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NEXT GENERATION QUALITY OF LIFE MEASURES

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Abstract

The Quality Adjusted Life Year (QALY) is an analytical dead end. After some 30 years it has been realized finally by those in health technology assessment that the QALY is a mathematically impossible construct due to the fact that both direct and indirect preference scores are ordinal. At the same time, it has also been realized that basing formulary decisions on assumption driven simulations violates the recognized standards for normal science. If we are to make value claims for competing products we need an entirely new approach to reporting on quality of life (QoL) among other attributes. The purpose of this commentary is to propose a set of standards that should be observed for value claims, with specific reference to QoL claims from the perspective of patients and caregivers. This is a critical step. It is one thing to maintain the QALY is an impossible construct; it is another to point to a positive way forward to next generation value measures.

INTRODUCTION

All value claims for pharmaceutical products and devices must meet the standards that apply in normal science [1]. Unfortunately, the overwhelming majority of patient reported outcome (PRO) claims fail to meet the required standards [2]. These include generic quality adjusted life year claims (QALYs) as well as disease specific PRO measures. At the same time assumption driven lifetime simulation models also fail these standards, notably those claims for pricing and access produced by the Institute of Clinical and Economic Review (ICER) [3]. We are in the unfortunate situation, after 30 years of QALYs and imaginary simulation modeling, that we now realize we cannot invent evidence to support formulary submissions.

An entirely new approach to value claims is required. Fortunately, we know the standards that should apply to value claims and, in respect of quality of life (QoL) we have a successor to the QALY that meets these standards. Continued insistence on developing assumption driven model simulations for imaginary value claims is an untenable situation; the QALY and assumption driven simulation modeling are both analytical dead ends. We must abandon pseudoscience.

The purpose of this brief commentary is to make explicit the standards that must apply to value claims, with particular reference to disease specific and patient centric QoL.

MINIMUM STANDARDS FOR VALUE CLAIMS

There are six standards that must be met for credible and evaluable value claims, including clinical endpoints, patient reported outcomes (PROs), QoL and, and resource allocation. Failing to meet any one of these standards means the value claim must be rejected.

1. **MEETING THE STANDARDS OF NORMAL SCIENCE**

The single most important standard is to meet the requirements of normal science: *All value claims must be credible, evaluable and replicable.* If not, like the QALY, the claim is nothing more than pseudoscience and must be rejected. Invented value claims have been the mainstay of health technology assessment for 30 years.

2. **SUBMITTING VALUE CLAIM PROTOCOLS**

Manufacturers and others submitting value claims must demonstrate how the claim can be evaluated: *All value claims must be accompanied by an evaluation protocol.* Failure to provide a claims evaluation protocol must lead to a rejection of the claim.

3. **RECOGNIZING THE AXIOMS OF FUNDAMENTAL MEASUREMENT**

All value claims must conform to fundamental measurement standards; this means that the claim submitted must have ratio measurement properties with a true zero and invariance of comparisons: *All value claims should meet ratio measurement properties.*

4. **SUBMITTING SINGLE ATTRIBUTE CLAIMS**

Following the standards of measurement of the physical science, all value claims should be for a single attribute whether this is for clinical, outcomes, PROs, QoL or resource utilization: *value claims must be for single attributes defined by a ratio scale.*

5. **SUBMITTING DISEASE SPECIFIC CLAIMS**

As the patient (or caregiver) is the presumed beneficiary of therapy intervention, value claims to support that intervention must be *specific to a target patient population within a disease area.*

6. **REPORTING VALUE CLAIM EVALUATIONS**

Value claims must, in the case of formulary submissions, be evaluated and reported to the formulary committee or other health system decision makers in a reasonable or meaningful time frame: *Value claims must be reported in a meaningful timeframe.*

ABANDONING ICER

ICER evidence report simulation modeling and value claims fail all of the standards detailed above. The failure is complete; there is no way the ICER modeling framework can be salvaged. Health technology assessment has relied for far too long on a consensus that creating evidence through assumption driven lifetime models is acceptable. Health care decision should not be based on assumptions and claims that can never be empirically evaluated. The temptation to invent evidence must be rejected.

