Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

Dear Members of the Committee,

In 2025, an estimated 618,120 will die of cancer, yet only 4% of patients will participate in clinical trials**.** Meanwhile, drugs that have passed Phase 1 trials sit on shelves, waiting up to two decades to be approved for market, while real human beings die because they can't access them. HB 701 will change that.

I'm writing this testimony while my infant daughter is asleep, my husband Jake is dead, and the drug that might have kept him alive long enough to meet her languishes on a shelf—out of reach of other dying husbands and fathers.

When Jake was first diagnosed with tongue cancer, his doctor clapped a hand on his shoulder and said, "Don't worry, this won't be what kills you." We were assured that the standard of care would likely leave Jake without a small piece of his tongue and maybe some radiation burns. He had a long, generative life ahead of him. We were optimistic. We were about to start a family.

But just a few months after completing radiation, Jake's cancer recurred.

There are very few options for recurrent head and neck cancer. Surgery is one. A combination of chemotherapy and Keytruda—an immunotherapy drug that works for only 20% of patients with head and neck cancer, but works extremely well when it does—is another. Jake did both.

By the time Jake had surgery to remove the recurrent tumor, his aggressive cancer had spread. His entire tongue had to be cut out.

Two months later, before Jake had even healed from that devastating surgery, doctors found six new tumors in his neck and two in his lungs. The surgeon couldn't cut out any more cancer. Jake wasn't responding to Keytruda. The median life expectancy for a patient with recurrent metastatic head and neck squamous cell carcinoma (R/M HNSCC) is six months.

Six months.

We were willing to do anything.

But as we quickly discovered, there was very little we *could* do—and even less we could do easily.

For a patient on their third line of treatment, the standard of care is:

- Spend a few extra months suffering through a brutal chemotherapy regimen and then die.
- Or go immediately into hospice and die.

We didn't like either of those options.

As a biochemist and physician, I immediately began researching alternatives. Keytruda was still an R/M HNSCC patient's best chance at a durable response. But Jake wasn't a responder. Could he become one?

Although I'd found a treatment that might do just that, it became quickly apparent that the physician's and hospital's fear of lawsuits and regulatory pressure were going to prevent them from helping us:

Research at the University of Pittsburgh (and multiple other institutions around the world) showed that melanoma patients who didn't initially respond to Keytruda could become responders after receiving a fecal transplant—a procedure in which a patient receives a special enema containing healthy, disease-free feces from another person to change the recipients gut microbiome. An incredible forty percent of Keytruda non-responders in the study became responders.

Jake didn't have melanoma, but the principles of *change your gut bacteria, change your response* might still apply. It was certainly a better option than a gruesome death by strangulation as the tumors in his neck rapidly expanded.

I approached a gastroenterologist at Mayo Clinic, where I work. I explained that the University of Pittsburgh had completed a proof-of-principle Phase 2 trial. Fecal transplants are FDA-approved only for certain bacterial infections of the gut, but Jake was happy to sign a consent form for off-label use. The risks were minimal—far lower than the certainty of death. We had even found a known Keytruda responder who was willing to donate feces, saving the time and cost of screening new donors.

The gastroenterologist agreed. We would do it—but only after the Mayo Institutional Review Board approved it and the FDA authorized a single-patient Investigational New Drug (IND) application for compassionate use.

The entire process could take longer than Jake's life expectancy. We didn't have time.

We begged. We offered to pay for the procedure out of pocket. That got us slightly closer, but fear of regulation stopped the doctor. He refused to use our donor's Keytruda-responder stool. We could only use stool meant to treat intestinal infections (for which the procedure was FDA approved)—even though there was no research to suggest that a random healthy donor would have any influence on Jake's Keytruda response. The doctor said it was our only choice. *What if Jake had a complication and the donor stool was blamed?* It was too professionally risky.

It was too professionally risky.

Somehow, it was less risky to let Jake die.

We begged some more. Jake would consent to all risks. The donor would sign additional waivers. I would sign a legal release. Jake was already going to die, and fast. We just wanted a chance for him to live.

Then the physician rescinded their willingness to perform any fecal transplant at all.

They didn't have time to fight the red tape. They feared censure. They didn't want to buck the status quo. We would have to find another way.

