

Not the Last Word: Prizes for Cures

Joseph Bernstein MD

These days, a smartphone with a Global Positioning System app can generally pinpoint your location on the globe to within about 20 feet [11], but for most of human history, it was far too easy to get lost. The problem of navigation was particularly acute on the open sea. Although determining a ship's latitude could be easily derived from the position of the sun relative to the horizon,

determining longitude was a much harder problem—because of the earth's rotation, the sun's east/west coordinates are not fixed in the heavens.

Back in the 18th century, the naval powers of Europe were keen to find a solution to the longitude problem [21]. Mastery of longitude would make the business of war (not to mention the business of business) that much easier. To help encourage inventors to find an answer, the British government passed The Longitude Act in 1714 [4], promising a prize worth nearly USD 3 million in today's currency to anyone who could produce a practical method of determining longitude at sea.

It worked. Inventors recognized that determining longitude at sea is easy if you knew the time back in Greenwich, England. The sun's position overhead will tell you the time in your current location, and each hour's difference from Greenwich Mean Time represents 15° of longitude. John Harrison thus invented a "marine chronometer", an accurate clock that could withstand the jostling of ocean waves. In no time at all, every ship was equipped with one.

Harrison's triumph occurred long ago, but I think the lesson still applies. For that reason, I propose that the NIH and other large funding organizations should offer large prizes in return for

discoveries that lead directly to cures. The National Institute of Diabetes and Digestive and Kidney Diseases, for example, could offer a USD 5 billion award for the discovery of a method that completely reverses diabetes. Within orthopaedic surgery, a prize of USD 50 million for a method of inducing flexor tendon repairs to heal without adhesions, or for ACL repairs to heal at all, might yield practical solutions. Yes, these are non-trivial sums—the entire NIH annual budget is about USD 40 billion [15]—but our current system of research funding is not getting us to find cures fast enough.

The United States leads the world in funding scientific research, and accordingly, is the world's biggest source of progress in biomedical science. Yet for the most part, our country produces what Thomas Kuhn [13] called "normal science"—adding information to established knowledge. Cures, by contrast, may demand what Kuhn calls a "paradigm shift"—new ways of thinking that remain elusive to even extraordinary "normal" scientists.

Paradigm shifts may be particularly needed in orthopaedic surgery. As Scott Dye [9, 10] has noted, perhaps too much attention is paid in orthopaedic surgery to "structural and anatomic data" [1], whereas true cures might require interventions that improve the metabolic function of the joint—"tissue homeostasis" [10], as Dye calls it.

Needless to say, many musculoskeletal conditions do not have endpoints

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that are easily amenable to a Prizes for Cures approach. For instance, whereas a cure for diabetes is easily recognized (normal blood sugar after a glucose challenge), a cure for diseases that wax and wane, like arthritis, may defy easy definition. Other conditions that are characterized by clinical symptoms and not objective signs, like back pain, are also not well-suited to this method. And for some progressive diseases, like osteoporosis, delaying advancement without a cure can nevertheless be a large victory. Yet even if the hard cases are omitted, there is still an abundance of diseases for which Prizes for Cures competitions can flourish.

Prizes for Cures competitions, moreover, are likely to yield secondary gains in other fields. The original longitude prize, as noted, gave us better clocks. When more modern-day explorers at NASA responded to President John F. Kennedy's challenge to land on the moon (a tangible-goal effort, like Prizes for Cures) they not only succeeded their original aim, they gave us the cordless drill, the computer joystick, and scratch-resistant lenses, among many other spinoff technologies.

Even without secondary gains, Prizes for Cures are a good investment. Three million dollars for an accurate ship clock sounds like a lot, but it gave humankind control of the sea. A USD 5 billion prize to eradicate diabetes might also sound expensive, until you think about the USD 1 trillion the United States is poised to spend on diabetes treatment alone in the coming decade.

We need more cures, and prizes will help us find them.

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Back pain, arthritis, and trauma are the three most common musculoskeletal conditions reported [23], and would all benefit from new research funding that rapidly advances scientific discovery to improved treatments. But incentive prizes, while attractive mechanisms to accelerate translation, are not a replacement for traditional funding for research and training.

Well-designed incentive prizes have upsides and can advance a focused problem without pre-determining which team or approach is most likely to be successful, thereby reaching beyond pre-conceived "usual suspects" and providing an inherent mechanism to cut unsuccessful projects. By paying only for results, incentive prizes can leverage investment exceeding the value of the prize purse, while shining a spotlight on a problem and shifting people's views about what is possible [24].

Additionally, incentive prizes are particularly useful for technology innovation toward a well-defined problem, and are a regular part of funding mechanisms in US Advanced Research Projects Agencies. The Defense Advanced Research Projects Agency (DARPA) has offered incentive prizes for many years to accelerate milestone-based projects where a "Go/No Go" decision is required [5]. For example, the recent DARPA Launch Challenge was designed to launch payloads into orbit on extremely short notice, with no prior knowledge of the payload, destination orbit, or launch site, and to do it twice in a matter of days [6]. In the healthcare sector, the Department of Health and Human Services offers incentive prizes for the Division of Research, Innovation, and Ventures (DRIVE) program to accelerate the development and availability of transformative technologies and approaches to protect Americans from health

security threats [8]. The CARB-X program, possibly the largest public-private partnership in the world, uses a prize mechanism to incentivize pre-clinical antibiotic development [20].

