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VALE PHARMACOECONOMICS: A PROVISIONAL OBITUARY

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The term vale, a less final term for death, coming from the Latin for farewell, is used to announce the passing of a person. In this case the term is used to announce the passing of a sub-discipline in health economics which has dominated health technology assessment for over 30 years: pharmacoeconomics. The death is not widely appreciated or, indeed, anticipated, yet like the more prescient major newspapers where it is common practice draft obituaries ahead of the persons' actual demise, a 'draft' obituary for pharmacoeconomics is in order. When consciousness ceases, the obituary only needs a few tweaks to render it apposite for a timely publication.

Vale Pharmacoeconomics: A Provisional Obituary

If there is a leitmotif that has driven pharmacoeconomics, it is that if evidence to support value claims for therapy interventions is absent or only limited, then practice demands the evidence be invented as approximate information. Decisions can be successfully based on claims that lack the standards of normal science; they do not have to be credible, evaluable and replicable. Pharmacoeconomics, defined by Wikipedia as *the scientific discipline that compares the value of one pharmaceutical drug or drug therapy to another* thus stands out, from the early 1990s, in occupying the unique position of rejecting standards in normal science that have been in place since the 17th century. Hypothesis testing was rejected in favor of approximate information. It was so much easier to invent evidence, typically through lifetime assumption driven simulations, than the more tiresome task of proposing a research program to meet evidence gaps; it was also more profitable from a consulting perspective.

The pharmacoeconomics meme, the embrace of a belief system that denied common sense in claiming a scientific status, was further supported by a denial, or at best ignorance, of the axioms of fundamental evidence. The critical, if not fundamental error, was to rely upon the quality adjusted life year (QALY) as the gold standard, single metric to lay the foundations for comparative cost-effectiveness claims. The failure of the QALY was laid down in the 1980s with the commitment to generating multiattribute generic preference scores. None of the developers apparently paid any attention to the axioms of fundamental evidence. If you want to multiply estimated time spent in a disease state by a preference score to give a QALY equivalent, then the preference score had to relate to a single attribute with bounded ratio properties, defined by a true zero (death) and a capped perfect health art unity. This was never achieved because no one recognized this as the fundamental requirement to create QALYs. The consequence was obvious: claims for incremental cost per QALY and cost-per-QALY thresholds were mathematically impossible.

But the ignorance of fundamental evidence had more to offer. If value claims are to be empirically evaluable they must relate to a single attribute; a ratio scale. This has been the standard in the physical sciences for 350 years. The generic preference scores are based on a composite basket of disease are symptoms. The elements are not defined in single attribute ratio terms; they cannot be amalgamated. In consequence they lack dimensional homogeneity and construct validity. They are only ordinal scores.

It is unique in both the physical and social sciences to find dedication and belief in a thoroughly discredited analytical framework held by hundreds if not thousands of followers. Perhaps the only challenger would be the unwisely held and applied pseudoscience of eugenics; to which it can be argued that the imaginary QALY as successor has a key role in the denial of care to target patient groups.

Pharmacoeconomics experienced a lingering and acrimonious death. No paradigm shift is easy, but this one was particularly acrimonious when it became to dawn on practitioners that the initial decision by academic thought leaders, particularly in the United Kingdom, that the analytical status of assumption driven simulation modelling and the failure to subscribe to the standards of normal science, notably the axioms of fundamental measurement, doomed approximate information from the start. Most galling of all was the recognition that red flags had been raised but ignored. Whether by ignorance or design, the paradigm was promoted by those who should have known better. Perhaps the most shameful neglect was in measurement theory and the failure to consider, or even be aware of, Rasch Measurement Theory which had emerged in the 1960s and was widely acknowledged by measurement theorists. Added to this was the sublime belief in assumption driven claims. Again for thought leaders this represented a failure to recognoze Hume's problem and the failure of logical positivism. No assumption driven model stretching decades into the future could ever claim a unique status. This was the final nail in the pharmacoeconomics coffin: the approximate information paradigm yields a potential infinity of alternative imaginary value claims.

As could be imagined, the realization that for over 30 years formulary committees, health system decision makers had been gulled into accepting claims for pricing and access to care by an analytical framework that was manifestly deficient, was a shock and a source of embarrassment as claims based on the discredited modeling had been taken a face value. Even more of a shock was the recognition that blanket claims for cost-effectiveness made no sense as they attempted to create a single metric for benefits and costs that defied not just common sense but any semblance of analytical sense. In the United States there were a number of paradigm casualties. Pre-eminent among these was the Institute for Clinical and Economic Review (ICER) who maintained to the end, without any semblance of proof, that ordinal preference scales were actually ratio scales in disguise. Joining ICER, was the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) who had been the leading advocate for approximate information and, last but not least, a number of specialist academic research centers who had tied themselves to ICER and income for inventing evidence.

The psychological ripples from the demise of approximate information has been felt worldwide. Instruments such as the multiattribute EQ-5D-3L/5L which had been central to thousands of peer reviewed papers, which had featured in thousands of CVs were now seen as millstones, with further

damage from the growing awareness that the majority of disease specific patient reported outcomes (PRO) instruments also failed to meet the required measurement standards; they only produced ordinal scores. This was the last straw. Perhaps one could live with disease specific PRO claims, but to be told that they were equally deficient in measurement theory terms was too much. Accepted belief in the technology assessment meme was finally shattered, the QALY disappeared.

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