteria defining the reimbursement, and were linked to specific conditions such as « Conditional on improvement of cost-effectiveness to an acceptable level » and « Do not list at the submitted price ».

The private insurance sector has played an increasingly significant role in Canadian cancer care; currently up to 66% of Canadians have access to drug coverage through private insurers. With the continuous shift of inpatient care to the outpatient setting by the provinces, gaining access to a broader range of treatments than what is offered through the public cancer care scheme and, more importantly, more rapid care has become possible through private treatment clinics, funded through their private insurance or by drug manufacturers. This may change, however, in the near future, as insurance companies work to formalize reviews and implement stricter cost-containment strategies toward specialty classes of medications. In addition, with the launch of more oral oncolytics, the cost of these take-home medications, which was historically within the public sphere, is now falling to the private payers' responsibility.

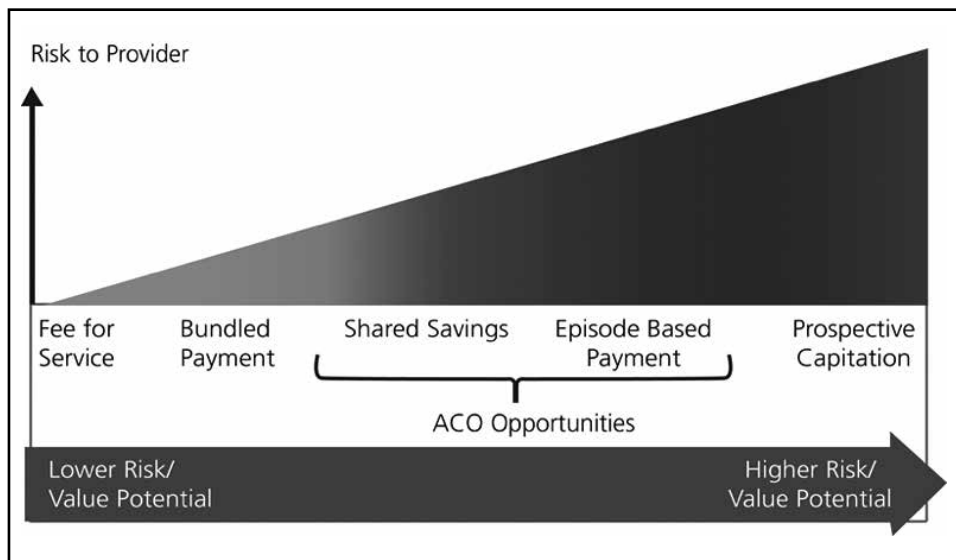
CANCER DRUGS NO LONGER A "SACRED COW" IN THE US

Several mechanisms for reducing cost and improving outcomes are being investigated at the moment. Clinical pathways rely on evidence-based algorithms to guide and standardize cancer care to the greatest extent possible, while still preserving a measure of physician autonomy in decision making for cancer care delivery. The model for bundled payments, as illustrated in oncology, involves paying an upfront fee to the oncologist for an entire "episode" of a patient's care. A 4-year-old pilot program launched by UnitedHealthcare, the nation's largest insurer, recently published encouraging but mixed results—the program providing upfront payments to doctors produced significant savings, but spending on chemotherapy drugs still increased more than expected [4]. Shared savings is a payment model that realigns incentives by allowing physicians to realize a percentage of whatever savings they can achieve through improvements in their care process. In a "medical home" setting, doctors may receive an additional fee to better coordinate patient care from so-called accountable care organizations (ACOs) where a larger health system shares some of the savings if it can manage patients' health for less money.

DRIVE TOWARD OUTCOMES-BASED PAYMENT ACCELERATED BY THE ACCOUNTABLE CARE ACT (ACA)

The ACA has accelerated the drive toward evidence-based treatment through a number of avenues, encouraging hospitals and doctors to integrate their operations and collaborate to control costs and improve care.

Graph 3. Emerging Value-based Payment Models in the US.



Several innovators such as Miami-Dade Accountable Oncology Program (Florida Blue), Moffitt Cancer Center in Tampa (Florida Blue), and Texas Oncology (Aetna) have been adapting the ACO model to oncology with the anticipated savings that can be derived from chemo pathway adherence (1%–3%), avoidance of hospital and ER visits (4%–7%), diagnostics (0.2%–0.5%), and end-of-life planning (0.9%–1.9%) [5]. As a partial solution to fragmented delivery of care, oncology patient-centered medical home (OPCMH) models have also emerged with the goals of coordinating care, improving quality, and streamlining costs.

A LOOK AT FUTURE EVIDENCE DEVELOPMENT STRATEGY IN THE US

Over time, payers will become more interested in advanced management strategies for cost containment, collaborating with ACOs and providers and offering financial incentives to them. With ACOs

and providers representing new stakeholders to the manufacturers, comprehensive value proposition is even more vital for the future to highlight the value of a product in the form of cost savings and/or improved outcomes to the payer, provider, and patient (e.g., reduction in emergency department utilization and hospitalization, decrease in total costs of an episode of care, fewer adverse events, survival, etc.).

Manufacturers must also develop a compelling economic value proposition to ensure clinical pathway inclusion, and optimize their investment in patient assistance programs (newly approved oral oncolytics will face high cost-sharing requirements; many plans will change their benefit designs—by adding more tiers or raising copay levels, for example—to increase cost-sharing). In addition, launch planning for an oral oncology medicine, compared with infused/IV formulations, requires

incorporating the dynamics among the provider, payer, and patient in the environment where new payment models are emerging and ACOs are driving evidence-based treatment and payment.

COMPREHENSIVE VALUE PROPOSITION TO MULTIPLE STAKEHOLDERS

By closely monitoring the trends around market access opportunities and challenges in key revenue potential markets, manufacturers must balance the requirements and practices of many different markets in designing a global trial program, selecting endpoints, and implementing post-marketing real-world studies. Overall, striking a balance in promoting innovation, thereby improving patient care, while also addressing health care costs has become ever more challenging at a time when the scientific promise is greater than ever and the value paradigm is constantly shifting from multiple stakeholders' points of view.

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The deadline for submitting nominations is Friday, January 2, 2015.

How (Not) To Assess the Social Value of Medical Interventions for Ultra-Rare Disorders (URDs): Recommendations from the URD Evaluation Project



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KEY POINTS

- Many drugs for ultra-rare disorders (URDs) fail to meet conventional cost effectiveness thresholds.
- An international panel of experts (in the fields of HTA, health economics, and orphan drug regulation) argue that this failure is primarily due to deficiencies of the underlying logic of cost effectiveness.
- Hence a need is postulated for the adoption of alternative evaluation principles, which better capture social value (i.e., the public's "social preferences", such as cost value and social utility analysis).

In many jurisdictions legislation has been enacted to encourage the development of treatments for rare or "orphan" diseases. Health economists, however, have expressed concern that drugs for orphan disorders "may impose substantial and increasing costs to the healthcare system," [1] and, indeed, "the five most expensive drugs in the world" [2] all happen to be medications for ultra-rare disorders (URDs).

In the US, "orphan diseases" are disorders with a prevalence of less than 200,000 affected persons; in the EU, prevalence must be less than 5 per 10,000 of the population. No official definition of "ultra-orphan disorders" (URDs) has been adopted globally. Rather, this informal subcategory was introduced by the National Institute for Health and Care Excellence (NICE), who applied it to drugs for conditions with a prevalence of less than 1 per 50,000 persons.

Many drugs developed to treat URDs will not meet the cost effectiveness thresholds stipulated by regulatory bodies like NICE, i.e., not to exceed a cost of 20,000£ to 30,000£ per QALY gained. Given the largely fixed costs of research and development, it seems plausible that this challenge will increase in relevance with decreasing prevalence rates, and it will be most pronounced in URDs. The introduction of an exceptional "ultra-orphan" category by NICE can thus be interpreted as a defensive move, responding to political and public pressures that NICE experienced as a reaction to negative appraisals. It also can be seen as an attempt to protect NICE's evaluation framework, while at the same time recognizing that this framework "somehow does not work" for "ultra-orphan" drugs.

Apparently, there is a serious mismatch between reimbursement policies based on the logic of cost effectiveness, with cost per QALY benchmarks, on the one hand and international policies designed to encourage research and development into rare and ultra-rare disorders and their effective treatment, on the other hand. As such, there is an unmet need for a coherent value framework reflecting all attributes of health technologies deemed relevant by the public ("social preferences"), while at the same time remaining consistent with prior normative commitments as entailed by institutional and legal traditions. Such a framework should reflect the goal of fair access to effective interventions (for patients), the need for incentives for research, development, and "innovation" (for manufacturers of drugs for URDs), and a set of clear principles for setting limits (for policy makers and payers).

In order to address this situation, the "URD Evaluation Project" was initiated by the not-for-profit Institute for Innovation & Valuation in Health Care (InnoVal^{HC}). Two international expert workshops were convened in conjunction with the Annual European ISPOR Congresses in Berlin, Germany, 2012, and in Dublin, Ireland, 2013. The situation analysis focused on the principles underlying the current evaluation framework, rather than actual evaluation policies implemented by HTA agencies and regulatory bodies (primarily those concerned with pricing and reimbursement decisions), or evaluation practice when principles and policies are applied to real-world problems. Besides a prevalence of less than 1 per 50,000, characteristics of URDs under consideration should include that the conditions are severe, are chronic, represent clearly defined biological

entities (i.e., are not "created" by artificial "slicing" of a biologically much broader and more prevalent indication), and are associated with a broadly accepted high unmet medical need. The typical case the workshop participants had in mind were treatments that are effective for one URD only (such as enzyme replacement therapies for hereditary lysosomal storage disorders); certain adjustments of a rather technical nature may be necessary when one drug works in more than one URD indication.

