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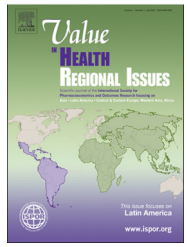

Considering Multicriteria Decision Analysis (MCDA) Simple Scoring as an Evidence-Based HTA Methodology for Evaluating Off-Patent Pharmaceuticals (OPPs) in Emerging Markets

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ABSTRACT

Off-patent pharmaceuticals (OPPs) represent more than 60% of the pharmaceutical market in many emerging countries, where they are frequently evaluated primarily on cost rather than with health technology assessment. OPPs are assumed to be identical to the originators. Branded and unbranded generic versions can, however, vary from the originator in active pharmaceutical ingredients, dosage, consistency formulation, excipients, manufacturing processes, and distribution, for example. These variables can alter the efficacy and safety of the product, negatively impacting both the anticipated cost savings and the population's health. In addition, many health care systems lack the resources or expertise to evaluate such products, and current assessment methods can be complex and difficult to adapt to a health system's needs. Multicriteria decision analysis (MCDA) simple scoring is an evidence-based health technology assessment methodology for evaluating OPPs, especially in emerging countries in which resources are limited but decision makers still must balance affordability with factors such as drug safety, level interchangeability, manufacturing site and active pharmaceutical ingredient quality, supply track record, and real-life outcomes. MCDA simple scoring can be applied to pharmaceutical pricing, reimbursement, formulary listing, and drug procurement. In November 2015, a workshop was held at the International Society for Pharmacoeconomics and Outcomes Research Annual Meeting in Milan to refine and prioritize criteria that can be used in MCDA simple scoring for OPPs, resulting in an example MCDA process and 22 prioritized criteria that health care systems in emerging countries can easily adapt to their own decision-making processes.

Keywords: emerging markets, generic pharmaceuticals, health technology assessment, HTA, MCDA, MCDA simple scoring, multicriteria decision analysis, off-patent pharmaceuticals.

Introduction

Delivering effective, universal, and efficient health care is an important policy goal in every country in the world, whether that country is developed or emerging. The fundamental difference between emerging markets and developed markets is a matter of implementation of good manufacturing practice (GMP) standards and bioequivalence. In developed markets, GMP standards have been fully implemented in parallel with the acceptance of bioequivalence, where a ±20% variance is accepted as a standard definition of generic products. Nevertheless, most emerging countries do not yet fully implement bioequivalence or even pharmaceutical equivalence, in which two products have the same active ingredient at the same dose. Thus, different policies for health technology assessment (HTA) need to be considered to make value-based decisions in generic purchasing. This article looks at the current need for such assessment and the use of multicriteria decision analysis (MCDA) simple scoring as a potential solution.

Because many emerging countries are heading toward universal coverage, quality and affordable off-patent pharmaceuticals (OPPs), which include international nonproprietary name generics, branded generics, and off-patent originators, have a critical role in maximizing the value to the public health system through improved reliability. At the same time, manufacturers who supply drugs of increased quality and quantity should be considered for incrementally similar increased reimbursement. Especially in emerging countries, a value-based HTA for patients treated by OPPs can significantly contribute to improved population health outcomes. Many health systems implement HTA to

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evaluate patented pharmaceuticals; nevertheless, HTA methodology is seldom applied to OPPs. This lack of HTA methodology for OPPs becomes especially concerning in emerging countries, in which OPPs are used to treat most patients (more than 60%) [1].

Historically, the fundamental assumption of lowest-price policy decisions for OPPs in emerging countries is based on the premise that all OPPs are the same. Given the critical role OPPs play in providing and retaining coverage for populations in emerging countries, this reliance on the assumption, although excluding other criteria such as product quality (i.e., GMP), stringent bioequivalent criteria, value in use (persistence and adherence), clinical outcomes, and additional nondrug costs, may prove to be an inadequate method for providing adequate health care [2,3]. Therefore, the International Outcomes Research Board, a group of academia and industry experts, has undertaken an initiative to develop an evidence-based HTA methodology for off-patent products and has conducted significant work in this area at both the theoretical and the practical implementation level in emerging countries. From their work, MCDA simple scoring is emerging as a useful approach that can be applied to pharmaceutical pricing, reimbursement, formulary listing, and drug procurement. This method can be adapted easily to suit specific characteristics of individual health care systems, of particular interest to those searching for a sound methodology to evaluate OPPs. In November 2015, a workshop was held at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Annual Meeting in Milan to refine and prioritize criteria that can be used in MCDA simple scoring for OPPs, resulting in an example MCDA process and tool that health care systems in emerging countries can adapt to their own decision-making processes.

