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A FAILURE OF PHARMACY PRACTICE: THE ACADEMY OF MANAGED CARE PHARMACY FORMAT FOR FORMULARY DECISIONS (VERSION 4.1)

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Abstract

Despite its apparent popularity, Version 4.1 of the Academy of Managed Care Pharmacy's (AMCP'S) Format for Formulary decisions is fatally flawed as a template for developing and evaluating value claims for pharmaceutical products. The flaws are obvious: (i) there is no concept of the standards of normal science where any claim must be credible, evaluable and replicable; (ii) that all value claims must recognized the limitations imposed by the axioms of fundamental measurement; and (iii) a that assumptions based on past observations cannot support modeled claims for future outcomes. These are standards that are fundamental in the physical and more mature social sciences (e.g., economics); unfortunately AMCP in consort with agencies such as the Institute for Clinical and Economic Review (ICER) and the professional group the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) have ignored these standards in measurement and logic for the past 30 years. While it is most unlikely that AMCP will admit to these flaws, the fact remains that we must abandon the invention of evidence to support formulary submissions and embrace a new paradigm for value claims. The purpose of this commentary is to set out the basis for rejecting economic evaluations and the AMCP Format for Formulary Submissions, including modeling to support value claims, pointing the standards required for robust and evaluable evidence.

Keywords: AMCP failure, intelligent design, imaginary pharmacy practice, impossible QALY

INTRODUCTION: AMCP FAILURE IN PHARMACY PRACTICE

Abandoning a paradigm (or meme) is uncomfortable; few are prepared to renounce prior belief, even when the beliefs are demonstrably false. This is the situation found in health technology assessment where, for 30 or more years the thought leaders have dominated the debate over approximate information versus hypothesis testing [1] [2]. The classic example of misguided modeling to create value claims is the reference case of the Institute for Clinical and Economic Review (ICER) where lifetime models, developed by a handful of university based expert research centers, produce assumption driven simulation models that defy, not only the standards of normal science, but the axioms of fundamental evidence and even simple logic [3]. The Academy of Managed Care Pharmacy (AMCP) Format for Formulary Submissions is clearly in this tradition in its recommendations for economic evaluations based on invented evidence as key elements in formulary decisions [4].

The purpose of this brief commentary is to demonstrate that, as a basis for value claims, the ACMP Format is a failure. It fails to recognize the standards of normal science, the limitations of the axioms

of fundamental measurement and, but not least, the problem of induction in assumption driven imaginary value claims [5]. Put simply, the AMCP Format makes a mockery of formulary decisions and claims for pricing and access.

The argument for value claims, whether these refer to clinical attributes, patient reported outcomes (PRO) or resource utilization and costs Is straightforward. The three requirements are:

- **All value claims must refer to single attributes that meet the demarcation standards for normal science: they must be credible, evaluable and replicable**
- **All value claims must be consistent with the limitations imposed by the axioms of fundamental evidence: they must meet interval or ratio measurement standards**
- **All value claim assumptions must respect the logical requirement that assumptions from the past cannot support assumptions on claims for the future**

The AMCP format seems oblivious to these requirements. This is an odd feature given the myriad claims that respect these standards in pharmacy practice, notably for pivotal clinical trials. Perhaps, for the AMCP, value claims, including economic evaluations can neglect these requirements; a position consistent with that taken by ICER and ISPOR which reject completely these standards for value claims [6] [7]. The conclusion is that the AMCP is an unequivocal support of formulary decisions based on invented claims.

AMCP: THE STANDARDS OF NORMAL SCIENCE

Value claims for pharmaceutical products and devices must respect the distinction between science and non-science; or, to put it more bluntly, between science and metaphysics or pseudoscience [8]. The criterion for demarcation is clear cut, unless you are a relativist, where science is just another cultural practice that accepts a sociological interpretation of what science is, the answer is that if you hold to a belief in objective knowledge, where science expands our knowledge of the world, then the AMCP Format is a failure for pharmacy practice. The distinction between science and metaphysics and pseudoscience is that the latter excludes from consideration, as Wootton puts it, the very feature which makes scientific arguments distinctive: their appeal to superior evidence [9].

