Diagnostic errors occur in all areas of medicine, but the 'Big Three' causes of major harm are missed vascular events (e.g., stroke, heart attack, pulmonary embolus), missed infections (e.g., appendicitis, meningitis), and missed cancers (e.g., lung, breast, or colon cancer). Stories from survivors (or family members) who have lived through such diagnostic errors are often powerful and moving. Below is a real-world story of a young man whose STROKE was missed, with devastating and tragic consequences.

We explain how further research through a Centers of Diagnostic Excellence (CODE Program) could prevent future tragedies and simultaneously cut healthcare costs, resulting in high-value diagnosis.

The Stroke Example

Patient Story: John Michael Night is a 20-year-old young man who can no longer speak or move his arms or legs, but he is mentally intact ("locked in syndrome"). He can only communicate by blinking his eyelids. He needs full-time care to tend to his every daily need, at great financial cost to his family and the health system. At age 17, he was a champion lacrosse player headed to college on a full athletic and academic scholarship. Two days after a lacrosse match, he developed dizziness, vertigo, vomiting, and unsteady walking. He and his parents went to an emergency department, where the physicians focused on what they believed to be the effects of recreational drug use, despite the patient's and family's insistence he took no drugs. John was admitted to the hospital, but the diagnosis of stroke due to a damaged blood vessel in the neck was missed. Instead of receiving immediate treatment with clot-busting drugs and blood thinners to reverse his evolving stroke and prevent further damage, he was left untreated for three days. During that time, he underwent numerous expensive diagnostic tests for diseases he did not have. It was only when his stroke progressed to the point that he could no longer speak or move his limbs that the true diagnosis was identified; unfortunately, the window for treatment had passed. Even a one-penny aspirin, had it been given before the stroke progressed, might have prevented this tragedy.

Background: It would be easy enough to assume that John's problem is a rare, standout case. Unfortunately, there are tens of thousands of patients each year like John whose strokes are missed and thousands of them who suffer serious, preventable harms the way John did. Stroke affects more than 1 million Americans each year, mostly older adults with diseases that cause progressive blockage of blood vessels. But young people are affected more often than typically recognized, usually due to the sorts of blood vessel injuries that John suffered. Roughly 10% of all stroke patients are missed at first medical contact. The ones missed are not usually patients with typical stroke symptoms like weakness on one side and inability to speak. Instead, most patients who are missed have subtler strokes presenting with atypical stroke symptoms such as dizziness, vertigo, headaches, or mental confusion. Although only about 10-20% of strokes initially manifest with dizziness and vertigo as the main symptoms, the way John's stroke did, these patients are much more likely to be missed, especially if they are women, minorities, or, as John was, young. Dizziness or vertigo is the symptom most tightly linked to missed stroke, and likely accounts for at least half of all the missed strokes each year in the US. In total, there are roughly 45,000-75,000 US emergency department patients each year whose strokes present this way and are missed.

The Conundrum: Approximately 95% of the 4.4 million patients presenting dizziness or vertigo to acute care settings do not have strokes as a cause, so finding these strokes requires the ability to separate them from more common causes (like benign, readily-treated inner ear diseases) with high accuracy. Right now, we spend roughly $10 billion per year trying to diagnose such patients, mostly trying to find the small fraction with strokes. Widely available tests like computerized tomography (CT) brain imaging are frequently (but mistakenly) relied upon in daily clinical practice – unfortunately, these CT brain scans miss 80-90% of strokes like the one John suffered. Brain magnetic resonance imaging (MRI) is better, but is less widely available, a lot more expensive, and still misses 10-20% of strokes like this when the pictures are taken in the first 48 hours after the start of symptoms.

CODE Program Role: Fixing the problem that led to John's tragic misdiagnosis requires a "better mousetrap." Experts at Johns Hopkins University School of Medicine have now developed a way to look very carefully at tiny eye movements that allows expert physicians to tell the difference between stroke and benign ear problems in about two minutes at the bedside with 99% accuracy (better than even MRI scans, our current best available test). The problem is that there are only a few dozen capable experts in the country, and millions of patients with dizziness. Two promising strategies for disseminating this approach broadly include simulation-based training for emergency physicians to develop more expertise and computer-based diagnostic decision support using a novel device (a portable "goggles" technology) that measures these tiny eye movements and helps interpret the results. Neither of these approaches has yet been fully refined or studied in clinical practice. Methods to monitor the rate of missed stroke (needed to track the impact of interventions on the missed stroke rate) have been developed, but have not been formally validated across institutions. ***More research is needed***. Developing a CODE partnership (e.g., between an academic institution like Johns Hopkins and a physician's organization such as the American College of Emergency Physicians) that focused on research to optimally implement these solutions could be transformational, within 5-10 years potentially saving thousands of lives and an estimated $1 billion annually (the latter by eliminating unnecessary brain scans and admissions for patients with easily treated inner ear diseases).

