

<u>*Question:*</u> How many Americans die of cancer each year? <u>a)</u> 100,000 b) 200,000 c) 300,000 d) 400,000 e) 500,000 f) 600,000

Frontiers of Cancer Diagnosis and Care

A new <u>release</u> (proof copy) from the National Academy of Medicine (NAM) discusses the way forward to deliver optimal care of this dreaded disease. The release is available free of charge if you register with the NAM. If you have cancer or know someone who does, you may want to review the findings of this workshop report. Cancer spreads by activation of genes that foster unrestrained cell



division or suppression of genes that limit cell division. There are many genes in each category, and if enough of them escape normal behavior, then the patient develops cancer. The classic problem in cancer is how to destroy cancer cells without also damaging normal cells. Obviously, if the genome of the

cancer cells can be characterized in terms of how it differs from normal cells, then it may be possible to target destruction of cells that have the genetic anomalies.

The NAM document notes that the molecular 'underpinnings' of the anomalies may be complex. There were 2 workshops, the first focused on imaging and pathology and the second on analysis of complex computational data potentially available on each patient. The participants came up with many recommendations. Herein, I'll highlight a few of these, avoiding some of the technical and regulatory issues to focus on the patient. One set of recommendations involved developing patientcentered, clinician-friendly tools. Another involved the process of informed consent. I especially liked the sections on data sharing and promoting multidisciplinary teamwork.

I'd not recommend this book for casual readers, but for those battling cancer, it could provide some useful background to better enable you to engage in shared-decision making with your clinicians. You may want to review some information on genetics if you have not had a course in that subject before attempting to make sense of the workshop proceedings.

The Health of Our Children

Three experts writing in *The New England Journal* of *Medicine* surveyed the impacts of climate change on the health of our children. The backdrop for their opinions is the suit brought against the federal government by 21 children who are claiming that the government's failure to act to limit climate changes is a threat to their rights to life, liberty, and property. Among the threats are extreme weather events, pollution from wildfires, increasing threats of infectious disease, and food and water insecurity. Pollution from continuing use of fossil fuels is also listed as a threat.

There is little doubt that climate change is real and will cause an impact on the health of our children, but I'd like to give perspective on several of the anticipated changes. For example, the largest threat of harm from infectious diseases originates in the overuse of ordinary antibiotics that fosters increased susceptibility to drug-resistant bacteria and fungi. Food and water insecurity is a real problem in the U.S., but this is largely due to economic disparities that lead to the rearing of many children in households with insufficient resources to provide optimal nutrition and safe water. Air pollution tends to be a subtle problem with longterm consequences. Small, easily respirable particulates affect children living near busy roads and industrial sources, but the adverse effects may only emerge later in life. My point is that it is not just climate change that threatens the health of our children. There are many social factors that impede their health.



Another article I came across, published in the JAMA, directly addresses the harmful effects of air pollution in children. The expert writers describe a recent study with a unique design that adds to the epidemiological associations between asthma in children and air pollution. The investigation involved comparing rates of childhood asthma in various communities of Southern California with the reductions in air pollutants from 1993 through 2014. The study was unique because the communities were assessed at three time points, somewhat acting as their own controls. The findings showed that reductions in childhood asthma were most associated with reductions in nitrogen oxides and small, respirable dust particles. The writers lament the current tendencies of the Environmental Protection Agency to deny the links between air pollutants and childhood diseases such as asthma.

In my opinion, this is another case where an industry (oil and coal) buys the votes they need to tailor a federal agency's decisions, but the victims of the regulatory decisions (children) do not have the resources to buy votes that lead to control of federal agency decisions.

What Do You Smell?

I live in a household filled with smells. Some are pleasant, such as when my wife is baking a cake or pie. Others are unpleasant, such as during a poopy diaper change or an affectionate attack by my wet dog. Is the ability of older adults to identify smells associated with decreased mortality? A large <u>team</u> of investigators tested for an association in about 2,300 community-dwelling adults aged 71 to 82. The odor

> identification test consisted of asking participants to identify 12 odors common in ordinary life by choosing one of 4 answers for each odor identification. Subjects were placed in 3 groups according to the number of correct answers as follows: poor, less than 9 right; moderate, 9-10 right; and good, 11-12 right. Participants were tested in 1999 or 2000 and followed for 13 years. Just over 1200 participants had died by the end of the study.

Comparisons of those with good olfaction vs. those with poor olfaction showed a 46% reduced mortality after 10 years and a 30% reduction after 13 years. Those who scored their health as excellent or good at the beginning of the study had the highest tendency to die if they had poor olfaction. The diseases most associated with deaths were dementia and Parkinson disease. Weight loss was also associated with higher mortality. Although this study is interesting, I am uncertain how it might be applied to clinical medicine. Happy smells to you.

Safeguards for Robotic Surgery

Earlier this year the FDA released a 'safety communication' suggesting that use of robots to treat cancer patients may not be in their best interest. A couple of MDs <u>examined</u> the situation regarding the safety of robotic surgery. The authors note that robotic surgery has increased 3-fold in the past decade and that the U.S. is the largest user of this technology. The justification seems to be that the procedure is safer than alternatives. But has that been demonstrated? In a study of 24,000 patients undergoing removal of a kidney, robotic surgery was found to be no better than laparoscopic surgery.

The doctors note that the FDA's communication encouraged surgeons to have discussions about the pros and cons of robotic surgery with their patients, especially as it pertains to the specific surgeon's skills. The writers voice two fundamental concerns. Have hospitals allowed surgeons with skill in one type of robot-assisted surgery to expand to other surgeries without ample oversight? They also note that more attention must be given to the 'learning curve' when physicians are allowed to apply robotic-assisted surgery. They call for proficiency-based benchmarks of skill. They also call for surgeons to be forthcoming with patients about the effectiveness of robotic surgery. But then the writers suggest that more evidence must be developed for or against robotic surgery. So, what should the surgeon tell his patients when the answers about risk and benefit are not available? Any patient anticipating robot-assisted surgery should review trusted articles about this procedure for their specific medical problem. This will facilitate a more balanced shared-decision making process with the surgeon.

