



# **PHCY 5141 PRINCIPLES OF HEALTH ECONOMICS AND OUTCOMES**

## **INTRODUCTION**

### **A NEW START IN HEALTH TECHNOLOGY ASSESSMENT**

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Welcome to the Spring 2023 *Principles of Health Economics and Outcomes (PHCY 5141)* course *A New Start in Health Technology Assessment – three credit hour course for PharmD and MS level students*. PHCY 5141 is a 3-part, 14-module course designed to provide a theoretical and practical foundation for the appropriate methods and application of techniques in health technology assessment (HTA); ones that meet the standards of normal science and fundamental measurement. Meeting the evidence needs of formulary committees, practitioners, patients and other health system decisionmakers is critical for effective health care delivery and the meaningful assessment of pharmaceutical products and devices.

The commitment in health technology assessment to the construct of assumption driven modeled simulations to create lifetime imaginary claims for comparative cost-effectiveness is being increasingly recognized as an analytical dead end. Introduced as a framework for creating non-evaluatable approximate modeled information it lacks any commitment to the standards of normal science or the requirements of Rasch or modern measurement theory; none of the claims make for product pricing and access meet standards for credibility, empirical evaluation or replication <sup>1</sup>.

Based on the mathematically impossible quality adjusted life year (QALY), there is a pressing need for a new start in health technology assessment to ensure that the standards for product assessment meet those of the physical and more mature social sciences such as education, psychology and economics. These are the objectives PHCY 5141 at the University of Wyoming.

The course is in three parts: (i) required evidentiary standards for product and therapy assessment; (ii) the failure of approximate modelled information for therapy decisions; and (iii) value claims and protocols for a new start in product evaluation that meet required scientific standards with feedback for ongoing disease area and therapeutic class reviews. The course proposes a new start in HTA to meet the needs of health system decision makers; a framework of analysis that is not only consistent with the standards of normal science and fundamental measurement, but one that focuses on capturing needs-fulfillment quality of life of patients and caregivers. The importance of rejecting on-evaluable value claims for conducting and assessing outcomes research will be emphasized. This rejection provides a firm empirical basis for evaluating long-term clinical outcomes and outcomes-based contracting.

The rationale for this new start paradigm is given in more detail at the end of this introduction together with key references.

Existing textbooks are out of date (and misleading) in terms of the appropriate analytical framework and techniques for health technology assessment and supporting products over their lifetime. The references have been selected because they support the arguments presented in the modules to support a new start in the techniques of health technology assessment and formulary submissions. The notes for the 14 modules are extensive (94,000 words) and effectively substitute for a textbook. The references for each module are extensive; but with key references marked [\*]. Wherever possible the references can be downloaded from the web (URL links provided).

For students not enrolled at the University of Wyoming, a three-credit course transfer for PHCY 5141 is subject to approval by the student's College or School of Pharmacy faculty, before application, acceptance and enrollment. The University of Wyoming reserves the right to limit enrollment subject to available resources.

## **PRE-COURSE READING**

Before beginning this course, please read the following key references:

Langley PC and McKenna SP. Measurement, modeling and QALYs [version 1; peer review: 2 approved] *F1000Research* 2020, 9:1048 <https://doi.org/10.12688/f1000research.25039.1>

Wright B, Linacre J. Observations are always ordinal; measurements, however, must be interval. *Arch Phys Med Rehabil.* 1989; 70(12):857-60  
[https://www.researchgate.net/publication/20338407\\_Observations\\_are\\_always\\_ordinal\\_measurements\\_however\\_must\\_be\\_interval/link/5563b02408ae9963a11ef326/download](https://www.researchgate.net/publication/20338407_Observations_are_always_ordinal_measurements_however_must_be_interval/link/5563b02408ae9963a11ef326/download)

Langley P. Nothing to Cheer About: Endorsing Imaginary Economic Evaluations and Value Claims with CHEERS 22 [version 1; peer review: 2 approved]. *F1000Research* 2022, 11:248 (<https://doi.org/10.12688/f1000research.109389.1>)