While we searched, Jake underwent another round of chemo. The side effects were devastating—he lost weight, grew weak, was constantly nauseated, and struggled to get through the day. We needed an alternative, but one rooted in science. I suddenly understood why quack cancer clinics promising miraculous "alternative" cures like high-dose IV vitamin infusions thrived on the dollars of desperate patients. We were willing to try anything. But we wanted to try something that actually had a chance of working.

Our only option was to fight our way into a clinical trial.

I've been a physician for 13 years. I've worked in hospitals, cared for thousands of patients, and coordinated care. I was unprepared for the bureaucratic and personal nightmare of navigating the clinical trial system.

The first shock? Ill patients, many undergoing chemotherapy which leaves them vomiting and immunocompromised, must *physically show up* at hospitals to establish care—often hundreds of miles away—just to learn whether a matching trial even has an open slot.

We tried calling hospitals first, asking if a trial had space before traveling. The answer was always the same: No one could tell us anything until Jake had an appointment.

We'd have to get Jake —who could barely walk to the bathroom—on a plane. First, for the screening appointment. Then again, to sign consents, which occurs separately from the screening appointment. Alternately, we'd have to pause his chemo, which was only barely beating back the rapidly advancing cancer.

"I only have two, maybe three trips in me," Jake said.

I didn't know how he could even do that much.

I wasn't just about to lose my husband, and our future baby wasn't just about to lose her father.

Science was about to lose a data point. I don't say this to be crass or cynical. Data points—real sick people trialing drugs—are what keep other people's husbands and fathers from becoming statistics.

Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

The biggest bottleneck in the clinical trial system is recruitment and retention. It's hard to get patients, and it's hard to keep them. According to *JAMA*, the clinical stage (phases 1, 2, and 3) accounts for 68% of total trial costs. The longer a trial takes, the more sites shut down due to poor recruitment. The longer it takes for a drug application to reach the FDA, the harder it is for patients to participate, and the more expensive the process becomes.

Why do we make it so hard for dying patients to access the only treatments that might save them?

Thankfully, some hospitals allowed telemedicine-based screening. But there was a catch: to legally use telemedicine—even just for a clinical trial screening, not for diagnosis or treatment—a patient had to be physically within the same state as the hospital.

These telemedicine restrictions had been lifted during COVID without issue, yet they were reinstated just before Jake became ill.

Of the twenty trial sites we found, eight allowed telemedicine screenings. Thanks to those, we were able to schedule all Jake's appointments within a week.

Even getting that far—knowing how to find compelling trials, what to ask for, connecting with the right coordinators—required a level of expertise I had only after nearly twenty years in medicine. How would the average patient manage this? They wouldn't.

Neither of our top two trial sites had slots available for Jake. If not for telemedicine-based screenings—an option *not available at all* at many hospitals due to outdated laws—we would have missed Jake's last chance. Instead, during screening appointment #7, Jake was able to secure an open spot at a trial at UCSD, pending eligibility testing.

Two days later, he had another dose of chemo and signed the consent forms to join the study, all in the same day. If not for UCSD also allowing remote consent signing—a rarity amongst hospitals, but another *simple* change that could save lives—Jake would have lost his spot in the study. Instead, he provided a quick signature via Docu-Sign after a thirty minute phone call

The trial drug, Petosemtamab, halted Jake's cancer almost immediately. It had none of the brutal wasting effects of chemotherapy.

Suddenly Jake could think again. We took walks, started writing a book, even went to the gym. I got pregnant with our daughter via IVF.

Jake was lucky. At the time, Petosemtamab was only available in the U.S.A. to a handful of patients, and only at the UCSD study site.

70% of trial patients had a similar, positive response. Petosemtamab was lengthening the lives of patients with advanced, metastatic disease by a median of six months, with some patients still on the drug at two years. That number is revolutionary for metastatic head and neck cancer patients. For comparison, the last big breakthrough in treatment was a brutal chemo regimen that extended patient's lives, and their suffering, by only two months.

Why was Petosemtamab, such an incredible option, unavailable to most?

The drug is currently languishing in additional trials. Merus, the makers of Petosemtamab, have recently started phase 2 trials that may take years to complete before an application for approval is even filed.

If Petosemtamab had been available under right-to-try laws, we wouldn't have wasted precious time navigating a broken system. It might have halted Jake's cancer sooner. It might have saved part of his tongue. It might have made surgery successful. He might have gained years. He might still be alive. Yet the drug sits on the shelf collecting dust while the patients who would benefit die.

