six primary prevention trials included in the Antithrombotic Trialists' meta-analysis had a predicted risk of a first coronary event above 1% per year, so the results from the available data in these intermediate-risk individuals are not, on their own, reliable.[2]

Four trials involving intermediate-risk individuals are ongoing and might yield more-reliable evidence. In each of these trials of aspirin in the primary prevention of cardiovascular disease, a slightly different strategy has been adopted to identify individuals at intermediate risk. The Aspirin to Reduce Risk of Initial Vascular Events (ARRIVE) study[7] is a large-scale, randomized, double-blind, placebo-controlled trial in which investigators have enrolled over 12,000 men and women with intermediate risk of a first coronary event predicted, using a modification of the Framingham Risk Score, to be about 1.5% per year. Researchers in the Aspirin in Reducing Events in the Elderly (ASPREE) trial[8] are enrolling elderly individuals aged ≥70 years, who are at intermediate risk by virtue of their age alone. In both A Study of Cardiovascular Events in Diabetes (ASCEND)[9] and the Aspirin and Simvastatin Combination for Cardiovascular Events Prevention Trials in Diabetes (ACCEPT-D),[10] individuals with diabetes mellitus but no known vascular disease are, likewise, at intermediate risk. High levels of adherence and follow-up are necessary in all these ongoing trials to provide reliable evidence about the absolute benefits and risks of aspirin for primary prevention in various groups of individuals at intermediate cardiovascular risk.

Until the results of these trials are available, judgments about prescribing long-term aspirin therapy for apparently healthy individuals at intermediate cardiovascular risk should continue to be made on a case-by-case basis, and are best informed by the available meta-analyses of the large-scale individual trials designed *a priori* to test aspirin for primary prevention.[2,3] General guidelines that advocate the routine use of aspirin in all apparently healthy individuals do not seem to be justified. The increasing burden of cardiovascular disease in developed and developing countries underscores the need for the more-widespread use of drug therapies of proven net benefit in the primary prevention of cardiovascular disease, such as statins to lower LDL-cholesterol levels, and various drugs to lower blood pressure.[2]

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THERAPY

Affect and affirmations—a 'basic' approach to promote adherence

William H. Shrank and Niteesh K. Choudhry

Efforts to improve health-care quality and efficiency will fail if patients with chronic disease do not adhere to medications and healthy lifestyles. A novel, psychological approach is to change behavior using 'affect' and 'affirmations'. We explore this strategy's potential, when added to the existing arsenal of interventions, to improve adherence.

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As we strive to identify approaches to improve health-care quality while reducing its cost, we frequently offer incentives to providers to enhance care coordination, reduce variability, and improve efficiency. However, even the most efficient and coordinated health-care delivery system will not meaningfully improve outcomes if patients with chronic disease do not adhere to their prescribed medications and a healthy lifestyle. Efforts to reform the health-care system must, therefore, include a committed effort to increase patient engagement and accountability for their outcomes—a recognition that patients have a central role in managing their chronic disease.

> "...positive reinforcement can be a very potent behavioral motivator"

Health-services researchers are increasingly exploring how best to promote healthy behavior in patients. Some of these interventions address specific barriers by simplifying care, improving patient education, offering reminders, or even reducing financial barriers to either medication use or healthy behavior.[1–3] Alternative strategies have tried to engage patients in new ways—notably by rewarding them, creating social networks, or encouraging them through motivational interviewing.[4,5] These approaches build on psychological and behavioral economics principles that suggest that positive reinforcement can be a very potent behavioral motivator.

These interventions hold promise, but the amount of benefit they provide is often modest. A more-basic approach might be needed—one that motivates patients to manage their chronic conditions using principles from B. F. Skinner and Madison Avenue advertisers. Perhaps we need to find a way to make doing the right thing 'feel good' to patients—in the same way that expensive television commercials persuade consumers to associate certain emotions with their products, or in the way that pharmaceutical manufacturers have distributed small gifts to providers to generate familiarity and loyalty.

