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VALUE IN HEALTH

Experimental and Observational Data and Formulary Listing

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Introduction

The Regence Group is a Blue Cross, Blue Shield plan in the Pacific Northwest that covers approximately two and a half million people resident in the states of Washington, Oregon, Idaho, and Utah. The Pharmacy Department at Regence is responsible for reviewing all drugs that are ultimately placed on their formulary and also for drug policy. The evolution of the use of medication reviews in managed care plans, how evidence is used to make formulary decisions, and the role of the Pharmacy and Therapeutics Committee in the decision-making process, are discussed.

Evolution of Medication Reviews

Medication reviews of evidence that inform formulary decision-making have been utilized by health insurance organizations in the United States for many years. Approaches to conducting these types of reviews have evolved over time from manual methods of assessing formulary kits and abstracts of some published literature, to the application of sophisticated electronic processes that facilitate the processing of huge amounts of information and lead to a much more comprehensive assessment of pertinent information (Fig. 1). Notably, The Regence Group was instrumental in the early development of the Academy of Managed Care Pharmacy dossier, a medical data source that is currently widely used in the United States. Other tools and sources of information include evidence tables, pharmacoeconomic modeling, Food and Drug Administration (FDA) docket material, primary and secondary literature, and practice guidelines from nationally recognized agencies. At The Regence Group, we are now at the stage where best practice is not only having evidence, but is also being consistent with how that evidence is used. As such, the approach we take is to formulate the key research questions in the context of the goals of a particular analysis and then apply a reproducible, systematic method comprising a critical appraisal framework that is transparent to the general public. Indeed, with due regard to transparency, all of the information that we evaluate for formulary decisions is readily available on RegenceRx.com [1].

Although drug and technology assessments are continually being undertaken by multiple well-funded and high-quality agencies that provide access directly to relevant information; such as the Cochrane Library [2], National Institute for Health and Clinical Excellence [3], Clinical Evidence [4], Agency for Healthcare Research and Quality [5], The Canadian Agency for Drug's and Technologies in Health [6] and the FDA [7], our assessment process agenda is not necessarily aligned with the timing of publication. This is partly because of the way information is used in our appraisal process and partly because of time pressures for producing formulary decisions within the US health-care environment.

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Evidence-Based Medicine Decision-Making

At The Regence Group, our best practice framework for evidence-based medicine decision-making comprises systematic evaluation, study data audit, critically appraising the evidence, and compilation of best information for informing formulary decisions in the form of a drug monograph. The systematic evaluation starts with a predefined search strategy that comprehensively gathers information in the form of randomized controlled trials, meta-analyses, systematic reviews, and observational studies about relevant end points and populations. As mentioned previously, the sources for this are myriad and can lead to collections of hundreds of publications (Fig. 2). Critical appraisal of the studies is done using a modification of the Delfini Group's process (http://www.delfini.org/—March 21, 2010) which typically reduces the number of publications that are deemed reliable to, on average, about 15%, and upon which the formulary considerations are made.

As is the case with many other managed care plans, we simplify the information selected by the critical appraisal of the evidence into categories of "inferior value," "equivalent value," and "superior value." Inferior value typically means that a product may have a lesser clinical benefit than existing options, or there is some sort of a safety issue that suggests the product may not bring any clinical benefit and, in fact, may bring harms to the patient population. Equivalent value, which comprises about 85% of the evidence, refers to drugs that, unless there are significantly different clinical properties, are considered to be not very different from existing therapies; i.e., there are already multiple similar drugs of the same class with a similar mechanism of action. The last category, superior value, is reserved for products that may indeed bring additional clinical benefit to the armamentarium of existing products.

Establishing a Systematic Review Process

The Consolidated Standards of Reporting Trials statement [8] details 22 descriptions of informational elements that are important in determining whether a study provides value to your assessment. Using this as a template, we create a checklist for each study that is identified by our search strategy. We then apply a validity and usability grading scale based on that of the Delfini Group [9] (Fig. 3). According to this scale, Grade A is a straightforward designation of utility; Grade B encompasses a high and a low category accommodating the fact that the evidence may be