The story of Petosemtamab is the story of dozens of promising drugs for terminal diseases that exist but remain out of reach.

HB 701 will change that.

As Jake once wrote:

"When I am dead and buried, at least those who I love and who love me will know the FDA protected me and millions of others like me from ourselves. Thanks, FDA. But the dead do not vote and do not agitate for change, so the system is likely to grind on."

Jake's voice isn't silenced just because he's dead.

Those who still love the dead—who know the dead could have suffered less, could have spent their last months with family instead of fighting bureaucracy—will keep agitating for change.

I won't stop.

Not until terminal patients are given more opportunities to live than they are given opportunities to die.

We can do better.

Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

Simple, easily enacted changes—like allowing telemedicine screening for clinical trial slots and remote consent signing—would help the system work more efficiently. Expanding right-to-try access would give dying patients the chance to live better *right now.*

This testimony isn't just about love for my husband. It's about love for progress and innovation. Jake wanted his death to mean something. Part of that meaning came from pushing science forward.

HB 701 won't just save lives.

It will improve the quality of the lives being saved.

As Jake wrote:

"It's too late to save my tongue, but it may not be too late to save the tongues and lives of others."

The best arguments for change come from the man who died waiting for it:

- Jake's arguments for why we need clinical trial improvements
- Jake's plea for a better "right-to-try system" and the tragedy of the invisible graveyard
- Additionally, my three-part essay on the Kafkaesque experience of trying to participate in a clinical trial can be found here:
    - Part 1
    - Part 2
    - Part 3

To read more about our personal stories, go to JakeSeliger.com and BessStillman.substack.com.

Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

The dead and dying at the gates of oncology clinical trials

I was reading Tyler Cowen and Daniel Gross's book *Talent: How to Identify Energizers, Creatives, and Winners Around the World*, and in it they write: "You can open doors for other people at relatively low cost (perhaps zero cost) to yourself just by making some options more vivid to them.... You embody *something*, and that something will stir some others into action" (237). That's a lot of what Bess and I are doing when we write about clinical trials, where getting the wrong answer means death: thus, our extensive focus on it, and the healthcare system more broadly. We're trying to open doors, especially for people who are sick or who don't realize what their options are.

Right now, according to "The pharma industry from Paul Janssen to today: why drugs got harder to develop and what we can do about it," apparently "Only 6% of cancer patients take part in clinical trialsnationally in the US, for instance, and the number is generally lower in other countries and for other conditions." A lot of cancer patients don't need clinical trials and are healed by existing treatments, but, even granting that standard-of-care often works, 6% seems low—it may be low because of poor guidance combined with fatalism. If my experience is representative,[1] a lot of cancer patients aren't getting adequate help understanding the system and finding a trial. Bess and I only succeeded in finding a clinical trial to keep me alive because of our own perseverance and obsessiveness; we were explicitly encouraged by multiple oncologists not to bother and to let me die. My primary oncologist at the Mayo Clinic Phoenix offered zero guidance, aid, or advice. I can't tell how common

this is, though feedback so far seems to indicate the answer might be "pretty common." For a normal person without some of our traits, background, and resources, getting an optimal clinical trial would be far harder, if not impossible—and it was already hard for us. I'm still puzzled that more people with poor prognoses on standard-of-care treatments aren't working to get the best clinical trials they can.

What's the barrier? Mindset, and discouragement from oncologists, is probably one problem. A guy named Richard Chen, whose profile says he wrote two books on clinical trial recruitment, said: "First, FDA's remit is not, and has never been, to get therapies to patients." He also said: "Its primary mission first and foremost, is to prevent unsafe drugs from injuring patients." If the FDA's remit isn't to get therapies to patients, that's bad, and its remit should change. The second comment is pure, unintentional comedy. Right now, I'm a dead man walking. The FDA is preventing "unsafe" drugs from injuring me, so that I can be "injured"—which is to say, killed—by a recurrent/metastatic squamous cell carcinoma infestation. If I'm injured or killed by a drug, that's not so different from my ultimate trajectory anyway, and the knowledge that can be created from my situation might accelerate treatments and save the next guy's life.