It is a moot point as to whether or not recipients of simulated assumption claims as advocated in the AMCP Format have the skills to interpreted the model, recognizing its imaginary nature, and incorporate (or ignore) the modelled claims, undoubtedly for a product price that will be claimed to be cost-effective. Compared to ICER, however, it is not clear whether AMCP endorses and requires thresholds to be applied to the modelling. In any event, this would be redundant as no manufacturer is going to submit a modelled claim that does not meet threshold requirements; or even admit to the possibility. A situation made all the more ridiculous when there is no chance of the claims ever being empirically evaluated with the model submitted as commercial in confidence unless there is a decision by the manufacturer to present the model as a peer reviewed paper as a marketing exercise. In this

case there is the opportunity to 'review' the model; an opportunity that is most unlikely to be taken up. In the past 30 years thousands of AMCP type model claims have been published; these typically support the product, which is not surprising, with financial support provided by the manufacturer. Editorial assessment appears to be minimal. In one instance, the journal being the ISPOR product *Value in Health*, 12 simulated model claims were published with all favoring the product and 11 support by the manufacturer [10]. Other issues of *Value in Health* follow the same pattern, joined by journals such as *PharmacoEconomics* and the *Journal of Medical Economics* [11] [12] [13] [14]. This is an unfortunate outcome of a commitment to building imaginary non-evaluable value claims which AMCP should have been aware of in drafting the AMCP Format. Instead, AMCP is a participant in a wasteland of non-evaluable imaginary information intended to support formulary decisions, but not effective pharmacy practice.

The pervasiveness of the current technology assessment paradigm, and its possible input to the lack of awareness of health evaluation practitioners of the axioms of fundamental measurement are the PubMed reference counts; with the criteria [QALY AND {model OR simulation}] the head count is 13,358 [12-20-2015]. If this is indicative, this represents a formidable amount of misinformation, to which AMCP has contributed its share. This reinforces the belief that the dominant 'consensus' in health technology assessment is the need to invent modeled evidence as a marketing claim for cost-effectiveness. The case for this is seen in the most widely used textbook in health technology assessment that lays out the steps to develop imaginary value claims; a primer for assumption driven simulation modelling, typically over a hypothetical lifetime for the target patent group. As noted below, with the lodestar of an ersatz claim or the umbrella term 'cost-effectiveness' pointing to a single metric value claim. It is entirely consistent with the so-called strong program; truth is consensus among the practitioners, with probabilistic sensitivity analysis the ultimate defense. Unfortunately, as noted below, there can be no 'preferred simulation'. In logic, any assumption about the future has the same status; Hume's problem of induction (David Hume 1711-1776) [15] .

Reviewing the AMCP Format, the only conclusion we can come to is that AMCP subscribes to the approximate information or non-science meme of health technology assessment. If value claims are made, AMCP sees no difference between those value claims that support the growth of objective knowledge and those that are the product of assumption driven simulations where there is no intention of expanding objective knowledge in pharmacy practice. The question AMCP fails to address is whether formulary decisions should be based on invented evidence for comparative clinical benefit claims or should commit to real world evidence, where the former is an analytical dead end.

AMCP: MEASUREMENT AND RESPONSE

If a value claim, whether clinical, a patient reported outcome (PRO) or otherwise, is to have any credibility then it must respect the axioms of fundamental measurement. This restricts claims to those that meet interval or ratio measurement properties [16]. This has been accepted since the seminal contributions to measurement theory by Stevens in the 1940s and Rasch and Luce and Tukey in the 1960s [17] [18] [19] [20]. The AMCP Format authors are, as far as can be ascertained, unaware of this

limitation on the levels of evidence; instead the belief appears to be that ordinal scales can be assumed to have ratio measurement properties [21]. This is an absurd assumption; ordinal scales cannot support claims for response to therapy as they do not support invariance of comparison. All they can support, as the scores are just ranked, is nonparametric statistical evaluation. The AMCP Format's modelling overview (Section 4.0B) provides the framework for an imaginary framework to quantify 'the risk-benefit tradeoff of the product and its economic value'. This is an impossible objective; certainly, as demonstrated on numerous occasions, it can be attempted but the results defy the standards of normal science and the axioms of fundamental evidence, and should be ignored. , Decision-based cost-effectiveness models are not an effective means to assess the overall potential value of health technologies as the AMCP Format claims (Section 4.1.1B); the question itself makes no sense as the metric for 'overall' potential value is irrational.

