The Y Takes On Diabetes

By using YMCAs, an insurer hopes to launch a coordinated attack against the disease

By Jennifer Corbett Dooren

A new health program being rolled out at YMCAs across the country shows the potential for a community-based organization to deliver a nationwide health-care intervention.

The Y's target is diabetes. Research has shown that the program, which combines exercise, dieting and individual counseling, can have a big impact in reducing incidences of diabetes. Impressed by the research, insurers and employers are providing direct funding as the YMCA seeks to enroll participants in the program and induce them to reach weight-loss targets.

If it succeeds, the YMCA diabetes-prevention program could help slow the spread of a disease for which about 79 million U.S. adults are currently at risk. What's more, it could encourage other uses of large community-based groups to attack specific health-care issues in a national coordinated way.

Indeed, there is nothing to stop other large nonprofits with footholds in communities across the country from playing a similar role as "adjunct providers in the health-care system," says Jonathan Lever, vice president for health strategy and innovation at the Chicago-based YMCA of the USA, the parent organization of YMCAs around the U.S.

The Y effort is based on a simple model. The YMCA gets reimbursed by insurance companies and employers for people who enroll in the yearlong diabetes-prevention course. If class enrollment goals are reached, and if participants lose 5% to 7% of their body weight over the year, the Y gets additional payments.

Brandon Sullivan for The Wall Street Journal

LET'S MOVE Sarah Shimchick leads a Phoenix YMCA diabetes-prevention class on a half-hour walk that includes talks on healthier eating.

Pounds Of Prevention

The YMCA's diabetes-prevention program (figures are through 2011)

438 Classes started

3,525 Total participants (completed or attended one session)

211 Class locations

24 States where program is offered

5.1% Average weight loss for people who attended nine or more sessions

4.4% Average weight loss for people who attended four or more sessions

Source: YMCA of the USA
The Wall Street Journal

Saving Lives and Money

The reason insurers and employers are willing to ante up: Preventing diabetes can save them and the health-care system enormous amounts of money. According to Tom Beauregard, an executive vice president of **UnitedHealth Group** Inc., the Minneapolis-based insurance company that set up the reimbursement mechanism, it costs about $3,700 a year on average to treat a person with prediabetes, or those with elevated blood sugar that's not high enough to be considered diabetes. But treating someone with advanced stages of diabetes tops $20,000.

Type 2 diabetes is a disease characterized by high blood-glucose levels caused by the body's inability to either make or properly use insulin, according to the Centers for Disease Control and Prevention in Atlanta. At least 26 million Americans already have the disease, which increases the risk of a host of other medical problems such as heart attacks and strokes.

The YMCA classes are designed based on a diabetes-prevention study by the National Institutes of Health that compared the effectiveness of the diabetes drug metformin and a program aimed at helping people lose at least 7% of their body weight through diet, exercise and individual behavioral counseling. The results, published in 2002, showed those in the lifestyle-intervention group cut the risk of developing diabetes by 58% over three years, while those on metformin had a 31% reduced risk.

Costly Decision

However, the lifestyle-intervention approach was criticized for being too costly. Researchers at Indiana University later refined the lifestyle course and worked with the YMCA in Indianapolis to see if similar results could be achieved through classes led by less-expensive, non-medical professionals. The yearlong course that resulted, which starts with 16 weekly classes followed by monthly classes—encourages people to find ways to exercise 150 minutes a week and cut calories by focusing on the amount of fat consumed. The course also provides strategies to help people make permanent behavioral changes.

Based on the results from Indiana and another test site in Kentucky, the Centers for Disease Control provided funding for the YMCA to offer the classes at a handful of facilities.

Then the effort got a major boost in 2010, when UnitedHealth Group approached the YMCA and the Centers for Disease Control about scaling up the program and setting up a reimbursement program.

Game Changer

"It really changed the dynamic," says Jonathan Lever, vice president for health strategy and innovation at the Chicago-based YMCA of the USA. Classes are now offered at 48 YMCAs in 26 states, and the Y plans to add more. The Centers for Disease Control is also continuing to provide some funding for start-up costs such as training additional lifestyle coaches and providing program materials. The YMCA gets reimbursed up to $500 per participant—but less if people fail to achieve weight-loss goals or don't attend the majority of classes.

UnitedHealth Group has set up a division called the Diabetes Prevention and Control Alliance, which markets the YMCA program to United Healthcare members, other employers and even other insurance companies. **General Electric** Co. offers the program to its employees.