Moreover, we already have an example of a medical area that works well with minimal FDA interference: surgery. Maxwell Tabarrok describes the situation in "Surgery Works Well Without The FDA: The best evidence against the FDA:"

> *Despite extreme information problems and a complete absence of federal oversight, surgery seems to work well. Compared to similar patients on the waiting list, 2.3 million life years were saved by organ transplants over 25 years. The WHO claims that "surgical interventions account for 13% of the world's total disability-adjusted life years." Coronary artery surgery extends lifespan by several years for $2300 a year. Cataract surgery and LASIK can massively improve quality of life for a few thousand dollars.*

Regarding drugs, particularly drugs for people who are already effectively dead, like me, we should be moving closer to a surgical model.

I think Chen is a smart and well-meaning person. But he's so bureaucratized, and he's so imbibed the FDA's line, that he doesn't realize the Kafkaesque absurdity of telling me, a dying man who's failed all standard therapies, that the FDA is protecting me from potentially unsafe drugs, so that I can safely die of cancer. If the FDA didn't flex their paternalism quite so aggressively, terminal patients could at least consent to try something that *might* help them, which is better odds than trying nothing and waiting for a certain end. Look, if the FDA wants to have long trial periods for dubious drugs like those meant to lower cholesterol or whatever, fine. Once a person has a fatal diagnosis, however, that person is probably, like me, a lot more inclined to take a flyer on what's available and see what happens. And we should be allowed to do that. We're terminal, not without capacity. If the FDA's remit is, ultimately, preventing patient injury, maybe they should ask themselves if they're causing injury with their current approach?

Knowledge among patients and oncologists seems to be another barrier, according to "Why drugs got harder to develop:"

> *Many patients are willing to take part in clinical trials in principle, but awareness is poor. About 50% of the time when patients are invited to clinical trials they accept, but 90% are never invited to participate, mainly because most patients are not treated in settings that conduct trials. Patients are also not necessarily aware of or educated about the benefits of trials, and how they may enable them to access a high standard of care. Leading clinical research centres often have too many studies and not enough patients. When it comes to the trial itself, the site may be far from where the patient lives, requiring them to travel or even relocate for the duration of the trial — without adequate support for doing so.*

Poor awareness is consistent with my experience—no one explicitly told me to seek clinical trials. Bess writes about the dearth of oncologists referring their patients to clinical trials in "Please be dying but not too quickly: part three" and I've written about this issue as well, but, as I mentioned above, if I'd followed my then-oncologist's guidance, I'd have done some palliative chemo and then died. That doesn't seem like an optimal outcome. If I die, Bess will be lonely. In spaces like oncology, I'd expect patients to be more like me—that is, highly motivated to attempt to not die. I don't wholly understand what's going on, which is why I titled my last essay on the subject "Puzzles about oncology and clinical trials."

I guess (or infer from behavior) that most oncologists aren't penalized or rewarded for helping their patients find and enter clinical trials. In the

emergency room, a doctor who routinely misses heart attacks or strokes will find his or her license attacked and him or herself in a court room. In oncology, there's apparently no real effort to consistently help patients who've exhausted standard treatments. It's not, I guess, part of the professional elements of the profession, which I find surprising. Sure, many patients are likely elderly and too sick to pursue clinical trials, but a fair number must be like me: motivated and able to undertake somewhat arduous efforts to prevent or delay death.

One reason too few people participate may be logistical:

> *To get enough patients to fill up large trials companies need to conduct trials at multiple sites. The more sites involved in a trial, the greater the logistical complexities involved in coordinating that the protocol is executed appropriately across sites, the data is collected to a good standard, and the drug is distributed to all sites as needed. This all increases costs. More sites also increases variance in execution, and improper trial conduct can delay or even sink a development program. According to data from Tufts university, >80% of trials fail to recruit on time, actual enrolment times are typically around double the planned timelines, and ~50% of terminated trials result from recruitment failures. An estimated 11% of trial sites fail to recruit a single patient, and another 37% don't reach their target enrollment criteria.*

There are efforts to create "virtual" trial sites—in other words, to allow clinical trials to proceed at local sites that reach some minimum threshold of competence. To use myself as an example, if the petosemtamab trial I'm doing

at UCSD included a real virtual site component, petosemtamab could be shipped to HonorHealth in Scottsdale or one of the Ironwood Cancer Centers in Chandler, and I could receive my infusions and monitoring locally, with the data reported to UCSD and/or Merus (the drug company). Although that would mean "more sites involved in a trial," it also means less responsibility at each site. The "recruitment failures" issue is interesting in light of the fact that almost no trial sites seem to do basic, modern marketing.