Langley P. Facilitating bias in cost-effectiveness analysis: CHEERS 2022 and the creation of assumption-driven imaginary value claims in health technology assessment [version 1; peer review: 2 approved]. *F1000Research* 2022, 11:993 (<https://doi.org/10.12688/f1000research.123709.1>)

## **COURSE STRUCTURE**

The course is presented in three parts:

- Part I: Required evidentiary standards for product and therapy assessment (4 modules);
- Part II: The failure of approximate modelled information for therapy decisions (5 modules); and
- Part III: Formulary submission value claims and protocols for a new start in product evaluation

Each of the 14 modules comprises: (i) a PowerPoint slide show with audio; (ii) Downloadable PowerPoint slides (each with audio); (iii) detailed notes to support the presentation; and (iv) discussion question for the module.

## **PHCY 5141 MODULES: PART I**

The four modules in Part I have two objectives. First, to detail the required evidentiary standards for any value claim for product performance in terms of (i) the standards of normal science and (ii) the failure of assumption driven multiattribute modeled simulations to produce value claims that meet the required standards; this is achieved by deconstructing the recently released Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Guidance for creating imaginary cost-effectiveness claims.

The first three modules represent a theme that underpins the role for a new start in health technology assessment: understanding the importance of demarcating science from non-science, the critical role of Rasch or modern measurement theory to transform observations to measurement and the need to reject assumption driven modelled simulation based upon the notion of the realism of assumptions to justify model claims for cost-effectiveness.

The modules are:

Module 1: Science versus non-science: *Understanding the importance of demarcation in the acceptance of value claims*

Module 2: Ratio and interval measures: *Appreciating the importance of interval and ratio measures to support value claims*

Module 3: Assumptions and Hume's problem of induction; *Understanding that assumptions cannot be used to validate modeled value claims*

Module 4: CHEERS 22: Tenacity of false belief systems in pharmacoeconomics: *Consider the potential impact given the limitation of CHEERS 2022 guidance*

## **PHCY 5141 MODULES: PART II**

The five modules that comprise Part II of the course focus on the failure of assumption driven modeled simulations in health technology assessment, in the quest for approximate information, to pass the demarcation test: they fail to meet standards for credibility of claims, the ability to be empirically evaluated and replicated in other target patient populations within a disease area. The practice of health technology assessment with the belief in assumption driven simulations means that it is non-science or pseudoscience.

The modules are:

Module 5: Truth is not consensus: *Consider whether there is any justification for lifetime modeled claims in formulary decisions*

Module 6: Failure of multiattribute generic preference measures: *Understand the case for rejecting multiattribute preference measures in value claims for therapies*

Module 7: The impossible QALY: *Understand why, despite its acceptance, why the QALY based on ordinal scores must be rejected*

Module 8: Impossible value claims: *Consider the case for single attribute ratio value claims in formulary submissions*

Module 9: Abandoning models in value claims: *Consider the circumstances under which modeled value claims are acceptable*

## **PHCY 5141 MODULES: PART III**

Finally, the modules in Part III of the course set out the standards for establishing and evaluation value claims for therapies in health technology assessment that ensure that they are a firm basis for formulary submissions. Not only must all value claims be presented as single attributes whether for clinical claims, patient reported outcome claims, drug utilization and resource utilization, but they must be supported by an evaluation protocol and, if required, support outcomes-based contracting and ongoing disease area and therapeutic class reviews.

The modules are:

Module 10: Guidelines for value claims in formulary submissions: *Introducing a proposed format for therapy value claims that meet required evidentiary standards*

Module 11: The patient voice: need fulfillment quality of life: *Introducing the needs-fulfillment quality of life measure for patients and caregivers*

Module 12: Selecting PRO claims: *Introducing criteria for evaluating measurement standards for disease specific PRO claims*

Module 13: Formulary submission guidelines: *Proposal for a formulary submission package for value claims and protocols*

Module 14: Questions a formulary committee should ask; *Questions to address to ensure value claims meet standards of normal science and fundamental measurement*

At the conclusion of each module, participants can download (i) a copy of the slides; and (ii) notes and references to support the slide presentation.