Mr. Beauregard says the alliance uses insurance claims data and demographic information to identify who in a company is at risk for developing diabetes, which includes people who are overweight or have another condition like elevated cholesterol levels or high blood pressure.

Coping With Munchies

The program appears to work because it's simple and focuses on realistic exercise and weight-loss goals. It's aimed at helping participants give each other strategies for coping with late-night munchies, for example. The program also allows people to use YMCA facilities to exercise free of charge while they are participating in classes.

Sarah Shimchick, a program coordinator at the Valley of the Sun YMCA in Phoenix, explains that initial diet advice focuses on counting fat grams and helping participants aim to lose 5% to 7% of their body weight, which often equates to about 15 pounds for people to see health benefits and prevent the transition to diabetes.

Fred Lopez, 48, who works for a law firm in Phoenix, says he gradually packed on an extra 30 pounds. "I exercised somewhat but I really wasn't committed on the diet side." A couple of years ago his doctor put him on Trilipix after a blood test showed he had "extremely high" levels of triglyceride, a type of fat in the blood.

Last year, Mr. Lopez says, his wife saw a flier at their local YMCA offering the diabetes-prevention program, and they both enrolled. Mr. Lopez says he has lost 25 pounds, exercises almost daily and feels terrific. "I have more energy, and I'm no longer exhausted at night." At his latest doctor's visit, Mr. Lopez was taken off Trilipix.

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Drug Discovery Gets an Upgrade

Pharmaceutical companies are using powerful computers to increase their chance of success

By Jonathan D. Rockoff

Computers are taking some of the luck out of drug discovery.

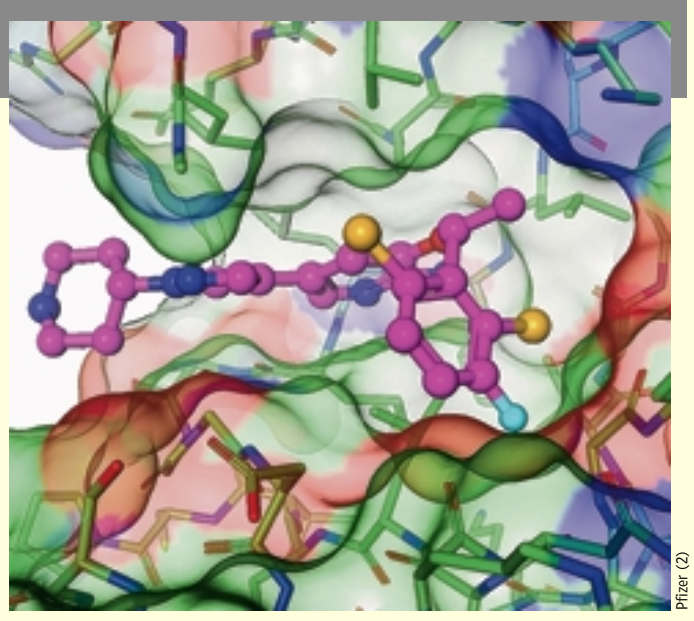
After decades spent searching for compounds in nature that might have medicinal potential, most major drug companies are now also designing medicines virtually. Aided by powerful computational analyses that help identify a target for a drug, researchers manipulate molecules on their computer screens to create custom-made compounds that attack disease-causing proteins.

This method of tailoring molecules is known as structure-based design. It was used to create Xalkori, a therapy launched by **Pfizer** Inc. last year to treat a rare and intractable form of lung cancer. It also has played a role in an Alzheimer's disease treatment being developed at **Eli Lilly & Co**, an antibiotic crafted by **GlaxoSmithKline** PLC that is in midstage trials and a **Sanofi** SA blood thinner in the final stages of development.

With computer-aided design, pharmaceutical companies are finding treatments they might never have discovered otherwise, even with considerable investments of time and expense, says Magid Abou-Gharbia, the director of Temple University's Moulder Center for Drug Discovery Research and the former head of drug discovery at Wyeth.

"You will actually increase the chance of success for coming up with a clinical [drug] candidate" by using it, he says.

FINDING A FIT Jean Cui (center) used data from computer analysis to devise the cancer drug Xalkori, which works by locking into and blocking a protein essential to a form of lung cancer (right).



Pfizer (2)

Keys and Locks

Structure-based design is quite different from traditional drug-discovery techniques, says Jean Cui, the scientist credited with discovering Xalkori.