I'm not hugely optimistic about fomenting real change. Real change is slow in a society like the United States, which has been characterized since the 1970s overwhelmingly by complacency, stasis, and status-quo bias. One sees that in our inability to build new housing, our inability to build new ships for the Navy, our refusal to accelerate subway development, our preference for interminable litigation over infrastructure, the Jones Act, the FDA, dishonest and tuition-seeking universities, and the innumerable other veto players who, like Richard Chen, are great at saying "no" and unable to say "yes." I hope we can build O'Neill Habitats that will allow a re-opening of the frontier and a new space where the dreamers who are tired of hearing "no" can instead create a new polity where it's possible to say "yes." The United States is huge on safetyism instead of true safety—and human flourishing.[2] We can and should do better. I doubt we will, however, because the people who most need FDA reform are dead. They're not writing. They're not doing podcasts. They're not agitating Congress.

Still, sometimes change happens, and the bureaucratic inertia is somehow overcome. For example, voucher and charter schools seem to continue to ascend, despite entrenched and intense monied union interests opposing

them, and decades after their intellectual foundations were laid. Marijuana legalization seemed unlikely until it happened. Psychedelics look like they're on the path to medical legalization, at the very least, and possible general legalization; based on my experiences, psychedelics are both safer and far more interesting than alcohol. SpaceX has revolutionized the space game, and I'd have incorrectly predicted failure. Tesla is the sole bulwark against state-affiliated and subsidized Chinese companies owning the entire electric car market. Who knows what's possible? I don't hope for this, but if someone in some senator or senior house member's family gets cancer, and that senator or house member learns what I've learned, FDA reform might become a vital issue for that person. Few people I've seen online have defended the current system (there are some—just not a lot).

The fact that the current ossified, slow system has persisted as long as it has is an argument for it continuing. Good enough is good enough, right? Moreover, the way the press responds to events helps perpetuate stasis: if a drug has negative side effects, including potentially death, that gets plastered all over the news. Investigations are launched. Scapegoats are sought. If a drug works, and saves lives, the response is muted. The articles go unread. The beneficiaries are happy but don't start campaigning for more and better medical treatment, faster. One person who dies from a drug outweighs one hundred who might be saved by another. It reminds me of all the press given to any kind of airline accident, even one without casualties, while 40,000 people a year die in car crashes, without most of them making headlines.

One person on LinkedIn said this about Bess's clinical trial essay-guide:

> *An extraordinarily damning overview of the way things operate currently, that puts everything we complain about from within the industry into perspective. Thanks for sharing this Brad [Hightower—mentioned above] – as you say, a must read that underlines how we must all work together to improve things.*

It might be a damning overview, but it also turns out that seemingly everyone working in or adjacent to clinical trials knows about the problems already. That includes everyone from the researchers themselves to the drug companies to the hospitals to the oncologists to the support staff. If a lot of people have known for a long time how bad the system is, and no one has managed to coordinate sufficiently to make substantial improvements, that implies that the problems will persist. Can Bess and I be the catalysts that finally galvanize some change? That'd be great, and yet I'm pessimistic. There's a saying in investing: "The market can stay irrational longer than you can stay solvent." Call this Seliger's Law: "A broken system can stay broken for longer than people have the time, energy, and ability to try fixing it."

Still, Bess and I would like to try to make the world a better place, to the extent we can, and within whatever limits our abilities and skills may impose, and trying to nudge the clinical trial system into a better equilibrium is part of our effort. It's too late to save my tongue, but it may not be too late to save the tongues and lives of others. In an alternate world, petosemtamab, or a cancer vaccine, would've been approved and available in Oct. 2022. I'd have gotten surgery, and then petosemtamab, which is way less toxic than chemotherapy. Maybe that wouldn't've saved my tongue—but maybe it would've. Oncologists

are reluctant to use chemotherapy, but modern alternatives like petosemtamab should help people like me in the future.