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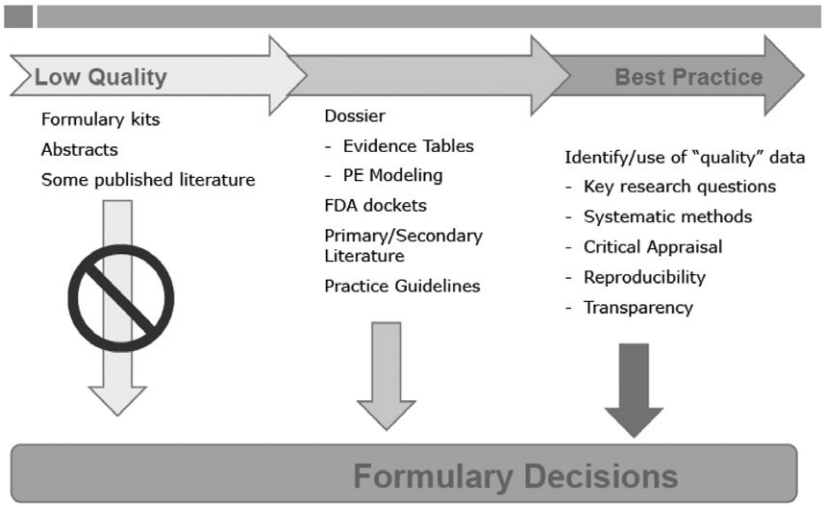

Figure 1 Evolution of medication reviews.

potentially strong and therefore might be sufficient in making useful health-care decisions. Then there are Grades U and Grade X that encompass uncertainty and lack of utility; information in these grades is typically not considered by the Pharmacy and Therapeutics Committee. In addition to assigning a grade to the evidence, for added transparency, we also prepare a critique that summarizes our findings based on the critical literature review for each of the studies. This will have the salient points for the physicians on the committee to use to decide whether or not they will consider the evidence in making the ultimate formulary decision.

Reasons for Excluding Data

There are many reasons why studies end up being considered unreliable sources of evidence:

- lack of transparency of methodologies including randomization, allocation, and blinding methods;
- large numbers lost to follow-up;
- problematic choices of outcomes rendering the data meaningless to the population of a managed care organization;
- lack of intent to treat analysis;
- nonsignificant findings from underpowered studies;
- post hoc analyses

By way of example, if we consider 24 randomized controlled trials, including a total of approximately 8000 patients, that examined the efficacy of a new medication for the treatment of seizures, nerve pain, fibromyalgia and anxiety, we find that the reported study conclusions are that the drug is effective for treating these conditions compared to placebo. Nevertheless, when we subject these trials to our critical appraisal process, we produce somewhat different conclusions (Fig. 4). Indeed, on assessing the quality of the data it appears there is only potentially useful information for this particular drug from one trial. So, our conclusions are somewhat different from the study authors in that although we did find evidence of treatment value

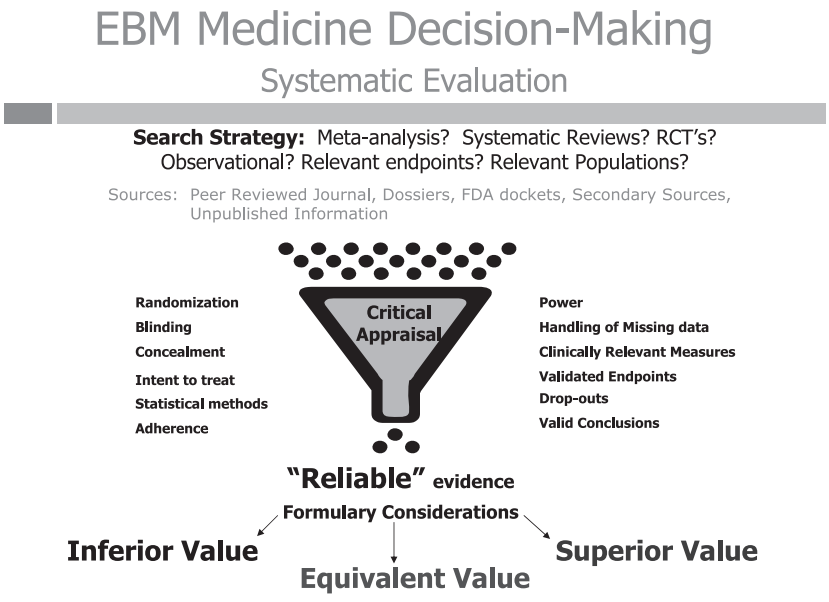

Figure 2 Systematic evaluation for evidence-based decision-making in medicine.