The panel reached a consensus that a number of typical challenges must be expected when dealing with interventions for URDs. The most serious ones fall into one of two categories, i.e., a) the need to establish evidence of clinical effectiveness, and/or b) the need to demonstrate "value for money":

a) Developing treatments for URDs is a more challenging, complex, and sometimes more risky endeavor than developing treatments for more common diseases, as often less clinical / medical research is often available for ultra-rare diseases, resulting in a limited clinical understanding; there is usually a very small number only of physicians with specialized expertise, who are based in few specialized centers; there exist unusual difficulties to produce robust clinical evidence; this, combined with difficulties to generate a large volume of evidence for URDs based on randomized clinical trials may lead to higher levels of uncertainty surrounding effect size estimators; significant hurdles exist when trying to identify and accurately diagnose patients with ultra-rare diseases; because the small number of patients are often geographically dispersed, multiple clinical trials sites must be established for

only a few patients; and ongoing post-marketing requirements, including registries and risk management plans, must be created and maintained globally for only a small number of patients; as a consequence, in a significant number of cases, the safety and efficacy profiles of orphan drugs have been incomplete, and often marketing authorizations were based on small scale studies addressing surrogate endpoints only [3]. The experts recognized the need for ongoing R&D for highly innovative and life-saving products for URDs, in order to increase clinical disease understanding and produce robust evidence on the clinical effectiveness of interventions (“technologies” in the broadest sense).

b) Further challenges are economic in nature; they concern the efficiency or “value for money” offered by URD treatments: currently established methodologies to determine “value for money” vary widely internationally, with a stronger utilitarian tradition (as for example, in England) generally leading to a higher acceptance of “efficiency first” evaluation principles, whereas stronger emphasis on a rights-based approach (and a corresponding legal tradition, as for example, in some continental European countries such as France and Germany) has led to a stronger reliance on approaches based on unmet medical need and on evidence of comparative clinical effectiveness for the allocation of health care resources.

In *applied health economics* – in contrast to neo-classical welfare economics – health outcomes – rather than “utility” – are usually considered to be the appropriate benefit for evaluation. This “extra-welfarist” view has been gaining popularity because of the wide-spread belief those basic necessities “such as life, health, and citizenship [...] should be distributed less unequally than the ability to pay for them” [4]. Usually the extra-welfarist evaluation paradigm is accompanied with the assumption that the objective of collectively financed health schemes ought to be maximization of the aggregate health gain produced for the population covered by the scheme. If health gains are measured in terms of quality-adjusted life years (QALYs), extrawelfarism then translates into QALY maximization, a normative hypothesis that has been endorsed on grounds of an alleged “consensus in the literature” [5].

Notwithstanding claims of distributive neutrality, however, this approach implies considerable constraints on the preferences to be taken into account. Any contextual variable(s) – beyond individual health gain – potentially influencing the *social desirability* of (and hence the social willingness-to-pay for) health services would necessarily violate the basic assumption that all QALYs are created equally. If however there were other objectives beyond the maximization of population health (which represents the goal of allocative efficiency), such as the wish to be treated with dignity and respect, or concerns about equity and, these quite obviously would either result in differential cost per QALY benchmarks as a function of these concerns, or might even require an entirely new evaluation paradigm. This issue has been de-

scribed using the notion of *horizontal equity* (i.e., the equal treatment of equals) versus *vertical equity* (i.e., the unequal but equitable treatment of unequals).

It is noteworthy that, in an attempt to escape from contentious interpersonal comparisons inherent in economic concepts of “allocative efficiency”, politicians and health care policy makers in jurisdictions such as the United States and Germany have deliberately decided to refrain from the computation of cost per QALY gained, in essence restricting themselves to the evaluation of comparative effectiveness (e.g., PCORI in the US) or, at best, of *technical efficiency* (e.g., methods guidance by IQWiG in Germany).

With either approach, there remains the need to establish fair boundaries with regard to coverage (reimbursement) and pricing.

The panel noted a number of serious problems that arise when traditional *Health Technology Assessments* (HTAs) include *cost utility analyses*, with quality-adjusted life years (QALYs) as a measure of health-related outcomes and their individual valuation) for URDs:

a) *Social value*, as indicated by the social preferences of the population covered by a National Health Scheme (NHS) or an insurance plan, is not identical with an aggregate of individual utility.

b) Rather, *social preferences* include equity concerns and a “sharing” perspective. Perhaps the best documented contextual variable is *severity of the initial health state*. People consistently show a strong preference to prioritize health care for the worse off, and this priority has been found to be largely independent from the improvement achieved by an intervention. In contrast to QALY-based valuation, *capacity to benefit* might be less relevant, as people appear to value additional health gains lower, once a certain (however, not readily quantifiable) minimum effect has been shown to be achieved by an intervention. Other *patient attributes* that have been found to exert an impact on the public’s prioritization preferences include (younger) age, parent and caregiver status, and (non) smoker.

c) Finally, the decision rules of the logic of cost effectiveness will lead to “*all-or-nothing*” decisions on programs, depending on whether they are located above or below the cut-off line for efficiency. People are not indifferent to the fact, however, that this way certain groups of patients would be entirely excluded from receiving health benefits.

d) In light of the observations above, QALYs, conceptualized as a preference-based measure of individual health-related outcomes combining quality and length of life, fail to capture the full value of URD technologies; hence they need to be complemented by or replaced with alternatives that include societal preferences, such as concerns for equity in access to treatment.

e) Current (*cost per QALY*) *ICER thresholds* used for cost-effectiveness (or more precisely, “cost-utility”)

analysis are largely arbitrary; their application may lead to positively unethical conclusions. Of note, the very *existence of such thresholds* (outside the confines of the narrow extrawelfarist framework) depends on the validity of the QALY maximization hypothesis, whereas systematic reviews of the literature have convincingly shown that this assumption is “descriptively flawed” [6]. Attempts to apply modifiers to account for severity of disease (so called “*equity*” or “*severity weights*”) in economic assessments of technologies for URDs have not fully reflected the large number of contextual variables, and cannot resolve the underlying issues with regard to fair chances to have access to effective treatment.

f) Interestingly, studies further suggest that the *importance of costs* may be overstated by conventional health economic evaluations, since cost-minimization, cost-effectiveness, cost-utility, and cost-benefit analyses, by definition, focus significantly on cost; in contrast to this, the public appears not to be well prepared to deny patient treatment merely on the basis of cost – which apparently constitutes a social preference related to some kind of fairness or rights-based reasoning similar to the dislike of “all-or-nothing” decisions, but does not necessarily imply valuing “*rarity*” *per se*; whereas *costs per patient* for URD treatment in many cases will necessarily tend to be (much) higher than cost per patient for more common disorders, given the research and development (R&D) issues delineated above, in combination with the fixed cost nature of R&D expenses, logistical challenges, and (sometimes) manufacturing complexities.

Collectively, the panel concluded that the findings and observations summarized above underscore the need for an evaluation paradigm capturing social norms and preferences in a better way than the conventional logic of cost effectiveness, with potentially far-reaching implications for the evaluation of URDs.

While recognizing the challenges associated with developing clinical interventions for URDs, the panel agreed that evidence for improvement of surrogate endpoints only should be no more than an interim attitude. The panel agreed that even for URDs it should be feasible and expected to set up multinational randomized controlled trials, designed to show relevant clinical endpoint benefit.

If a broader *social value perspective* was to be adopted in a consistent manner, then there could be simultaneous implications for the definition of social opportunity cost (or value foregone), with social value being driven by the existence of a program (i.e., for example the value people attach to living in a society that does not simply abandon certain groups of patients, who are unfortunate enough to suffer from a high cost illness) and opportunity cost by its budgetary impact. This would obviously shift the focus from cost per patient to cost on the program level, which indeed reflects the perspective of a real-world decision maker.

Promising alternative evaluation principles (better reflecting the public's social preferences) prominently include cost value analysis using the person trade-off method [7], social utility analysis using the relative social willingness-to-pay (RS-WTP) instrument [8], or – as an interim solution – multi-criteria decision analysis (MCDA) frameworks.

ACKNOWLEDGMENTS

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The complete recommendations of the expert group are available online at: www.innovat-hc.com: M. Schlander, S. Garattini, P. Kolominsky-Rabas, E. Nord, U. Persson, M. Postma, J. Richardson, S. Simoens, O. de Solà Morales, K. Tolley, M. Toumi: Consensus Statement: "Determining the Value of Medical Technologies to Treat Ultra-Rare Disorders (URDs). Consensus Statement based upon an International Expert Workshop [Final Version of July 19, 2013] InnoVa^{HC} Discussion Paper No. 27 (Wiesbaden, Germany, July 2013); ISBN 978-3-941609-26-6.

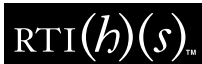
*A full publication outlining the rationale underlying the consented recommendations is currently in press: Schlander M, Garattini S, Holm S, Kolominsky-Rabas P, Nord E, Persson U, Postma M, Richardson J, Simoens S, de Solà Morales O, Tolley K, Toumi M. Incremental cost per quality-adjusted life year (QALY) gained? The need for alternative methods to evaluate medical interventions for ultra-rare disorders. *J Comp Effect Res* 2014;L3:399-422. *

WEB CONNECTIONS

There are many venues one can search for published economic evaluations. If you wanted to only search for economic evaluations with regards to children's health, you should refer to the Pediatric Economic Database Evaluation (PEDE): <http://pede.ccb.sickkids.ca/pede/database.jsp>. There are over 2,632 economic evaluation citations published from January 1, 1980 through December 31, 2013 included in the database. Health state utility weights, which were reported in the cost-utility analyses included in the PEDE are also available. There are 1,703 health state utility weights available. Based on information reported on the website, the types of economic evaluations included in PEDE are: 64% CEAs, 24% CUAs, 8% CBAs, and 4% CMAs. There are several resources to thank for supporting this project and of note is the start-up funding which was from The Hospital for Sick Children (SickKids), which is affiliated with the University of Toronto. SickKids is a health care, teaching and research centre dedicated exclusively to children.

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The International Society for Pharmacoeconomics and Outcomes Research New CEO and Executive Director – Nancy S. Berg



The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) is pleased to announce that Nancy S. Berg joined the association on October 22, 2014, as its CEO and Executive Director, succeeding ISPOR Founding Executive Director, Marilyn Dix Smith, RPh, PhD, who announced her retirement in 2013.

