Medication Formularies in the Personalized Medicine Environment

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A medication formulary is a list of "approved" drugs, usually indexed by class or by indication. Generally, formularies are used by health plans and pharmacy benefits managers, and are assumed to include drugs which provide the greatest overall value for all stakeholders in patient care.

Historically, formulary proponents have argued that participants simply did not need the variety of available FDA-approved medications—that every medication in a drug class was equi-therapeutic, and the cost of allowing all drug options would not justify the health benefits.

In 2016, however, these arguments are weak. Today, we know a one-size-fits-all approach to pharmacotherapy is not appropriate for all patients and that reducing drug spend does not always reduce *overall* healthcare costs.

Introduction and History

Medication formularies have been popular since the early 1970s. Started in hospitals by Pharmacy and Therapeutic (P&T) committees, formularies were intended to control costs and streamline inventory management by limiting the array of medications prescribed within each therapeutic class. The P&T committee would examine issues such as: is it necessary to have a dozen different cephalosporin antibiotics in the hospital pharmacy's inventory *or* can the entire spectrum of bacteria sensitivity be covered with *only four* cephalosporin products? Thus, the P&T committee, led by clinicians and pharmacists (not administrators), would examine the literature and select a few cephalosporin products for the hospital by using clinical and pharmacoeconomic criteria. This effort demonstrated to be cost-effective in reducing inventory burden in hospital pharmacies.

With the advent of Pharmacy Benefit Managers (PBMs) in the early 1980s, the same formulary approach was propagated on a much larger scale, but for a different purpose. Then and now, formularies were used to limit the number of medications in each class, thereby strengthening PBM negotiating power with the pharmaceutical manufacturers for best pricing based upon volume incentives. This practice had the opposite effect on pharmacies. Because each PBM developed its own list of 'preferred drugs' for each therapeutic class, community pharmacies had to (try to) stock every medication in every class, to cover every PBM's formulary.

Over time, PBM-manufacturer pricing negotiations devolved to post-invoice rebates provided by the drug companies directly to the PBMs. Recent legislation has prompted PBMs to share with customers the extent of these rebates. Some PBMs have become completely transparent, showing customers the precise rebate detail from each drug company. Other PBMs obscure this information, blurring the calculations regarding how rebates are shared.

Continued Challenges with the Rebate System

There are two germane conceptual and even ethical issues to consider. First, from an economic perspective, market distortion resultant from PBM business models has led to neither reductions in medication inventory (i.e., carrying-cost savings) nor overall medication cost contraction. In fact, the cost of

drugs in the US continues to trend dramatically upward. Perhaps if all rebates garnered by the PBMs were fully transparent, this cost escalation would be less drastic.

Second, the long-needed government-catalyzed transformation to personalized medicine is contrary to the formulary-approach to care. Within a 'personalized medicine' construct, medication selection *first* considers which medication best fits the patient's existing medication regimen, drug history, allergies, genotype, etc. However, today, the integrity of the decision-making process is compromised when a formulary only includes one or two of an entire class of drugs – the one or two with the best rebate-incentives. Thus, clinicians must abandon their efforts toward personalized, patient-specific medication recommendations and consent to prescribing a possibly sub-optimal treatment.

Relevance Today

Transformation from the historic formulaic approach to a personal approach is long-needed. The incidence of Adverse Drug Events (ADEs) in the U.S. is chilling. With 4.3 billion prescriptions filled in the United States in 2014[1], medication treatment is the most common medical intervention, and its imprecise use represents the fourth leading cause of death and contributes to an estimated 45 to 50 million adverse drug events (ADEs) annually[2,3,4], with 2.5 to 4.0 million of those ADEs considered serious, disabling or fatal[5,6]. If the status quo is perpetuated, these tragedies will continue.

Pharmacists know that each medication within a drug class is different (by definition and science), and that formulary committees must cease assuming that pharmaceutical products with different active ingredients are interchangeable. There is sufficient ADE literature to attest to the need for a person-by-person approach to medication selection. We *ought not* base our prescribing decisions on the economics of monetary rebates; we *ought* to base our prescribing decisions on what is the very best targeted medication for each patient, using personalized science. Certainly, that is the approach each of us would prefer for ourselves and our families. A one-size-fits-all approach to pharmacotherapy is intolerable in a personalized healthcare environment.

Pharmacists are on the front line of the war against ADEs.

We are calling for a migration from population-based formularies to a personalized formularies, based solely on the characteristics of each patient. These personalized formularies would not penalize a patient with "prior authorizations" and higher copays for the medications that are most appropriate for him/her. These personalized formularies would be dynamic, guiding prescribers with person-specific rules: for patients without the functional gene/enzyme to metabolize* six of the seven statins[7], the seventh statin would be preferred (to avoid the muscle cramping that otherwise occurs); and for patients whose medication profiles increase risk for cardiac arrhythmia, drugs with the least risk for inducing cardiac arrhythmia would be preferred (because additional drugs with the same heart risk which could trigger the arrhythmia).

Without such a change, medication-related problems will continue to be a leading cause

* Metabolize, in this instance, means that the person's gene/enzyme, which normally would transform the drug to become water-soluble and permit it to be excreted by the kidneys, is compromised.

of death. A fresh approach that personalizes and optimizes medication regimens, focuses on outcomes, and does NOT further enable PBMs to decide which medications people should be taking based on pharmaceutical manufacturers' rebates will help our society finally make a break-through on enhancing pharmacotherapy quality in healthcare.

References

1. Murray Aitken et al., "Medicine Use and Spending Shifts: A Review of the Use of Medicines in the U.S. in 2014," IMS Institute for Healthcare Informatics, April 2015.

2. Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA 2013;309:657-9.

3. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA. 1998;279:1200-5.

4. Office of Disease Prevention and Health Promotion, Department of Health and Human Services. National action plan for adverse drug event prevention. Available at URL: http://health.gov/hai/ade.asp.

5. Budnitz DS, Pollock DA, Weidenbach KN, et al. National surveillance of emergency department visits for outpatient adverse drug events. JAMA 2006;296:1858-66.

6. Budnitz DS, Lovegrove MC, Shehab N, et al. Emergency hospitalizations for adverse drug events in older Americans. N Engl J Med 2011;365:2002-12.

7. Ramsey LB, Johnson SG, Caudle KE, et al. The Clinical Pharmacogenetics Implementation Consortium guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update. Clin Pharmacol Ther2014;96:423-8.