### **INSTRUCTOR AVAILABILITY/CONTACT INFORMATION**

Office Hours: by appointment for Zoom and via electronic mail to UW account. Responses to emails will occur within 48 hours

### **ASSESSMENT**

There will be three literature critiques (25 points each), a mid-term and final written short answer examination (50 points each) and an assessment of up to 50 points for class participation.

Total score out of 225 will be translated to the following grades (corrected by 0.44):

A: 90.0 -100.0

B: 80.0 – 89.9

C: 70.0 – 79.9

D: 60.0 – 69.9

F <60.0.

### **LITERATURE CRITIQUE**

Your critique should comprise four sections: (i) Introduction; (ii) Summary; (iii) Critique; and (iv) Conclusions. Maximum 1500 words Use DOCX format, Times New Roman (12) with reference numbers in text and references included at end.

Remember, the literature critique should reflect the course content and objectives: Is the stated purpose of the paper/commentary and the arguments presented relevant to the claim in this course that current standards of health technology assessment are at an analytical dead end?

Issues you should consider are:

- Is the purpose of the paper/commentary clearly stated?
- Have the author(s) indicated what motivated them?
- Does the paper/commentary provide context for their arguments?
- How convincing do you find their stated purpose?
- How convincing do you find the arguments?

The papers you are asked to critique are:

Schommer JC, Carlson AM, Rhee TG. Validating pharmaceutical product claims: questions a formulary committee should ask. *J Med Econ.* 2015;1-7 [Report due 19 March]  
<https://www.tandfonline.com/doi/epdf/10.3111/13696998.2015.1108917>

Langley P. Let a Thousand Models Bloom: ICER Analytics Opens the Floodgates to Cloud Pseudoscience. *Inov Pharm.* 2021;12(1): No. 5 [Report due 2 April]  
<https://pubs.lib.umn.edu/index.php/innovations/article/view/3606/2668>

Langley P. Concerns with Patient Reported Outcome Measurement and Value Claims for Therapy Response: The Case of Mavacamten and Symptomatic Hypertrophic Cardiomyopathy (SHCM). *InovPharm.* 2022;13(2): No. 16 [Report due 16 April]  
<https://pubs.lib.umn.edu/index.php/innovations/article/view/4861/3198>

## **MID COURSE AND FINAL EXAMINATION**

Each examination will consist of 10 statements. You will be asked if you agree, are unsure or disagree with each statement and give the reasons for this response (max 400 words each statement response). Each examination counts 50 points. Questions for the mid-term will be distributed on March 26 and returned by April 2. Questions for the final will be distributed on April 16 and returned by April 23.

## **LIVE SESSIONS AND DISCUSSION QUESTIONS**

From March 5, 2023 (Sunday: Course Introduction 1 hour) to April 23, 2023 (Sunday); 3 hours starting at 5pm Wyoming time (Zoom). The discussion question(s) for each session will be found at the end of the slide presentation for each module, starting with Module 1. Prior to the introductory session on March 5, 2023 you will be expected to have reviewed the pre-course reading.

## COURSE SCHEDULE

Date	Modules	Topic(s)
<b>Sunday March 5</b>		Introduction: Course Objectives (One hour)
<b>Sunday March 12</b>	1 2	Science versus Non-Science in Health Technology Assessment Ratio and Interval Measures for Health Technology Assessment
<b>Sunday March 19</b>	3 4	Assumptions and Hume's Problem of Induction in Modeled Value Claims CHEERS 2022: Relevance for Modeled Value Claims
<b>Sunday March 26</b>	5 6	Truth is not Consensus Failure of multiattribute generic preferences
<b>Sunday April 2</b>	7 8	The Impossible QALY Impossible value claims
<b>Sunday April 9</b>	9 10	Abandoning Models in Value Claims Guidelines for value claims in formulary submissions
<b>Sunday April 16</b>	11 12	The patient voice: need fulfillment quality of life Selecting PRO claims
<b>Sunday April 23</b>	13 14	Formulary submission guidelines Questions a formulary committee should ask

## **PHCY 5141: A NEW START IN HEALTH TECHNOLOGY ASSESSMENT**

Welcome to the School of Pharmacy, University of Wyoming course PHCY 5141 *A New Start in Health Technology Assessment*. This is a 3-unit course designed to introduce a new start for the evaluation of pharmaceutical products and devices.

