2015 TOP CANCER DOCTORS

Newsweek

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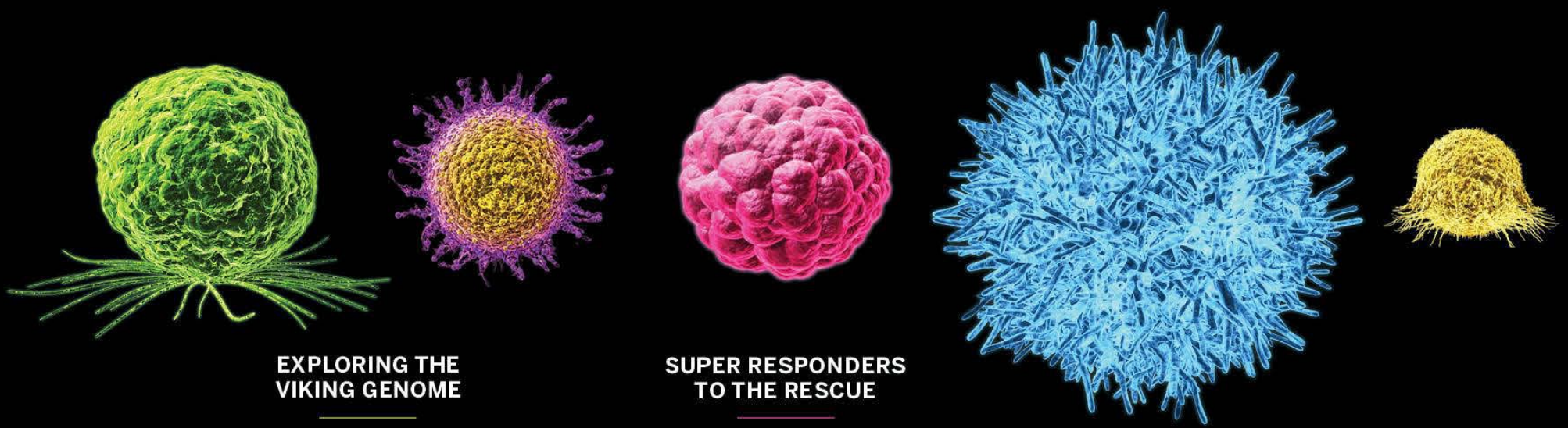

EXPLORING THE VIKING GENOME

SUPER RESPONDERS TO THE RESCUE

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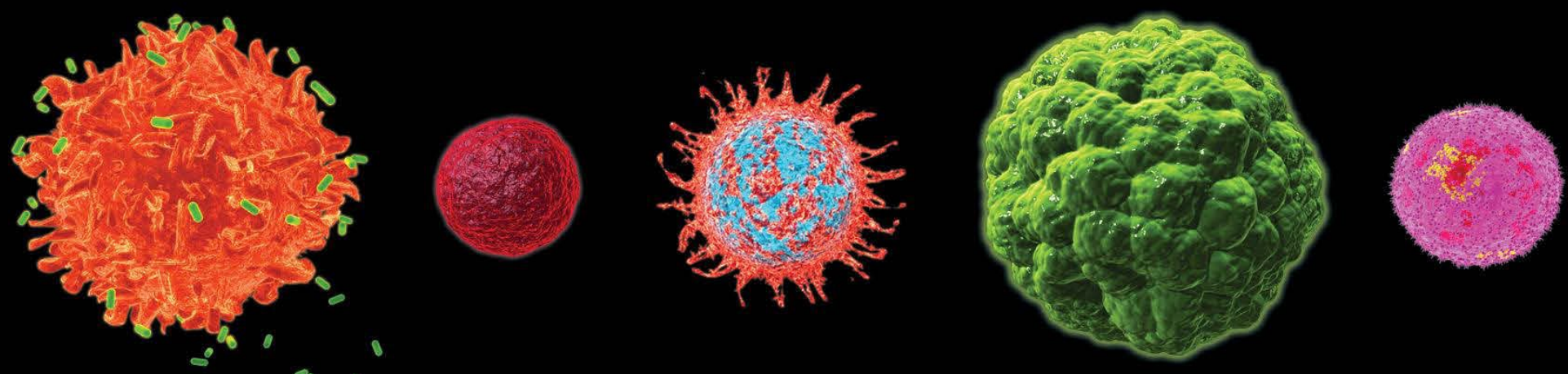
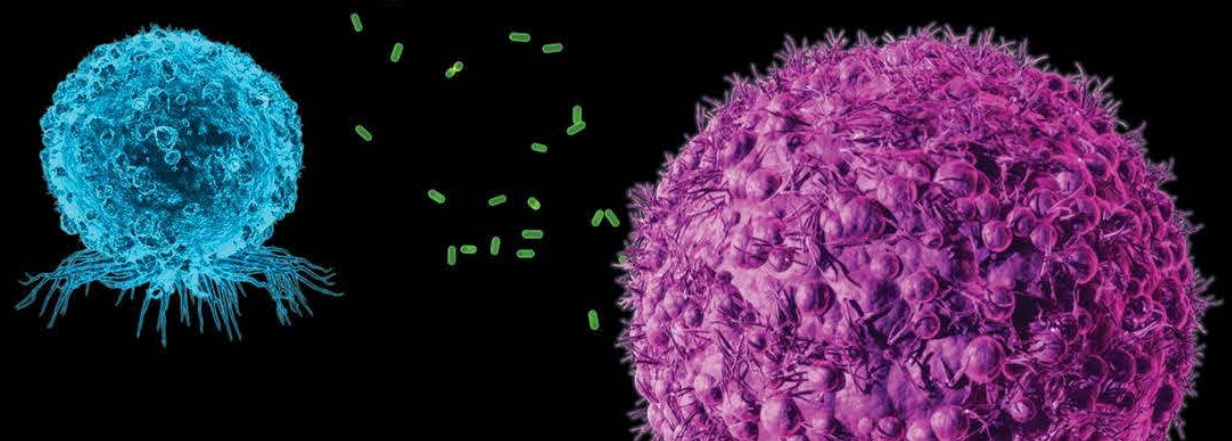


MAKING MEDICAL RADIO WAVES

THE TRAGIC LACK OF MEDS FOR KIDS

THE DRUG IS TOO DAMN EXPENSIVE!

