Transforming modern medicine doesn't have to be high tech or expensive



uch of the progress in medicine since I was a medical student has involved expensive, hightech diagnostic tests and therapies — a trend that has accelerated recently and worries health economists and politicians alike because it boosts healthcare costs.

That's why we mustn't forget that there is an important role as well for ingenious, low-tech, less expensive approaches.

The most recent cancer breakthrough, a <u>treatment for advanced lymphoma called "CAR-T"</u> approved by the FDA in October, is an utterly astonishing tour de force.

In a complex, multi-step process, it involves removing immune system cells known as T cells from each patient and sending them to a highly specialized manufacturing center where they are genetically altered to include a new gene that directs the T cells to target and kill the cancer cells. The modified cells are then infused back into the patient.

This is the second such approved treatment: a different <u>CAR-T therapy for a form of acute lymphoblastic</u> <u>leukemia</u> was given the green light by regulators in August. This approach is the epitome of personalized medicine.

Animal experiments suggest that CAR-T therapy could transform the treatment of other kinds of cancers as well, but the Brave New World of high-tech medicine won't come cheap. The cost: a staggering \$373,000 per patient for the lymphoma treatment and \$475,000 for leukemia. (That is not a misprint.)

lowetech 2d6 18 2 nknown Another remarkable genetic engineering feat was <u>reported</u> in the journal *Nature* in November. An experimental gene therapy procedure <u>used to transform and grow sheets of healthy skin</u> <u>saved the life of a 7-year-old boy</u> who suffered from a genetic disease, junctional epidermolysis bullosa, that had blistered and destroyed most of his skin.

He was on the verge of death, but two years after the treatment with genetically engineered cells produced by a multinational team, he has healthy skin and leads a normal life. That is another treatment whose cost will be well into six digits, if it is ever commercialized.

FDA just approved for marketing a clever combination product, the first "digital" drug. It combines a tiny chip comprised of minerals like silicon, magnesium and copper inside tablets of Abilify, a drug used to treat schizophrenia, bipolar disorder and other mental illnesses.

In the stomach, it transmits a signal to an adhesive patch worn on a patient's torso, which records the dosage and time of ingestion and relays that information to a smartphone app. That provides a record of the patient's adherence to his medication schedule. The price hasn't yet been announced, but it's certain to be steep.

Another similar product can measure and provide real-time data on the concentration of gases in the

human gastrointestinal tract.

A revolutionary high-tech medical innovation almost ready for the clinic is xenotransplantation, the transplanting of animal organs into humans. Improved immunosuppressant drug regimens and increasing numbers of pig lines that have been gene-edited to eliminate antigens that would cause rejection by the human recipient are a potential game-changer.

The experiments in which porcine organs have been transplanted into monkeys are very promising. Like CAR-T therapy, xenotransplantation will be hugely expensive, given the development costs and liability considerations.

A variation on the theme of transplantable – or more accurately, *implantable* organs — is "bioprinting," of tissues and organs, using sophisticated 3D printers.

It has been known for more than a decade that living cells can be sprayed through the nozzles of inkjet printers and remain viable, and various research groups are now using multiple print heads to spit out different cell types accompanied by chemicals that help to maintain the correct structure, such that layer of **cells are Bound** to grow into functional, living tissue.

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Possibilities include kidney and liver tissue, skin, bones and

cartilage, as well as the networks of blood vessels. R&D in this sector is remarkably advanced and progressing rapidly. According to an <u>article</u> in *The Economist* in January:

They have implanted printed ears, bones and muscles into animals, and watched these integrate properly with their hosts. Last year a group at Northwestern University, in Chicago, even printed working prosthetic ovaries for mice. The recipients were able to conceive and give birth with the aid of these artificial organs.

Some academic physicians are touting high-tech variations of "telemedicine," including real-time personal monitoring and reporting of data to healthcare providers.

Dr. Eric Topol, a cardiologist at the Scripps Research Institute in La Jolla, California, <u>wrote</u> recently that "real progress in containing costs and improving care will require transforming the practice of medicine itself . . . to move much more aggressively into the era of smart medicine, using high-tech tools to tailor more precise and economical care for individual patients." The most advanced radiation therapy machines are hugely expensive. The one that went online at the Hampton University Proton Therapy Institute in 2010 cost a cool \$244 million.

However, high-cost, high-tech "innovation" isn't always an improvement. A recently completed, multi-year study of almost 24,000 patients with kidney cancer by researchers at the Stanford University School of Medicine <u>found</u> that robot-assisted laparoscopic surgeries are associated with increases in operating times and cost compared with traditional (non-robot-assisted) laparoscopic surgeries. There was no statistical difference in clinical outcomes for patients or length of hospital stay.