Acute Kidney Injury from Contrast Media

A long <u>review article</u> by 3 MDs in *The New England Journal of Medicine* addressed what is known about the link between use of iodinated contrast agents and risk of acute kidney injury. Historically, use of such media have been clearly associated with acute kidney injury based on increases in serum creatinine, a substance cleared from the blood by the kidney. These contrast media are used in diagnosis of several cardiac conditions. The predicament is that cardiologists may be reluctant to use such media based on an unfounded fear that they will cause harm to their patient. This has the potential to get things wrong in patient care. But the jury is not in.

The writers point out several studies suggesting that modern contrast media are not the direct cause of acute kidney injury – it is a mere association. Interestingly, they offer a panorama of strategies to limit the risk of kidney injury in vulnerable patients (those with preexisting kidney problems), including use of the bare minimum amount of contrast media necessary to produce optimal images. They call this a true 'controversy' in medicine, leading to the suggestion that more research should be performed.

I'd suggest that patients with limited kidney function ask their clinician how risk of kidney damage from use of contrast media will be mitigated. Is the media essential for diagnosis? The situation is further complicated by the fact that kidney function declines with age just as the potential for use of contrast media in diagnosis becomes more likely.

Phosphate Binders in End-Stage Kidney Failure

A couple of MDs <u>comment</u> on a recent study that compares two kinds of phosphate binders that could be used to lower phosphate in folks with end-stagerenal disease (ESRD). The study in question compared two phosphate binders, finding that they were roughly equivalent in safety and effectiveness, at least short-term. One is much more expensive than the other. The problem posed by the writers is that no one has shown in a well-controlled study that *any* phosphate binder is effective in managing the course of ESRD and mortality.

There is plenty of evidence associating higher serum phosphate levels with higher mortality in hemodialysis patients. There is also mechanistic evidence that phosphate levels may be associated with calcification of blood vessels (i.e. a marker for increased risk of cardiovascular disease). The writers contend that reductions in serum phosphate are merely a surrogate marker for *possible* progression of ESRD and mortality. The reviewers poetically note that "until trial data [of binders compared to placebo] are available, patients and clinicians remain adrift in a sea of phosphate data that lack grounding by a suitable landmark." In my opinion, this is only one of the many medical seas in which clinicians and patients are adrift.

Perspectives on Opioid Dangers

In an article highlighted in *Annals of Internal Medicine*, a <u>physician describes</u> a new study in which a relationship was found between dentist prescribing of opioids and subsequent use and abuse of opioids. The study design was retrospective, using an insurance database and looking at nearly 15,000 people between the ages of 16 and 22 that were prescribed opioids in 2015 by a dentist. This was matched to a group that had not received any opioids. In the following year after prescribing of an opioid or a mock-placebo (control group), the exposed group had a 5.8% incidence of use or abuse of opioids, whereas the 'placebo' group had only an 0.4% incidence. The writer takes this finding to be 'newsworthy' and calls for better control of dental opioid prescribing.

A good friend of mine lost his daughter to misuse of an opioid after a dental procedure. Sadly, when the dentist prescribed the drug, he was unaware of her history of abuse. As far as the study goes, I'd point out that the data are from 3 ¹/₂ years ago. One must hope that dentists have tightened their collective grip on irresponsible opioid prescribing. Parents of young people who receive potentially painful dental procedures must monitor any opioid prescriptions. By now these should be rare.

In a review <u>article</u> in *The New England Journal of Medicine*, 3 MDs put the opioid epidemic in perspective. From 1999 to 2017, 700,000 Americans died of drug overdose, most of them from opioids. In Americans aged 24 to 34 years old, the fifth leading cause of death is opioid related overdose. The writers offer the following general strategies for physicians:

- Are opioids really necessary given their risk?
- If so, limit the dose and duration
- Avoid any dose escalation
- Insist on proper disposal of unused drugs
- Reduce doses in patients with serious, chronic pain
- Do not prescribe in combination with other sedative drugs
- Monitor long-term, patient-users for opioid abuse

• Consider having naloxone available

To some extent, patient advocates should ask questions about all the topics above depending on the needs of the patient(s) they are looking after. Do not leave all the safety strategies to the physician. I would add that one should consider alternatives to opioids. Some folks I know were prescribed an opioid, but took a different class of pain relievers.

A couple of experts <u>wrote</u> their views in the *JAMA* on how to treat opioid-use disorder (OUD). They add to the daunting statistics above, noting that in 2016, 2 million Americans were diagnosed with OUD; however, estimates are that only $1/3^{rd}$ of OUD patients have received treatment in the past year. The writers are emphatic that OUD is a brain disorder, not a moral failure. They write that there is no excuse for failure to use medication-based treatments for OUD.

New Warning on Insomnia Drugs

At the end of April, the FDA issued a new 'boxed' warning about rare, but serious complications from use of certain insomnia drugs. Boxed warnings are the FDA's highest level of warning. The trade names include Lunesta, Sonata, and Ambien. The warnings focus on unsafe behaviors while virtually asleep to include, sleep walking, sleep driving, and sleep cooking. Those who experience these episodes seldom remember what happened. I'd recommend that if you must use one of these drugs, have some way to monitor your behavior after taking them. The Mayo Clinic provides a guide on how those with insomnia may use over-the-counter sleep aids or avoid drugs all together.



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