Cancer vaccines exist, though trials are moving achingly slowly. A company called Transgene is testing a cancer vaccine called TG4050 on patients with initial head and neck cancer diagnoses—the same diagnosis I had in Oct. 2022. TG4050 is moving to a Phase 1b and 2 trial; according to the company, "The compelling initial Phase I data presented with NEC at ASCO 2023 showed that all evaluable patients treated with TG4050 monotherapy developed a specific immune response and remained disease-free." I wish I'd remained disease-free; instead, I have no tongue and am likely to die soon.

Despite my pessimism, "Why drugs got harder to develop" says:

> *Yet, even though there are major forces pushing against drug developers, there is a sense that the industry is still underperforming, and that it could do more. One reason for optimism can be seen in the recent flattening of the slope of Eroom's law following decades of declining productivity. It remains to be seen whether the recent uptick is a sustained turnaround or not. The pessimistic view is that it is illusory, a result of how drugmakers have side-stepped fundamental productivity issues by focusing on developing drugs for niche subpopulations with few or no options where regulators are willing to accept less evidence, it's easier to improve on the standard of care, and payers have less power to push back on higher prices: rare disease and oncology in particular. It's no coincidence that investment has flowed into areas where regulatory restrictions have been relaxed and accelerated approvals are commonplace: 27% of FDA drug*

> *approvals in 2022 were for oncology, the largest therapeutic area category, and 57% were for rare/orphan diseases*.

That seems better than nothing. Maybe Congress and/or the FDA is responding to the Richard Chin logic I note above. The FDA has created systemic problems, and it can also create systemic solutions. For example, the FDA doesn't really account for the time-value of money,[3] which is especially important in a high-interest-rate environment:

> *As a more general point, it would help if regulators could be more predictable and transparent in their decision making. In a survey of drug and device industry professionals, 68% said that the FDA's unpredictability discouraged the development of new products. It can be hard to predict how regulators will react to a certain dataset in the context of high unmet need, so companies can be inclined to 'submit for approval and pray', even after receiving negative feedback on the data package from regulators during prior interactions.*

"Hard to predict" means that many people stop pushing a drug before they start. Companies are competing for investable cash with all other companies; the more time-consuming (read: expensive) the FDA makes the process, the fewer drugs will even be attempted. "Why drugs are harder to develop" suggests the FDA be more accountable to patients:

> *A straightforward start to improve transparency across the industry would be for the FDA to disclose the formal 'complete response letters' (CRLs) issued when they reject a drug which contain the reasons for rejection. Making this information public would give future developers*

> *insight into the regulator's thinking on a disease, with minimal downsides. How companies represent their CRLs to the broader market today is often misrepresentative of the actual reasons for rejection, potentially misleading patients as well as future investors and drug developers in the indication.*

I'm not the only one thinking about reform; pretty much everyone in the industry is. To return to a point I raised at the beginning of this essay, reforms could also make clinical trials easier for patients to access. Bess and I spent thousands of dollars and countless hours learning how the clinical trial system works and then how to participate. Initially, no one comprehensively helped us on this journey; my original oncologist at the Mayo Clinic Phoenix was and likely still is sluggish. Mayo Phoenix has a great ENT department but appears to be poor in oncology, which is surprising for an organization with a reputation for cancer care. Bess and I had to learn what we know piecemeal, which is part of the reason we're trying to describe comprehensively what we've learned and how other people's experiences can be made better.

The best trial for head and neck cancers is petosemtamab, and that trial is being hosted at UCSD. Bess and I are lucky enough to have the resources necessary to get me there twice a month from Arizona for infusions, thanks in large part to the generosity of friends and strangers who've contributed to the Go Fund Me. I've been saying that being sick for an extended period of time has at least three components to it: health itself; financial well-being; and managing healthcare. Drop any one of the three and the other two are likely to fall too. Very few people can help my health or healthcare directly, but the contributors to the Go Fund Me have made the financial challenges easier.

What'd make things better for everyone, however, is reforms like virtual trial sites. The healthcare team at UCSD has been great, but being infused locally would negate the need to be away from home six days a month, the cost of flights, hotel, and the huge energy expenditure all that entails. The process of getting a clinical trial medication can and should be less expensive and arduous than it is. I can see why most people who might want to participate in the better clinical trials for their illness run out of money and energy to pursue those trials. Bess and I were ready to move anywhere. Fortunately, we've not had to move somewhere expensive and far from family and friends. We were ready to, though. We may still have to one day—and maybe, but hopefully not, soon.