Typically, a drug works by attacking a disease-causing protein that is interacting with other molecules in an unhealthy way. By connecting to the protein, a drug can stop it, thereby restoring healthy interactions or compensating for unhealthy ones.

A drug connects to a protein much as a key fits into a lock. For most of their histories, drug makers looked for the keys while ignoring the locks. Drug companies sifted through natural substances found in soil, as well as collections of dyes and industrial chemicals and failed compounds from previous drug research-and-development programs. They would test those samples for any impact on diseased cells and, if they were lucky, find one that worked. This is how penicillin was discovered.

Over the years, companies speeded up the process. They accumulated vast libraries of potential compounds—the end of the Cold War opened up a trove of new molecules collected by Eastern European laboratories—then used robots to quickly run through hundreds of thousands of samples to see if any showed medicinal potential.

Yet, drug screening remained dependent on a company's good fortune to chance upon a promising compound. When researchers hit on a new medicine, they often wouldn't know for years why it worked, only that it did. They didn't know what the key or lock looked like.

Frustrated, a Merck & Co. scientist named Joshua Boger left to start a company that aimed to take much of the luck out of drug discovery. His firm would figure what a lock looked like, so it could fashion a better key to fit into it. The company, Vertex Pharmaceuticals Inc., established in 1989, was among several conceived with this mission.

"I felt every project wasn't using all the information available to it, and one of the kinds of information left out most often was the structural information, telling you what a drug was supposed to do," says Dr. Boger, now a board member at Vertex, based in Cambridge, Mass., whose hepatitis C therapy, Incivek, was approved last year.

Determining the shape of a lock isn't easy, however. Because proteins run from X-rays taking their snapshots, scientists must first crystallize them so they can't escape and then deduce their shape by looking at the patterns left by the X-rays deflecting around them. This requires thousands of interference patterns and powerful computers to analyze them.

Then, researchers must fashion a custom molecule to fit into that lock. Coming up with the right shape can be difficult. Moreover, the molecule also must connect, or bind, to the target. And to be a successful drug, a molecule must have other properties. It can't be metabolized by the body too quickly or slowly, and it must be able to be synthesized and manufactured in large quantities.

Because of those challenges, structure-based design is more an instrument for boosting companies' drug-discovery efforts than for revolutionizing them, researchers say. It provides information that is helpful and sometimes crucial for discovering new drugs, but it can't generate the ideal candidate without other information and work.

"It doesn't tell us everything, but it gives us a very good clue," says Tony Wood, who heads chemistry at Pfizer.

Scientist's 'Aha' Moment

Xalkori wouldn't have been discovered in the early 2000s if not for structure-based design, according to researchers at Pfizer.

In 2003, Pfizer bought Pharmacia, the owner of the biotech firm Sugen, where much of Dr. Cui's early work on Xalkori took place. Researchers were trying to block a protein called c-Met that was found to play an important role in the growth of cancer tumors. They hit upon a naturally occurring molecule that connected to c-Met, and synthesized some prototype molecules.

But even with further refinement, these prototype molecules didn't have the properties—such as avoiding quick metabolism in the body—needed to make it a workable drug, Dr. Cui says.

Scientists turned to structure-based design for help. The researchers crystallized the c-Met protein with one of the prototype molecules hooked up to it, fired X-rays at the arrangement and, using computers, deduced the structure of the protein and how the prototype molecule fit into it like a key in a lock.

They emailed the results to Dr. Cui, who began trying to come up with an entirely new molecule that would bind to c-Met and possess properties suitable for a drug. It was difficult, Dr. Cui recalls. The new molecule would have to connect to a site on the c-Met protein that scientists hadn't expected, and it required a tight squeeze into a small space. Dr. Cui says she found herself trying to solve the puzzle all of the time.

In May 2002, after five months of thinking about it, the design came to Dr. Cui while she was at home watching her two daughters play. The next morning, she took a rough sketch of the design to her boss, and soon colleagues were making compounds virtually on a computer and in test tubes for further study. Within weeks, Sugen decided it would try to turn this molecule into a drug. By February 2003, testing in animals showed that the molecule could stop tumor growth. After the Pfizer acquisition, researchers there further refined, synthesized and studied the molecule until Xalkori emerged ready for testing in humans.

The work showed that Xalkori, known chemically as crizotinib, bound to and blocked the tumor-causing activity of a protein called ALK, as well as c-Met. Xalkori was approved last year for non-small-cell lung cancer caused by a genetic hitch affecting the ALK protein. Researchers are still probing its use in other cancers involving the c-Met protein.

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