The course that the commitment to assumption driven modelled simulation to support cost-effectiveness claims is an analytical dead end. It meets neither the standards for normal science nor the required measurement standards. The new start delivers a comprehensive package to support formulary submissions, prospective research courses to discover new facts for therapy response as well as the necessary inputs for outcomes-based contracting.

The focus of this course is to examine the appropriate theoretical and practical foundation for the methods and application of techniques in health technology assessment (HTA) that meet the standards of normal science and fundamental measurement<sup>2</sup>. This involves meeting the evidence needs of formulary committees, practitioners, patients and other health system decision makers and is critical for effective health care delivery, together with the meaningful assessment of pharmaceutical products and devices by pharmacists in everyday practice. At the same time, we require disease specific single attribute and direct patient centric measures of the benefit of a new therapy to patients and caregivers. This can be achieved by the latent construct of need-fulfillment to produce unidimensional, linear and interval measures applying the Rasch model of instrument development.

### **COURSE STRUCTURE**

PHCY 5141 in three parts: (i) required evidentiary standards for product and therapy assessment (4 modules); (ii) the failure of approximate modelled information for therapy decisions (5 modules); and (iii) formulary submission value claims and protocols for a new start in product evaluation (5 modules). The course aims to make the case for rejecting 30 years of much misplaced and wasted effort in HTA. In the early 1990s the decision was made that in order to make the case for new pharmaceutical products at product launch; hypothesis testing was to be abandoned in favor of creating assumption driven modeled approximate information to support formulary decisions<sup>3</sup>. This was uncritically accepted by leaders in the field and detailed in textbooks and practice guidelines<sup>4</sup>. It was also uncritically accepted by academic centers, government agencies and analysts despite warnings to the contrary<sup>5 6</sup>. The result was the acceptance for publication of thousands of cost per quality of life (QALY) assumption driven imaginary claims which fail to meet the standards of normal science and fundamental measurement and their continued application by groups such as the Institute for Clinical and Economic Review (ICER)<sup>7 8</sup>. At the same time this acceptance of assumption driven modelled claims is open to abuse and bias<sup>9</sup>. We are still locked into this belief system with the recent publication of the CHEERS 2022 guidance for submitting imaginary modeled claims to academic journals<sup>10 11</sup>.

The new start paradigm provides a theoretical and practical foundation for the appropriate methods and application of techniques in HTA that meet the standards of normal science and fundamental measurement. Meeting the evidence needs, including outcomes contracting, of formulary committees, practitioners, patients and other health system decisionmakers, including minimizing



bias, is critical for effective health care delivery and the meaningful assessment of pharmaceutical products and devices <sup>12</sup>. This course proposes a new start in HTA to meet the needs of health system decision makers; a framework of analysis that is not only consistent with the standards of normal science and Rasch or modern measurement theory <sup>13</sup>, but one that focuses on capturing needs-fulfillment quality of life of patients and caregivers. The importance of rejecting non-evaluable value claims for conducting and assessing outcomes research will be emphasized. This rejection provides a firm empirical basis for evaluating long-term clinical, quality of life and resource utilization outcomes, including engaging with health systems to identify and even contract for key value claims as part of disease area and therapeutic class reviews.

Many practitioners are aware of the manifest deficiencies in modelled claims <sup>14</sup>. Yet the majority persevere in the belief that formulary committees are prepared to accept imaginary claims to support pricing and access decisions. The problem, is that by changing assumptions any number of competing modeled claims can be presented <sup>15</sup>. At the same time, journal editors are presumably more than happy to publish any number of simulated imaginary claims, driven by assumptions, which have no relation to reality for an impossible unknown future.