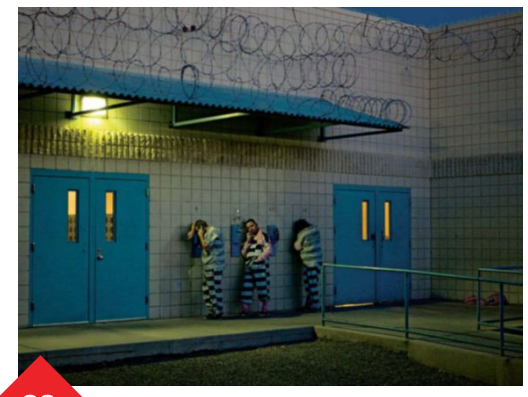


Newsweek

DOWNLOADS

01

HOW CHINA HELPED IRAN GO NUCLEAR



02

TALK IS NOT CHEAP: INSIDE THE SHADOWY BUSINESS OF PRISON PAY PHONES

03

TWO NUMBERS: FORGET STUDENT LOANS—DAY CARE WILL COST YOU AN ARM AND A LEG

04

THE CITY TAKES ON THE STATE: DE BLASIO AND CUOMO'S FEUD WON'T END WELL

NEW WORLD

SPECIAL HEALTH SECTION:
DISPATCHES FROM THE FRONT LINES
OF THE WAR ON CANCER

BIG SHOTS

COCKTAIL HOUR

PEACE FIGHT

FROM WHITE HOUSE TO BIG HOUSE

BATTLEGROUND

piracy to Violate the International Emergency Economic Powers Act (One Count); Violation
International Emergency Economic Powers Act (Two Counts); Conspiracy to Commit Money
dering (One Count); Conspiracy to Commit Wire and Bank Fraud (One Count); Wire Fraud
Counts)

LI FANGWEI

(FBI)

HOW CHINA HELPED IRAN GO NUCLEAR

THE U.S. HAS INDICTED KARL LEE FOR SELLING ADVANCED MISSILE AND NUCLEAR TECHNOLOGY AND MATERIALS TO IRAN.

Somewhere on the grimy streets of an industrial city in northeastern China walks one of the world's most dangerous men. Stocky and fleshy-faced, with a mole on his upper lip, Li Fangwei keeps a low profile and operates under a half-dozen aliases. In another time and place, he might have strutted about his criminal empire like a colorful cocaine

kingpin, machine-gunning rivals and showering the locals with soccer stadiums. But Li's brand of business requires more discretion: He sells advanced missile and nuclear technology and materials. To Iran.

Indicted in New York last year for Iran sanctions-busting and money laundering, Li—known in the West as Karl Lee—operates out of Dalian, the Yellow Sea shipping center formerly known as Port Arthur. Once talkative, he no longer answers his phone. Employees at a half dozen of his companies contacted by Newsweek said they'd never heard of him.

But Lee is well known to U.S. government officials and prosecutors who have kept close watch on his illicit missile and nuclear technology business for the past decade. To them, he's second only to A.Q. Khan, the notorious Pakistani scientist who gave Iran, North Korea and Libya road maps to the bomb. "A.Q. Khan is in a class by himself," says Robert Einhorn, a top former nonproliferation official in the Clinton and Obama administrations. "But if Khan occupies places 1, 2, 3 and 4, then Karl Lee is clearly No. 5 on down.... He's done a lot of damage."

Other experts uniformly agree. "He's the greatest serial proliferator in the world, judging by the sanctions on him," says Valerie Lincy, executive director of the Wisconsin Project on Nuclear Arms Control, a private, nonpartisan research organization.

"Karl Lee's importance as a supplier to Iran's missile program can't be overstated," says Nick Gillard, an analyst with Project Alpha at King's College London, which has closely tracked Lee's transactions. "If you were to take apart an Iranian missile, there's a good chance you'd find at least one component inside that's passed through Lee's hands." In recent years, Gillard says, Lee has graduated from selling technology and advanced metals made elsewhere to becoming a producer himself of "highly sensitive missile guidance components such as fiber-optic

gyroscopes, making the leap from middleman to high-tech manufacturer."

Which makes him a wild card in the sweeping arms deal with Iran that extends the ban on selling ballistic missiles and parts to Iran for another eight years. If China can't—or won't—control him now, Congress will never vote to lift sanctions on Iran, suggests Senator Mark Kirk of Illinois, a leading Republican hawk. "While this administration may temporarily waive some Iran sanctions laws to advance flawed negotiations, Congress will never vote to permanently repeal these laws until the Iranian regime's nuclear ballistic missile and terror threats end once and for all," Kirk said in a statement to Newsweek.

But that's the rub. Starting with the Clinton administration over a decade ago, China's response to behind-the-scenes protests from U.S. officials over Lee's activities has ranged from "never heard of him" to "go fish," according to present and former officials. And that remains unchanged, judging by Beijing's response to an inquiry about Lee from Newsweek last month. In a prepared statement, the spokesman for China's Washington embassy insisted that Beijing takes proliferation of weapons of mass destruction "seriously," but "as for the specific case [of Lee], I don't have further information for you."

