ISPOR Report

22nd Annual European Congress

Copenhagen, Denmark November 2019

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Foreword

Matt Griffiths, Head of HTA & Health Economics

Fresh and recovered from successful conferences at both ISPOR New Orleans and HTAi in Cologne earlier in 2019, Costello Medical were pleased to maintain a strong presence at the annual ISPOR Europe conference in Copenhagen this November. As with previous years, a sizeable number of us (11 staff from across our UK, Singapore and US teams) travelled out to the conference, winter coats packed in anticipation of the Danish weather. Between meeting existing clients and making new contacts at our exhibitor booth, attending the many presentations, workshops and panel discussions, and delivering our own 2 issue panels and 8 research posters it's hard to imagine how we'd manage with any fewer attendees!

We were pleased this year to contribute 2 distinct (though not unrelated) topics to the ISPOR agenda via our issue panels. On a personal level I was delighted to moderate my first ISPOR issue panel, which discussed the causes and potential solutions to issues of HTA capacity and the risks this poses for delayed access to patients. I was honoured to be joined by 3 excellent panellists in Dr Lesley Tilson (NCPE), Professor Mike Drummond (University of York) and Eric Low (Eric Low Consulting) and so pleased to find the panel well attended by an enthusiastic and engaged audience who contributed plenty of questions. The topic of HTA capacity is one that I believe will only increase in relevance, not least due to the emergence of more multi-indication therapies and the potential for the relentless march of real-world evidence (RWE) to drive increased re-appraisal of therapies. It was on this latter topic that my colleague, Craig Brooks-Rooney, delivered our second issue panel, inviting Adrian Towse (Office of Health Economics), former colleague Jeanette Kusel (NICE Scientific Advice) and Anna Halliday (Novartis) to debate the question of whether a formal system for using RWE to revisit the HTA decision would be worth it, and what any such system should look like.

In addition to our panels, we were delighted to be represented at the conference by 8 Costello Medical research posters, covering topics that included: early prediction of survival estimates for immune-oncology (IO) therapies; rare disease utility studies; reporting standards for expert elicitation exercises and a conceptual methods poster exploring the use of expected value of perfect parameter information in the context of expert-derived opinion.

Reflecting on the conference presentations as a whole, I would have to summarise my main take-home message as: **big data is here**. That might seem a facile statement to make – big data and digital technologies are, of course, not new topics for ISPOR and other similar conferences, or indeed wider political discussions. We've known this is on its way for a while. However, in previous conferences I've always had a sense that big data has been discussed as something relatively inert that will sit patiently and wait for us to work out how to feed this into our regulatory and assessment frameworks. This year felt like a shift in tone, with much more discussion of the "inevitable" disruptive influence (positive and negative) of the "big tech" companies as the digital health industry grows. The second and third plenary sessions – both more compelling than many plenaries we've seen in recent years – did an excellent job of laying the groundwork for future debate on the trade-off between making the most of what digital technologies have to offer, whilst ensuring appropriate regulation and maintenance of a "human", empathetic approach to healthcare. It is certainly a very interesting time to be working in this field, and we're excited to navigate the regulatory and HTA landscape as it responds to this disruption.

With that setting of the scene, it is my pleasure to invite you to read this year's report.

The Conference

22nd Annual European ISPOR Congress

Copenhagen, Denmark, 2nd–6th November 2019

Digital Transformation of Healthcare: Changing Roles and Sharing Responsibilities

5,500+
healthcare stakeholders from over 90 countries

2,500+
presentations

Costello Medical research contributions:

2
issue panels

8
original research posters

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Incorporating RWE in Decision Making

Big data as a source of RWE

With the rise of digitised healthcare, big data has been increasingly identified as a potentially valuable source of RWE. However, uncertainties around the methodologies for harnessing big data have posed challenges to its application in healthcare decision making. ISPOR Europe focussed on the potential of big data and explored the advances that the scientific community has made with addressing some of these issues. At the same time, the overarching question remains – can we trust big data?

Previous ISPOR congresses highlighted concerns from the perspective of regulatory and reimbursement decision makers, who challenge the credibility of RWE due to the lack of transparency in its methods and reporting. Ongoing efforts to develop guidance that address inconsistencies continue, with the Real-World Evidence Transparency Initiative updating on their draft white paper, which provides guidance on study registration of hypothesis evaluating treatment effectiveness (HETE) studies.