Nancy has 30 years of experience in technical and scientific association leadership, and has been an entrepreneur and business consultant to commercial and nonprofit organizations.

Prior to joining ISPOR, Nancy was President and CEO of the International Society for Pharmaceutical Engineering (ISPE), a 501(c)(6) organization. During her tenure with ISPE, Berg was responsible for transformational change at ISPE, the world's largest professional society fostering dialog and education on technical, scientific and regulatory best practices in the pharmaceutical and biotech industries. She was the architect of the Society's Strategic Plan, focusing ISPE's energies and expertise on high-value, ground-breaking initiatives related to drug shortages, quality metrics, global manufacturing quality, facility and supply chain issues and patient experiences in clinical trials.

Nancy has been instrumental in creating synergies between pharmaceutical industry stakeholders, bringing together diverse groups of professionals, regulators, and partner organizations to work on issues of shared concern. Berg's work with the US Food and Drug Administration (FDA) and ISPE's Drug Shortages Initiative is particularly noteworthy; in one project, she led teams of ISPE Members to complete groundbreaking research recently cited by FDA in its strategic plan and in senior official U.S. Congressional testimony. ISPE recently announced the industry's first Drug Shortages Prevention Plan, a collaboration involving Members and Regulators in Europe and North America as well as Phase 1 of its Quality Metrics Study, conducted to help identify a set of common metrics for use by industry and health authorities in assessing product quality and patient safety.

Under her leadership, ISPE strengthened its internal operations. The organization introduced a strategic redirection of focus in Europe and Asia, while in North America, the Society, in late 2014, opened an office in Washington, D.C., in addition to its headquarters in Tampa, FL and regional offices in China and Germany. Nancy has been catalytic in evolving ISPE's visibility and in building more contemporary business operations, streamlining governance processes and developing new revenue sources. The inaugural Pharma EXPO tradeshow (3 – 5 November 2014,

Chicago), an event for the pharmaceutical industry managed in partnership with PMMI, was developed and launched on her watch.

Nancy also served as Executive Director/CEO of the Society of Manufacturing Engineers (SME), a 501(c)(3) organization, based in Dearborn, Michigan from 2000 to 2006 when she left the society to launch her own consulting business focused on helping shape growth and improve the effectiveness of businesses, start-ups and nonprofit organizations. While at the helm of SME, she directed the day-to-day operations of the \$30-million/year, 200-employee organization and its worldwide businesses, including events, training and expositions, publishing, technical communities, membership operations, and the SME Education Foundation (also a 501(c)(3) entity).

At SME, Nancy built, repositioned, and streamlined operations, established a more customer-driven culture, and integrated product and market development initiatives. She designed and launched the association's strategic plan, Plan 2010 and she and her management team were recognized by leading professional organizations, such as the American Society for Training and Development and the International Association of Business Communicators, for these efforts.

Prior to being selected as SME's executive director and general manager, Nancy was director of expositions at SME, responsible for overseeing 21+ international trade shows and educational events. Under her leadership, SME's tradeshow activities grew exponentially and SME was named a top 10 trade show management company in the 1997 & 1998 Tradeshow Week Data Books. As a result of her strategic leadership, SME grew to have four of the nation's top 200 trade shows recognized by Tradeshow Week. During this time, Berg spearheaded joint ventures, partnerships and strategic alliances with more than 100 associations, agencies, governments, institutions and organizations around the world and led ISPE's entry into major global markets.

Nancy joined SME in 1982 as staff manager for Robotics International of SME (RI/SME), an association specializing in robotics technology. In 1984, she assumed responsibility for product development in the Expositions Division. Later, as Expositions Director, she also became responsible for strategic and financial planning, sales, communication and services, and education and show event management. Earlier in her career, Berg worked in both the manufacturing and service industries.

Nancy also consulted with organizations on strategic and growth planning, leadership, sales and marketing, effective operations and business transformations. She has helped businesses become more effective, more influential, and more relevant by thinking strategically; planning long term; focusing their positioning and marketing around smart objectives, partnerships; and developing great leadership and committed employees.

Throughout her career, Nancy has been recognized as a ground-breaking leader with a hands-on style. During her tenure with SME, she was the youngest person to head a global engineering/technical organization. In 2014, she was awarded The Joseph X. Phillips Professional Lifetime Achievement Award by ISPE for her regulatory work. She has been named one of Detroit's "Top 100 Most Influential Women" by Crain's Detroit Business and one of Michigan's Top 50 Women by Corp! Magazine. She also received the Women of Achievement Award, Business & Industry by the YWCA of Western Wayne County Michigan among other recognition.

Nancy has been engaged in education and business issues at national and international levels. She has been recruited to serve on many government initiatives involving business, community, development, growth, and revitalization issues. She served on the Board of National Science Foundation-sponsored educational coalitions, as well as other boards and committees. She is a volunteer fundraiser for the Leukemia and Lymphoma Society's Team in Training Program cycling events. She is a leader in her church and has served as professional advisor to executives and companies across many industries.

Nancy is a graduate of the University of Michigan-Flint and is married to Timothy Jackson.

"The role of ISPOR has never been more important to the global health care community, including researchers, clinicians, health technology developers, assessors, and decision makers," says Nancy. "I am proud to be joining at a time when the work of ISPOR and its members is more critical than ever and look forward to contributing my career experience to the Society's future success."

We welcome Nancy to ISPOR and look forward to her impact towards ISPOR's success. 

Value in Health Volume 17, Issue 8

The following articles will be included in the the December 2014 issue of *Value in Health* (Volume 17, Issue 8):

FEATURED ARTICLE

US Valuation of Health Outcomes Measured Using the PROMIS-29

ISSUE HIGHLIGHTS

Commentary

Toward a Functional Definition of a 'Rare Disease' For Regulatory Authorities and Funding Agencies

Economic Evaluation

Mapping from the Health Assessment Questionnaire to EQ-5D: the Impact of Different Algorithms on Cost-effectiveness Results

Patient-Reported Outcomes

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ISPOR 17th Annual European Congress—New Challenges, New Frontiers!

Malgorzata (Gosia) Juszczak-Punwaney, MPOlSc, MA, Manager, International Development (Europe, Africa and Western Asia), ISPOR, Lawrenceville, NJ, USA, and Stephen Priori, Director, Publications, ISPOR, Lawrenceville, NJ, USA

A record 4,800 attendees from over 80 countries travelled from their corners of the world to take part in the ISPOR 17th Annual European Congress, embracing the theme, “New Challenges for Improving European Health Care.” The Congress, held on November 8-12, 2014 in Amsterdam, The Netherlands was a great example of ISPOR’s increasingly crucial role in addressing the challenges and opportunities of global health systems.

PLENARY SESSION FOCUS: EUROPEAN HEALTH CARE
The Congress plenary sessions offered a variety of topics, focusing on the Congress’s theme of new challenges in European health care.

The First Plenary Session entitled, “Creating Sustainable Health Systems in Europe” addressed moving health systems across Europe in which health care delivery is both affordable and of the highest possible quality. Speakers included Richard Sullivan, MD, PhD, Director, Kings Health Partners Institute of Cancer Policy & Global Health, London, London, UK; Maureen P. M. H. Rutten-van Molken, PhD, MSc, Professor of Economic Evaluations of Innovative Health Care for Chronic Diseases, Institute for Medical Technology Assessment/Institute of Health Care Policy and Management (IMTA/IBMG), Erasmus University Rotterdam, Rotterdam, Netherlands; and Zoltan Kalo, MSc, MD, PhD, Professor of Health Economics, Department of Health Policy and Health Economics, Eotvos Lorand University (ELTE) and Founder & CEO, Syreon Research Institute, Budapest, Hungary. The session also featured Lieven Annemans, PhD, MMan, MSc, Professor of Health Economics, Ghent University, Ghent, Belgium. Having Professor Kalo as a speaker in one of the sessions brought attention to current challenges many Central & Eastern European countries face during the process of creating sustainable health systems. Prior to the session, Bengt Jönsson, PhD, Professor of Health Economics, Stockholm School of Economics, Centre for Health Economics, Stockholm, Sweden, received the 2014 ISPOR Avedis Donabedian Outcomes Research Lifetime Achievement Award (see page 24 for presentation and acceptance remarks).

2014-2015 ISPOR President Adrian Towse, MA, MPhil, President and Director, Office of Health Economics, London, UK moderated the Second Plenary Session on: “Earlier Access to Innovation - Is It Worth It?” This session featured speakers representing three different perspectives – regulatory agency, industry, and health technology assessment (HTA) – where adaptive licensing, coverage with evidence development, and other programs to deal with evidence uncertainty were discussed. Representing the regulatory agency perspective was Hans-Georg Eichler, MD, MSc, Senior Medical Officer, European Medicines Agency (EMA), London, UK. Giving the industry perspective was Richard Bergstrom, MScPharm, Director General, European Federation of Pharmaceutical Industries and Associations (EFPIA), Brussels, Belgium. Alric Ruther, MD, PhD, Head, Department of Health Care Quality, International Affairs, Institute for Quality and Efficiency in Health Care (IQWiG), Cologne, Germany, and Carole Longson, PhD,

Director, Centre for Health Technology Evaluation and Executive Director, National Institute for Health Care & Excellence (NICE), London, UK represented the health technology assessment (HTA) perspective. The Third Plenary Session entitled, “Health Care Evidence: Can We Get To The ‘Real World?’” featured speakers Lars Pedersen, MSc, PhD, Professor, Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark; Hilary Pinnock, MB, ChB, MD, MRCGP, Reader, Asthma UK Centre for Applied Research, Centre for Population Health Sciences, University of Edinburgh and General Practitioner, Whitstable Medical Practice, Whitstable, Kent, UK; and Sebastian Schneeweiss, MD, ScD, Professor of Medicine and Epidemiology, Harvard Medical School, Boston, MA, USA. The session moderated by Finn Borlum Kristensen, MD, PhD, focused on a core ISPOR research and methods area: the need for “real world” evidence expressed by many health HTA bodies and payers and post-authorization efficacy studies expressed by the European Medicines Agency (EMA).