It is not often appreciated, but the current analytical framework supports a belief system in imaginary value claims that is unique in the physical and social sciences; rejecting the standards for the discovery of new, yet provisional facts, that has been accepted for the 375 years since the scientific revolution of the 17<sup>th</sup> century. While practitioners in HTA or pharmacoeconomics claim it is a branch of economics, this is wishful thinking. It is totally at variance with the standards of analysis both in mainstream economics and in the applied discipline of health economics, the study of the production and consumption of health and healthcare; we must not confuse the ‘standards’ of non-science with those of science. HTA follows a belief system which has more in common with that prevailing in the middle-ages; one beginning only to be overthrown with the scientific revolution of the 17<sup>th</sup> century by figures such as Bacon, Galileo, Descartes and Newton. In this context it is worth remembering the motto of the Royal Society (founded in 1660): *nullius in verba* (take nobody’s word for it). This is rejected in HTA by asking, with assumption driven claims, that we take any person’s word for it; any assumption driven non-empirically evaluable claim is presumably as good (or bad) as any other.

It is worth quoting Richard Dawkins, the evolutionary biologist, on differentiating science from non-science (or simply faith in creating non-evaluable approximate information value claims):

*.....the selective forces that scrutinize scientific ideas are not arbitrary or capricious. They are exacting well-honed rules and they do not favor self-serving behavior. They favor all the virtues laid out in textbooks of standard methodology: testability, evidential support, precision, quantification, consistency, intersubjectivity, repeatability, progressiveness, independence of cultural milieu and so on <sup>16</sup>.*

Measurement is critical if value claims for competing products are to have any credibility. If the tools used to support claims for measuring response are irrelevant, failing to meet required measurement standards, then we have to question almost all direct and indirect generic preference scores and the overwhelming majority of patient reported (PRO) instruments. Most fail the axioms

of fundamental measurement and the tools of simultaneous conjoint measurement that have been practiced in other social sciences for 60 years.

At the same time, value claims must be disease specific tailored to specific attributes relevant to formulary decisions whether these are for clinical claims, quality of life claims or drug and resource utilization claims. The target must be to develop instruments that meet ratio or interval measurement properties. Assumption driven simulated blanket claims for comparative cost-effectiveness are totally unacceptable.

It is not so much that HTA is at a crossroads; the decision to take the wrong road was made decades ago. No, we must seriously question the pharmacoeconomic belief system (or meme). This will be defended; the wagons will be pulled into a circle. There is no option: we require a paradigm that makes analytical sense and which brings us back to the standards we have long ignored. This is the purpose of this ACPE Certificate Course from the School of Pharmacy, University of Wyoming.

### **FROM MEME TO PARADIGM**

It is now increasingly recognized that the existing belief system or meme in health technology assessment (HTA), designed to capture blanket non-evaluable claims for cost-effectiveness through the invention of assumption driven simulations incorporating incremental cost-per-QALY claims and thresholds, is an analytical dead end. Despite the widespread acceptance of this meme evidenced by the leading textbook by Drummond et al, and the recently endorsed Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) guidance statement and the proposed complement and possible successor to the EQ-5D-5L multiattribute generic measure the EQ-Health and Wellbeing (EQ-HWB) generic instrument<sup>9 10 17</sup>. The meme fails to recognize the standards of normal science which all claims must be credible, empirically evaluable and replicable, and the standards of fundamental evidence where, following the seminal work of Rasch in the 1950s, all claims for measurement must have unidimensional interval or ratio properties; a requirement recognized for over 50 years in measurement theory<sup>4 5</sup>. The acceptance of the current HTA meme, the self-replicating belief system, cannot be described as a paradigm; a necessary framework which supports Popper's notion of the evolution of objective knowledge in a user accessible and management framework by discarding black box simulation models<sup>18</sup>.