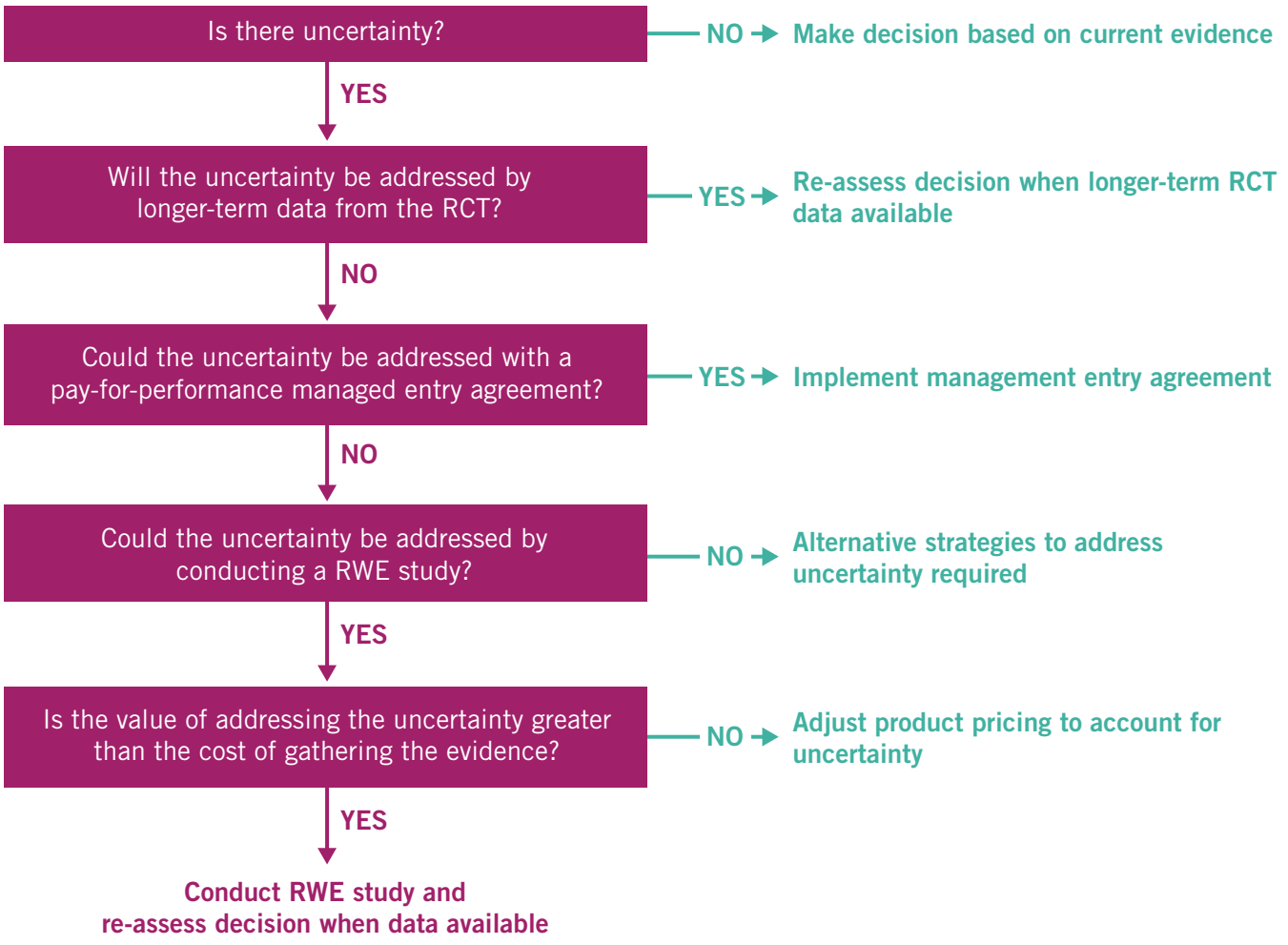
Across sessions at ISPOR Europe, discussions moved beyond the limitations of retrospective/observational data, to critical considerations of methodological approaches that may overcome these, such as difference-in-differences analyses (page 11) and studies employing propensity score matching. Proponents of RWE argued that observational data can be used to answer interventional queries when a robust causal model is built.