EMPOWERING THE PATIENT
Recognizing the need for greater patient involvement in health care decision making, the ISPOR Congress provided a platform for discussion on patient experiences and role in contributing to quality health care and improving health outcomes worldwide. During the ISPOR Patient Representatives Roundtable, experts from numerous patient-focused organizations, such as EURORDIS discussed the value of patient involvement in HTA and how to best engage patients in the decision-making process. The ISPOR Patient Representatives Roundtable is now considering actions to improve the role and perception of patients in health economics and outcomes research as well as create good practices.

HTA CAPACITY BUILDING WORLDWIDE
“This Congress increased the awareness of health economics issues specific for CEE,” said Maria Psenkova, RNDr, President, ISPOR Slovakia Chapter. “It provided the ground for finding solutions in HTA decision making and capacity building across the entire region.” The ISPOR HTA Roundtable, which brought together key European HTA representatives, served as an opportunity to share new developments in HTA at the European level as well as discuss the needs, for capacity building not only in Europe but around the world. The Congress, which offered several sessions focusing on Central and Eastern Europe (CEE), was attended by almost 1000 representatives from the CEE region, the majority of who were the members of ISPOR Central & Eastern Europe Network. Over 550 registrants attended Issues Panel 3: How Desirable, Feasible, And Acceptable Is The Inclusion Of Real-World Evidence In HTA Decision Making Across Europe?, which examined the importance and issues surrounding the inclusion of real-world evidence into drug development and drug assessment for regulatory and reimbursement decision making in Europe.

HEALTH POLICY TRENDS IN ASIA
Despite its European venue, the Congress was well attended by ISPOR members from Asia. The ISPOR Asia Consortium Business Meeting brought

together over 50 representatives from 10 ISPOR Regional Chapters in countries, such as: China, Japan, India, Israel, South Korea, Malaysia and Iran. Discussion topics included current health policy trends in Asia and opportunities for future growth and development. The Vision 2020 statement was an important part of the agenda, as the Consortium celebrates this year its 10th anniversary.

ALL-TIME HIGH FOR SHORT COURSES
ISPOR pre-Congress Short Courses on Saturday and Sunday eclipsed previous attendance records, with over 2,700 registrants enrolling in 25 Short Courses, with 15 courses being sold-out prior to the Congress. Reimbursement Systems for Pharmaceuticals in Europe alone had 300 registrants, an all-time high for an ISPOR meeting or congress. “Attending the Congress was a fruitful and positive experience, and the combination of capable speakers and great audience provided the recipe for success,” said Mahmoud Elmahdawy, PharmD, President, ISPOR Egypt Chapter and Chair-Elect, ISPOR Africa Network. “ISPOR short courses relating to pricing of pharmaceuticals and biotech products were quite informative and delivered in a very practical approach, which greatly enriched the learning experience.”

ISPOR REGIONAL CHAPTERS, ISPOR ARABIC, AND ISPOR AFRICA NETWORKS FORUMS
ISPOR Forums presented by ISPOR Regional Chapters, ISPOR Arabic, and ISPOR Africa Networks brought awareness to health economics & outcomes research in Europe, Western Asia, and Africa. For instance, collaborative presentations delivered by experts from ISPOR CEE Network focused on: capacity building in PE & HTA, benefits of innovative medicines, and policy challenges of rare diseases. “I found Forums sessions presented by the ISPOR CEE Network particularly interesting and relevant to health economic issues currently discussed in my country,” said Professor Dominik Tomek, PharmD, MPH, PhD, ISPOR Board of Directors Member and Chair-Elect, ISPOR CEE Network Education Committee.

As Amsterdam provided much to enjoy and the Congress had much to offer, it is apropos to close with, as the Dutch say, “*Afwisseling verheugt*” (Variety pleases).

ISPOR will gather again on May 16-20, 2015 in Philadelphia, PA, USA for the ISPOR 20th Annual International Meeting. We hope to see you there to celebrate our 20th anniversary, as well as at the 18th Annual European Congress in Milan, Italy, at the Milano Congressi, 7-11 November 2015. Thanks for attending the ISPOR meetings this year! 

To see the 17th Annual European Congress Program Committee, go to: <http://www.ispor.org/Event/ReleasedPresentations/2014Amsterdam>

To view the ISPOR 17th Annual European Congress Podium and Poster Research Presentation Award recipients and presentations, go to: <http://www.ispor.org/awards/17euro.asp>

ISPOR 17th Annual European



First Plenary Speaker
Richard Sullivan, MD, PhD

“Where else to discuss European health care research and policy than ISPOR-Amsterdam?”



Does The Data Speak For Itself? A Look At Adequate Data Generation To Meet The Differing Requirements Of Multiple HTA and Reimbursement Bodies In Europe Issues Panel (l-r): Timothy R Auton, MSc, PhD, Omar Dabbous, MD, MPH, Friedhelm Leverkus, MS, Mira Pavlovic, DrPH



ISPOR 17th Annual European Congress Program Committee Co-Chairs Finn Børlum Kristensen, MD, PhD (l), Carin A. Uyl-de Groot, PhD, and ISPOR President Adrian Towse, MA, MPhil



Second Plenary Speaker
Hans-Georg Eichler, MD, MSc



ISPOR 17th Annual European Congress
Poster Session and Exhibit Hall



Budget Impact Analysis: Applications & Design Issues Short Course

“... a great opportunity for learning and exploring new approaches in pharmacoeconomics. The environment of congress was amazing.”

Congress Photo Highlights



*Second Plenary Session: Earlier Access To Innovation - Is It Worth It?
(l-r): Carole Longson, PhD, Alric R  ther, MD, PhD, Richard Bergstr  m, MScPharm,
Hans-Georg Eichler, MD, MSc*

"... the ISPOR conference has been very useful both as a learning and sharing of knowledge opportunity and also as an opportunity to network within the industry."



First Plenary Session respondent Lieven Annemans, PhD, MMan, MSc



First Plenary Session- Creating Sustainable Health Systems in Europe



ISPOR 17th Annual European Congress meeting area



Generating Evidence for Pharmacoepidemiology, Health Outcomes, and Epidemiology through Direct-To-Subject Study Approaches Workshop



Capacity Building in Pharmacoeconomics and HTA in Central & Eastern European (CEE): Opportunities in Education and Training Forum (Josip Culig (I) and Olha Zaliska)



ISPOR 17th Annual European Congress Social Event at the NEMO Science Center

ISPOR Avedis Donabedian Outcomes Research Lifetime Achievement Award Presentation and Recipient Remarks: Martin Buxton and Bengt Jönsson, PhD

The 12th Avedis Donabedian Outcomes Research Lifetime Achievement Award was presented at the ISPOR 17th Annual European Congress, on 10 November 2014, Amsterdam, The Netherlands. At the session, the ISPOR Avedis Donabedian Award Committee Chair Mark Sculpher, PhD, introduced Martin Buxton, to present the award. The following is Martin Buxton's introduction of Bengt Jönsson, followed by his acceptance speech.

AWARD PRESENTATION

Martin Buxton

I am delighted to present this year's Avedis Donabedian Lifetime Achievement Award to Bengt Jönsson.

As the recipient of this award four years ago, I recall the pride in being honoured in this way, BUT also a very strong sense, indeed an element of embarrassment, that there were many others equally, if not more, deserving of the honour. And, amongst those at the top of that list of deserving names, I would have placed Bengt.

I first met Bengt in 1974 at a meeting of the UK Health Economists Study Group at the University of Kent, when I acted as a discussant of a paper of his entitled, "Ex post and ex ante cost-benefit analysis: the cases of poliomyelitis and kidney failure." This paper, if I recall correctly, was material that subsequently formed part of his PhD thesis which he defended at the University of Lund in 1976.

In the years that followed that first meeting, I met Bengt regularly as a professional colleague at conferences and meetings. More recently, we have become good friends and for parts of the year at least are near neighbours. As a friend, I know he is great company, with a wide range of interests and knowledge that goes well beyond his professional expertise. But, this award is not granted simply for being a great guy: it is for a lifetime of professional achievement.

For those of you who perhaps don't know Bengt's distinguished career, or have only met him in recent years, I will try to summarise some of his many roles and contributions that have made him such an important part of the international health economics community.

He began his academic career at the University of Lund in Southern Sweden in 1969 and completed his PhD there. That PhD was I know, heavily influenced by discussions with the late Professor Alan Williams at University of York – someone we share as a key influence and 'hero'. In 1979, Bengt

founded the Swedish Institute for Health Economics (IHE) - with which he is still closely involved - and soon after he became professor of health economics at the University of Linköping where he founded the Centre for Medical Technology. Both these institutions that he founded have remained key parts of the Swedish infrastructure for undertaking research in health economics and health technology assessment.

In 1991 he moved to the Stockholm School of Economics, and whilst he has now retired, he retains an Emeritus Professorship and remains very active travelling around the world to lecture and to advise. But that brief outline of his academic career fails to give a true sense of his enormous influence on the growth of health economics and through that on health and pharmaceutical policy in Sweden, Europe more generally and indeed around the world.

A direct impact has been that he seems personally to have been part of the education of virtually all the many health economists that have been trained in Sweden. But his influence goes far beyond the world of health economics and health economists. In a breadth of involvements and collaborations, very much in the spirit that ISPOR seeks to encourage, he has worked with leading clinicians in a wide range of specialties, with governments and local authorities, with hospitals and with the pharmaceutical industry. It takes a special talent to be respected and listened to by all these parties, and he has gained that respect not just from the wise advice he offers, but from the knowledge that he has also been prepared to sit in the hot seat and has helped to make the difficult decisions that are involved in managing a major teaching and research hospital.