The AMCP Format provides no guidance to those developing value claims of the need to respect these axioms; indeed the AMCP Format reads as if the axioms of fundamental measurement are irrelevant. If an instrument for assessing therapy response is to meet required standards then it must be designed to have the required measurement properties. Many clinical response assessments do precisely this; unfortunately the overwhelming majority of generic and disease specific PRO measures do not. Thus reflects, in large part, the various authors lack of understanding of the constraints imposed on their manipulation of scales to create summary and aggregate response measures [22]. The false belief that Likert scales are ratio scales that can be aggregated and manipulated to give summary and overall scores is a classic yet widespread misapplication as they only ordinal. Such measures have no place in formulary decisions and pharmacy practice.

AMCP: INVENTING PHARMACY CLAIMS

AMCP recognizes the importance of real world evidence and schemes to encourage evidence development; as long, presumably, that the evidence collected meets required measurement standards. For the AMCP Report, limitations on data for decision making do not include apparently fundamental measurement (Section 4.1.1B). The problem, of course, is with new products and the limited data available to support value claims at product launch. The response in health technology assessment has been to invent non-evaluable value claims, approximate information, through lifetime simulation modelling and non-evaluable assertions that the product is cost-effective. Hypothesis testing and the development of research programs to meet evidence gaps have been rejected in favor of approximate imaginary information [2]. The AMCP Format accepts this completely. This sets pharmacy practice in an ambiguous position: in subscribing to the AMCP Format as a professional standard, should formulary committees accept imaginary modeled claims as evidence to be treated equally with claims based on value claims that meet required measurement standards? In other words, should formulary committees abandon the distinction between value claims that meet the required scientific standards and non-science claims?

The embrace of imaginary claims is made clear in the AMCP Format options for modelling techniques Section 4.1.2B). Three techniques are proposed each of which defies the standards of normal science

in supporting value claims: (i) decision trees; (ii) Markov (cohort) models and (iii) patient level simulations (discreet event simulations). Unless there is a stated objective that the claims from these models are designed to be empirically evaluable, the result is claims that lack any credibility, evaluation and replication. The question of cost-effectiveness analyses conducted alongside clinical trials is recognized (Section 4.1.3B); once again these limitations apply, in particular any attempt to collapse trial claims into a sig le metric for cost-effectiveness.

The failure of the AMCP Format is evidenced in its commitment to hypothetical lifetime models where it advises that the format requires a *time horizon …long enough to reflect all important differences in costs and outcomes between the technologies being compared* (Section 4.2.1B). This ensures, of course, that the resulting value claims will fail the standards for credibility and empirical evaluation; together with the further requirement that the analytical framework fir imaginary claims must be presented as incremental costs and outcomes analyses.

Models that create imaginary claims are clearly non-science; for the AMCP Format the focus is on optimal assumption driven models that yield imaginary invented value claims. An acceptance that puts the AMCP squarely in the same corner as ICER with its reference case for creating imaginary claims and the ISPOR standard for imaginary formulary claims. Just as ICER should be ignored so should any claim that is based on the AMCP Format proposed modelling options; formulary committees and other health system decision makers should be made aware of this failure in pharmacy practice.

AMCP: THE IMPOSSIBLE PREFERENCE SCALE

Preference estimates for the AMCP Format models should, apparently, *be derived from studies surveying either patients or the general population using either direct or indirect elicitation methods* (Section 4.2.1B). Unfortunately, given the AMCP Format's disregard of the axioms of fundamental measurement, the preference estimates that are recommended all suffer from a basic flaw: they are ordinal scales. The AMCP Format presumably assumes that any direct or indirect preference score has ratio measurement properties. If so, these mystical ratio scales lack (i) invariance of comparisons; (ii) a true zero (required of a ratio scale) and (iii) dimensional homogeneity (unidimensionality) and hence construct validity. This last point follows from the preference reporting on health states with multiple symptoms (or attributes) and response levels. Unless there are ratio scales for each attribute, they cannot be combined (and it is unclear while we would attempt to combine them anyway as each would support a value claim). Ordinal preference scores cannot support claims for response to therapy; AMCP should acknowledge this as a key element in evaluating therapy claims.

