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-evaluable 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 [1].

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

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

OVERVIEW: A NEW START PARADIGM IN HEALTH TECHNOLOGY ASSESSMENT

The focus of PHCY 5141 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; A new start in HTA. This involves meeting the evidence needs of formulary committees, practitioners, patients and other health system decision makers which is critical for effective health care delivery, together with the meaningful assessment of pharmaceutical products and devices by pharmacists in every day practice.

This new start in HTA rests on three premises:

- All value claims for therapy impact, whether for clinical endpoints, PRO, drug and resource utilization must meet the standards of normal science for credibility, empirical evaluation and replication;
- All value claims must be for instruments supporting single attributes that meet Rasch measurement standards or rules as interval or ratio scores in order to capture response to therapy; and
- All value claims must be supported by a protocol detailing how the claim is to be assessed and reported.

The proposed new start demonstrates 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 not the required measurement standards. The new start delivers a comprehensive package to support formulary submissions, prospective research programs to discover new facts for therapy response as well as the necessary inputs for outcomes-based contracting.

THE CHALLENGE OF THE NEW START

Health care decisions cannot be based on imaginary, assumption driven claims for cost-effectiveness. Unfortunately, current analytical standards in pharmacoeconomics or health technology assessment (HTA) fail to meet the required evidentiary standards. We have to do better than rely on the multiattribute QALY as a gold standard in creating approximate information; unless the QALY can be demonstrated to have interval measurement properties, capturing a single unidimensional attribute, health technology assessment has no claim to relevance. Rather there is a concern the current standards in health technology assessment encourage a belief in the importance of consciously rejecting the standards of normal science and fundamental measurement. By 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 [2]. Rasch measurement is not knew; it was proposed and accepted in the 1950s but ignored in health technology assessment with the commitment to multiattribute generic instruments and patient reported outcomes that produce nothing but ordinal observations or raw scores: observations are always ordinal, measurement must be interval.

We have to backtrack; to admit that the commitment to observations rather than measurement has effectively crippled health technology assessment. What was overlooked, and continues to be overlooked, is that meaningful measurement is based on the properties of interval scales and that Rasch measurement is the only necessary and sufficient means to transform ordinal observations to interval, linear measures [3]. If this lesson is rejected, then health technology assessment has nothing to say in capturing patient response to therapy. We have to do better.

This is the purpose of PPCY is to bring health technology assessment in from the cold. The key point is that the Wyoming program 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 [4] . This was uncritically accepted by leaders in the field and detailed in textbooks and practice guidelines [5]. It was also uncritically accepted by academic centers, government agencies and analysts despite warnings to the contrary [6] [3]. 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) [7] [8] . At the same time this acceptance of assumption driven modelled claims is open to abuse and bias [9] . 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 [10] [11] as well as the mooted successor to the QALY, the EQ-Health and Wellbeing (EQ-HWB) multiattribute instrument which, unfortunately, continues the tradition in patient reported outcomes of ignoring the standards of Rasch measurement, confusing polytomous observations with measurement, producing nothing by raw scores [12].

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 [13]. This program 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 [2], 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.

BELIEVING IMAGINARY CLAIMS

Many practitioners are aware of the manifest deficiencies in modelled claims [14]. 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 [15]. 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 17th century [13]. 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 17th 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 anybody'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* [16].

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 in health technology assessment that makes analytical sense and which brings us back to the standards we have long ignored; the required standards for the 21st century.

FURTHER INFORMATION AND PROGRAM COORDINATOR

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

Elliott M Sogol PhD RPh FAPhA
Director Postgraduate and Continuing Education
School of Pharmacy
College Of Health Sciences
University of Wyoming
Email: esogol@uwyo.edu

REFERENCES [KEY REFERENCES *]

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