I cannot list all the many instances of these significant interactions: but a few examples serve to illustrate the breadth and depth of his influence:

- he led the health economics analysis of the landmark 4S study of simvastatin and played a key role in research on osteoporosis to develop cost-effective intervention thresholds linked to fracture risk assessment;
- he has been a member of the Karolinska University Hospital Board, of the National Social Insurance Board in Sweden, and of SBU (The Swedish Council on Technology Assessment in Health Care);



ISPOR Avedis Donabedian Lifetime Achievement Award in Health Outcomes presenter Martin Buxton (l) and 2014 ISPOR Avedis Donabedian Lifetime Achievement Award in Health Outcomes recipient Bengt Jönsson, PhD

- he is a Past President of Swedish Health Economics Association (SHEA), and of the International Health Economists Association (iHEA);
- he is a member of the European Academy of Cancer Sciences and recently he has been very involved in trying to understand and remove some of the major inequalities that exist in cancer care in Europe;
- he has advised the Swedish Government and the EU on a range of issues and is currently vice chair of the EU Expert Panel on effective ways of investing in health; and, of course,
- he has participated in numerous advisory boards for most of the major pharmaceutical companies.

Earlier this year marked a land-mark birthday for Bengt and a Festschrift [1] was produced with 30 papers from leading health economists from around the world and a celebratory conference held in Stockholm with many local Swedish and international participants. What was most striking about that book and the conference was the breadth of his contributions that it evidenced, the world-wide nature of his influence and the immense esteem and affection that so many people have for him.

By any definition, he has had a lifetime of achievement which richly deserves recognition and celebration in awarding him the 2014 ISPOR Avedis Donabedian Lifetime Achievement Award.

REFERENCES

[1] Culyer AJ and Kobelt G (eds.). Portrait Of A Health Economist, Essays By Colleagues And Friends Of Bengt Jönsson. IHE, Lund, Sweden 2014. <http://www.ihe.se/portrait-of-a-health-economist-3.aspx>.



RECIPIENT REMARKS

Bengt Jönsson, PhD

Thanks to ISPOR, the Avedis Donabedian Award Committee, and all who have contributed to this great honour. It is also feels very special to be presented with this award by Professor Martin Buxton, who was there when it all started, and has been a colleague and friend during the whole journey.

Forty-one years ago, I came to the University of York in England to meet Professor Alan Williams for a discussion about my planned thesis in public finance, focusing on public expenditure and cost-benefit analysis. In our discussions he suggested that I should focus on health economics, and he directed me to a collection of readings on Health Economics, edited by Cooper and Culyer, which had just been published. During my stay, I read the 15 papers included in the book, and talked to Tony Culyer, then Assistant Director of the Institute of Social and Economic Research at the University of York. After that, I changed the subject for my thesis.

From the reading there were two observations that stimulated my interest. The first was the observed variations in medical practice and resource utilisation, which indicated great opportunities for improvements in allocative efficiency. I later learned that the same observation was behind the development of outcomes research, and Avedis Donabedian's classic paper from 1966, that I was not aware of at the time. The second observation was the importance of new medical technology for improvements in outcome and cost-effectiveness, in particular pharmaceutical innovation; what economists call dynamic efficiency.

Some years later, I came in contact with the growing development of health technology assessment (HTA) in the US which was based on the observation that many methods used in clinical medicine were not based on scientific evidence, and there was a need for development of new policy instruments for the management of innovation in health care.

It was very stimulating to work in the intersection between the emerging fields of health economics and HTA at that time, but there was very little support; no academic positions or research grants. The pharmaceutical industry played an important

role for development of health economics in Europe, through the funding of OHE in London (1962), and IHE in Sweden (1979). The first chair in health economics in Sweden was established 1981, and I was appointed to that in 1982, and in 1987 the first government HTA agency in Europe was established in Sweden (SBU).

The introduction of cost-effectiveness as a criterion for reimbursement of drugs in Canada and Australia in the early 1990s gave an important stimulus for the development of pharmacoeconomics, but as the founders of ISPOR in 1995 know well, it was not obvious that we two decades later should see a development to a Society with over 16,000 members, of which 4500 are here at this conference in Amsterdam. It shows the power of an idea whose time has come.


When a younger colleague congratulated me on the Award, she added, "Is it not a little sad for you, to have spent such a long career in health economics, during a time when nobody cared very much about your research. Now everybody is interested and talks about it, and it is time for you to retire."

Let me first say that I am not sad at all, particularly not on a day like this. Looking back, it is a great inspiration to be involved early in any scientific development, and a great satisfaction to see it succeed. It has been pure pleasure to introduce new students to the field, work together with them, see them succeed and take over. I also think that the studies we have done and published and all the competence we have built, now located in government, health care, industry and consultancy, had a significant impact on health policy; even before the creation of specific national and international institutions and mechanisms for decision making based on pharmacoeconomics and outcomes research. But there is certainly more that needs to be done. It is easy to observe that we today have similar variations in the use of health technology between and within countries as forty years ago, which indicates further opportunities for improvement. The importance of providing information for rational decisions about medical innovations, and

correct incentives for innovators is also the same; exemplified with the theme for this Congress. I am happy for all new students in our field of scientific inquiry that have such interesting and important issues to work with. The most important advice to any young scientist is: choose an important question for your research. Methods are important, but they are tools, and should be chosen and developed to answer the question. Without an important question, there will never be an important answer.

I have had my "fair inning," as Alan Williams should have said, but that does not necessarily mean that it is all over yet. But I like to end this talk with thanks to all of you, not only for the Award and the professional recognition, which of course means a lot, but also for everything that came along with it: the opportunity to meet and work with exceptional persons and to develop long term friendships. I feel very privileged.

It has been debated if health economics is best defined as a discipline or a topic. I think that for me, it can also be defined as a lifestyle! Finally, a special thanks to Gisela and Linus, for your decision to share this lifestyle with me.

(Bengt Jönsson's latest book, The Value of New Medicines, can be downloaded for free at: <http://www.sns.se/forlag/value-new-medicines-0>) 

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The ISPOR Awards Program is designed to foster and recognize excellence and outstanding technical achievement in pharmacoeconomics and outcomes research.



Sean Sullivan, PhD, Chair, ISPOR Scientific Awards Committee and Stergachis Family Professor and Director, University of Washington, Pharmaceutical Outcomes Research and Policy Program, Seattle, WA, USA.

The following awards will be presented at the ISPOR 20th Annual International Meeting, May 16-20, 2015, Philadelphia Marriott Downtown, Philadelphia, PA, USA.

ISPOR Bernie O'Brien New Investigator Award

Nominations Due By February 13, 2015

The ISPOR Bernie O'Brien New Investigator Award was established in 2004 to honor the long-standing commitment of Bernie J. O'Brien, PhD to training and mentoring new scientists in the fields of outcomes research and pharmacoeconomics.

The Award consists of a plaque, complimentary meeting registration, an unrestricted research grant of US\$5,000.00 and up to US\$1,500.00 for travel expenses.

All nominations must include a letter of support for the nominee and a current edition of the nominee's CV essay indicating the reason for your nomination.

For complete background, criteria, selection process, and nature of the award can be found at: http://www.ispor.org/awards/Obrien_investigator.asp.

**Nominations should be sent to: awards@ispor.org
For information, contact Angela Buziak,
Coordinator, Publications
and Communications, at: abuziak@ispor.org**

ISPOR Award for Excellence in Methodology in Pharmacoeconomics and Health Outcomes Research

ISPOR Award for Excellence in Application of Pharmacoeconomics and Health Outcomes Research

Nominations Due By February 13, 2015

The ISPOR Award for Excellence in Methodology and Application in Pharmacoeconomics and Health Outcomes Research were established in 1997 to recognize outstanding research in the field of pharmacoeconomics and outcomes research methodology and outstanding practical application of pharmacoeconomics and outcomes research in health care decision making.

The Award, presented at the ISPOR Annual International Meeting to the corresponding author of the paper, consists of a plaque, complimentary Annual International Meeting registration, roundtrip air fare, hotel, meal and miscellaneous expenses for two days, based upon current ISPOR travel policies.

Only ISPOR members may submit nominations (either their own publications or others). All nominations must include a brief cover letter indicating the reason for the nomination. Supporting documentation MUST include a PDF of the nominated paper.

For complete background, criteria, selection process, and nature of the award can be found at: http://www.ispor.org/awards/methodology_.asp and http://www.ispor.org/awards/application_.asp.

ISPOR POLAND CHAPTER

"A Very Important Element of Pharmacoeconomic Education in Poland"

"Therapeutic and Diagnostic Device Outcomes Research is the first such comprehensive publication available in Polish language, which as a whole deals with the subject of clinical effectiveness assessment and economic efficiency of products used in medical diagnosis and treatment. It provides necessary information for the Polish medical decision makers, payers, health care experts, analysts, clinicians and patients. It is a very important element of Pharmacoeconomic education. We have dealt so far mainly with drugs and now we have a 'bible' for medical devices. I am sure that this translation will be welcomed by Polish readers."

– Joanna Lis, MSc, PhD, President, ISPOR Poland Chapter

For more information about the Polish translation of Therapeutic and Diagnostic Device Outcomes Research, please visit the ISPOR Poland Chapter at: <http://www.ispor.org/RegionalChapters/Chapter/Poland>

ISPOR also offers Therapeutic And Diagnostic Device Outcomes Research in Portuguese, and a Spanish version is currently in development.

For more information and additional translated ISPOR books, visit: <http://www.ispor.org/publications/BooksIndex.asp>



Connection and Collaboration: Student Activities at the ISPOR 17th Annual European Congress

Brendan J. Kelly, 2014 – 2015 ISPOR Student Network Chair and PharmD Candidate, Touro University California, Vallejo, CA, USA



The ISPOR 17th Annual European Congress was held in Amsterdam, The Netherlands, November 8-12, 2014. As in previous years, one of the main objectives for the ISPOR Student Network is increasing connections and collaboration among student members. The ISPOR Student Network has been experiencing exponential growth as we induct new student chapters and members. This year's Congress provided students the platform to maintain connections and the opportunity to discuss ideas to increase collaborative efforts in Europe and other regions.