Investigators in two studies published in January 2012 employed this technique.[6,7] In both studies, high-risk patients for whom healthy behavior is essential to reduce downstream adverse events and excessive health-care costs were recruited. Peterson and colleagues focused on patients immediately after percutaneous coronary intervention, and attempted to increase physical activity[6]—an important predictor of subsequent events. Ogedegbe and colleagues targeted African–American patients with hypertension and in primary care, and sought to increase adherence to essential medications,[7] also an important predictor of downstream adverse health consequences and costs. In both studies, the researchers aimed fundamentally to change the way that patients felt about their self-management by inducing a positive affect (an improved mental state that follows small positive experiences) and using self-affirmation (which draws on past experiences to make an individual feel proud).

In these two studies, performed by many of the same investigators, patients were randomly allocated to an active comparator arm (intensive patient education) or to an intervention arm (in which patients also received an affective, behavioral intervention). The affective intervention included a workbook chapter focused on the constructs of positive affect and self-affirmation; bimonthly inducement of positive affect and self-affirmation by telephone; and small, unexpected, bimonthly gifts mailed several weeks before follow-up calls. Positive-affect induction consisted of reminding patients to "think about things that make you feel good" and take a moment each day to enjoy positive thoughts.[6,7]

After percutaneous coronary intervention, Peterson and colleagues found a significant increase in the likelihood that patients in the intervention arm met self-reported exercise goals compared with the control group (55% versus 37%; $P=0.007$).[6] With affective intervention, patients experienced nearly double the improvement in kilocalories expended per week at 12 months compared with control patients (602 kcal versus 328 kcal; $P=0.03$).[6] In the population of patients with hypertension, Ogedegbe and colleagues found that the affective intervention increased medication adherence by 6% compared with controls (42% versus 36%; $P=0.049$), although actual blood-pressure control was not improved.[7]

Some people might think that the affective approach is superficial and does not sufficiently address the severity of the clinical picture for patients with heart disease. However, the ends seem to justify the means. If a simple intervention can effectively engage, motivate, and encourage patients to lead healthier lifestyles, then concerns about the nature of the intervention would run counter to efforts to improve public health. The authors did not specify (as they should have) the cost of the intervention, but we can assume that this endeavor was not prohibitively expensive, which adds to the appeal of this approach. Moreover, these studies were not the first to use affect and motivation to promote healthier lifestyles. Motivational interviewing has previously been shown to improve adherence in various clinical conditions by providing education and affirmations to patients.[5,8,9] Efforts to compare motivational interviewing with the affective approaches described here will be helpful to determine best practices.

Changing patient behavior is extremely difficult. Patients do not adhere to activities that they know can improve their health for many reasons, such as the time needed to perform the behavior, the complexity of the behavior, cost, poor understanding, cultural concerns, poor motivation or self-efficacy, or cognitive or physical limitations. As a result, no single intervention is likely to affect all those causes, and even the most-successful interventions often offer only marginal changes in behavior.

Neither of the affect studies 'solved' the problem of nonadherence to healthy lifestyles or appropriate medication use, but both showed great promise. The magnitude of the improvement in exercise rates in the study by Peterson and colleagues was extremely large.[6] In the study by Ogedegbe and colleagues, the 6% improvement in medication adherence,[7] particularly in comparison with an active comparator arm, is consistent with some of the most-effective interventions available to improve adherence.[2] The lack of an improvement in blood-pressure control was surprising considering evidence from the randomized, controlled MI FREEE trial,[10] in which an intervention to eliminate co-payments for effective cardiovascular medications led to similar improvements in adherence to those seen in the study by Ogedegbe and colleagues, and were associated with significant improvements in vascular outcomes.

Nevertheless, an affective-intervention approach seems to hold great promise and could be applied in addition to other approaches to influence patient behavior. As shown in these studies, affective intervention improved behavior above and beyond the benefits from an educational intervention.[6,7] These results suggest that this affective strategy could be offered as one of a menu of interventions to improve medication use and healthy lifestyles. Ultimately, providers should learn to understand the specific barriers to healthy behavior in individual patients, and target the precise intervention that will most-efficiently lead to healthy lifestyles and medication adherence.