Faced with such laissez-faire responses, the Obama administration began ratcheting up pressure on Lee last year, designating more of his companies for sanctions, hanging a $5 million reward on his head and issuing an Interpol "red notice" for his arrest if he travels outside China. The FBI also seized $7 million of his assets and issued a "wanted" poster with a blurry picture of the smirking, tousle-haired 42-year-old. As fast as they hit Lee's operations, however, he closes them and pops up under new names and accounts. And he remains beyond the reach of the Justice Department, protected by a web of Chinese officials, sources say, and limits his foreign travel to direct flights to Tehran.

Many officials who have tracked Lee for years are fed up. Quiet diplomacy hasn't worked, they say. It's time to castigate China publicly for protecting Lee and demand that it turn him over for prosecution here. "It's way past time for naming and shaming," says Einhorn, who personally discussed Lee with Chinese officials during the Clinton administration.

Presented with the opportunity to do just that this month, however, Obama administration officials retreated with responses worthy of ink-spraying squids. The State Department official responsible for nonproliferation declined an interview request. The Justice Department refused to say whether the U.S. has formally asked China to turn over Lee. And a senior administration official, speaking strictly on a not for attribution basis, offered only boilerplate on how the U.S. and China "continue to deepen" their "cooperation on nonproliferation and counterproliferation issues." To be sure, he said, "the United States continues to consider Karl Lee a priority proliferation threat."

That was it. The administration was chary, of course, of saying anything that might rattle the Iran-talks steamroller. But sooner or later, with pressure building from Washington hawks, it's likely the administration is going to have to confront China on Lee's missiles or maybe watch the entire diplomatic enterprise go into a ditch. The question is how.

Oddly enough, U.S. law enforcement officials know almost nothing about Lee's family, education, party connections and lifestyle—a reflection, perhaps, of how they've been stonewalled by their Chinese counterparts for the past decade. By tracking his commercial transactions, however, they think they've identified companies registered under the names of his father, Li Guijian, and two brothers, Li Fangchung and Li Fangdong.

But where did Lee get his technical and business expertise? Where did he learn to speak English? They don't know. Is he living large like Pablo Escobar? They don't

think so, although they say he's fond of luxury cars and nice suits. That's it. Beyond his business dealings, he's a cypher. "We have worked on him a long time," says Matthew Godsey, a Chinese-speaking senior research associate at the Wisconsin Project, chuckling. "It's hard to pin down who he is personally."

Investigators know Lee was born in Heilongjiang, a hardscrabble province bordering on Manchuria, in 1972, when China was being turned upside down by the ultra-leftist Cultural Revolution. By the time he was in high school, however, the country was well on the road to exuberant, state-guided capitalism, aided by its nascent ties with the United States. But how Lee made the leap from the rustic far northeast to the booming port city of Dalian to world-class notoriety as Khan's heir in the black market nuclear-arms business remains a mystery—at least in Washington. One government investigator says Lee had a grandfather who was a "legendary colonel in the People's Liberation Army" during the Korean War, which probably helped.

In any event, by the early 2000s Lee was "connected," as the gangsters say. A classified 2008 State Department cable obtained by WikiLeaks described him as "a former government official who has been using his government connections to conduct business and possibly protect himself from Beijing's enforcement actions."

"If you're trying to think through why the Chinese don't [stop] with this guy," a congressional staffer who has been tracking Lee says, "there are two explanations and possibly more. One, they like what he's doing—and you have to ask why. Or two, he's got to be paying people off."

Or both. Indeed, lots of government and party officials probably have their beaks in Lee's businesses, the congressional staffer says. "That's the Chinese way of doing business."

"This is an area where it's pretty important to have contacts either in the security apparatus or the military, and preferably both," a Beijing source involved in counterproliferation issues told Newsweek. "The industry is littered with former security types.... My assumption has been all along that he's not just some entrepreneur who built up a company and then decided to sell things to Iran. That's not how this works."

Payoffs? He shrugged.

But there are other motives driving Lee's high-wire act of dodging repeated U.S. indictments and sanctions, observers say. Many Lee-watchers think he's really Beijing's man in Tehran, a very useful cutout for arms sales, a "private businessman" whom they can pretend is freelancing while they keep close relations with the Iranians. At some point, this thinking goes, Beijing knows that the United States and Iran will eventually come to some sort of nuclear agreement that will lift the sanctions. When that day comes, Lee's covert missile and nuclear technology sales will have put China at the head of the line in the Iran arms bazaar.

Until then, the likelihood that Lee will ever be arrested and shipped to America to stand trial makes some experts laugh. For starters, a rising China can't be pushed around by Washington anymore. While it succumbed to pressure 20 years ago and quashed some arms dealing with Iran, today it knows the Obama administration needs it more than it needs Washington for help on a range of issues, from the Iran deal to North Korea to trade and the vast amount of U.S. debt that China holds.

In the meantime, Lee has made himself virtually irreplaceable to both Beijing and Tehran, if only because of "the amount of time that Iran has invested with him," a federal investigator says. "The degree of tradecraft that he has used makes him a seasoned veteran," he adds, referring to Lee's skill in working through dozens of fronts under

multiple aliases. “It takes time to develop somebody else like him, and clearly he’s able to act freely within China. So you’ve got someone who can move freely, who has been trained for over a decade and uses really good tradecraft. That’s kind of hard to replace.”

He is, in short, much like Nicolas Cage’s character in Lord of War, a Russian-born American by the name of Yuri Orlov who deals arms to a score of bad guys on behalf of clients like the CIA, which wants to keep its hands in the savage conflicts hidden. In the movie, a zealous Interpol agent (Ethan Hawke) finally tracks down Orlov and throws him in a cell. The agent thinks it’s the end for Orlov, but the arms dealer assures him he’s wrong.