Student and Faculty Lunch

To connect students and faculty members, the ISPOR Student Network congregated for the annual **Student & Faculty Welcome Reception**. The reception was held on Monday, November 10th, at the Amsterdam Café in the RAI Conference Center. All students and faculty were invited to the reception, which stimulated interaction among academics from all international ISPOR regions. The reception was a great success, drawing 75 attendees to the event, a 25% increase from last year's reception. The event hosted a raffle for students to win prizes, including Health Care, Cost, Quality and Outcomes: ISPOR Book of Terms and four annual ISPOR memberships. **Daniel C. Malone, RPh, PhD**, ISPOR 2014 – 2015 President-elect, participated in the raffle and presented the prizes to the winners. **Joshua Brown, PharmD**, from the University of Kentucky, Kentucky, USA, commented on the success of the student activities and student presence at the Congress stating, "I've been involved with the ISPOR Student Network for a number of years now and it's great to see how much we've grown and evolved!"

As the Student Network expands, it is our mission to develop the organization while maintaining internal connections. We continue to develop our platforms for student interaction and provide resources for students to develop professional careers. In order to meet the goals of the mission, the ISPOR Student

Network introduced two new events at the Congress: The **Student Research Showcase** and the **Student Network & Faculty Advisor Luncheon**.

The **Student Research Showcase** was held on Monday, November 10th, and was highly attended by approximately 90 attendees. The theme was, "Outcomes Research Having a High Impact on New Challenges for Improving European Health Care." The showcase featured four student speaker presentations: **Jane YC Chan, MA, MSc**, from the London School of Economics, London,


England, UK, presented, "Does Price Matter? The Impact of Cost information on patient Decision Making," **Henk Broekhuizen, MSc**, from the University of Twente, Enschede, The Netherlands, presented, "Patient Preferences and HIV drugs: What About Uncertainty?" **Frank Moriarty, BSc, HRB, PhD**, from the Royal College of Surgeons in Ireland, Dublin, Ireland, presented, "Potentially Inappropriate Medicines and Potential Prescribing Omissions in Older People and their Association with Healthcare Utilization: A Retrospective Cohort Study," and **Carina Schey, PharmD**, from the University of Groningen, Groningen, The Netherlands presented, "Assessing the Relationship Between Individual Attributes Identified in Review of Multi-Criteria Decision Analysis (MCDA) of Rare Diseases and Annual Treatment Costs in Rare Endocrine Disorders." Event attendees described the Student Research Showcase as a brilliant opportunity for students to share and discuss research findings and the student engagement has created a bridge for continued involvement, as students become professionals in their respective areas of research.

The second new event held on Tuesday, November 11th, was the **Student Network & Faculty Advisor Luncheon**. The European ISPOR student member and chapter participation has increased substantially over the past couple of years, justifying the need to increase the presence of the Student Network during the European Congress to continue to progress and build the Student Network internationally. This is the first time a luncheon has



Frank Moriarty, BSc, HRB, PhD, Royal College of Surgeons in Ireland, Dublin, Ireland, presenting "Potentially Inappropriate Medicines and Potential Prescribing Omissions in Older People and their Association with Healthcare Utilization: A Retrospective Cohort Study," at the Student Research Showcase.

been held at the European Congress to congregate the chapter presidents and faculty advisors to discuss challenges and opportunities faced within individual chapters. The faculty advisors of the ISPOR Student Network have invaluable experience and the event gave the students the opportunity to connect with our valuable resources. The luncheon also served as a forum for the European Meeting Planning Committee to discuss concepts and ideas for the 18th Annual European Congress, which will be hosted in Milan, Italy.

Overall, the ISPOR 17th Annual European Congress was a huge success for the Student Network! The expansion of student membership and chapters in the European region was complemented by increased student presence at the Congress. And, as students from all around the world convened, our student activities provided opportunities for us to connect and collaborate. In addition, we were contacted by students interested in starting new student chapters! One student, Fabian Degener from the University of Groningen, The Netherlands, expressed his interest in starting an ISPOR Student Chapter. Mr. Degener commented, "Being a student, we are always seeking new prospects. The Student Network is a great opportunity for us [students] to network and exchange ideas for new projects." As a closing comment, it was great meeting everyone at the Congress and I look forward to our continued growth and success within the ISPOR Student Network! 



73 ISPOR REGIONAL CHAPTERS



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SHORT COURSES

SATURDAY, MAY 16

ALL DAY COURSES 8:00AM-5:00PM

INTRODUCTION TO PHARMACOECONOMICS

Learn how to incorporate pharmacoeconomics into study design and data analysis, how to collect and calculate the costs of different alternatives, determine the economic impact of clinical outcomes, and identify, track, and assign costs to health care resources.

BAYESIAN ANALYSIS – OVERVIEW AND APPLICATIONS

This course provides an overview of the Bayesian approach, its applications to health economics and outcomes research, and hands on experience using WinBUGS.

MORNING COURSES 8:00AM-12:00PM

INTRODUCTION TO DATABASE ANALYSIS OF OBSERVATIONAL STUDIES OF TREATMENT EFFECTS

This course introduces analytic techniques and best practices to improve causal inference in studies using retrospective databases, including stratification analysis, multivariable regression, propensity scoring, instrumental variable, and structural modeling techniques.

INTRODUCTION TO MODELING METHODS

This course introduces the principles and practice of decision analysis. Participants evaluate the appropriateness of decision analysis, construct simple decision trees, understand basic mechanics of tree evaluation and sensitivity analysis, and acquire skills in the interpretation of a published decision analysis.

INTRODUCTION TO PATIENT-REPORTED OUTCOMES

Conceptual, methodological, and practical methods for measuring quality of life, health status, and other types of health outcomes are presented. Theoretical frameworks, reliability, validity, responsiveness, methods of administration, respondent and administrative burdens, and issues of analysis and interpretation are discussed.

INTRODUCTION TO CONJOINT ANALYSIS

This course introduces the conceptual basis for quantifying decision-maker preferences for medical interventions and the practical design and analytical issues that must be addressed to obtain valid empirical preference estimates.

ELEMENTS OF PHARMACEUTICAL / BIOTECH PRICING I – INTRODUCTION

This course gives participants a basic understanding of the key terminology and issues involved in pharmaceutical pricing; the tools needed to build and document product value are explored through a series of exercises.

AFTERNOON COURSES 1:00PM-5:00PM

META-ANALYSIS AND SYSTEMATIC REVIEWS IN COMPARATIVE EFFECTIVENESS RESEARCH

This course discusses six key areas: 1) comparative effectiveness research; 2) impetus for meta-analysis and systematic reviews; 3) basic steps to perform a quantitative systematic review; 4) statistical methods of combining data; 5) reporting of results; and 6) appraisal and use of meta-analytic reports.

UTILITY MEASURES

This course explores concepts of health-related quality of life in terms of their differences and similarities, methods used to capture utilities (standard gamble, time trade off, and rating scales), and instruments to measure quality of life (EQ-5D, Health Utilities Index, and SF-36).

MODELING: DESIGN AND STRUCTURE OF A MODEL

This course provides hands-on experience in constructing a decision analysis tree including Markov models, Monte Carlo simulations, sensitivity analysis, determination of probability values, and transition probabilities.

CASE STUDIES IN PHARMACEUTICAL / BIOTECH PRICING II – ADVANCED

This course employs case studies to lead participants through the key steps of new product pricing, with focus on the need to thoroughly analyze the business environment and the need to closely integrate pricing, reimbursement, and PE strategy for a new product with clinical development and marketing strategies.

COST-EFFECTIVENESS ANALYSIS ALONGSIDE CLINICAL TRIALS

This course presents design, conduct, and reporting of cost-effectiveness analyses alongside clinical trials. Analyses guided by an analysis plan and hypotheses, an incremental analysis using an intention to treat approach, characterization of uncertainty, and standards for reporting results are presented.

ADVANCED PATIENT-REPORTED OUTCOMES

This course provides an in-depth discussion of both the methods that are used to validate and refine PRO measures (including ePROs) and the analytic methods used to model PRO data over time in clinical trials.

SUNDAY, MAY 17

MORNING COURSES 8:00AM-12:00PM

DISCRETE EVENT SIMULATION FOR ECONOMIC ANALYSES – CONCEPTS

This course provides a basic understanding of key concepts of discrete event simulation and will focus on the use of these simulation models to address health economic (and device-related) problems.

STATISTICAL METHODS IN ECONOMIC EVALUATIONS

This course examines statistical approaches that address common features of resource use and cost data, including distributional characteristics, censoring, hierarchical data structures, and potential confounding.

RISK-SHARING / PERFORMANCE-BASED ARRANGEMENTS FOR DRUGS AND OTHER MEDICAL PRODUCTS

Theory and practice of “pay-for-performance” or “risk-sharing” arrangements are analyzed, along with several examples of performance-based schemes from Europe, the United States, and Australia.

NEW! DEVELOPMENT OF CONCEPTUAL MODELS

The course reviews important practical aspects of the development of conceptual models using a series of case studies to illustrate the role of clear conceptual models in the iterative process of model development.

APPLICATIONS IN USING LARGE DATABASES

This course reviews the databases CPRD (UK database), GE Centricity electronic medical record (EMR), and Medicare (USA databases). Each database is discussed in-depth including how to access information and how researchers utilize this information.

PATIENT-REPORTED OUTCOMES – ITEM RESPONSE THEORY

Applications of IRT have increased considerably because of its utility for instrument development and evaluation, assessment of measurement equivalence, instrument

linking, and computerized adaptive testing. This short course discusses the basics of IRT models and applications to improve health outcomes measurement.

USE OF INSTRUMENTAL VARIABLES IN OBSERVATIONAL STUDIES OF TREATMENT EFFECTS

Sample selection models provide a test and correction for the presence of selection bias, enabling an investigator to obtain unbiased estimates of treatment effects. This course discusses various models and their applications, in particular instrumental variables.