The result is that health technology assessment, as practiced for the last 30 years, is unique in its commitment to non-empirically evaluable claims for cost-effectiveness<sup>3</sup>. This analytical framework denies progress and the discovery of new facts in therapy impact; resting instead on the hope that formulary committees will factor in imaginary claims for cost-effectiveness into their decision-making. To those who, over the past 30 years, have been trained and believe implicitly in the role of modeled approximate information to drive decisions, putting hypothesis testing to one side, these claims, as exemplified in the practice guidelines for modeling produced by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), must appear irrational<sup>2</sup>. After all, quality adjusted life years (QALYS) have been a cornerstone of economic evaluations; unfortunately, the QALY is an impossible mathematical construct as it involves multiplying time spent by an ordinal utility or preference multiattribute score<sup>19 6</sup>. But multiattribute or composite scores, given the standards of fundamental measurement<sup>20</sup>. Once

these measurement requirements are recognized aggregate scores from Likert scales must also be rejected; they are only accepted if we can demonstrate that the relative value of each response category are treated as being the same, and unit increases across the rating scale are given equal value. The result is that that all multiattribute generic and disease specific instruments are nothing more than ordinal observations; the authors of these instruments fail to recognize that the Rasch measurement model provides the necessary and sufficient means to transform ordinal counts into linear measures to support value claims in HTA <sup>6 12 21</sup>.

Unfortunately, current analytical standards in pharmacoeconomics or health technology assessment (HTA) fail to meet the required evidentiary standards. The misplaced focus on approximate information, assumption driven simulated and non-empirically evaluable modelled claims for cost-effectiveness. At the same time, in focusing on disease specific value claims, and rejecting multiattribute generic preferences and quality adjusted life years (QALYs), there is a pressing need to understand the impact of modern or Rasch measurement rules to construct patient reported outcome (PRO) instruments that support meaningful claims for response to therapy.

## **CORE VALUE CLAIMS**

The proposed new start in HTA puts aside imaginary assumption-driven simulations and impossible claims for cost-effectiveness, including the mathematically impossible QALY, in favor of a transparent commitment to single attribute value claims, supported by protocols, that are empirically evaluable to support formulary decision making; a concrete and transparent approach to support managerial decisions. An approach consistent with both the standards for normal science recognized in other disciplines and the limitations imposed on patient-reported outcomes by the axioms of fundamental measurement; a course that meets the neglected evidence requirements in health system decision-making.

The focus of the proposed new start in HTA is agreement on core value claims in disease areas and for target patient populations. These value claims must encompass, at least for the entry of new product or first assessment of existing products: (i) clinical [instrument based] claims; (ii) patient reported outcome claims [disease symptoms as well as aspects of quality of life as a latent construct], (iii) drug utilization [uptake on market entry and compliance], and (iv) other resource utilization impacts [as units not costs]. The three premises for value claims are:

- All value claims must be proposed as single attributes which meet the standards of normal science: credibility, empirical evaluation and replication
- All value claims must meet Rasch standards for fundamental measurement (interval or ratio measures]
- All value claims must be presented with a supporting protocol for evaluation and reporting within a meaningful timeframe

The Certificate Course makes clear that these three premises are the basis for any guidance documentation to manufacturers for formulary submission. Submissions that fail to meet these standards must be rejected. This means that the majority of patient reported outcome (PRO) instruments, multiattribute and disease specific will be rejected; they will fail Rasch standards <sup>22</sup>. Single attribute PRO claims must be unidimensional with at least interval measurement properties,

captured by either Rasch dichotomous modeling, the polytomous Rasch Rating Scale Model or Partial Credit Rasch Model<sup>5</sup>. Also excluded will be assumption driven simulation models with non-evaluable claims for cost-effectiveness; the use of quality adjusted life year (QALY) claims and non-evaluable constructs such as multiattribute efficiency frontiers.

The overall intent is to apply the criteria that can justify HTA as science and not non-science or pseudoscience; it must meet the demarcation criteria<sup>23</sup>.

## MEASUREMENT

A recurring theme in the Certificate Course is the imperative of measurement from the requirement that before responses from assessments can provide measurement, they have to be transformed to provide measurement properties. This is made an imperative in Rasch or modern measurement theory where, following Andrich and Marais, *assessment* is the engagement of that entity with some instrument, with a protocol recording the observations or counts of the engagement, while *measurement* involves some kind of transformation and is defined as the *estimation of the amount of a unidimensional trait relative to a unit*. The unit derives from a scale of equal units that provide the measurement on linear continuum while scaling locates an entity on that scale. Assessment precedes measurement; we measure the properties of entities that are of interest, not the entities themselves; for example, we don't measure persons but the manifested psychological attributes, traits or constructs of that person that are of interest. To capture the construct of interest we require a procedure to manifest or assess the property of interest.