Both of us also wish that there were greater transparency around which trials are doing well in terms of patient outcomes and which trials aren't doing so well. We've learned via experience that right now, there's no substitute for establishing care at a bunch of sites and listening to the oncologists there. Oncologists running trials will often tell you how things are going for trials that've been running for a while. If they're enthusiastic about a trial, it's often because they see a lot of patients doing well on it. They have observational data that outside docs and institutions have to wait months, maybe years, to get wind of.

Sometimes they'll also steer patients away from trials that aren't producing enough positive results. I'm grateful to the docs who've quietly advised us against floundering drugs. Some oncologist meetings produce non-public intel about which trials are most promising, provided enough patients have received the drug in question; the oncologists won't know much if you're like

the first or fifth or tenth human to be dosed with a novel substance, but a lot of these trials have built up years of data. If a site has run through dozens or as many as 100+ patients, the oncologists will have a sense of whether it's working, even if nothing "official" has been released.

This is one of innumerable tiny facts and practices about effectively participating in clinical trials that we've discovered. I've never read anyone else who's put out things like this, just like I've never read anything remotely like Bess's clinical trial guide-essay, "Please be dying, but not too quickly." Somehow, a lot of this essential information isn't making it into the larger information ecosystem. The lack of quality information has been driving my writing over the last five months, including my last essay, "On not being a radical medicine skeptic, and the dangers of doctor-by-Internet." We collectively can and should be doing better. I'm trying to be part of the solution. In reading this, and passing it to others, you're part of the solution, too.

If you've gotten this far, consider the Go Fund Me that's funding ongoing care.

- See also Alex Tabarrok's "Conditional Approval for Human Drugs," in which he says "I think that the FDA's excellent arguments for conditional approval apply to human drugs as well as to (other) animal drugs and even more so when we recognize that human beings have rights and interests in making their own choices." And he also ends on a hopeful note: "Dare I say it, but could the FDA be lumbering in the right direction?"
- Part III of Bess's clinical-trial odyssey has recommendations for improvements.

Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

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[1] Which I hope it isn't, and yet the emails I've been getting indicate that my experience is distressingly common.

[2] The book ***Where is My Flying Car?*** by J. Storrs Hall is good on this. We should have so many nuclear power plants that power is almost too cheap to meter, we should have O'Neill Habitats that re-open the political frontier in order to let the non-complacent gather and advance the human condition, and we should have progressed much further in curing cancer and making biology a variable rather than a constant. That we're content to creep and crawl on the earth rather than soar into the heavens is an indictment of our whole society. Too many lawyers, too few makers.

[3] Bess asked what the time-value of money is. Briefly, it's how much an investment or investor would lose or gain from alternatives. Take a simple example: you can invest a million dollars in a company running a clinical trial, or in a money-market fund paying 5% a year. If you invest in the money market fund, you wind up with $1,050,000 at the end of the year. If FDA delays cost you a year, you've effectively lost the $50,000—you have more like $950,000! Inflation matters in these calculations, too.

This is also why delays to housing construction are so evil.

Bess Stillman, MD / PO Box 998, Carefree, AZ 85377 / drbstillman@gmail.com

I am dying of squamous cell carcinoma, and the treatments that might save me are just out of reach

Alex Tabarrok writes about how "when the FDA fails to approve a good drug, people die but the bodies are buried in an invisible graveyard." I'd like to make that graveyard a little bit more visible because I'm going to be buried in it, in a few weeks or months. A squamous cell carcinoma tumor appeared on my tongue last September; the surgery for it occurred in October, followed by radiation in December – January, but the tumor reappeared at the base of my tongue in April. A massive surgery on May 25 appeared to produce "clean margins" (that is, no tumor cells remained where the surgeon operated), albeit at huge cost: I have no tongue any more, just a "flap" of muscle where it used to be, and no ability to swallow solid foods ever again. Monday I'm starting chemotherapy, but that's almost certainly going to fail, because a CT scan shows four to six new gross tumors, four in my neck and two, possibly, in my lungs.

So what *might* help me? MRNA tumor vaccines. Head and neck squamous cell carcinomas (HNSCC) are notoriously treatment resistant, and mRNA vaccines have shown huge promise. Why aren't they happening faster? Because the FDA is slow. There are some trials underway (here is one from Moderna; here is another), and, although I'm trying to enroll, I may be too late, since my cancer moves so aggressively. The FDA was loathe to approve initial mRNA human trials, even when those trials would have been full of people like me: those who are facing death sentences anyway.