INTRODUCTION TO BUDGET IMPACT ANALYSIS

This course describes the methods used to estimate the budget impact of a new health care technology. Both static and dynamic methods for estimating the budget and health impact of adding a new drug to a health plan formulary are presented.

AFTERNOON COURSES 1:00PM-5:00PM

NEW! INTRODUCTION TO BIG DATA ANALYSIS: GRAPH ANALYTICS

Issues related to node-typed, edge-typed, and directed graphs, using the resource description framework (RDF) to describe information in a graph, the use of SPARQL, and the application of inferential rules and ontologies to the dataset are discussed.

BUDGET IMPACT ANALYSIS: APPLICATIONS AND DESIGN ISSUES

This course provides hands on experience utilizing an Excel-based approach to create and modify budget impact analysis models and cost calculators. Applications focus on design issues related to accuracy of budget impact estimation as well as applicability to decision makers.

DISCRETE EVENT SIMULATION FOR ECONOMIC ANALYSES – APPLICATIONS

This course is structured around practical hands-on discrete event simulation exercises. Topics include: components of a DES; how to build a model; modeling of processes and resource use; and modeling of variables and decisions.

NETWORK META-ANALYSIS

The fundamentals and concepts of network meta-analysis are presented, motivated by instructive and real examples implemented with the WinBUGS package.

USE OF PROPENSITY SCORES IN OBSERVATIONAL STUDIES OF TREATMENT EFFECTS

This course discusses how propensity scores can be used to mitigate confounding, the advantages and disadvantages of standard adjustment relative to propensity score-based methods, details of propensity score methodology, and risk adjustment models.

ADVANCED DECISION MODELING FOR HEALTH ECONOMIC EVALUATIONS

This course considers key aspects in the development of decision modeling, how models can be made probabilistic to capture parameter uncertainty, how to analyze and present results, how results should be interpreted, and decisions should be made.

NEW! USING MULTI-CRITERIA DECISION ANALYSIS IN HEALTH CARE DECISION MAKING: APPROACHES & APPLICATIONS

This course reviews the use of MCDA in health care applications and the different approaches employed. Issues related to selecting the right data approach, criteria definition, scoring performance, weighting criteria, and uncertainty analysis will be demonstrated.

COMPLETE SHORT COURSE DESCRIPTIONS
AVAILABLE AT WWW.ISPOR.ORG

ISPOR 20TH ANNUAL INTERNATIONAL MEETING

May 16-20, 2015 • Philadelphia Marriott Downtown • Philadelphia, PA, USA



CALL FOR ABSTRACTS

Abstract Submission Begins: October 15, 2014 / Abstract Submission Deadline: January 15, 2015

SUBMISSION INSTRUCTIONS

All abstracts and proposals MUST be submitted through ISPOR's online abstract submission system by January 15, 2015. Abstracts accepted for other ISPOR meetings can NOT be submitted and a research abstract that was submitted to another meeting and copyright transferred is not allowed.

SUBMISSION INSTRUCTIONS, EXAMPLES & SPECIFIC EVALUATION CRITERIA AVAILABLE AT WWW.ISPOR.ORG

RESEARCH ABSTRACTS

Outcomes research on all health care interventions (including drugs, devices, behavioral modification programs, surgery, disease prevention, gene therapy, screening, diagnostic procedures, and health education) and on all diseases or health disorders are considered. Research abstracts (except for conceptual papers) must be organized by OBJECTIVES, METHODS, RESULTS, CONCLUSIONS. All accepted research abstracts are published in *Value in Health* as submitted. Accepted research is presented as a 15-minute podium presentation or poster presentation (with a poster author discussion hour). Abstracts are evaluated on the quality of the study (or concept) and quality of the abstract presentation.

Research topics include: **Clinical Outcomes Studies, Cost Studies, Patient-Reported Outcomes & Patient Preference Studies, Health Care Use & Policy Studies, Research on Methods, Conceptual Papers.** See the ISPOR website for research subtopics, diseases, and health care treatments.

ISSUE PANEL PROPOSALS

Issue panel proposals should show real debate on new or controversial issues in health economics and outcomes research or real debate on the use of outcomes research in health care decision making. Issue panel proposals must be organized MODERATOR, PANELISTS, ISSUE, OVERVIEW. Accepted issue panels are one hour in duration with a moderator and 2-3 panelists representing different organizations. Panelists should present distinct views about the topic.

Issue Panel topics are: **Clinical Outcomes Research Issues, Economic Outcomes Research Issues, Patient-Reported Outcomes & Patient Preference Research Issues, Health Policy Development Using Outcomes Research Issues, Use of Real World Data Issues.** See the ISPOR website for issue panel subtopics.

WORKSHOP PROPOSALS

Workshop proposals should show novel and innovative experiences in the conduct of outcomes research (including, but not limited to, experiences with conjoint analysis, large database analysis, modeling, observational studies, record review, surveys, sensitivity analysis, and patient registries) or novel and innovative experiences in the use of outcomes research (clinical, economic, or patient-reported/patient preference outcomes) in health care policy development. Workshop proposals must be organized by DISCUSSION LEADERS, PURPOSE, DESCRIPTION. Accepted workshops are one hour in duration with a minimum of 2 and maximum of 4 discussion leaders (more than one organization must be represented). An audience interactive element must be included in the proposal and during the workshop.

Workshop topics include: **Clinical Outcomes Research, Economic Outcomes Research, Patient-Reported Outcomes & Patient Preference Research, Health Policy Development Using Outcomes Research, Use of Real World Data.** See the ISPOR website for workshop subtopics.

PRELIMINARY PROGRAM

MONDAY, MAY 18: 7:15AM-7:45PM

FIRST PLENARY SESSION: TAKING STOCK OF THE LEARNING HEALTH CARE SYSTEM: WHAT HAVE WE ACHIEVED AND WHY DOES IT MATTER?

Nearly a decade ago, leaders envisioned a pathway to a learning health care system, where research is closely integrated and rapidly translated into practice by making use of electronic data that can track patients across health care providers and time. Since then, there has been substantial public and private investment to make this vision a reality. This session critically examines how far we have come and what the implications are for comparative effectiveness researchers, payers, patients, and the life sciences industry.

* 48 Research Podium Presentations * 5 Issue Panels * 7 Workshops * 7 ISPOR Group Forums * Exhibits * 700 Research Poster Presentations – Session I & II

TUESDAY, MAY 19: 7:15AM-7:45PM

SECOND PLENARY SESSION: COST-EFFECTIVENESS AND CLINICAL PRACTICE GUIDELINES: HAVE WE REACHED A TIPPING POINT?

In recent years, both oncology and cardiology professional organizations have embraced the explicit consideration of cost-effectiveness and the value of treatments in developing and updating clinical practice guidelines and clinical pathways. This is a new development in the U.S. health care system, and one which is complicated by the pluralistic nature of the system. The impact that it could ultimately have on medical practice is not clear neither in terms of access to care and providers nor in terms of incentives for innovation. This session will explore the implications of this change for the range of stakeholders involved, including U.S. private insurers, clinicians, patients, and federal government programs.

* 10 Issue Panels * 14 Workshops * 7 ISPOR Group Forums * Exhibits * 700 Research Poster Presentations – Session III & IV * Evening Social Event

WEDNESDAY, MAY 20: 7:15AM-4:00PM

THIRD PLENARY SESSION: BIG DATA, BIG SYSTEMS, AND BETTER EVIDENCE: WHAT PROGRESS?

What could the growing interest in big data mean for health delivery systems and patients? This session will explore the challenges for incorporating big data into health system decisions and processes. A number of related questions will be explored. What is the potential role of big data in our ability to measure the performance of health systems in terms of effectiveness and efficiency? Can big data be used to improve evidence and clinical decision making? Is there a need for new analytical approaches? How will these developments affect patients?

* 5 Issue Panels * 10 Workshops * Exhibits * 350 Research Poster Presentations – Session V

**COMPLETE INFORMATION AND
REGISTRATION AT WWW.ISPOR.ORG**



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ISPOR 5TH LATIN AMERICA CONFERENCE



3-5 September 2015
Santiago, Chile

*Increasing Access to Health Care in Latin America:
Making Better Decisions for Greater Equity*

CALL FOR ABSTRACTS

Abstract Submissions Opens: 19 January 2015
Early Registration Deadline: 21 July 2015



**CO-ORGANIZED BY: International Society for Pharmacoeconomics and Outcomes Research (ISPOR)
ISPOR Latin America Consortium & ISPOR Chile Regional Chapter**

Supporting Institutions (as of November 2014)

- Institute for Clinical Effectiveness and Health Policy (IECS), Argentina
- Institute for Health Technology Assessment (IETS), Colombia
- General Health Counsel (CSG), Mexico
- Interdepartmental Center for Health Economics (GRIDES), Brazil
- General Coordination for HTA, Department of Science and Technology (CGATS/DECIT), Brazilian Ministry of Health, Brazil
- SaluDerecho (An initiative focusing on prioritization, equity and constitutional mandates in health), Washington, D.C.

Conference Program Planning Committee

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Rony Lenz Alcayaga, MA, Professor, School of Public Health, University of Chile and Head Consultant, Lenz Consulting, Santiago, Chile

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Department of Scientific Affairs, Public Health Institute of Chile, Santiago, Chile

Mario Giorgio Saggia, MBA, Independent Health Economics Consultant, São Paulo, Brazil

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Diego Rosselli, MD, MEd, MHP, Associate Professor, Health Economics, Javeriana Papal University, Bogota, Colombia

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For information, please email laconsortium@ispor.org.

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For information, please email exhibit@ispor.org.

EDUCATIONAL SYMPOSIA

These sponsored presentations are open to all delegates. The sponsor organization chooses a subject of interest and arranges suitable speakers for the presentation.

For information, please email symposia@ispor.org.



ISPOR 5TH LATIN AMERICA CONFERENCE

3-5 September 2015, Santiago, Chile

ISPOR SHORT COURSE PROGRAM

ALL DAY SHORT COURSES (8:00-17:00)

INTRODUCTION TO HEALTH ECONOMICS

(Presented in Spanish)

Track: Economic Methods

Level: Introductory. This course is suitable for those with little or no experience with pharmacoeconomics.