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The Sepsis Example

Patient Story: Rory Staunton was a 12-year-old boy with the dream to grow up to be a pilot—he had fallen in love with the story of "Sully" and the miracle landing of the disabled jet on the Hudson River. For his 12th birthday, his parents gave him a helicopter tour of New York City. His life was joyous, and he had big plans for the future.

Rory was diving for a ball at recess one day. He got the ball but scraped his arm. That night he awoke from sleep with pain in his leg; by the morning he had a high fever and was vomiting. He couldn't go to school the next day. His pediatrician thought he had the stomach flu, a viral infection, but sent him to the emergency department (ED) to treat his dehydration from the vomiting. In the ED they sent "stat" (immediate) blood tests, but no one followed up on the results; they agreed with the pediatrician that it was a benign stomach virus and sent him home after giving him intravenous fluids. The next day Rory couldn't get off the couch, wasn't eating, and had a high fever that couldn't be controlled. His parents tried to get through to the pediatrician multiple times, without luck; by the time she saw Rory for the second time, he was already in grave shape. The family went straight to the ED and Rory was admitted directly to the intensive care unit, but it was too late—he died within 24 hours of streptococcal sepsis, a complication of the simple scrape on his arm, from a bacterial skin infection that went undetected.

Background: Sepsis is life-threatening organ dysfunction caused by the body's own response to severe infection. Sepsis has a devastating annual impact on patients in the US and around the world, and affects patients of all ages. Depending on the clinical criteria used, there are roughly 850,000 septic patients seen in US EDs every year. Sepsis accounts for at least 20-30% of hospital deaths each year in the US, costing the healthcare system over $24 billion annually. The Sepsis Alliance, the largest sepsis advocacy group in the US, believes that this disease is the *leading* cause of death in US hospitals. A key area of focus in the fight against sepsis is early recognition and treatment of infection. The time-sensitive aspect of this disease is crucial because after the onset of severe sepsis, mortality rates increase by 7-10% every hour that treatment is delayed. Around 70% of sepsis cases are community-acquired, and public education and awareness campaigns encourage individuals to seek out treatment early enough to prevent unnecessary harm. The burden then falls to our healthcare system to make the diagnosis as quickly as possible… a goal that in the past, as in this case, has been challenging to meet.

The Conundrum: This is a 'needle-in-the-haystack' problem—how is a clinician supposed to think of sepsis, when so many patients present with fever, and the vast majority of these have some other, less worrisome condition? There are still no definitive diagnostic tests or "biomarkers" for sepsis, so diagnosis relies on identifying clinical 'red flags.' Unfortunately, in this case, red flags like leg pain, mottled skin were dismissed; abnormal blood tests were not followed up; and deteriorating trends in Rory's vital signs during his ED stay were not recognized.

CODE Program Role: Major advances in the diagnosis of sepsis have been achieved in recent decades, including new consensus-based definitions, revolutionary new lab tests that identify bacteria in hours instead of days, and checklists where front line staff are encouraged to consider sepsis if the patient meets a specified number of criteria (fever, fast heart rate, etc). Despite all of this progress, thousands still die in our country each year from delayed diagnosis and treatment of sepsis. ***More research is needed.*** The problem is not lack of ideas—what's needed is dedicated research funding to develop and test the ideas that already exist. One promising idea is to use 'big data' and artificial intelligence to look at all of the electronic data available on a given patient to identify patients at risk as early as possible, by having computers monitor thousands of potential predictors continuously, instead of relying on nurses or physicians to use a one-time checklist that can only account for a handful of variables at a time. This has already been done, with smart algorithms outperforming expert human judgment, yet these algorithms are not yet in routine clinical use. Developing a CODE partnership (e.g., between an academic institution and an electronic health record vendor) that focused on research to optimally implement such intelligent solutions could be transformational. In parallel, we need to be researching the most effective organizational approaches to enhancing communication and improving awareness and recognition of 'red flags' by staff and patients. Improving early diagnosis of sepsis by just 10% might save the US over $2B in healthcare costs. Even larger improvements, and commensurate savings, could be realized with a focused, coordinated research effort.

