Cardiometabolic Risk Factors: Novel Approaches Can Improve Patient Outcomes

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The outlook for cardiometabolic health remains suboptimal in 2013, despite considerable awareness of the health consequences and the associated costs of cardiometabolic risk factors, including cardiovascular disease, diabetes, dyslipidemia, hypertension, and obesity. There is not much that has not been said about these top killers of Americans. Yet despite all the research and the published literature, new treatments, and well-documented high morbidity and mortality associated with heart disease, type 2 diabetes, and obesity, the incidence of each of these conditions continues to climb.

As an example, in 2011, 16.3 million Americans had chronic heart disease, 76.4 million had hypertension, 5.7 million had heart failure, and 7 million had a stroke—all directly increasing the mortality risk from heart disease. In 2007, approximately 25.8 million Americans had diabetes, and many millions more had prediabetes. Unless new approaches to diabetes therapy become available in the coming years, it is projected that approximately 21% of the American population will have type 2 diabetes by 2050.

Heart disease remains the leading killer of Americans, and even with the many antihyperglycemic drug classes, less than 50% of patients with diabetes reach the American Diabetes Association’s glycemic goal of hemoglobin A1c <7%. Why has the transition from epidemiologic research and well-conducted clinical trials into standards of care apparently been so ineffective? Are the therapeutic options inadequately perceived in terms of efficacy, safety, cost or convenience, even in the presence of data that would suggest otherwise? As with so many other facets of medicine, potential contributors are diverse, and remediation requires a concerted effort on the part of many stakeholders to isolate, and then address each of the mediating variables.

For example, considering the serious health implications of obesity, it is surprising that it took until 2013 for the American Medical Association to classify it as a disease, possibly because obesity was mainly assumed to be the result of lifestyle or behavior. It may take yet another generation of personalized medicine research to fully identify biologically based risk factors for development of obesity and cardiometabolic complications, beyond those which already can be deduced in diabetes, and as has already begun in heart disease. As in so many other conditions, it may be the interaction of genetic, sociodemographic, and other characteristics that yielded the highest specificity and sensitivity in this regard.

A number of recent developments are noteworthy in their ability to disentangle these issues. Hulsmans and Holvoet recently noted that not all obese patients are at the same risk of developing cardiometabolic complications. Therefore, they say, “there is an urgent need for novel biomarkers for early identification of obese patients at high risk. Possible candidate biomarkers are microRNAs, which are highly conserved non-coding RNA molecules of approximately 22 nucleotides that exert post-transcriptional effects on gene expression.” This is a promising start that will enable more effective targeting of subgroups of obese patients with efficient risk-mitigation strategies.

Obviously, the costs associated with the management of illnesses linked to the presence of cardiometabolic risk factors continue to rise in tandem. In 2007, the estimated total US cost for diabetes was $174 billion. In 2010, the direct cost for cardiovascular disease was $272.5 billion, which is expected to reach $818.1 billion by 2030. Similarly, the total cost related to obesity is projected to reach $861 billion to $957 billion by 2030. These numbers alone are sufficient to drive home the link between clinical and economic priorities.

The articles in this theme issue of American Health & Drug Benefits provide significant contributions to the literature and highlight for all healthcare stakeholders the importance of focusing on cardiometabolic risk factors.

Spinler and colleagues have conducted the first non-claims-based analysis of data from the national cardiovascular registry PINNACLE, to identify Medicare beneficiaries with multiple chronic cardiovascular conditions who are eligible for medication therapy management (MTM), a modality that has been shown to improve outcomes and reduce costs in patients with chronic diseases. The authors point out that many eligible patients are not participating in MTM programs, in large part because of a lack of knowledge of these programs’ benefits. These data therefore not only support tailored therapy for Medicare beneficiaries at risk, but also imply the need for an effective communication program within the subpopulation, a theme that is apparent in other articles in this issue. Spinler and colleagues charge providers to explain to patients the benefits of MTM programs and encourage their participation. They call on providers to educate patients on why enrolling in such programs can help to improve their
health outcomes and reduce overall costs. Tzeel aptly notes in his perspective, “as the authors so eloquently state, ‘we believe that promoting the utilization of such programs to eligible patients should be the responsibility of all healthcare providers within the framework of care advocated by the ACC within the framework of the patient-centered medical home for CV care.’”

Also in this issue, Banerji and Dunn elucidate the increasing prevalence of diabetes and the staggering economic implications, focusing their analysis of the literature on a lack of medication adherence among patients with type 2 diabetes as one of the principal culprits for the dire state of this disease. Banerji and Dunn call for innovation in drug therapies that will focus on patient convenience and ease of use to enhance adherence, suggesting that these are crucial to improving outcomes and reducing the morbidity and mortality rates far beyond the trends seen with currently available medications. Their article serves to emphasize that issues of cost and convenience are as important as efficacy and safety in promoting adherence. They provide some hope in their review of new treatment approaches in the current pipeline that may offer new solutions to lagging adherence as well. As Bourret observes, “Banerji and Dunn aptly make the case for a call to action for aggressive change and innovation in the management of patients with type 2 diabetes and the development of new pharmaceuticals that reduce cardiovascular risk, result in less weight gain, and improve adherence and health outcomes.” The status quo, they suggest, is no longer acceptable.

And in a one-of-its-kind presentation, Hawkins-Taylor and Carlson resurrect the events surrounding the case of BiDil, noting the need to consider sociocultural parameters, including race and ethnicity, in drug development. The US Food and Drug Administration (FDA) approval of this first and only drug specifically indicated for a racial group resulted in a controversy that, the authors show, has implications for the future development of targeted therapies, especially in the age of personalized medicine. In 2005, when BiDil was approved for the treatment of heart failure in African Americans, the potential impediments associated with introducing combination therapy as a unique treatment in a self-identified patient subgroup was not fully appreciated by different stakeholders, although it was mentioned in the FDA’s approval.

As Murphy notes, “In a literature replete with references to personalized medicine tailored to variations in genetics and disease-related phenotypes, the case study presented by Hawkins-Taylor and Carlson…emphasizes the importance of incorporating sociodemographic variables into this definition.” With all the focus on race, the authors emphasize, lost was the main clinical message—the need to manage heart failure with a combination of vasodilator therapies in African Americans. The role of genetics and biology, extracting information from data which would resonate with a demographic minority and their providers, did not factor in within the debate about the utility of this particular therapy, but in the age of personalized medicine, resurrecting this case from its recent past has important implications for drug developers, policymakers, providers, and payers. The lesson, Murphy says, is that “failure to achieve meaningful adoption after approval, despite a methodologically rigorous pedigree, emphasizes the importance of ensuring clinical and commercial stakeholder convergence during, not after, the drug development process.”

Finally, Mahgerefteh and colleagues review the evidence for the 2 new therapies approved by the FDA in mid-2012 for the treatment of obesity, highlighting the current public crisis of obesity and the need for improved therapies. The authors focus on the potential benefits seen in clinical trials with these 2 drugs, with independent and new mechanisms of action, which, in addition to weight reduction, have also been shown to improve blood pressure, blood glucose levels, and lipid levels. As Felicetta says in his perspective, “Time, and real-world data, will tell whether these…medications are indeed able to live up to the promises they offer.”

With the aging of the US population and increasing life expectancy, the toll of heart disease, diabetes, and obesity will reach unsustainable levels that may exceed current projections. This theme issue is a call to action to patients, providers, payers, researchers, drug manufacturers, and policymakers. The challenges are many, and the needs for innovation and change are urgent. ■

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References