“Let me tell you what’s going to happen,” Orlov says, sitting in handcuffs. “Soon there will be a knock on that door, and you will be called outside. There will be a man in the hall who outranks you.... First, he will complement you on the fine job you have done...that you are to receive a commendation, a promotion. And then he’s going to tell you I am to be released. You are going to protest, you’ll probably threaten to resign, but in the end I will be released.

“The reason I will be released is the same reason that you think I’m going to be convicted: I do rub shoulders with some of the most vile, sadistic men calling themselves leaders today,” Orlov continues. “But [for] the president of United States, who ships more merchandise in a day than I do in a year, sometimes it’s embarrassing to have his fingerprints on the guns. Sometimes he needs a freelancer like me to supply forces he can’t be seen supplying.”

Somewhere in China, there’s probably a policeman who thinks world peace would be served—and his career enhanced—by arresting Karl Lee. But that would be foolish. “You call me evil,” Orlov says, “but unfortunately for you, I am a necessary evil.” At least to Beijing.

With Bill Powell in Dalian, China.

Jon Lowenstein/NOOR/Redux

TALK IS NOT CHEAP: INSIDE THE SHADOWY BUSINESS OF PRISON PAY PHONES

CRITICS SAY THE INDUSTRY IS RIFE WITH EXORBITANT FEES AND SWEETHEART DEALS TO LOCAL SHERIFFS. WILL THE FCC ACT?

Last year, when Joanne Jones learned that her son Nate had been arrested, the last thing she worried about was her phone bill. The police in San Marcos, Texas, had charged

him with aggravated robbery, but when Jones tried to call him in jail, she quickly realized it was going to cost her. There was a $3.99 “wireless administration fee” and a $2 “non-use” fee, not to mention the cost of the call, about $10 for a 15-minute conversation.

Over the past year, Jones, 60, an occupational therapist in Warwick, Rhode Island, has racked up over $1,000 talking to her son behind bars. The money goes to Securus Technologies, a Dallas-based company that’s one of the largest players in the prison tech industry. The company employs 1,000 people in 46 states, contracts with 2,600 jails and prisons across North America and provides service to more than 1 million people. Every day, inmates and their families place about 400,000 calls on Securus phones, according to company statements. And because they can choose only the one provider in their jail or prison, business has been booming for Securus.

Yet critics say the company, along with the industry in general, is getting rich off exorbitant fees and sweetheart deals to local sheriffs. “This is about shifting the cost of the police state onto the backs of the poor people being policed,” says Paul Wright, executive director of Human Rights Defense Center.

Securus says it’s not doing anything wrong. Company officials say that their business isn’t wildly profitable and that their margins are comparable to other phone operators such as Verizon and AT&T. But leaked documents from a Securus investor presentation, published by The Huffington Post and reported elsewhere, show that in 2014 Securus earned $114.6 million in profits on revenues of about $404 million—margins comparable to those at companies like Apple and Google. In an email, Securus CEO Rick Smith says the website received the presentation “illegally,” and in a letter to the Federal Communications Commission (FCC), a Securus lawyer wrote, without elaborating, that

“the figures set forth in the article are simply incorrect or taken in the incorrect context.”

Either way, the FCC is now closely watching the industry. By the end of this summer, it will expand its regulations on the prison phone business. The new rules could lower rates for inmates and their families, and reduce the amount of money sheriffs receive from the fees charged for those calls. As FCC Commissioner Mignon Clyburn says, “People should be treated with as much dignity and respect as possible, even if they are incarcerated.”