An important stakeholder in this discussion is patients. Obvious questions on privacy and security arise when we consider the use of patient data for RWE generation. Panellists of the plenary sessions – representing academia, private companies and the public sector – illustrated the complexities of data accessibility and ownership. One panellist suggested that trust is broken when companies use data for purposes other than what is agreed as a "common good"; however, what may be defined as this "common good" remains to be determined. There is a clear need for technology developers, researchers, healthcare providers, non-profit organisations, patients and other relevant stakeholders to agree on when, how and what big data can be used (or used for), before we can start to move from the "trough of disillusionment" to the "slope of enlightenment".

RWE for addressing uncertainty

The issue of uncertainty around clinical evidence was raised in numerous sessions, especially in the context of revolutionary therapies with less robust evidence bases such as cell and gene therapies and medical devices.[1, 2] It was widely agreed that RWE should be used to supplement randomised controlled trials (RCTs) in order to address the uncertainty surrounding long-term outcomes, safety, adherence and costs, among many other outcomes that are difficult to address in short-term RCTs. This is not a new concept; however a number of suggestions were put forward to provide solutions for practically utilising RWE to bridge the knowledge gaps resulting from RCTs. In Issue Panel 12 (A Formal System for Using Real-World Evidence to Revisit the HTA Decision – More Trouble Than it's Worth?), the question was raised as to whether HTA bodies could introduce a formal process to revisit initial HTA decisions with RWE obtained post-adoption of a new technology. While this approach could reduce uncertainty around best estimates of value for money, it was highlighted that in some cases continuation of the clinical trials would address uncertainty, or uncertainty could be addressed with performance-based payment schemes. RWE should therefore be used when uncertainty cannot be addressed by other means, and when addressing the uncertainty is worthwhile.

Figure 1: Considerations when addressing uncertainty



Another point raised was the importance of allowing manufacturers to be able to increase as well as reduce prices based on the results of RWE studies. Relatedly, it was noted that this reinforces a potential role for indication-based pricing in allowing differential pricing for specific populations that benefit from health technologies to a greater or lesser extent.

Overall, while there are clearly benefits of using RWE to address decision uncertainties, one of the common messages from panels at ISPOR was that use of RWE should in no way disincentivise the submission of robust, thorough, RCT evidence, which remains the gold standard expected by regulatory and HTA authorities. However, decision makers are increasingly aware of the need to reduce residual decision uncertainty, with NICE in particular expected to provide guidance on this following its health technology evaluation methods review in 2020.

Matt Griffiths, Head of HTA & Health Economics

"ISPOR conferences in previous years have frequently debated the extent to which RWE will allow us to overcome some of the limitations of an RCT-based evidence package. This year it felt like the conversation had moved on substantially, with widespread acceptance of an important role for RWE in HTA, and increased focus on discussing the details of "how" we can ensure we're making best use of all the data that is increasingly readily available.

As noted above, panellists consistently projected the message that RWE should supplement RCT data, not disincentivise its generation. However, in the context of accelerated regulatory pathways and the increasing openness of healthcare systems to managed access agreements, the notion that robust, gold standard RCT data is still systemically incentivised and RWE will stay neatly in a box marked "supplementary to RCT" seems a little disconnected from reality. Multiple cell and gene therapies, and many novel therapeutics in oncology particularly, have passed regulatory and HTA hurdles despite a lack of RCT data and high levels of uncertainty. Obviously, context is important and for a number of these therapies there are good reasons why RCT data is not viable or would not actually resolve the uncertainty in a reasonable timeframe. However, with healthcare systems increasingly providing a roadmap to access in the absence of RCT data, combined with exciting methodological advances (for example the use of machine learning) that move analysis of real-world data (RWD) closer to reasonable inference of causality, are we sure that we still have systemic incentivisation of manufacturers to conduct thorough RCT-based research and we aren't moving towards a post-RCT world despite what the panellists said? RWE certainly has a number of advantages over evidence from RCTs and an important role to play. However, if we do abandon the gold standard requirement for RCT data, let us hope this is done with eyes open as to the extent to which advanced methods allow RWE to satisfactorily 'replace' what RCTs offer in terms of causal inference, and not simply as a reaction to increasing RWD availability combined with pressure to grant early access and rely on RWE 'after the fact' in advance of us fully understanding what RWE is actually able to tell us."

Updates on the Evaluation & Pricing of Curative Therapies

Craig Brooks-Rooney,
Scientific Director

Having followed the evolving discussion on evaluating and funding curative therapies across the past few ISPOR conferences (covered in our previous reports from ISPOR Europe 2018 and ISPOR 2019), I approached this year's European meeting searching for new ideas and conversations on this topic.