But the return on investment for incentive prizes may be deceptive. The winner-take-all approach means that the many losing teams collectively "waste" huge amounts of time and resources that could have been used for other scientific endeavors. Shouldn't cost estimates of incentive prizes also include both direct costs for project winners and opportunity costs incurred by the losing teams? Indeed, the benefit of traditional research mechanisms and risks to losing teams is implicitly recognized in current competitions. Even many years into successful incentive prizes, DARPA uses prize challenge funding sparingly and is a small percentage of their total budget (~1% in FY2018) [7]. And although research funding is known to be a wise investment [18], quantifying its direct return on economic and health outcomes is extremely complex due to the difficulty in measuring relevant parameters in a holistic manner, the non-linear relationships between research and innovation, and the time lag between discovery and outcomes [2].

When might an incentive prize be the right funding mechanism? When the goal of the project is clear, the benefits are large, there are measurable requirements on the path to implementation, technical innovation is a required part of the solution, and when the broader costs are considered. We need to recognize that prizes can distract from other large societal problems or approaches where systematic investigation and progress can provide the most impactful results. Importantly, "cures" often involve innovations in scientific discovery and

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technology, as well as education and implementation [22].

Grand challenges are another funding option that can focus a broader scientific community to accelerate work toward societal major goals [18]. This approach offers funding on focused topics that capture the public's imagination to create an "all-hands-on-deck" effort with more diverse approaches and greater number of "winners" than incentive prizes, while also building research infrastructure and developing the careers of trainees [24]. The NIH BRAIN [16] and Cancer Moonshot initiatives use the grand challenge approach [17] to provide funding that addresses complex multifactorial diseases. The current NIH Helping to End Addiction Long-term Initiative is a trans-agency effort to speed scientific solutions to address the national opioid public health crisis.

Current research funding for musculoskeletal diseases remains incommensurate with the size of the disease burden [19]. For example, back pain is a leading cause of global disability and solutions will require research that improves knowledge of the complex relationships between anatomical pathology, disability, pain and socio-economic factors [12]. Addressing back pain and other musculoskeletal disorders therefore requires broad funding to support diverse research teams with long-term commitment to improve understanding and treatment of these diseases. I agree with Dr. Bernstein that incentive prizes can play an important role in healthcare discovery, yet feel they must remain only a small part of a balanced research portfolio.

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True innovation, like John Harrison's marine chronometer, takes

time—many decades in Harrison's case [3]—and the ability to weather failures and criticism from the powers that be. In orthopaedics, we could shoot for paradigm-shifting discoveries, but without being afforded the time or the patience to fail, we often settle for "incremental" science instead.

The musculoskeletal community has yet to solve many of the major orthopaedic problems that affect millions of our patients including intervertebral disk degeneration, effective healing of rotator cuff tendons and ACL tears, straightening of the curved spine without fusion, brachial plexopathy, and osteoarthritis.

A lack of cures for these orthopaedic conditions is not caused by a lack of passionate young surgeon-scientists. The Clinician Scientist Development Program, sponsored by the Orthopaedic Research Society, turns away far more surgeon applicants than it can accept each year, and those who attend repeatedly express the desire to have time dedicated to both clinical and research work. Having a career that includes both is synergistic—the needs of a surgeon's patients fuel the urgency to find a "cure", rather than conducting, as Dr. Bernstein points out, Kuhn's "normal science" [13].

The lack of cures also does not stem from a lack of available technology. New tools, like ribonucleic acid sequencing and proteomics, help us address orthopaedic diseases in ways we could not in 2001. We can take advantage of new disease-specific models that will allow us to understand the biology of many of the problems we currently face as surgeons. While these techniques are available, they require resources to conduct and expertise to interpret.

In the 1960s, our country put an enormous amount of money into

the space program, long before a man landed on the moon. The funding was provided as the research progressed. This approach of adequate resourcing and teamwork led to a successful mission to the moon within a decade.

This type of support is currently offered for research in other medical specialties. Since 2001, the NIH has awarded more than USD 440 billion in medical research funding [14]. And if Nobel Prizes are used as a metric for "paradigm shift" discoveries, then it should be considered a successful program—27 Nobel Prizes have been awarded to NIH-funded investigators (in fields of medicine other than orthopaedics) during that 18-year period. However, the National Institute of Arthritis and Musculoskeletal Medicine (which funds awards in Orthopaedic Surgery, Rheumatology and Dermatology) receives less than 2% of the overall NIH budget [14]. While prizes for cures is certainly an interesting proposal, I would be more in favor of providing the orthopaedic surgeon-scientists in our midst the time, resources, and encouragement to pursue their passion to find these cures.

We can do this. We can provide time by providing dedicated research days every week for surgeon-scientists. We can provide resources by joining with our patients to campaign to Congress to have NIH funding be proportional to the burden of disease. Lastly, we can recognize that the pursuit of "paradigm shift" cures can take decades, much as Harrison's chronometer did, and we can continue to provide sustained encouragement and support to these clinician-investigators with mentoring, collaboration, and simple recognition that we appreciate their efforts. If we can provide surgeons-scientists the time,

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resources, and encouragement to pursue their passion for a cure, then we will begin to see the “paradigm shift” advances our field so sorely needs.

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