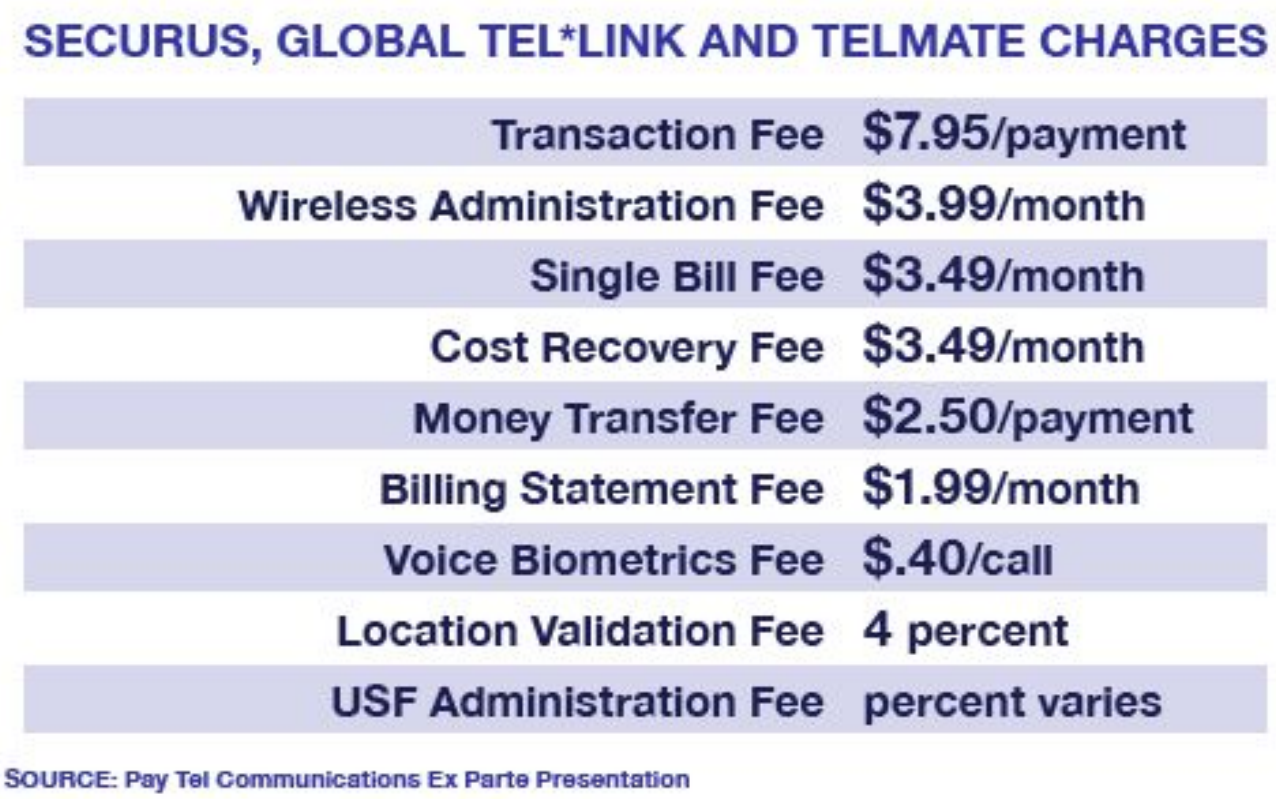
Ripping Phones From the Wall

One of the main things the FCC may target are the billions of dollars in commissions that companies like Securus pay local sheriffs. Jail and prison administrators say allowing inmates to talk on the phone costs them money, as they need to pay guards to monitor the calls. Yet the fees seem unusually hefty; some sheriffs may collect up to 90 percent of the call revenue, which can amount to millions of dollars a year. And there’s little oversight once the money is in the bank. “Every single filing I’ve ever seen from the sheriffs is about the money,” says Wright. “They aren’t giving a rat’s ass about safety.”

In the past year, more than 200 sheriffs have filed letters to the FCC, threatening to rip the phones from the wall if the government takes away their commissions. “They don’t have to provide a call service,” says Jonathan Thompson, executive director of the National Sheriffs’ Association.

The size of the commissions—and the price at which companies like Securus place their rates—are often big factors in winning bids with jails and prisons. At Hays County Jail, where Jones’s son is incarcerated, Securus collects $9.29 for each 15-minute call he places, the maximum time inmates are allowed to use the phone. Yet in 2011, the San Marcos Mercury reported that Securus pays

up to 58 percent of that, $5.39, back to the Hays County Sheriff's Office.



Critics say commissions paid to sheriffs help drive up prison phone fees. Credit: Pay Tel Communications Ex Parte Presentation

This relationship has become a good selling point for prison tech companies. Over the past 10 years, Securus claims, it has generated some $1.3 billion in commissions for local sheriffs. But critics like Peter Wagner, executive director of the Prison Policy Initiative, say the commissions are why it's so expensive for inmates to make calls. Wagner says Securus and other prison tech companies have "a financial incentive in making sure that the rates are as high as possible."

'Where the Real Money Is'

If Securus is paying such high commissions, how can it possibly make substantial profits? The answer, analysts say, is simple: Prison tech companies have increased fees to recoup lost revenue from the commissions. "Rather than actually selling phone service and making money as a phone company," Wagner says, "the phone calls are just a gimmick in order to charge the fees, because that's where the real money is."

Securus appears to be getting rich from the fees, which are not included in sheriffs' commissions. "The companies playing the fee game look generous because they are promising to share up to 99 percent of the rate revenue with facilities," Wagner wrote in a June report. "But that 'generosity' is only possible because the company is hiding the revenue it collects from fees."

Investors still seem enthused. In 2013, Abry Partners of Boston bought a major stake in Securus for $640 million, valuing the company at around $1 billion. At the same time, Securus has expanded into a variety of new services, including video visitations and electronic monitoring. Over the past 39 months, Securus has purchased 13 companies, and it recently opened a 10,000-square-foot "technology center" to show off its new products.

But Securus's recent growth might be cut short by the new regulations. In the lead-up to the FCC's decision, dozens of Americans have sent letters to Washington urging action. The prison phone business "is rife with greed, shameless profiteering and the exploitation of vulnerable consumers," wrote Michael Hamden, a lawyer in North Carolina, earlier this summer. "Industry executives have colluded with correctional professionals to bilk millions of dollars from prisoners and their families."

Joanne Jones agrees. Recently, she wrote Smith two letters, urging him to reduce the cost for families trying to talk to their loved ones behind bars. Smith, she says, has not yet responded to her. (He also declined to comment on Jones's case.) "It makes me ill," Jones says. "Their fees and their rates are unethical and immoral, and I just don't understand how they can get away with it."

Eric Markowitz is a senior writer with the International Business Times. Follow him on Twitter @EricMarkowitz.

Vidhya Nagarajan

TWO NUMBERS: FORGET STUDENT LOANS—DAY CARE WILL COST YOU AN ARM AND A LEG

THE AVERAGE COST FOR CHILD CARE CAN CREEP UP TO AS MUCH $16,000 ANNUALLY IN THE U.S.

It’s the most common unsolicited advice new parents receive: Start saving for college. But the financial challenges

of parenting come due much earlier—before a child is even out of diapers. In the U.S., the price for a year of infant day care has already surpassed that of some four-year public universities, according to a report published by Child Care Aware of America, a national nonprofit that advocates for affordable options for families.

Working parents who don't have a doting grandparent nearby can expect to fork over as much as $16,000 a year to ensure their baby is fed, diapered, cuddled and entertained by a trained professional. In most states, the average annual cost for child care also surpasses the average amount to keep a roof over the family.

Families in the Northeast pay the most for center-based care; in Massachusetts, center-based infant care costs an average of $16,549 per year. The expense is far less for families living in the South and cheapest in Mississippi, where day care may add up to just $5,496 out-of-pocket. But even the least expensive care is still unmanageable for a lot of families. In many states on the West Coast, for example, the average cost of care adds up to 14 percent of the state median income for a married couple with children. Nationwide, the situation is most dire for single-parent families, where the cost of care is more than 23 percent of the median income.