AMCP: THE IMPOSSIBLE QALY

A continued lack of appreciation of the limitations of fundamental measurement is a major oversight in the AMCP Format. The AMCP Format accepts the proposition that the QALY allows for 'assessment of overall health care value' (Section 4.2.1B). The fact that is overlooked is that in order to create a

QALY, multiplying time spent in a disease state by a preference score requires the preference score to have ratio measurement properties. The generic preference scores both direct (standard Gamble and Time Trade Off) and the indirect scores (EQ-5D-3L/5L; HUI Mk2.3, SF-6D) only have ordinal properties. They were not designed as bounded ratio scales fixed at 0 = death and 1 = perfect health. Instead we have scales which lack the necessary properties with algorithms for the indirect scores that generate negative values or states worse than death; there is no true zero. A recent attempt to create US values for EQ-5D-5L multiattribute health states found that of the 3,125 health states, 20% (or 625) had negative values [23]. Unless you have belief in a mystical ratio scale, which ICER apparently does, the QALY, therefore, is an impossible mathematical construct as ordinal scores do not support multiplication [24].

In claiming that the various preference scores capture overall health care value, AMCP overlooks the differences between the various scores in terms of the health dimensions covered, the number of response levels, the description and severity of response levels and the construction of the various scoring algorithms. While these differences may be of limited interest given the ordinal nature of the resulting preference scores, there is a more fundamental issue regarding the apparent benefits of generic versus disease specific scales. The existing generic scales fail not only the axioms of fundamental measurement but also any assessment of required dimensional homogeneity and construct validity. It is doubtful if any attention is given to them in allocating health care resources; a task for which they are not equipped in any event. AMCP should look to value claims specific to target populations in disease areas as central to pharmacy practice and formulary decisions.

The fact that the AMCP Format fails to recognize the QALY as an impossible construct is not surprising; this lack of understanding is shared not only by leaders in the field of technology assessment but by thousands of technology assessment acolytes around the globe (and journal editors). For these people the impossible QALY is alive and well. Once the fact that the QALY is an impossible construct is recognized it nullifies simulated imaginary claims for cost-effectiveness. This is seen clearly in the ICER evidence based models, produced by expert groups, typically affiliated with colleges of pharmacy, who appear equally oblivious to these limitations and should know better.

AMCP: ASSUMPTIONS

In common with the thought leaders at ISPOR and the expert modeling groups support ICER, the AMCP Format overlooks a simple point in logic: the problem of induction. First proposed by the Scottish philosopher David Hume in 1748, the point made is blatantly obvious: *The whole of our science assumes the regularity of nature…. Yet there is no way in which this assumption can be secured. It cannot be established by observation, since we cannot observe future events. And it cannot be established by logical argument, since from the fact that all past futures have resembled past paths it does not follow that all future futures will resemble future pasts* [25].

The problem of inductions is overlooked entirely by the AMCP Format in its emphasis on high quality data sources as the basis for assumptions to population imaginary models; but the notion of 'high

quality' is irrelevant unless this is a justification for the realism and relevance of these models in defining a known future world (Section 4.2.2B). These 'high-quality' data support the parameter estimates for the model; they should be linked to the respective assumption which should be listed. What the AMCP Format forgets is that you cannot justify the merits of one assumption over another from existing data sources. An assumption is an assumption; the model builder might claim that his/her choice of assumptions relating to future clinical effectiveness, adverse events, unit costs, utilities, practice patterns and compliance over the next 20 or 30 years are 'realistic', as required in the AMCP Format models, but this reflects the analyst's psychology rather than any appeal to logic. While the AMCP might defend this abuse of logic by an appeal to the application of sensitivity analysis, the same defense can be used of any number of models driven by different (yet 'realistic') assumptions for the selected therapies in a hypothetical patient population. Perhaps the users of the AMCP Format should be made aware of the limitless possibilities of competing modeled value claims where there is no basis for judging one set of imaginary assumptions and their claims as superior to another. The AMCP Format allows this; there is no attempt to set criteria for competing model superiority. Perhaps AMCP should proceed down the same road as the National Institute for Health and Care Excellence (NICE) where there are academic specialists, contracted to universities, who are devoted to examining the entrails of imaginary modelled claims to judge whether the proposed model or an alternative is more 'realistic'. Building a professional career on assessing the realism of assumptions regarding therapy impact in the future is, of course, a pointless exercise.