The critical distinction, as Wright and Linacre, express it is between observations, counts of observed events and the transformation to quantitative measures, the arithmetical property of linear scales. In the terminology of measurement theory, the transformation from ordinal (or nominal) data to interval (or ratio) linear measures. This sets the objectives in modern measurement (but not quite modern as it has been recognized for some 60 years or more) to transform observations or instrument assessments, the entities construct of interest, to a unidimensional, interval (or ratio) scale. To enable this transformation, we require procedures or rules, these are provided by a unique solution which is termed Rasch measurement. Why unique? Because the Rasch measurement model provides the necessary and sufficient means to transform ordinal counts to linear measures.

The failure in the current HTA belief system is that, with only a handful of exceptions (which have been red flags for decades) the many HTA practitioners, the authors of thousands of peer-reviewed and published papers, have not recognized the need to transform ordinal observations to interval measures; measures which must have unidimensional properties. We are locked into a 'measurement' meme which denies the ability to provide meaningful measures of response to therapy defined in unidimensional and interval terms. Instead, the gold standard is to create, from raw counts or observations, multiattribute measures which fail at the first hurdle; bringing down with them the multitude of studies that provide incremental cost-per-QALY claims, where the QALY is an impossible mathematical construct.

In contra-distinction to the CHEERS 2022 guidance for submitting assumption driven non-evaluable cost-per-QALY claims to journals is the recently released (at almost the same time as CHEERS 2022) are the Rasch Reporting Guidelines for Rehabilitation Research (RULER)<sup>24 25</sup>.

These are not a recent innovation; studies reporting Rasch measurement in the context of rehabilitation outcomes were first reported in 1988. The purpose of RULER is to provide peer-reviewed, evidence-based and consistent guidance for reporting studies that apply Rasch measurement theory in a rehabilitation context so that there are uniform expectations on how to write and evaluate research on rehabilitation outcomes assessments. The RULER template is one that should be applied across disease areas if we are to evaluate Rasch-based claims for therapy response. Such a commitment from decision makers should be seen as an essential part of a new start in health technology assessment, incorporated in submission guidelines for health systems.

## **ASSUMPTIONS**

A further theme for the Certificate Course is what we may call the ‘misuse of assumptions’; in other words, a failure in simple logic to recognize the implications of Hume’s problem of induction. This misuse is pervasive, despite the preoccupation of philosophers of science with its implications over the past 250 years or more since its first appearance in the work of David Hume (1711-1775), a Scottish philosopher in 1748. The issue is the relation, if any, between claims from the past and claims on the future; expressed as the notion of the realism of assumptions. The application is pervasive: the construction of assumption driven simulated model claims on the future, typically the lifetime of a hypothetical population, to make a case for incremental cost-per-QALY claims and, supported by sensitivity analyses, threshold-based recommendation for cost-effectiveness, pricing and product access. This was effectively demolished by Russell in 1912 with his example of the farmer who feeds a chicken each day to fatten it up until the day when the former comes out, the chicken approach expecting to be fed and the farmer wrings its neck. Put less evocatively: the fact that all past futures have resembled past pasts does not mean that all future futures will resemble past futures. Induction, or confirmation of a claims, is logically impossible. We cannot even argue probabilistically because the data on which the claim is based are only a sample of all possible claims. Hence, we cannot say that one assumption or set of assumptions (and there can be dozens from the literature and even guesses from experts) to support a simulation model are any different (less, equally or more realistic) than any other. In short, no one simulation model, such as those produced by the US Institut of Clinical and Economic Review is any better (or worse) than another. Apart from the fact that these models are multidimensional, lack evaluable claims and were only designed as vehicles for approximate information; in the last case, of course, it not clear as to what they are approximating. Add to this the fact that these models are an invitation to reverse engineering to support a sponsor’s claim for cost-effectiveness at a price that meets the sponsors revenue projections.