Patricia Cole, director of government relations at Zero to Three, a national nonprofit that advocates for early childhood education, says staffing costs are the biggest driver for the astronomical expense. That doesn't mean workers are paid well; the average income in 2013 for a full-time child care professional was $21,490. But infant care is labor-intensive and demanding. A baby may require as many as eight diaper changes and four bottle feedings a day, so more caretakers are needed at infant care centers than at centers for older children.

"Different states have different requirements," says Cole. "Some states might require one staff person for every four

children. Others might go up as high as every staff member for six infants."

Add cribs and other equipment, special transportation vehicles and laundry service to the mix and the cost begins to add up quickly.

Most parents have little choice but to pay for day care from the time their children are very young, often as little as six weeks after the baby is born. That's if Mom's even lucky enough to work for a company that allows time off; only 12 percent of Americans employed in the private sector have access to paid family leave, according to the U.S. Department of Labor.

Cole says several bills have been introduced in Congress to improve the situation for working families. One bill, from Senator Bob Casey (D-Pa.), closely matches an item in President Barack Obama's 2016 fiscal year budget, which proposes expansion of tax credits for child care costs. The budget would triple the maximum Child and Dependent Care Tax Credit for families who have annual household incomes up to $120,000 and children under 5. If this were to occur, families could claim up to $3,000 a year in tax credits per child.

Mark Lennihan/Getty

THE CITY TAKES ON THE STATE: DE BLASIO AND CUOMO'S FEUD WON'T END WELL

YOU CAN'T FIGHT CITY HALL, UNLESS YOU'RE THE GOVERNOR, AND CUOMO AND DE BLASIO ARE REALLY GOING AT IT.

The city never agrees with the country. If you embrace one, you spurn the other. The divide harks back to the rift between Alexander Hamilton, the New Yorker who saw

cities as the future of America, and Thomas Jefferson, the gentleman farmer of Monticello, who compared cities to sores that vitiate the body.

The American antipathy to cities informs the assignation of state capitals, only 17 of which are in the largest city in their respective state. In New York, this divide is especially pronounced. New York City accounts for about 43 percent of the state's population and is the acknowledged world capital of finance, media, culture and Cronuts. That makes for a perennially testy relationship between the global metropolis and Albany, the state capital. New York City can hardly repaint a crosswalk without Albany, whose governor and Legislature must answer not only to Brooklyn and the Bronx but to Butternuts (pop. 1,786) and Almond (pop. 458). In the end, Jefferson's vision prevails, the large city sapped of strength by competing country interests.

"New York is the nation's largest city, yet it has to go on bended knee to a scruffy, dysfunctional state government, based in what it looks upon as a hick town," says New York Daily News state affairs columnist Bill Hammond. Similar conflicts sprout across the land, perhaps most notably in the dispute over the minimum wage, which has risen in cities like Seattle and San Francisco thanks to local legislators intrepid enough to act on their own. Such efforts, though, have met with blowback. "As city after city has voted to give low-wage workers a raise in recent years, state after state has passed laws limiting local governments' power to do so," reports the Pew Charitable Trusts.

There is only so much the city can do in a system that grants enormous power to the state capital. The perfect example of that limit is Albany, where the city's aspirations are trumped on everything from the subways, run by the state's Metropolitan Transportation Authority, to rent control, which falls under the auspices of the Division of Housing and Community Renewal.

The political knife fight now taking place in New York is especially odd because both the governor, Andrew Cuomo, and the mayor, Bill de Blasio, are city guys who identify, at least nominally, with the white ethnics of New York City's outer boroughs. Both are Democrats who worked together in the federal Department of Housing and Urban Development under President Bill Clinton. They both have national ambitions, but it is their exceedingly public disagreement that has lately garnered attention.

De Blasio asked Albany for extended mayoral control of the city's public schools and funds for an affordable housing program. Legislators from both parties rebuffed him, giving de Blasio only one year of school control and an eviscerated housing plan. "Mr. de Blasio's camp was dismayed" upon learning of what Albany had to offer, said The New York Times, which added that "the frustration appeared to be reaching near-existential levels" in City Hall.

These were not the first indignities suffered by the mayor at the capital's hands. De Blasio's signature campaign program in his 2013 mayoral bid was universal pre-kindergarten, which he intended to fund with a tax on the wealthy. But that would require approval from Albany, where Republican legislators have considerable strength and where the governor is aligned with Democrats on social issues but contemptuous of their long-standing fealty to public sector unions. Cuomo gave de Blasio $300 million for the pre-K program but without increasing taxes, thus claiming some ownership over the mayor's signature program. De Blasio also picked a fight against charter schools, loathed by his teachers union supporters. On Albany's "Lobby Day" in 2014, de Blasio attended a teachers union rally, but Cuomo upstaged him by showing up at a huge demonstration of charter school students bused up from New York. De Blasio lost that one too.

By this past spring, de Blasio was accustomed to losing, but having an anonymous source in the governor's

office—almost certainly the governor himself—call him "bumbling and incompetent" was a fresh insult on top of legislative injury. Bloodied and on the ropes, de Blasio hit back. In an interview at the end of June, he unloaded on Cuomo, accusing him of having a "lack of leadership" and harboring a "vendetta" against those who cross him. "I think he believes deeply in the transactional model," de Blasio sneered. Cuomo took this with the glee of a seasoned politician. "The mayor was obviously frustrated he didn't get everything he wanted from the legislative session. Welcome to Albany," Cuomo said with condescension.