AMCP: DIRECT MEDICAL COSTS AND LIFETIME BENEFITS

Value claims for the impact of competing therapies should be expressed in resource units (e.g., CPT codes) and unit costs relevant to the particular formulary committee. If not, then any claims for costs should be rejected out of hand: typically the claim fails the standards of normal science. This fairly obvious point seems not to have occurred to the authors of the AMCP Format as it seems clear that in modeled simulations the thought that the cost assumptions could be potentially evaluable is absent. Instead, the focus is on the 'realism' of the cost assumptions as justification, apparently to quantify costs for the next 20 to 30 years; the assumed costs and benefits associated with the natural course of a disease. This leaves the door wide open to any assumed claims for the costs and benefits over the course of a disease, with the authors recognizing that the claims for costs and benefits would never be open to empirical assessment. Recipients of these non-evaluable claims would be expected, without question, to take these at their face value as integral to formulary decisions for cost-0effectiveness in a managed care environment; denial of access to therapy would be justified by imaginary claims of future, but unknown, direct medical resource utilization and the applied unit costs, in a single cost-effectiveness metric.

It should be clear by now that the current technology assessment paradigm is an entirely hollow concept. Certainly, with the support of the impossible QALY, any number of stages of disease benefit streams could be simulated. The stages of disease could be different, defined by any number of state transition matrices, and any of the multiattribute generic instruments that create ordinal preference scores. There is no gold standard ordinal preference score to support a gold standard QALY. Attempts

have been made but the discussants not only failed to select the most popular ordinal score the EQ-5D-3L but failed to consider any measurement constraints. The fact that all these instruments create ordinal and not ratio scores was absent from the discussion. This debate was irrelevant; the QALY is an impossible construct yet defended as a critical requirement [26].

If benefits defined by QALY are impossible, then we have to fall back on, of necessary, a single metric that captures the overall health status of respondents irrespective of their current experience of disease and the presence of stage of disease co-morbidities. This is obviously impossible. Yet AMCP subscribes to this chimera. Whether this reflects a lack of awareness or a simple belief in the meme content of the current paradigm is unknown; what is known is that the entire edifice of benefits and costs is a shambles defined in terms of scientific standards, measurement and even simple logic.

AMCP: EUGENICS

If the imaginary cost-per QALY imaginary calculus is accepted as a valid basis for resource allocation in health systems and unavoidable therapy rationing, this raises the issue of the basis for denying patients access to therapy. Such a framework for access denial raises the specter of eugenics and the evidence base for denying care [27]. The relevance of the experience with eugenics is important in evaluating the AMCP Format because, as Pigliucci notes eugenics is *a perfect example of the social perniciousness of scientific blunders* [8]. Whether we wish to attach the term 'blunder' to the existing health care technology paradigm, as detailed in the AMCP Format, is a personal choice. What is clear is that pharmacy practice has been undermined by the uncritical acceptance of recommendations from groups such as ICER for pricing and access to therapy where the foundation defies normal science. Eugenics is now discredited, but in the application of assumption driven imaginary simulations it has come in through the back door, hidden by a veneer of metaphysical or pseudoscientific respectability claiming to create a universal cost-effectiveness metric to support health care allocation.

This raises the question of the criteria for denial of care. In the eugenics literature, from a Soviet central planning perspective, there is clearly a need for a metric which captures, at the margin, the cost and benefits of competing therapy interventions to support resource re-allocation. While this is an overly simplistic position in health care resource allocation decisions, the application of an ICER (or AMCP) recommendation for social pricing and denial of care based on imaginary claims will still resonate as a eugenics index under a notionally fixed health system budget.