While the debate at previous meetings tended to adopt the view that current value frameworks do not adequately capture the value of curative technologies, in Copenhagen there was an acknowledgement that HTA agencies have approved most FDA/EMA-approved curative therapies on the market. Clearly therefore, current value frameworks have not proved a barrier to access. Nevertheless, there continue to be proponents of incorporating novel elements of value into value frameworks for curative therapies, with Professor Stephen Palmer arguing that quality-adjusted life year (QALY) weightings should be used to adjust for novel elements of value. There is an expectation that NICE will take a lead in this area, given the ongoing review of its methods of technology evaluation, in 2020.

One of the bigger questions raised at the conference was the long-term effects of curative therapies on the dynamics of the healthcare market. Mike Drummond highlighted that in small patient populations, there are likely to be few competing curative therapies, limiting the competition during patent protected periods. This is exacerbated by the substantial first-mover advantage of curing the prevalent population, leaving a smaller population of incident patients for future therapies to compete for. This also results in the market being less attractive to generic manufacturers, thus potentially leading to long monopoly periods for originator products.

Ultimately, this brings us to a question posed in several sessions at the conference: how should consumer surplus be allocated between manufacturers and the healthcare system? Traditionally this has been captured by manufacturers during the monopoly pricing period and by healthcare systems when generics enter the market. This is particularly relevant for conditions that are currently very expensive to treat over a patient's lifetime, whereby a curative treatment could result in substantial avoided long-term costs: should such savings be captured by the manufacturer (reflected in a high price for the curative therapy) or shared with the healthcare system?

One option mooted is a mandatory price cut upon patent expiry, mimicking the effect of a generic entry. Another option is to adjust the price from the outset to reflect a better sharing of the consumer surplus or cost savings throughout the lifecycle of the product. While evaluation frameworks may be broadly suitable for curative therapies, our payment models may yet need to be reworked if these market dynamics play out. Costello Medical will be conducting research for a 2020 ISPOR conference examining these potential trends further – we would welcome collaborators on this!

Facilitating Patient & Clinical Expert Involvement in HEOR & HTA

Empowering patient involvement

As expected, the topic of how to better represent and incorporate patient opinion in HTA decision making made a reappearance at ISPOR Europe this year. Although a largely undisputed goal within the HTA community, how to go about this in a consistent, practical and equitable manner remains contentious. As we noted after HTAi, the increasing discussions around patient preference studies and projects such as PREFER highlight the growing momentum in this field.[3, 4] This was further supported by strong attendance at the Health Preference Research Special Interest Group meeting held at ISPOR Europe, where it was clear that those with an academic interest in this field are making strides in terms of methods.[5] It was, however, interesting to hear an acknowledgement that health preference studies need to be more frequently and better reported, including steps such as registration of protocols on the International Academy of Health Preference Research (IAHPR) website as standard, in order to promote validity of these methods and share good practice within the wider HTA community.[6] Furthermore, the challenge of how such methods can be adapted for use in a time-pressured industry setting, where almost inevitably the discussion around preference studies happens too late in clinical development, continues. It is at this interface where we believe agencies like Costello Medical can play a key role in working alongside academics and together with industry clients to develop methods for gathering patient preference data that balance academic rigour with industry demands.

An example of a creative approach for analysing patient opinion, albeit in a different context, was presented in a workshop moderated by Sheela Upadhyaya (NICE).[7] Together with Paul Connor (Kyowa Kirin International) and Christian Hill (MAP Biopharma), they shared the example of the NICE highly specialised technologies (HST) appraisal for burosumab, a treatment which was recommended by NICE in 2018 for the treatment of X-linked hypophosphataemia (XLH).[8] Sheela and Paul discussed how NICE and the manufacturer collaborated effectively and openly throughout the appraisal process, with Sheela commending Kyowa Kirin on their transparent approach to the limitations of burosumab and their available data. The workshop described a thematic analysis of 110 responses received from patients and families on the Evaluation Consultation Document, which identified key differences between clinician and patient opinion.[9] When asked at which stage such an analysis would have been most valuable, Paul suggested at the time of NICE scoping discussions, enabling such data to be built into the HTA submission. One of the fantastic things about this example was the huge number and quality of the comments and video interviews contributed by patients; it was clear that Metabolic Support UK had played a key role in supporting the patient community as they navigated this process, and this enabled the collection of such a robust and valuable data set.