Those who know history know that the feud between city and state will not end well, fun as it may be to watch. In 1966, John Lindsay strode into City Hall in lower Manhattan as the Republican answer to John F. Kennedy. "GOP Hope," said the cover of Newsweek in the spring of 1965, showing a dashing Lindsay in front of the city's skyline, a coolly confident smile on his delicate patrician lips, hair sculpted to perfection. At his inauguration, Lindsay promised urban renewal and racial uplift, so unabashedly messianic he makes the Barack Obama of the hope-and-change days look like a milquetoast actuary. New York "is a city in which there will be new light in tired eyes," Lindsay vowed.

The tension between New York City mayor Bill de Blasio and New York Governor Andrew Cuomo is nothing new: former mayor John Lindsay, pictured here on the cover of 'Newsweek' in 1965, famously and frequently clashed with then-Governor Nelson Rockefeller during eight years in office.

Credit: Newsweek

Eight years later, Lindsay's eyes were glazed over by an unending procession of defeats: debilitating and deeply embarrassing strikes by transit and sanitation workers, a teachers strike stemming from a nasty fight between Jewish

educators and black activists in Ocean Hill-Brownsville, a blizzard that kept Queens buried long after Manhattan was cleaned, a “riot” by blue-collar workers furious at Lindsay’s opposition to the Vietnam War, a “blue flu” strike by the police department. “Fun City,” as his New York was once famously branded, had become broken and broke by the time Lindsay left office in 1973.

The man who stood in Lindsay’s path was then-Governor Nelson Rockefeller. Much as Cuomo and de Blasio share certain superficial characteristics, so did Lindsay and Rocky, both Ivy League–educated uptowners flirting with the left wing of the Republican Party (Lindsay: Upper West Side, Yale; Rockefeller: Upper East Side, Dartmouth). Lindsay was grand in vision and contemptuous of those who did not share it. Rockefeller was the shrewd backroom dealer, eager to show he was more than just his name but rarely shy when it came to using the immense influence that name suggested.

During the 1968 garbage strike, Lindsay asked Rockefeller to call in the National Guard. The governor retorted, “You can’t move garbage with bayonets.” In 1971, as the city’s finances continued to deteriorate, he rebuked Lindsay publicly in a lengthy letter to The New York Times, imperiously lecturing his downstate rival on fiscal probity: “I know how difficult it must be for you to make adjustments similar to those I had to make.”

Lindsay, for his part, called Rockefeller a “tool of the White House” of Richard Nixon and branded his Fifth Avenue apartment Berchtesgaden, a favorite Hitler retreat. In a famous slogan from the 1969 campaign, Lindsay called being mayor of New York “the second-toughest job in America,” suggesting a low opinion of Albany. Nor was this merely electioneering bluster. “I’ve told Nelson that in power, complexity, and responsibility, my job dwarfs even his and that he ought to keep that in mind,” Lindsay had told journalist Nat Hentoff the year before.

"The mayor thought the governor autocratic; the governor thought the mayor incompetent," says Richard Norton Smith, author of the recent On His Own Terms: A Life of Nelson Rockefeller. In the end, the two men wore each other down, neither achieving the national prominence he sought. Rockefeller was appointed vice president, but as he once said, he "never wanted to be the vice president of anything." Lindsay's own run for the presidency in 1972 was a disaster; his try at the Senate, in 1980, didn't go much better. By then, he was widely seen as the man whose profligate spending had brought about the 1975 financial crisis. A return to law practice proved as inauspicious as a return to politics; despite the impression that Lindsay was to the manner born, his finances were such that, in 1996, Rudy Giuliani gave Lindsay a city sinecure so that the man once branded the Republican answer to JFK could simply have health care.

Joseph Viteritti, a professor of public policy at Hunter College and the editor of Summer in the City: John Lindsay, New York, and the American Dream, notes that Lindsay saw himself as a "national spokesman for cities," while de Blasio is a "voice for economic justice" who wants to be heard across the nation, eagerly using City Hall as his bully pulpit. Earlier this year, de Blasio touted a national progressive agenda; his trips to Iowa and Washington, D.C., have some pundits wondering whether he is already tired of City Hall.

Yet neither city nor state triumphs when its top dogs go for each other's throats. "By the time Rockefeller and Lindsay were finished torturing each other, the city was on the verge of bankruptcy, and the state's finances were as brittle as a maple leaf in November," writes Terry Golway of Capital New York.

Financial ruin on the scale of '75 is not likely to result from the Cuomo–de Blasio fight, but stories of legislative dysfunction are still injurious. The sooner this stops, the better for all, except perhaps the tabloids. Seeking to put

an end to the squabble, the prominent Republican Alfonse D'Amato, a former U.S. senator, invited the pugilists to a "pasta summit" at Rao's, the impossible-to-get-a-table Italian legend in East Harlem. It was a charming gesture of goodwill. Both the mayor and the governor declined.

Rebecca Arnold/The St. Luke Foundation for Haiti

HAITI'S CERVICAL CANCER EPIDEMIC

IN MUCH OF THE WORLD, THE DISEASE HAS BEEN ALL BUT CURED, BUT IN DEVELOPING COUNTRIES IT REMAINS A COMMON KILLER OF WOMEN.

The pain and the irregular bleeding told Nanotte Pierre there was something wrong. But none of the doctors she visited over a decade could tell her what it was. An infection, they thought, but none of their expensive therapies put an end to the problem. Instead, it worsened.

In 2013, Pierre's younger sister, who made her living selling sweets on the street, was working outside a Haitian gynecology clinic called Klinik Manitane. Nearby, a river of plastic foam and plastic bottles choked a drainage ditch, and the sun scorched the road until it swirled with dust. But the clinic was pleasant, and the women who'd come to see a health care professional waited on benches shaded by a salvaged UNICEF tent.

