PHCY 5141
PRINCIPLES OF HEALTH ECONOMICS AND OUTCOMES

INTRODUCTION

REJECTING PSEUDOSCIENCE:

A NEW START IN HEALTH TECHNOLOGY ASSESSMENT

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Welcome to the Fall 2022 *Principles of Health Economics and Outcomes (PHCY 5141)* course *Rejecting Pseudoscience: A New Start in Health Technology Assessment*. This is a 3-unit 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. Unfortunately, current analytical standards in pharmacoeconomics or health technology assessment fail to meet the required evidentiary standards. The misplaced focus on approximate information, assumption driven simulated modelled claims for cost-effectiveness fails both the standards for normal science and fundamental evidence. It is an analytical dead-end. This course presents a necessary new start in the assessment of value claims for competing pharmaceutical

products and devices. 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.

STUDENT LEARNING OUTCOMES AND GOALS

At the end of the course, you will be able to:

- Understand the deficiencies of health technology assessment techniques as defined by pharmacoeconomics in terms of the standards for normal science and fundamental measurement
- Recognize the importance of a new framework for economic evaluations in formulary decision making
- Identify the appropriate measurement constructs for value claims in therapy impact
- Identify the appropriate health technology assessment framework for a given situation
- Differentiate the options in economic analysis for value claims
- Understand the limitations of simulation modeling in creating value claims
- Recognize the limitations of QALYS and patient reported outcomes (PRO) claims
- Construct appropriate resource utilization and cost claims
- Understand the importance of the patient (or caregiver) voice in value claims
- Critically assess value claims for competing therapies

READING AND REFERENCE MATERIALS

There is no textbook for this course as there is none that meets the required standards for health technology evaluation. Instead, the course is built around a series of 14 modules with slides/audio presentation supported by extensive notes and 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.

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

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

- Four modules that make the case for the standards of normal science and the rejection of pseudoscience:
    - Science versus non-science
    - Ratio and interval measures
    - Assumptions and Hume's problem of induction
    - CHEERS 22: Tenacity of false belief systems in pharmacoeconomics

- Five modules that address the failure of created approximate information:
    - Truth is not consensus
    - Failure of multiattribute generic preference measures
    - The impossible QALY
    - Impossible value claims
    - Abandoning models in value claims

- Five modules that detail the standards for a new start in formulary submissions:
    - Guidelines for value claims in formulary submissions
    - The patient voice: need fulfillment quality of life
    - Selecting PRO claims
    - Formulary submission guidelines
    - Questions a formulary committee should ask

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 literature 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 Due October 30 (25 points)

Langley P. Let a Thousand Models Bloom: ICER Analytics Opens the Floodgates to Cloud Pseudoscience. *Inov Pharm*. 2021;12(1):No. 5
https://pubs.lib.umn.edu/index.php/innovations/article/view/3606/2668 Due November 18 (25 points)

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
https://pubs.lib.umn.edu/index.php/innovations/article/view/4861/3198
Due 30 November (25 points)

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 6 November and returned by 13 November. Questions for the final will be distributed on 27 November and returned by 4 December.

LIVE SESSIONS AND DISCUSSION QUESTION

From 16 October (Sunday) to 4 December (Sunday); 3 hours starting at 5pm Wyoming time. 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 first session on 16 October you will be expected to have reviewed the Introduction and Module 1

COURSE SCHEDULE

Date	Modules	Topic(s)
16 October	INTRO	Introduction: Course Objectives
	1	Science versus Non-Science in Health Technology Assessment
23 October	2	Ratio and Interval Measures for Health Technology Assessment
	3	Assumptions and Hume's Problem of Induction in Modeled Value Claims
30 October	4	CHEERS 2022: Relevance for Modeled Value Claims
	5	Truth in not Consensus
6 November	6	Failure of multiattribute generic preference
	7	The Impossible QALY
13 November	8	Impossible value claims
	9	Abandoning models in value claims

20 November	10 11	Guidelines for value claims in formulary submissions The patient voice: need fulfillment quality of life
27 November	12 13	Selecting PRO claims Formulary submission guidelines
4 December	14 Wind-up	Questions a formulary committee should ask What have you gained (or lost) from this course?

FURTHER INFORMATION AND PROGRAM COORDINATOR

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

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OVERVIEW: A NEW START IN HEALTH TECHNOLOGY ASSESSMENT

These modules present the case that the existing approach to health technology assessment (HTA) or pharmacoeconomics is an analytical dead end. More to the point: we have wasted some 30 years in advocating the creation of value claims that lack any scientific credibility. The reason is quite straightforward: The International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the Institute for Clinical and Economic Review (ICER) and academic groups, following leaders in the field, have rejected the standards of normal science: the requirements that all value claims for response to therapy have to expressed as single attributes that are credible, evaluable and replicable [1].