The obvious point is that there can be any number of model simulations; each driven by its own set of assumptions [4]. If the claims are non-evaluable we have no basis on which to judge one set of claims from another. All we can do is challenge assumptions or, as ICER has done, revisit prior assumptions with real world data some years after product launch and produce a new set of pricing and access recommendations. A singularly worthless exercise.

NEXT GENERATION QUALITY OF LIFE

Rejecting invented evidence also means rejecting ordinal multiattribute preference scores and the QALY. Both are well past their use by date; indeed, if they ever had one in the first place [5]. Fortunately, given the importance attached to value claims for QoL in formulary decisions it is reassuring to know that we have next generation measures for QoL suitable for clinical trials and observational studies that meet all the required standards. These are patient centric , disease specific measures that avoid community preference for health states, and their unfortunate eugenic implications, with ratio rather than ordinal properties.

Avoiding community preferences for health states defined in terms of a bundle of symptoms and functions, does not mean that the next generation measures ignore clinical symptoms and functional status. The potential contribution of these attributes is seen through the lens of the patient (or caregiver) as elements in a broader holistic framework. As the patient (or caregiver) is the ultimate beneficiary of a therapy intervention the value claim focuses on the need of the patient and the extent to which that need is fulfilled. It is the benefit a patient derives from an intervention specific to a disease state defined in the patient's own terms.

Patient focused QoL measures are not new; they have just been ignored in favor of ordinal multiattribute preference measures [6]. Developed over the past 40 years for specific chronic disease states there are now some 30 disease states covered (including: atopic dermatitis, psoriasis, growth hormone deficiency, Crohn's disease, depression, asthma, COPD, sickle cell disease, herpes, ulcerative colitis). These various measures are based on a coherent outcome model. They determine the extent to which respondents can meet their fundamental human needs. Items or statements are presented (with a binary True/Not true response) derived directly from relevant patients (and caregivers) and provide data on the value these groups derive from alternative interventions. This ability is clearly related to the symptoms and functional limitations they experience. However, in contrast to clinician

determined HRQoL quality of life measures such as the EQ-5D, these new measures generate a basis for a single index of patient value or QoL rather than adding together (inappropriately) a basket of clinical outcomes defined as ordinal scales.

As disease specific measures they identify the overall impact of living with a particular disease from the patient's perspective. This provides the framework for evaluating the extent to which patient (or caregiver) needs are met with competing therapy interventions. The items selected for each instrument are based upon intensive interviews with patients and an extended process of item selection through the application of Rasch Measurement Theory [7]. Items finally selected are ranked in terms of difficulty of a need being met and the ability of the respondent to meet that need expressed in probabilistic terms. The number of items selected is relatively small, typically in the range 25-30. The instrument can be completed in 4 or 5 minutes.

This single index of patient value is transformed to a bounded ratio scale that is unique to each instrument [8]. This creates the Need-QOL (or N-QOL) measure, which is robust and accurate, meeting all the required standards detailed above. As the N-QOL is on a bounded ratio scale in the range 0 =no needs are met to 1 = all needs are met It can be used to create need-based quality of life claims by multiplying time in a disease stage by the N-QOL score to create the N-QAL. By design, negative values are impossible. Scores for different instruments across disease states can be compared.

OVERVIEW

The advent of the disease specific N-QOL means the end of multiattribute ordinal preference scores and the impossible QALY. This provides an assured basis for value claims that represent he need of patients (and caregivers) and a measure of the extent to which that need is met. The key development that has made this possible is the ability, recently developed, to transform single index of patient value from these instrument to a bounded ratio scale with all necessary properties to evaluate need and its determinants as well as robust and accurate measures of therapy response.

The next step, given the number of instruments already developed, is to initiate a research program to evaluate need in these diverse disease areas, supported by trials and observational studies to create value claims for therapy interventions. There is no longer any need to invent evidence for non-evaluable QALY claims..

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