There are plenty of variations on high-tech medicine that are inexpensive and highly cost-effective. An example is an intervention used regularly at Stanford's Lucile Packard Children's Hospital: the <u>use of</u> <u>virtual reality (VR) goggles</u> to allay pain and anxiety in children undergoing painful or threatening medical procedures. The kids can be "whisked away to swim under the sea, zap flying cheeseburgers in outer space, catch basketballs using their heads and fly on paper airplanes through the sky."

Presumably, the goggles could also be used on kids (or even adults for that matter) who come to the emergency room for anything that induces anxiety – which, especially in a young child, could be almost anything from any asthma attack or appendicitis to a broken arm.

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Another example is illustrated by a recent article in the

American Journal of Medicinethat describes how a single blood test can ascertain that a patient in the emergency room is not having a heart attack and so can forego the inconvenience and expense of additional invasive tests or unnecessary hospitalization.

The highly sensitive blood test measures levels of cardiac troponin, a protein involved in muscle contraction; if the level was below the limit of detection of the test, there was greater than 99 percent likelihood that the patient was not experiencing a heart attack and was at very low risk of other cardiac adverse events for at least 30 days.

That innovative approach, made possible by the new high-sensitivity blood test, is advantageous to patients and helps to reduce healthcare costs.

There are other innovative, inexpensive low-tech or mid-tech approaches that can markedly improve Americans' health. A colleague recently told me about specialized flooring in a home for seniors in Denmark.

Not only was the flooring "cushioned," but it also contained electronic sensors every few inches, so that an attendant sitting at a central console could tell if there was any sudden change in distribution of weight – for example, going from standing on two legs to weight distributed evenly over a broad area of floor. If a senior fell in his unit with the door closed, an attendant could detect the fall and be in the room in a matter of seconds.

To measure the potential benefits of a low-tech version of this sort of approach in a rigorous way, a research group in New Zealand <u>compared rates of falling and injuries</u> from falls on low-impact flooring (LIF) compared with standard vinyl flooring on an "older persons health ward."

Falls were prospectively monitored with written reports of all incidents, noting the location and consequences of each fall. The frequency of falls and injuries on LIF and those occurring on standard vinyl flooring (controls) were compared.

The investigators found that over the 31 months of the study, there were 278 falls (among 178 persons who fell). The rate of falls was indistinguishable in the two groups, but "fall-related injuries were significantly less frequent when they occurred on LIFs (22 percent of falls versus 34 percent of falls on control flooring)." And many of those averted injuries were serious: "Fractures occurred in 0.7 percent of falls in the LIF cohort versus 2.3 percent in the control cohort."

Falls are both a cause and effect of declining health in the elderly. They are the leading cause of injuryrelated visits to emergency rooms and the primary cause of accidental deaths in Americans over the age of 65. Thus, the New Zealand study provides a compelling rationale for adding low-impact flooring to nousing for seniors, along with <u>other modifications</u>.

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A recent article in the New England Journal of Medicine

illustrates how low-tech, low-cost nutritional supplementation might reduce the likelihood of a genetic predisposition to preterm birth, at a time when highly sophisticated gene therapy approaches are impractical and premature (no pun intended).

Preterm birth (defined as birth before 37 weeks of gestation) affects almost 10 percent of pregnancies in the United States and is the leading cause of death in neonates and children under the age of five years.

The study, in 43,568 women of European ancestry, found that "six maternal genomic loci that were robustly associated with gestational duration and that contained genes in which the established functions are consistent with a role in the timing of birth. Three of these loci were also associated with preterm birth."

Because of the multiple genes involved and the fact that the results show only an *association* with preterm birth, not *causation*, gene therapy is beyond scientists' capabilities.

However, the study did suggest a simple, low-tech, low-cost solution – selenium supplements during pregnancy. The rationale is that one of the genes identified is involved in the incorporation of the element selenium into proteins that serve a critical role in the body and have been linked to birth and preterm birth.

In addition, as <u>noted</u> by the authors, "Malawi, the country with the highest global risk of preterm birth, has a high prevalence of selenium deficiency." Thus, the monitoring of selenium levels and selenium supplementation in pregnancy should certainly be studied.

The high-tech miracles of modern medicine will continue to garner headlines, but to advance American healthcare, simpler and relatively inexpensive innovation is also essential.

Henry I. Miller, a physician and molecular biologist, is the Robert Wesson Fellow in Scientific Philosophy and Public Policy at Stanford University's Hoover Institution. He was the founding director of the Office of Biotechnology at the FDA. Follow him on Twitter <u>@henryimiller</u>.

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