Course Description: This course is designed to teach clinicians and new researchers how to incorporate pharmacoeconomics/health economics into study design and data analysis. Participants will learn how to collect and calculate the costs of different health care or health care economic evaluation alternative treatments, determine the economic impact of clinical outcomes, and how to identify, track, and assign costs to different types of health care resources used. The development of economic protocols and data collection sheets will be discussed. Different health economics models and techniques will be demonstrated with case studies. These include: cost-minimization, cost-of-illness, cost-effectiveness, cost-benefit, and cost-utility analysis. Decision analysis, sensitivity analysis, and discounting will also be demonstrated and practiced. Participants will learn to compare and evaluate interventions such as drugs, devices, and clinical services.

APPLIED MODELING

(Presented in English, Portuguese, and Spanish)

Track: Modeling Methods

Level: Advanced. This course is designed for those with some familiarity with modeling methods, looking for hands-on practice in developing a model.

Prerequisite: This course is suitable for those who are familiar with modeling methods and/or those who have previously taken the ISPOR Short Course, "Introduction to Modeling."

Course Description: This course is a hands-on introduction to the use of software in the creation and analysis of cost-effectiveness decision models. The basics of cost-effectiveness decision making and building and analyzing a simple decision tree will be discussed. Markov modeling and Monte Carlo simulation will be introduced. All participants must bring a Windows laptop computer with a copy of TreeAge Pro Suite installed and running. You will be provided download and installation instructions when you pre-register for the course.

MORNING SHORT COURSES (8:00-12:00)

INTRODUCTION TO MODELING

(Presented in Spanish)

Track: Modeling Methods

Level: Introductory. This introductory course requires a basic familiarity with decision analysis.

Course Description: This course includes a review of Markov models, discrete event models, and other modeling techniques and their appropriate applications, including a review of the ISPOR Principles of Good Practice for Decision Analytic Modeling in Health Care Evaluations, as well as the recent ISPOR-SMDM guidelines (*Value Health* 2012). Using a series of related examples, the course will carefully review the practical steps involved in developing and using these kinds of models. Instructors will cover the practical steps involved in the selection and modeling of data inputs and practical aspects related to the determination of when, why, and how to handle stochastic (i.e., first order Monte Carlo Simulations) and probabilistic uncertainty (i.e., second order Monte Carlo Simulations). Issues related to the selection of model input parameters and their distributions for use in probabilistic sensitivity analyses will be considered.

HEALTH-RELATED QUALITY OF LIFE / UTILITY MEASURES

(Presented in Spanish)

Track: Patient-Reported Outcomes/Preference Methods

Level: Introductory/Intermediate. This course is for those with some experience with quality-of-life measures in health economic evaluation.

Course Description: Conceptual, methodological, and practical methods for measuring quality of life, health status, and other types of health outcomes will be presented. Utility measurement, a method of determining an individual's preference for a certain outcome represented by a quantitative score (utility), will also be reviewed. Methods for measuring preference-based outcomes like the standard gamble, time trade-off, and visual analogue scale will be demonstrated. Additionally, utility-based instruments such as the EQ-5D, HUI, QWQ, and SF-36 will be briefly discussed. Utility measurement, however, is not only about mastering these techniques; it is about using them in such a way that health care decision makers can apply the results, for instance in cost per QALY-analyses. For this purpose, one needs to be aware of shortcomings of the available utility measures and potential solutions. Furthermore one should be aware of the decision-making context and the way results are interpreted. To equip participants with expertise in the field of utility measurement, the most important issues will be discussed, such as potential insensitivity of generic instruments for particular disease specific problems, and to what extent adaptation of generic or disease-specific quality of life instruments may offer a solution. Also the issue of "whose values count: patient values or values from the general public?" will be discussed. Finally, faculty will turn to the interpretation in the context of resource allocation.

AFTERNOON SHORT COURSES (13:00-17:00)

EXTRACTING COST DATA FOR ECONOMIC ANALYSIS IN LATIN AMERICA

(Presented in Spanish)

Track: Economic Methods

Level: Intermediate. This course is designed for those with some experience with pharmacoeconomic analysis.

Course Description: This course will focus on practical aspects of cost development for pharmacoeconomic studies. The objective is to help the participant bridge the gap between understanding pharmacoeconomic theory and the practice of developing cost estimates. Factors to consider when costing pharmacoeconomic analyses, such as perspective, data sources, data classification systems, developing resource use profiles, obtaining unit costs, and making cost adjustments will be presented. Examples of issues encountered when identifying and extracting cost data will be discussed.

META-ANALYSIS & SYSTEMATIC LITERATURE REVIEW

(Presented in Spanish)

Track: Outcomes Research Methods

Level: Intermediate. This course is designed for those with some experience with pharmacoeconomic analysis/outcomes research methods.

Course Description: Faculty will discuss systematic literature review and meta-analytic methods used to assess the quality of evidence for health care interventions. Statistical approaches to pooling results from several studies and application of meta-analysis in pharmacoeconomic studies and health care decision making will be presented.

**Complete Short Course descriptions
available at www.ispor.org**



ISPOR 5TH LATIN AMERICA CONFERENCE

3-5 September 2015, Santiago, Chile

CALL FOR ABSTRACTS

Abstract Submission Opens: 19 January 2015 / Abstract Submission Deadline: 19 March 2015

SUBMISSION INSTRUCTIONS

All abstracts and proposals **MUST** be submitted through ISPOR's online abstract submission system by 19 March 2015. Abstracts will be accepted in Spanish, Portuguese, and English. Abstracts accepted for other ISPOR meetings can **NOT** be submitted and research published or presented at other national or international meetings is discouraged.

SUBMISSION INSTRUCTIONS, EXAMPLES & SPECIFIC EVALUATION CRITERIA AVAILABLE AT www.ispor.org

RESEARCH ABSTRACTS

Outcomes research on all health care interventions (including drugs, devices, behavioral modification programs, surgery, disease prevention, gene therapy, screening, diagnostic procedures, and health education) on all diseases or health disorders are considered. Research abstracts (except for conceptual papers) must be organized by OBJECTIVES, METHODS, RESULTS, CONCLUSIONS. All accepted research abstracts are published in *Value in Health* as submitted. Accepted research is presented as a 15 minute podium presentation or poster presentation (with a poster author discussion hour). Abstracts are evaluated on the quality of the study (or concept) and quality of the abstract presentation.

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WORKSHOP PROPOSALS

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Workshop topics include: **Clinical Outcomes Research, Economic Outcomes Research, Patient-Reported Outcomes & Patient Preference Research, Health Policy Development Using Outcomes Research, Use of Real World Data.** See the ISPOR website for workshop subtopics.

ISSUE PANEL PROPOSALS

Issue panel proposals should show real debate on new or controversial issues in health economic/pharmacoeconomics and outcomes research or real debate on the use of outcomes research in health care decision making. Issue panel proposals must be organized by MODERATOR, PANELISTS, ISSUE, OVERVIEW. An accepted issue panel is one hour in duration with a moderator and 2-3 panelists. Panelists should be from different institutions and/or work environments representing different perspectives on the debate.

Issue Panel topics are: **Clinical Outcomes Research Issues, Economic Outcomes Research Issues, Patient-Reported Outcomes & Patient Preference Research Issues, Health Policy Development Using Outcomes Research Issues, Use of Real World Data Issues.** See the ISPOR website for issue panel subtopics.

PRELIMINARY PROGRAM

THURSDAY, 3 SEPTEMBER 8:00-22:00

SHORT COURSE PROGRAM

*Introduction to Health Economics *Introduction to Modeling *Applied Modeling
*Extracting Health Care Data for Economic Analysis *Meta-Analysis & Systematic Literature Review *Health-Related Quality of Life/Utility Measures

Plus! *EDUCATIONAL SYMPOSIA *WELCOME RECEPTION

FRIDAY, 4 SEPTEMBER 8:00-21:00

FIRST PLENARY SESSION: IS HTA FAIR? ANALYZING THE HTA PROCESS IN LATIN AMERICA & ITS IMPLICATIONS FOR ACCESS TO HEALTH CARE

Health technology assessment (HTA) is increasingly being used by public and private payers in Latin America to assess the effectiveness and efficiency of health care technologies for their populations – but is it fair? HTA has been implemented as a way to enable better decisions that balance varied societal and stakeholder perspectives and needs, but there still persists the question of whether or not the decisions being made fairly represent all stakeholders. Panelists will discuss these issues from a perspective of working in the environment of fairness, while balancing the requirements of a rigorous scientific method to evaluate the usefulness of drugs and devices for their populations.

Plus! *EDUCATIONAL SYMPOSIA *ISSUE PANELS *WORKSHOPS *POSTER & PODIUM PRESENTATIONS *EXHIBITS

SATURDAY, 5 SEPTEMBER 8:00-17:30

SECOND PLENARY SESSION: ACCESS TO HIGH COST DRUGS IN LATIN AMERICA: WHO GOES FIRST?

Health systems in Latin America are currently experiencing constant pressure from patient groups, many of which are supported by the manufacturers themselves, as they seek access to high cost drugs via the prosecution of claims in the court system. The end goal of these claims is to ensure the financing of high cost medicines. In response to this trend, and given the natural complexity of pharmacological therapies, countries are now developing strategies to finance access to high cost drugs. Given the scarcity of available resources, it is necessary to prioritize their allocation. This session aims to review such activities in the region, and inquire about some of the critical aspects of prioritization, namely: Have certain health problems been favored and why? What types of drug therapies have high priority? Who makes these assignments? What criteria are used in the prioritization process? Are certain patient groups privileged and why? Are these solutions long or short term answers? In short, who comes first and who must wait for access to expensive drugs?

Plus! *EDUCATIONAL SYMPOSIA *ISSUE PANELS *WORKSHOPS *POSTER & PODIUM PRESENTATIONS *EXHIBITS

Over 800 attendees expected!



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