If AMCP is to enter this arena, then a decision has to be made as to how the modeled AMCP Format is to be interpreted and applied in health care resource allocation decisions. There is no hint in the AMCP Format guidelines that they want to emulate ICER and follow down the social pricing, price discounting imaginary rabbit hole. Apparently, the AMCP Format modelling is not intended to make suggestions regarding price discounting and the price that would be consistent with a cost-effectiveness claim for a specific health system

AMCP: COST-EFFECTIVENESS

For ISPOR, ICER and AMCP, the claim for overall cost-effectiveness rests on the application of QALYs in assumption driven imaginary simulations. The QALY is the lodestar, it is viewed as a generic metric that captures the health benefits relevant to decision making across a range of disease. There is no interest in a disease specific measure as this would disallow comparisons, although there is a range of disease specific quality of life instruments covering some 30 disease states that have applied Rasch Measurement Theory (RMT() to creating interval and, in some instances, bounded ratio scores that meet the required measurement standards [28]. For the QALY, as noted an impossible mathematical construct, the steps to claiming cost-effectiveness involve (i) simulation modelling of lifetime QALYs covering the stages of disease; (ii) simulation modelling for imaginary direct medical costs; (iii) undertaking an imaginary incremental cost-per-QALY assessment; and (iv) applying imaginary cost-per-QALY thresholds to assess the product price at which a claim for cost=effectiveness can be made. This is patently an absurd undertaking, driven by the need to make a single cost-effectiveness claim, as the exercise rests not only on a hypothetical simulation by assumption framework which under no circumstances can produce credible, evaluable a replicable value claim even if expressed in probabilistic terms, but a model which requires preference scores with ratio properties.

The AMCP Format appears not to recognize that unless the components of a cost-effectiveness claim are designed to meet the required ratio measurement standards for the elements of the claim where the costs are credible, evaluable and replicable (e.g. in terms of resource units) and the effectiveness claim meets the same standards, the overall claim is worthless. There is no doubting the attraction of a single metric, such as the application of probabilistic sensitivity analysis to ascertain the likelihood of a specific unit price being, in an imaginary sense, cost-effective. Attempting to deconstruct a composite cost-effectiveness claim is also fruitless, although it can point to the dubious nature of many of the 'realistic' assumptions that support the simulation modelling. Preferences or utilities, while only ordinal scores, are all too often from single studies as well often in simulations combining scores from different multiattribute generic instruments.

AMCP: VALUE CLAIMS PROTOCOLS

It should not be assumed that formulary committees or other health system decision makers are equipped to assess value claims; let alone those that defy the standards of normal science. The obvious solution is for the manufacturer to provide a protocol describing how the value claim, underwritten by the manufacturer, is to be assessed and reported back to the health system. In the case of the AMCP Format, value claims even if they meet the required standards, are apparently to be taken at face value with no attempt to evaluate them in the target treating population (which would be impossible). This leaves pharmacy practice in the air as the application of claims and protocols for imaginary future claims are clearly impossible as, implicitly, the AMCP Format denies their application.

Where a value claim meets the standards of normal science it should be evaluated. Protocols for evaluating claims were first proposed some 15 years ago and are a requirement of the latest version of the Minnesota formulary guidelines [29] [30]. In addition, the Minnesota guidelines also include a series of questions formulary committees should address to the manufacturer to establish the basis for the value claim. Of course, if (as in the case of AMCP) the modeled value claims are imaginary, then the question of a protocol does not arise and the claim should be rejected.

AMCP: CHALLENGING ICER

The endorsement by the AMCP of the analytical standards for creating imaginary cost-effectiveness claims, gives manufacturers and others the opportunity to challenge any recommendations from ICER for pricing and access; exactly the same opportunity is presented for claims based on the AMCP model. As the analytical requirements are essentially the same it would be quite straightforward to engage with an expert modelling group to address and modify the assumptions supporting the ICER model in terms of its structure and parameter values (e.g., transition matrices, preference scores). Given the interests of the manufacturer it would be unsurprising if the 'new' model in its choice of defensible assumptions came to the opposite conclusions to the ICER model with substantially reduced imaginary cost per QALY findings; essentially all that is required is to produce a competing set of preference scores.

