Exercise, especially strength training, builds muscle mass, so patients might not see any difference on the scale if they follow his advice to increase physical activity, he said. Instead, Lopez-Jimenez and his patients measure success with a blood pressure cuff, a hemoglobin A1c test, and other tools that assess metabolic function. “I tell these patients the main goal is to improve the metabolic parameters,” he said.

Magkos doesn’t disagree. “Exercise, whether you are metabolically healthy or unhealthy, will improve your metabolic health,” he said. While Magkos and his coauthors asked participants not to change their activity level while losing weight, the researchers did not collect information about physical activity.

When it comes to diet, the quality of calories consumed, not just the quantity, plays a role in reducing the risk of chronic disease and death in MONW individuals, research suggests. An analysis of data from the National Health and Nutrition Examination Survey (NHANES) found an association between a higher-quality diet, such as the DASH diet, and a lower mortality risk among MONW adults during an average follow-up of 18.6 years. The researchers did not find such an association among adults who had a normal BMI and were metabolically healthy. Previous studies assessing the effect of a healthful diet on the risk of chronic disease had focused on individuals whose BMI classified them as obese, the authors noted.

Although their BMIs were normal and, on average, similar, there was a notable difference between the metabolically healthy and metabolically unhealthy individuals, coauthor Anwar Merchant, ScD, MPH, DMD, said. The average waist circumference for the healthy group was 31.8 inches, compared with 34.1 inches for the unhealthy group, said Merchant, an epidemiology and biostatistics professor at the University of South Carolina’s Arnold School of Public Health.

Related research by Merchant and his coauthors suggested that improvements in metabolic health associated with a higher-quality diet are mediated by reductions in abdominal obesity.

Note: Source references are available through embedded hyperlinks in the article text online.
approved by the FDA between 1999 and 2012. They obtained drugs’ QALY gains relative to prevailing treatment options from the research literature, excluding studies with pharmaceutical industry sponsorship to eliminate that source of financial bias. To be conservative, for studies that compared a drug with multiple alternatives, the authors selected the most effective comparator (that is, the one resulting in the highest QALY gain). In total, they analyzed 135 drug-indication pairs, 76 with accelerated approvals, 59 with conventional approvals.

The study found that drug-indication pairs with expedited approvals had higher median QALY gains than those with conventional approvals: 0.182 vs 0.003 QALYS, respectively. Drug-indication pairs in multiple expedited reviews had an even higher median QALY gain of 0.307. These results suggest that the FDA’s expedited drug review programs include drugs that provide greater benefits than those undergoing conventional review. Indeed, to the extent the expedited programs handle drugs for conditions for which there is unmet medical need, relatively larger QALY gains are to be expected.

Limitations

Naturally, the study has some limitations. A major one is that not all drugs could be analyzed, because of lack of QALY data. In total, the sample included only 30% of all FDA-approved drugs in the 1999–2012 study period (57% of approved drugs that underwent expedited approval and 79% of approved drugs that underwent conventional approval were not included in the analysis). It is therefore possible that the results do not generalize to all FDA-approved drugs.

Another significant limitation is that drugs approved with expedited programs are done so based on surrogate end points, as are the studies used to attribute QALY gains. Surrogate end points are usually biomarkers that indicate improved health that can be measured more quickly than the outcomes we care most about, like survival. Basing FDA approval on surrogate end points is controversial because they may not have strong predictive power for the outcomes of interest. For example, a systematic review found that most surrogate end points used in cancer drug trials don’t correlate strongly with survival. Another study found that a majority of cancer drugs approved based on surrogate end points in recent years have unknown or no beneficial survival effects. The extent to which QALY gains based on surrogate end points reflect true QALY gains is uncertain.

QALYs have other, well-known limitations. For instance, they may not fully capture all our preferences for treatments. An extreme manifestation of this point is exhibited by the “rule of rescue,” which is the tendency for people to prefer to expend greater resources to aid patients close to death, even if greater QALY gains could be achieved by using those resources for others.

It is also possible that with more time, safety concerns will arise for drugs with expedited approval. Drugs subject to less FDA scrutiny are more likely to exhibit safety problems, be withdrawn from the market, or carry black box warnings. We should therefore continue to monitor these drugs and update the performance of expedited approval programs as more information is available. Of concern, over the 2009–2013 period, only a minority of drugs with expedited approval had their efficacy tested in a postmarket trial within 3 years. Regardless of one’s view of the quality of FDA review or any particular study of a drug, we should agree that the outcomes of FDA policies in general and of particular drugs with expedited approvals based on surrogate end points warrant additional scrutiny.

Because expedited review programs are intended for drugs that treat serious conditions and address unmet medical needs, accepting greater risk may be reasonable and more consistent with patients’ preferences. However, because many of these drugs also come with high price tags, financed with public funds through Medicare, Medicaid, and other programs, the patients’ point of view is not the only one of relevance. A consideration of cost is also reasonable from the point of view of taxpayers.

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