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Here is one story, from "Why the FDA Has an Incentive to Delay the Introduction of New Drugs:"

> *In the early 1980s, when I headed the team at the FDA that was reviewing the NDA for recombinant human insulin, . . . we were ready to recommend approval a mere four months after the application was submitted (at a time when the average time for NDA review was more than two and a half years). With quintessential bureaucratic reasoning, my supervisor refused to sign off on the approval—even though he agreed that the data provided compelling evidence of the drug's safety and effectiveness. "If anything goes wrong," he argued, "think how bad it will look that we approved the drug so quickly." (41)*

The problem is that delaying mRNA cancer vaccines kills people like me.

We need to have a much stronger "right to try" presumption: "When Dying Patients Want Unproven Drugs," we should let those patients try. I have weeks to months left; let's try whatever there is to try, and advance medicine along the way. The "right to try" is part of fundamental freedom—and this is particularly true for palliative-stage patients without a route to a cure anyway. They are risking essentially nothing.

When I am dead and buried at least those who I love and who love me will know the FDA protected me and millions of others like me from ourselves. Thanks, FDA. But the dead do not vote and do not agitate for change, so the system is likely to grind on.

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In computer science there is a convention in which one's first program prints "Hello, world." Now it is my turn to write "Goodbye, world." I'm crying as I write this and am sorry to have to go so soon. I have to give back the gift, though with great sadness.

Here is more about the FDA being slow and bureaucratic.

EDIT: Thank you for all the comments and emails. Many of you have asked what you can do to help, and one possible answer is to consider the Go Fund Me that's funding ongoing care. Apart from that, I'm being treated at the Mayo Clinic Phoenix, and they have a system set up for donations to support clinical trials, so maybe that is another answer; I hope that, in the future, others won't have to go through what I'm going through.

You may like some of the other essays I've written, like "I know what happens to me after I die, but what about those left behind?", or that Bess has written, like "How much suffering is too much?"

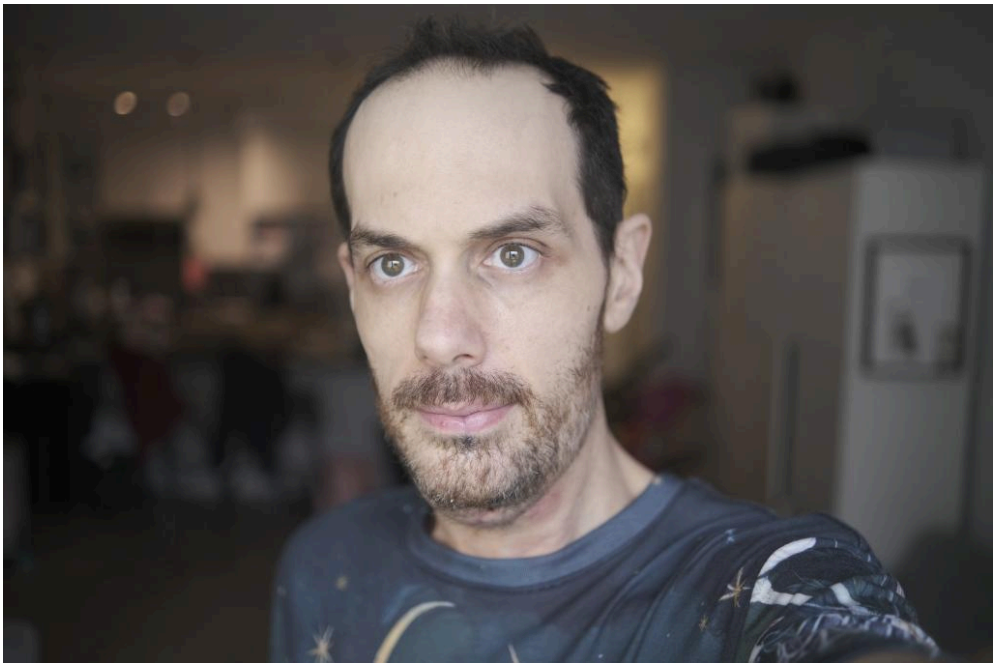

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Photo: Jacob Stillman on July 22, 2023.