Overall, the affective approach tested by Peterson and Ogedegbe seems to be an important way to engage patients and promote medication adherence and healthy lifestyles. The approach attempts to make a very basic, subconscious connection between happy feelings and certain behavior. This approach could represent a low-cost, highly effective way to reduce health-care costs and promote improved patient outcomes. Health-care reformers should continue to look to other disciplines for secrets to improved performance, reduced variability, and lower costs, in the hope of discovering novel strategies to enhance the efficiency of the health-care system.

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VALVULAR DISEASE

Super size me? Annular size and paravalvular leak after TAVR

Michael A. Quail and Andrew M. Taylor

Paravalvular aortic regurgitation (PAR) after transcatheter aortic valve replacement is common and independently associated with increased morbidity and mortality. The determinants of PAR are uncertain, but new data extend our understanding, and a simple practice change in preprocedural imaging could help dramatically to reduce the incidence of this important complication.

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Transcatheter aortic valve replacement (TAVR)[1] has become an established treatment for patients with severe aortic stenosis and prohibitive surgical risk. Preprocedural imaging, typically by echocardiography or CT, to assess the underlying anatomy and determine the appropriate device size and procedural feasibility, has an important role in planning for TAVR.[2] Inappropriate sizing can contribute to complications such as residual transvalvular gradients or paravalvular leak. Paravalvular aortic regurgitation (PAR) is common after TAVR and independently associated with increased morbidity and mortality.[3,4] An association with increasing annular size has previously been shown.[5] Strategies to reduce this common complication are urgently required.

In two timely papers published in February 2012 in the *Journal of the American College of Cardiology*,[6,7] undersized TAVR devices are identified as important contributors to the development of PAR, and 2D transesophageal echocardiography (TEE), which was predominately used to judge TAVR-device size in both studies, is suggested as the culprit. Willson and colleagues assessed the difference between the nominal size of implanted TAVR devices and the preprocedural annulus measurements by CT and TEE.[6] Using receiver-operating characteristic (ROC) analyses, the investigators showed that the magnitude of the difference predicted postprocedural PAR. The area under the ROC curve was greater for mean annulus diameter measured with CT (0.81, 95% CI 0.68–0.88) than with TEE (0.70, 95% CI 0.51–0.88). This analysis suggests two things: first, that the extent of the discrepancy between 'true' annular dimensions and the dimensions of the implanted valve accounts for observed PAR; and second, that this estimation is better performed by CT than TEE. On average, TAVR-device diameter was 2.2 ± 1.2 mm greater than the TEE-assessed annular diameter, and 0.6 ± 1.9 mm larger than the CT-assessed diameter, which implies that the operators intended a bigger TAVR–annulus difference than was actually achieved. On further analysis, the investigators dichotomized patients into those with a TAVR-device diameter ≥1 mm (oversized) or <1 mm (undersized) greater than the CT-measured annulus. The incidence of PAR was 2.2% and 21.4% in patients with an oversized or undersized TAVR device, respectively (OR 9.4, 95% CI 2.15–88.8, $P<0.01$). Patients with the greatest degree of undersizing (that is, an annulus bigger than the prosthetic valve) had the most-severe PAR. The researchers conclude by recommending CT-guided TAVR-device sizing, with at least 1 mm oversizing of the prosthetic valve relative to the CT-measured aortic diameter.

> "...undersized TAVR devices are identified as important contributors to the development of PAR..."

Jilaihawi *et al.* also used ROC analysis to predict PAR by the difference between TAVR-device dimensions and annular measurements by CT and TEE.[7] As in the study by Willson and colleagues, CT had the superior predictive capacity, particularly for maximum annulus diameter (area under the ROC curve 0.82, 95% CI 0.70–0.94, $P<0.001$). TEE fared worse than in the Willson study, and did not predict PAR (area under the ROC curve 0.64, 95% CI 0.46–0.81, $P=0.09$). After the poor performance of TEE on ROC analysis, subsequent