Lastly, the potential of digital technologies to facilitate collection and analysis of patient data was apparent throughout the conference. For example, disease tracking apps, such as for diabetes and championed by the #wearenotwaiting movement, can now allow patients to conduct their own small-scale analyses of treatments received whilst also contributing to the RWE available for that product.[10, 11] In addition, advancing digital technologies for brain imaging presented by Tristan van Doormaal (University Hospital Zürich) dramatically demonstrated the greater level of information that clinicians are able to provide to patients, a step that will in turn allow patients to provide better informed and more relevant data for use by other stakeholders. A point highlighted on several occasions though,

was the importance of respecting individual patient preferences, whether in terms of their desire to share data, be more or less involved in the drug development process, or to receive more or less information on their diagnosis and likely disease course. Therefore, as we look towards improving methods, efficiency and aligning on frameworks that are suitable across products, disease areas and geographies, it is critical that we do not lose the flexibility to accommodate individual preferences and respect personal choice.

Maximising the benefits of expert elicitation

Annabel Griffiths, Head of Rare Diseases

"We were delighted to hear an update from the University of York research project that is developing a reference protocol for expert elicitation in healthcare decision making. Results of this are summarised in the Structured Expert Elicitation toolbox and a full HTA report will be published by York soon.[12]

Considering the wide variety of methods and terminology (mis)used in this field, it was reassuring to see the protocol describe 9 broad principles that reflect different aspects of techniques such as Cooke's classical method, Delphi approaches and the SHeffield ELicitation Framework (SHELF). With a view to the protocol's wider adoption in the HTA community, the potential flexibility within each principle will be key, for example, to allow adjustments to accommodate expertise levels, time available and the nuances of a particular project or disease area.

As such, I hope the full report will provide guidance on the key methodological principles that must be fulfilled and where compromises can be made if necessary. It was encouraging to see the results of a pilot study whereby the protocol was applied to a previously completed NICE diagnostic appraisal, and key differences in elicited values reported. This suggests such research projects will offer valuable information to HTA bodies and therefore should encourage a move towards time investment in these studies from manufacturers. That being said, such a step up in terms of the time commitment required by both manufacturers and the experts involved in such exercises will be a substantial adjustment and it is inevitable, therefore, that it will be a long time before the gold standard methods are regularly applied in the industry setting."

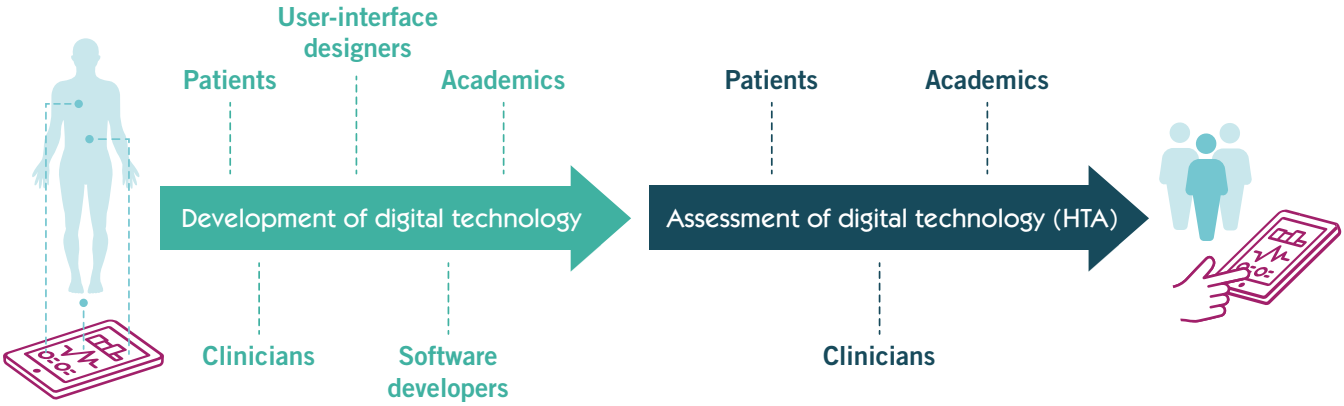
Expert involvement in the development & HTA of digital technology

Collaboration was a key theme of this year's congress, and ISPOR Europe would not be complete without discussion of cross-border collaboration to improve the availability of pharmaceuticals, covering the role of organisations such as the European Network for Health Technology Assessment (EUnetHTA), BeNeLuxA and the Fair Access and Pricing Scheme (FAAP).[13] However, particularly prominent at this year's congress was the emergence of a clear requirement for multi-stakeholder collaboration on a smaller scale to facilitate the uptake and utilisation of digital health, and to ensure the development of appropriate and relevant study outcomes for assessing digital health technologies.