Instead, the focus has been on assumption driven simulated claims that fail the demarcation test for science in terms of non-science; they are pseudoscience [2]. The modeled claims proposed in pharmacoeconomics are to establish invented claims the cost-effectiveness of competing therapies; a failed methodology. They fail not only because they reject the standards of the physical sciences and the more advance social sciences, but because the entire modeling framework is a logical and mathematical impossibility. It is an analytical dead end. If we are to provide a framework to establish the relative worth and impact of competing therapies, then the current methodology of invented outcomes and blanket modeled cost-effectiveness claims must be rejected.

Practitioners are aware of the manifest deficiencies in modelled claims [3]. Yet they persevere, as shown by the recently released CHEERS 22 guidance for construction and submission of imaginary value claims for competing products to leading journals; who have in turn endorsed them [4]. The belief is that formulary committees are prepared to accept imaginary claims to support pricing and access decisions. The problem, of course, is that by changing assumptions any number of competing modeled claims can be presented. A recent analysis of industry versus non-industry model claims has pointed to the presence of a significant systematic bias that favors claims sponsored by industry; modeled claims have been designed to create a required outcome to support sponsor pricing [5]. 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.

To understand why the pharmacoeconomics of health technology is an analytical dead end, it is proposed to review a recent guidance for creating imaginary modeled claims: CHEERS 2022 [6]. This review will offer, first, a detailed critique of why the current system belief in imaginary value claims should be abandoned and, second, why we need a new start in technology assessment that is meaningful to health system decision makers and which is not metaphysics or pseudoscience, but an analytical framework consistent with the standards of normal science.

There is, hopefully, more to HTA assessment than the creation of an endless number of assumption- driven imaginary simulations that leading journals are willing to publish. Of interest, perhaps, as marketing support, but of no relevance to formulary decision making as any imaginary claim is as valid (or invalid) as any other.

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 over 300 years [7]. While practitioners in 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 production and consumption of health and healthcare.

Unfortunately, HTA practitioners are devoted to a belief system which has more in common with that prevailing in the Middle Ages, and not overthrown until 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 [8]. Any non-empirically evaluable claim is 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 [9].

The purpose of this course is to set the stage for a critique, and even the rejection, of the current belief system in HTA ot pharmacoeconomics in favor of a new start in the evaluation of competing therapies in formulary decision making. The case is that we must accept that the standards of normal science are relevant to formulary decision making and value claims for therapy response.

In the last resort it is about measurement; 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. They all fail the axioms of fundamental measurement.

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. Blanket claims for comparative cost-effectiveness are totally unacceptable.

In short, as will be explored, a new start in health technology assessment rests on two requirements:

(1) All value claims for a product or therapeutic intervention must refer to single unidimensional attributes that meet the demarcation standards for normal science: all value claims must be credible, evaluable and replicable in a meaningful timeframe; and
(2) All value claims must be consistent with the limitations imposed by the axioms of fundamental measurement: they must meet interval or ratio measurement standards

It is no exaggeration to make the case that in pharmacoeconomics we have wasted 30 years; although no leader in this field, principally academic, will admit to this. After all, to base one's professional career on a series of false assumptions, and demonstrated lack of awareness of the standards of normal science, in particular fundamental measurement, is a failure few would care to acknowledge. If we add to this the extent to which literally thousands of students and analysts have followed this lead makes an admission all the more damaging. There are now thousands of publications generating mathematically impossible quality adjusted life years (QALY) models, none of which have any pretense to scientific credibility [10].

It is not so much that HTA is at the 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.

REFERENCESLEY

[1] ** Langley P. Nonsense on Stilts – Part 1: The ICER 2020-2023 value assessment framework for constructing imaginary worlds. *Inov Pharm*. 2020;11(1):No. 12 https://pubs.lib.umn.edu/index.php/innovations/article/view/2444/2348

[2] Pigliucci M. Nonsense on Stilts: How to tell science from bunk. Chicago: University of Chicago Press, 2010

[3] ** Langley P. Peter Rabbit is not a Badger in Disguise: Deconstructing the Belief System of the Institute for Clinical and Economic Review. *InovPharm*. 2021; 12(2): No 22 https://pubs.lib.umn.edu/index.php/innovations/article/view/3992/2855

[4] Husereau D, Drummond M, Augustovski F et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 22) Statement: Updated reporting guidance for health economic evaluations. *ValueHealth*. 2022;25(1):3-9

[5] Xie F, Zhou T. Industry sponsored bias in cost-effectiveness analysis: registry based analysis. *BMJ*. 2022:377

[6] ** 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)

[7] Drummond M, Sculpher M, Claxton K et al. Methods for the Economic Evaluation of Health Care Programmes (3rd Ed.). New York: Oxford University Press, 2015

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

[9] Dawkins R. A Devils Chaplain. New York: Houghton Miflin, 2004

[10] Langley P. The Great I-QALY Disaster. *InovPharm*. 2020; 11(3): No. 7 https://pubs.lib.umn.edu/index.php/innovations/article/view/3798/2697