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The Cancer Example

Patient Story: Sue Sheridan had recently suffered through her family's first diagnostic error. A diagnosis of severe jaundice was missed in her infant son, resulting in permanent brain damage known as kernicterus. Then came the second error, close on the heels of the first. Sue's husband Patrick developed neck pain. Physical therapy didn't help reduce the pain, nor did acupuncture. An orthopedic specialist finally ordered an MRI scan, showing a tumor (lump) impinging on Patrick's spine. At a well-respected teaching hospital they removed the lump. Based on the preliminary pathology report, the surgeon reassured the Sheridans that this was a benign tumor, in need of no further treatment. However, additional tests were later performed on the specimen, changing the final pathologic diagnosis. It turned out the tumor was actually an aggressive, malignant sarcoma requiring urgent chemotherapy. The pathologist faxed a report to Patrick's doctor, and it was added to his medical record, but Patrick's physician didn't see the report or act on it. Six months passed, at which point Patrick's pain returned and the lost pathology report was discovered. It was too late. The tumor by now had spread and invaded his spinal cord, and Patrick didn't respond to treatment of the now-advanced cancer. Sue reflects on the moment—"That diagnostic error ended his life." Patrick died at age 45, leaving his wife to raise their neurologically-impaired infant son on her own.

Background: Each year in the US, more than 1.6 million new cases of cancer are diagnosed and more than 600,000 die of the disease. Cancer sometimes kills despite our best treatments; what's alarming and intolerable are the many preventable breakdowns in our healthcare delivery system that contribute to poor outcomes. The most common problem is avoidable delays in making the diagnosis. Egregious, avoidable delays in diagnosis are found in every study that examines this issue, and may be more common in certain patient populations such as children, women, and minorities. Delays often start with physicians dismissing early, mild complaints such as fatigue or depression, with weeks, months or years elapsing before referral for appropriate testing or specialty consultation. Lost test results, as in Patrick's case, are frustratingly common; roughly 10% of critical test results aren't acted upon in a timely fashion, even in healthcare organizations with expensive, modern electronic medical record systems. In addition to delays, quality can also break down in cases where the pathologic diagnosis itself is wrong. Research on second opinions finds the diagnosis can change up to 10-20% of the time—sometimes from malignant to benign or benign to malignant. That means some patients get unnecessary toxic chemotherapy at great expense to the health system… and other patients die of a treatable disease without those treatments.

The Conundrum: Cancer isn't always obvious from the start, but figuring it out within days or weeks rather than months or years can be the difference between life and death. Missed opportunities for timely diagnosis reflect the complexity of healthcare delivery and may involve the patient, the physician, or the healthcare system. Patients may not seek age- and risk-appropriate screening, or they may dismiss mild or early symptoms such as fatigue or depression. Physicians may not go beyond an initial diagnosis such as an iron-deficiency anemia to determine whether there is an additional root cause underlying that condition, such as colon cancer. Or the system may simply fail through breakdowns in communicating critical test results, as happened in Patrick's case.

CODE Program Role: Preventing communication failures with critical test results seems like 'low-hanging fruit,' but this apparently simple problem has resisted early attempts at solutions, reflecting the difficulty in effectively 'closing the loop' among multiple healthcare providers in a complex health system. A promising new approach can automatically detect breakdowns in test results communication—so-called 'electronic trigger tools,' pioneered by researchers at the Michael E. DeBakey VA Medical Center in Houston, take advantage of data in the electronic medical record to identify cancer patients at risk for a diagnostic error, and seek to intervene before harm occurs. ***More research is needed*** to fully develop this new technology and explore how to best use it in clinical practice before it can be broadly disseminated. Developing a CODE partnership (e.g., between researchers at the Houston VA and a standards-setting organization such as the Office of the National Coordinator for Health Information Technology [ONC]) that focused on research to optimize standards for such electronic trigger tools for cancer diagnosis could be transformational. In parallel, we need to research how to maximize use of appropriate cancer screening and increase both timeliness and accuracy of cancer diagnosis, across care settings. Since US cancer care is projected to cost more than $150 billion per year by 2020, reducing diagnostic delays and avoiding misdiagnosis or overdiagnosis will likely produce major savings by reducing wasted healthcare resources.