Despite reported interest and enthusiasm in potential digital health technologies, uptake and retention for such products is often low: 83% of digital health technology publishers report fewer than 10,000 monthly active users, and 46% have fewer than 500 monthly active users, despite often high download rates.[14] A lack of relatability to patients and doctors may be contributory, and it was highlighted that mHealth app solutions are often developed to target non-existent problems, resulting in the neglect of real issues.[15] Collaboration between stakeholders including patients, clinicians and software developers throughout the development process will assist in the development of relevant, user-friendly and effective digital health products **(Figure 2)**;[10] increased patient involvement will be pivotal in ensuring that rapidly developing digital health technology is utilised to its full potential.

Collaboration is also required to develop an appropriate infrastructure for the HTA of digital health technologies.[10] In particular, there remains uncertainty around what would be clinically relevant endpoints to consider, and how "clinically relevant" should be defined. Additionally, how best to incorporate the "human factor" in HTA is yet to be determined; this appears to be even more important for digital technologies than pharmaceuticals, with issues surrounding privacy, perceived utility and perceived effectiveness, in particular. Given the rapidly evolving nature of digital health, better adapted approaches to HTA will be needed to ensure that robust methodologies are developed which both ensure quality and appropriate speed of assessment.

Figure 2: Multi-stakeholder collaboration in the development and assessment of digital technologies



5 Key Methodological Takeaways for Evolving Methods in Evidence Collection & Modelling

Difference-in-differences analysis

Difference-in-differences ("diff-in-diff") analysis is a method used to assess the causal effects of non-randomised interventions, such as policy changes, by comparing the difference in the outcomes of an "exposed" and "control" population before and after implementation of the intervention of interest.[16]

Underlying this methodology is the assumption that the control population provides an appropriate proxy for the counterfactual outcome in the exposed population, i.e. that the same change in the respective outcomes of the 2 populations would have been observed over time had the intervention not been introduced (the "parallel trends" assumption).

Approaches such as matching on pre-intervention outcomes can be adopted to reduce confounding in "diff-in-diff" analyses; however, care should be taken to avoid common pitfalls such as regression to the mean.

Surrogacy relationships

An interesting educational symposium sponsored by MSD discussed the validation and utilisation of surrogate endpoints in HTA of early cancer treatment.[17] Key take-homes from this session were as follows:

- A case study of a recent NICE appraisal found that the NICE Committee had expressed a preference for a Markov model over a partitioned survival model structure explicitly because the Markov structure did not rely on overall survival (OS) predictions derived from a surrogacy analysis that the Committee considered unvalidated and potentially flawed.[18] This highlighted the need to consider any assumed surrogacy relationships (and their validity) as an explicit factor influencing model design.
- Professor Andrew Briggs expressed his view that we should pay less attention to the dichotomous decision of whether a surrogacy relationship is or is not valid and instead focus on ensuring we adequately represent the uncertainty inherent in any potential surrogacy relationship. In this light he discussed how demonstration of a relationship between the surrogate outcome and final endpoint within your trial (i.e. trial-level surrogacy effect) requires less strong assumptions than assuming that a literature-reported relationship holds, but likely translates to more uncertainty in the relationship estimate (wider confidence intervals). There is often a trade-off between strength of the underlying assumptions regarding a surrogacy relationship and the level of uncertainty in the estimated relationship, and it is important to consider what assumptions can be supported and whether resultant uncertainty has been appropriately reflected.

Eliciting quality of life values from children/caregivers

Both groups have similar challenges surrounding the practicalities of valuation. All stakeholders agreed there is very little guidance available currently for best practices in valuing the quality of life (QoL) of these populations. Currently, although ~80% of the ISPOR audience agreed that carer burden should be accounted for quantitatively, for example via QALYs, none of the current QoL tools for carers are able to estimate QALYs. Likewise, concerns with the perspective to take when valuing the QoL of children were consistently raised, with EuroQoL using a value set defined by adults considering QoL from a child's perspective, but NICE arguing for valuation by the children themselves. Overall there was a call for more guidance on best practices, given the increasing numbers of NICE submissions including either carer or child QoL. Moving in this direction, new developments in measurement tools are potentially paving the way for new processes. For example, the E-QALY project, which aims to extend QALY domains beyond health, including to those judged as important by patients, social care users and carers. The project will start valuations next year, so may provide a practical solution in the near future.