The manufacturer through its retained model group could then proceed to hoist ICER by its own petard. The incremental model claims could be assessed against the various ICER cost-per-QALY thresholds, concluding that on ICER's criteria for a social price the product, given the new and claimed 'more realistic' model points to the fact that the manufacturers price was entirely reasonable. Discounts to achieve a required cost-effectiveness threshold would, by design, not be required; indeed, the case could be made that the price was understating its social value and could be justifiably increased as one more modeled addition to a global library of imaginary cost-effectiveness claims for specific products in a disease area.

This notion of a library is not as far-fetched as might be assumed; ICER in its evidence reports provides a brief overview of competing imaginary models as part of the model validation process which, not surprisingly, makes no reference to credible and evaluable value claims. The upshot is that an imaginary competitive 'new' model, which is essentially a marketing exercise, is just one more addition to what we might consider the global library of non-evaluable imaginary cost-effectiveness claims for pharmaceutical products. Surprisingly perhaps, there is a database or registry of some 10,000 cost-utility analyses covering the period 1776-2020 hosted by the *Center for Evaluation and Risk in Health Care* at the Tufts University Medical Center: the *Cost-Effectiveness Analysis (CEA) Registry* [31]. Unfortunately, the sponsors of this registry have overlooked the small point that as the various preference scores are ordinal, the QALY is an impossible mathematical construct. The entire exercise is, in retrospect, a waste of time.

Given the focus on assumption driven simulations that largely comprise the CEA registry, the developers of the data base, and manufacturers who subscribe to it, are clearly unaware of the standards of normal science, the axioms of fundamental measurement for single attribute value claims, and the problem of induction. The closest analogy to the Tufts registry would be the extensive relic collections held at the end of the 13th and beginning of the 14th centuries by figures such as Frederick III [1463-1525], Elector of Saxony and Albrecht of Brandenburg [1490-1545], Elector of the Holy Roman Empire, Archbishop of Mainz and Cardinal Archbishop of Mainz [32]. Relics and indulgencies, thanks to Martin Luther [1548-1546], with their associated steady income stream from the more credulous and ill-informed audience had largely disappeared by the mid-1520s.

CONCLUSIONS: PHARMACY PRACTICE

Given the manifest failings in the AMCP Format, the endorsement of assumption driven imaginary value claims, in respect of the development and evaluation of pharmaceutical products, points to the overdue need to reconsider pharmacy practice standards. We must reject the imaginary information meme in favor of a framework for value assessment that meets the standards of normal science. But this may not be what pharmacy practice for AMCP is about: perhaps it is to make decisions on invented composite cost-effectiveness claims. If so, health care decisions by formulary committees are in the unique position in both the sciences and social science in accepting invented evidence for non-evaluable claim decision making. Evidence from pivotal clinical trials is subsumed in a composite of assumptions, many involving false claims and even guesses for measurement status, in an attempt to capture a single hypothetical lifetime cost-effectiveness metric which defies empirical evaluation. Asking health system decision makes to accept imaginary simulated model claims for cost-effectiveness makes a mockery of the role of formulary committees in therapy choice.

It is not clear whether pharmacists advising formulary committees or the other committee members coming primarily from a medical background, are aware of this absurd promotion of imaginary value claims as key factors in formulary decisions. To say that they are poorly served by the AMCP Format would be a major understatement. Perhaps it's just the question of limited exposure or understanding of the philosophy of science and measurement theory (let alone simple logic). If so, AMCP might step in to remedy the situation. The obstacles are formidable and the AMCP response predictable. Proposing a successor paradigm is likely to be strenuously opposed given that so many in leadership positions in pharmacy management (including AMCP members) have much to lose. If professional careers in academia, government and industry have relied on the creation of assumption driven imaginary worlds then we can only expect opposition. This is unfortunate as we have the tools at our disposal to develop analytical frameworks to support meaningful, protocol driven value claims. We have a successor to the QALY if need fulfillment, patient centric quality of life is a desired disease specific value claim. We have the ability to assess other PRO claims in terms of the required measurement standards. Perhaps AMCP with its place in pharmaceutical practice might take the initiative; we should not hold our breath.

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