This critique does not deny the role of models and assumptions supporting those models; a common feature of research in the physical and more mature social science (supporting paradigms and not memes). If the model is designed to generate credible, evaluable and replicable claims then if it fails to meet assessment standards for provisional acceptance, the entrails or assumptions of the model can be reviewed.

## **PROTOCOLS**

Protocols are an integral part of the proposed new start in HTA just as they are integral to product development. Once, however, marketing approval is secured, the application of protocols is put on

the back burner (apart from Phase 4 trials) for value claims assessment. This is a critical mistake; if we are to support value claims assessment for a product over its life cycle, protocols are front and center in support of value claims, in providing a framework for evaluating and re-evaluating the merits of value claims. Recognizing the asymmetry between proof and disproof, a protocol should support a value claim in presenting that claim in a format that recognizes the role of falsification of claims; strictly, a protocol should maximize the likelihood of a value claim being falsified <sup>26</sup>.

Recognizing the importance of falsification as the demarcation criteria between science and non-science, the focus on falsification is the basis for the provisional acceptance of value claims over the product life cycle is essential. This sets the new start in HTA apart from the relativistic acceptance of non-evaluable formulary proposals, and claims for a fair price modelling driven by fixed parameters and limited assumption options. At all stages of product formulary acceptance and continued approval, placement and pricing there must be strong and explicit commitment to transparency and not black-box models to support ersatz outcome claims. Ongoing value claim protocols are the basis for this continued re-evaluation or evolution in objective knowledge, supporting if required outcomes-based contracting

At the same time the proposed new start recognizes that over a product life cycle pricing and access are provisional. At product launch information and extant value claims are limited. Pricing negotiations must reflect the standards of existing claims while requiring the initial formulary submission to present value claims to be assessed in a short and meaningful time horizon. The protocol details the assessment process and must be agreed with the health system. There is the possibility of core and supplementary claims, specific to indication approved disease areas or target patient populations. Ongoing pricing and access reviews will be dependent on the outcome of value claim assessments.

## **PATIENT BENEFIT**

If we are to provide an assessment of the direct benefit to patients and caregivers of a new therapy then this must be a direct and not an inferred benefit from purely clinical considerations <sup>27</sup>. Certainly, we can report the clinical outcomes of pivotal trials, but we need to move to a holistic measure that manifests the needs-fulfillment latent construct. Needs which are subjectively reported by patients and which can then be transformed to linear interval measures by applying Rasch rules. As patients are the ultimate beneficiaries of health care interventions, where quality of life is impacted significantly by health status, notably in chronic diseases, then we need to assess needs by the difficulty of meeting them and the benefit from meeting more of the needs from a new therapy. We put aside, therefore, terms such as ‘efficacy’ and ‘effectiveness’ in favor of ‘needs fulfillment’.

## **SUBMISSIONS: DISEASE AREA AND THERAPEUTIC CLASS REVIEWS**

The proposed new start sets the stage for evidence-based decision making; evidence which meets the required standards for normal science and fundamental measurement. To achieve this the Certificate Course proposes a format for the assembly of product dossiers, to include questions



that a formulary committee or other health system decision makers should address to ensure the submission is acceptable. These questions are relevant irrespective of whether the requested and submitted dossier, with protocol, is for the evaluation of a new product or device, for ongoing disease area and therapeutic class reviews or outcomes-based contracting.

The key point is data assembly; feedback from core value claims that are assessed with real world evidence to support the evolution of what Popper has described as objective knowledge. Therapy claims are not static; they represent a step in the discovery of new facts, to meet evidence gaps, in the support of a product over its life cycle. Creating simulated modelled assumption driven claims is not a starting point. Blanket claims for cost-effectiveness are not the basis for any process of discovery, particularly when they fail the standards of normal science and fundamental measurement.

## **FURTHER INFORMATION AND PROGRAM COORDINATOR**

For further information on this program for university credit, please contact:

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## **REFERENCES [KEY REFERENCES \*]**

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