Structured expert elicitation

Expert elicitation is widely used in HTA and is essential in cases of uncertainty. In the absence of appropriate guidelines for structured expert elicitation (SEE), a protocol* has been developed by the Centre for Health Economics (University of York) for use of SEE in healthcare decision making.[12, 19] This guidance provides a number of considerations for an elicitation exercise, including:

*This reference protocol is not intended as a prescriptive method, rather to serve as a guide to good practice. 1. Ensure diversity of experts (at least 5), focussing on gathering substantive expertise; include experts not involved in the task development; 2. Minimise and record conflict between experts; 3. Elicit simple observable quantities where possible; ratios or complex parameters (for example, regression coefficients) should not be elicited directly; 4. Capture dependence between variables; it is preferable to express dependent variables in terms of independent variables when experts lack strong normative skills; 5. Elicit beliefs from experts individually, even if a group interaction follows; 6. Explicitly explore between-expert variation; 7. To permit training of the expert, ensure face-to-face delivery where possible; training is crucial and should focus on avoiding bias and expressing uncertainty; 8. Collect rationales for how the experts made their judgements after the exercise; 9. Document and justify all SEE methodological choices.

Systematic evaluation of IO therapies

Given the novel mechanism of action, durable responses and potentially improved OS associated with IO therapies, there are challenges in adequately assessing the value of such therapies for the purposes of HTA. Therefore, in both an educational symposium and research poster, a potential checklist for manufacturers to consider when submitting a dossier for HTA scrutiny was proposed, with 'Addressed', 'Evidence generation required' or 'N/A' as the possible responses to the following criteria:[20, 21]

Mechanism of action	› Has the underlying biological model, and how it links with any survival analysis/statistical modelling, been clearly explained? › Have published external data or additional clinical trial data been presented as supportive evidence of long-term survivorship? › Has pseudo-progression been raised as an issue? If so, were outcome measures used in the trials that take this phenomenon into account?
Limited clinical trial evidence at HTA submission	› Have the trial endpoints been presented within the context of completeness (for example, censoring, numbers at risk)? › Have the surrogate endpoints been presented, and their relationship to long-term OS demonstrated?
Model structure and survival extrapolation methodology	› Has the use of non-standard models been justified, including their use in previous IO economic evaluations? › Has heterogeneity in treatment effect been explored and were any subgroup analyses based on mechanism of action and clinical plausibility? › Have any biomarker data been presented as the predicate for considering heterogeneity? › Has the survival analysis/statistical modelling been presented and justified both in terms of statistical performance and how it reflects the underlying biological model?
HTA submission	› Have RWD been included to support estimates of long-term OS? › Have the central points above been linked with payer, clinician, and patient perspectives on immunotherapy?

Further Information

If you would like any further information on the themes or research presented above, please do not hesitate to contact Matt Griffiths, Head of HTA and Health Economics at **matt.griffiths@costellomedical.com**.

Many of the presentations from the conference can be found on the **ISPOR website** (**www.ispor.org/conferences-education/conferences/past-conferences/ispor-europe-2019/program/program**).