Why Lowest-Price Policy Objectives Fall Short

In lowest-price–driven policies, the assumption that "OPPs are the same" is quite common, especially in developing economies. The off-patent originator has already gone through extensive testing and assessment, and it is presumed that the generic version of that medication will provide the same benefit for lower cost [3–5]. In a health care system that has limited resources but a desire to provide vital medication to as much of its population as it can, basing decisions on drug acquisition cost can seem like a practical way to get as much "bang for the buck" as possible.

Unfortunately, the fundamental presumption behind this thinking—that the branded and unbranded generic versions are identical to the originator in active pharmaceutical ingredients (APIs), dosage, consistency formulation, excipients, manufacturing processes, and distribution, for example—is not always the case. These additional variables can greatly affect the efficacy and safety of the product, negatively impacting not just the anticipated cost savings but also the health of the country's population. Table 1 presents the current status of GMP, pharmaceutical equivalence, and bioequivalence categories considered in generic policy decisions across 14 different emerging countries.

Even when pharmaceutical equivalence and bioequivalence have been achieved, evidence for their therapeutic evidence may be limited [3,5], and few emerging countries explicitly require bioequivalence and bioavailability studies [6]. In addition, there is a range of bioequivalence, and so one generic drug may actually be closer in bioequivalence to the originator than a second generic drug [3], but if cost is the only criterion considered, the drug that is the "closer match" to the original may be denied. Another factor that may affect the efficacy and safety of generic medications is the type of excipients used, which, although considered inactive substances with no effect on drug action, can sometimes have an effect on drug stability, adverse reactions, or how the active drug is dissolved and absorbed into the body's systems [4,7]. Biosimilars may have minor structural differences that may be connected to immunogenicity-related adverse effects [4]. A recent publication further discussed the challenges associated with various definitions around generic pharmaceuticals [6].

Manufacturing processes can introduce significant variables within OPPs. Investigations into pharmaceutical manufacturing processes across the globe reveal ingredient inconsistencies, sanitation and cross-contamination concerns, misrepresentations, poor storage conditions, and other potentially serious problems with the manufacture and delivery of branded/unbranded generic drugs [8]. Recent recalls in the United States involved issues with container closure systems, foreign particulate matter within injectable medications, and glass delamination within containers/closure systems, as well as contamination issues from compounding pharmacies [4,9,10]. Additional problems include the inability to verify a product's or ingredient's source and to confirm proper and sanitary handling throughout the chain of custody [11,12]. These problems are especially exacerbated during drug shortages, when manufacturers and suppliers must quickly seek alternatives to fulfill demand.

Clearly, if cost is the highest priority when making decisions on drug policy, the health care system in question may be opening itself to other concerns that could be detrimental to its overall goals of widespread health care at reasonable cost. This is precisely why HTA is used in developing countries to assess the value of OPPs. HTA allows decision makers to evaluate a drug's value on more criteria than just cost. HTA is, however, seldom used for OPPs, and therefore seldom used by policymakers in emerging countries, where OPPs make up the bulk of their treatment base. Even if HTA methods can help policymakers balance drug acquisition costs with benefits, most emerging countries have limited experience in using such methods.

Could MCDA Simple Scoring Be a Solution?

MCDA is a decision-making process in which a set of criteria are defined, ranked in terms of relevance and importance, and evaluated consistently. After a set of criteria have been defined and ranked by stakeholders and decision makers, each alternative is evaluated against the same set of criteria, creating an assessment of value for each alternative. Because it emphasizes relevant criteria and provides a consistent decision basis, MCDA increases the consistency, transparency, and legitimacy of health care decisions over other methods, which are often overly simplified, created ad hoc, focused on only a single facet or goal of health care such as cost-effectiveness, or swayed by political or special-interest motives [13–15]. The implementation of MCDA in health care has recently been growing, with the number of publications addressing MCDA usage in health care decision making ballooning from about a dozen in 2000 to more than 60 in 2011 [16].

MCDA benefits decision makers by providing a consistent framework for decisions, encouraging the inclusion of various stakeholders from different perspectives, presenting data in a consistent and digestible format, and allowing for the comparison of trade-offs between alternatives. MCDA benefits manufacturers by pointing out data gaps in manufacturers' research, helping manufacturers simplify and focus communications with decision makers on relevant information, and establishing a common language for discussions with policymakers, regulators, and other interested stakeholders. Because of these demonstrable benefits, decision makers indicate a positive attitude toward MCDA's potential to improve decision making [14].