References

1. Issue Panel 12: A Formal System for Using Real-World Evidence to Revisit the HTA Decision – More Trouble Than it's Worth? ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
2. ISPOR Forum: Real-World Evidence Transparency Initiative – Transparency in RWE – Moving Forward. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
3. Griffiths A. Reflecting on HTAi 2019 – What Can We Expect from ISPOR Europe?
4. Innovative medicines initiative (IMI). PREFER.
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6. International Academy of Health Preference Research (IAHPR).
7. Workshop 14: A Novel Approach to Improving Our Understanding of the Burden of a Rare Disease: The Use of Opportunistic Retrospective Qualitative Analysis of Public Responses to Highly Specialized Technology Appraisal. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
8. National Institute for Health and Care Excellence (NICE). Burosumab for treating X-linked hypophosphataemia in children and young people [HST8].
9. Ferizovic N, Mak C, Marshall J, *et al*. A qualitative analysis of the burden-of-illness associated with X-linked hypophosphataemia (XLH) in children and adolescents. Bone Abstracts 2019.
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11. TechRepublic. #WeAreNotWaiting: Diabetics are hacking their health, because traditional systems have failed them, 2016.
12. Workshop 18: Considering the Applicability of Guidance for Expert Elicitation in Healthcare Decision Making. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
13. Issue Panel 11: Cross Border Collaboration on Availability of Pharmaceuticals in Europe – What, Why And What If? ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
14. Research 2 Guidance. mHealth Developer Economics. 2019.
15. Second Plenary Session: Shaping the Digital Healthcare System. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
16. Third Plenary Session: Big Healthcare Data – Endless Opportunities for Research and Learning. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
17. Educational Symposium: Challenges and Promises of Early Cancer Treatment – Validating and Utilizing Surrogate Endpoints in Health Technology Assessment. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.
18. National Institute for Health and Care Excellence (NICE). Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease [TA558] – Appraisal Consultation Document.
19. Bojke L, Soares M, Claxton K, *et al*. Developing a Reference Protocol for Expert Elicitation in Healthcare Decision Making. Health Technology Assessment Reports (In Press) 2019. Available from: http://eprints.whiterose.ac.uk/151174/.
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Costello research contributions to ISPOR Europe 2019

Poster Presentations:

Allen G, Warnants E, Summers D, Evans J. Poster Presentation PBI44: Real-World Evidence in Gene Therapies: Recommendations Versus Reality. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Artignan A, Bobrowska A, Ashworth L, Murton M, Zemyarska M, Buchanan-Hughes A. Poster Presentation PNS413: Development, Validation and Concordance of Clinical Code Sets Used in Real-World Database Studies. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Bewicke-Copley H, Evans J, Newell I, Pritchett D, Ruban-Fell B, Griffiths A. Poster Presentation PRO156: Approaches to the Collection of Utility Values for Rare Diseases. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Gibson S, Atkinson M, Beale R, Wickstead R, Griffiths M. Poster Presentation PCN336: Parallel Scientific Advice from NICE and CADTH: Would One Submission Fit All? ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Lim S, Koh V, Yoshino M, Brooks-Rooney C. Poster Presentation PNS209: Impact of Generics and Biosimilars on Branded Drug Listing Decisions in Singapore. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Porteous A, Herbert K, Painter C. Poster Presentation PCN20: Accurate Predictions of Life Year Gains for Immuno-Oncology Therapies in the Long Term? An Analysis Based on Published Checkmate 057 Nivolumab Data. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

van Hest N, Griffiths M, Hearmon N. Poster Presentation PNS42: To What Extent Does Seeking Clinical Expert Opinion for Model Inputs Reduce the Cost of Uncertainty? A Conceptual Approach Using Expected Value of Perfect Parameter Information (EVPPI). ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

van Hest N, Upton E, Ader J, Woodhouse F, O'Connor M-E. Poster Presentation PDG85: Trust the Experts? Acceptance of Expert Elicitation in the National Institute for Health and Care Excellence (NICE) Single Technology Appraisal (STA) Process. ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Issue Panels:

Issue Panel IP2: Is Delayed Access Due to Issues of HTA Capacity a Necessary Reality or an Unacceptable Problem? ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

Issue Panel IP12: A Formal System for Using Real-World Evidence to Revisit the HTA Decision: More Trouble Than It's Worth? ISPOR 22nd Annual European Congress, Copenhagen, Denmark, 2019.

About Costello Medical

Costello Medical provides scientific support to the healthcare industry in the analysis, interpretation and communication of clinical and health economic data.

Our technical expertise spans medical education, advisory boards, value materials, scientific writing, publication planning, evidence development, statistics, health economic modelling and health technology assessment. A full description of what we offer can be found on our website: **www.costellomedical.com**.

Due to growing demand across an increasing range of service offerings and geographies, Costello Medical has grown organically since foundation in 2008 to a team of over 150 based in Cambridge, Manchester, London and Singapore, with offices opening in both Boston, USA, and Shanghai, China in 2020. Alongside our widening technical and creative capabilities, we remain committed to our core values of high quality scientific work coupled with excellent customer service at competitive and transparent prices. Our talented team has experience with a variety of leading pharmaceutical companies and a track record of success in a broad range of disease areas.