One day, the clinic was passing out appointment cards to the women outside and handed one to Pierre's little sister. She thought maybe Pierre should go in her place. Maybe the people there could finally do something about her problem.

It was a brutally hot August day when Pierre, 42, went to the clinic, and she felt seized with pain. There were women in front of her in line, but she wasn't leaving without seeing a doctor. When it was her turn, Pierre undressed and reclined on the exam table. A midwife sat down before her with a speculum, a light and a liquid smelling strongly of vinegar. The midwife was so surprised by what she saw that she immediately called over a doctor, who brought in another doctor, an American woman who entered the room by greeting Pierre in French.

When she inspected Pierre, her face became serious. Pierre did the only thing she could do. She lay there and prayed. "I have a God that won't let me down," she thought as the American doctor scraped out a piece of her with a long, scissor-like tool. The diseased flesh went to a lab, and for a month Pierre waited in pain. She worked at a local market, where she sells odds and ends, and she made arrangements for her sister-in-law to take care of her 14-year-old daughter when she was dead.

When the results came back, Pierre was told she had invasive cervical cancer.

If Pierre were American, she probably never would have gotten cervical cancer at all. In the developed world, it's largely a historical disease. But Pierre lives in Haiti, where

by some estimates the rate of cervical cancer is the highest in the world. Surgery is prohibitively expensive, chemotherapy drugs are limited and there isn't a radiation center in the country. One typical treatment option is group prayer.

We Cured Cancer

Death by cervical cancer is torture. In A Women's Disease, historian Ilana Löwy's book on the illness, she describes the final weeks in the life of Ada Lovelace, daughter of the poet Lord Byron, who died in 1852. "Maddened by pain that could no longer be controlled entirely by opiates, she could not be held in bed and threw herself against the furniture or on the floor." A century later, Argentine first lady Eva Péron, known as Evita, was in such agony at the end of her life because of her cervical cancer that doctors gave her a lobotomy in hopes it would quiet her pain.

There is good news, however. When people ask, "Why haven't we cured cancer?", part of the answer is that, for some forms of it, we kind of have. We've nearly solved cervical cancer. In the beginning of the 20th century, it killed more American women than any other kind of cancer. Now it is among the least lethal forms of the disease.

That's thanks to medical innovations developed over nearly two centuries. Doctors in the 1800s, with brash (and mostly fatal) surgical interventions and primitive speculums, studied "cancers of the womb" extensively. Even in those early days, doctors hypothesized that if cervical cancer could be detected sooner, it could be stopped. Once, by accident, a doctor who removed a cervical lesion for biopsy discovered that the removal had prevented the lesion from becoming cancerous. Through such observations, cancer of the cervix became the paradigm for how all cancers might one day be treated. As Löwy put it to me, the thinking was that "this is the way we should win the war on cancer. We should find it early, and we could solve it early."

Visible symptoms, however, never present themselves early enough. The pain Pierre experienced for years is not typical, and her doctors still aren’t sure it was connected to her cancer. Rather, irregular bleeding is usually the first indication that something is wrong, but this seldom occurs until the cancer has already spread to the uterus or beyond. By then, it's usually too late.

Around the turn of the century, doctors began to argue that screening apparently healthy women would save lives. In the 1920s, Georgios Papanikolaou, a Greek-born doctor working at Cornell University, developed a test that became known as the Pap smear, and in the 1940s the American Cancer Society promoted its regular use.

In the 1990s, researchers made another breakthrough. They discovered that virtually every case of cervical cancer has a single cause: the sexually transmitted human papillomavirus (HPV). Since the 2000s, HPV vaccines and new screening techniques that test for the presence of high-risk strains of the virus have opened up a remarkable prospect: Cervical cancer could one day vanish.

A woman walks through the downtown streets of Port-au-Prince, Haiti, March 24, 2011. Haitian women are highly susceptible to cervical cancer due in part to a lack of widespread preventative screening and early treatment options that are routine in the United States. Credit: Ramon Espinosa/AP

A Poor Woman's Disease

By some counts, Haiti has the highest incidence of cervical cancer in the world. It kills nearly as many women there as all other cancers combined. Meanwhile, in North America it’s responsible for less than 3 percent of female cancer deaths.

Worldwide, more than half a million women developed cervical cancer in 2012, and more than half of them died. Eighty-five percent of those cases occurred in the developing world. Even in the U.S, the disease is more prevalent among blacks, Hispanics and whites in Appalachia—groups with the least economic means. Cervical cancer is a disease of poverty.

In large part, this is because the latest prevention tools aren’t available or affordable in poor countries. Per capita income in Haiti is $810 per year, according to the World Bank, and many Haitians cannot pay for Pap smears. Even

if they could, there aren't enough laboratories or personnel to analyze them. According to U.S. doctors I talked to who work in Haiti, there are fewer than 10 pathologists in the entire country.

Sometimes tests are inconclusive, requiring follow-up. But many Haitian women can't take time from work to travel long distances for a screening. And if the results are positive, then what? Except for the wealthy elite, no one has money for treatment. There is no health insurance in Haiti.

One solution advanced by some public health experts is VIA, a low-cost alternative that stands for "visual inspection with acetic acid." Acetic acid is the main ingredient of vinegar. When it is painted onto the cervix, precancerous lesions turn white. Almost anyone can be trained to do it.

That's why that American woman, Dr. Rachel Masch, the executive director of Basic Health International, was at the Port-au-Prince clinic Pierre visited that day in August 2013. She was training midwives on the VIA procedure. Basic Health, working with the California-based aid organization Direct Relief and the Haitian nonprofit St. Luke Foundation, has screened thousands of women in Haiti's capital city and has likely saved several dozen lives through prevention.

Whenever they notice a dangerous-looking spot, they freeze it with a long metal prod super-chilled with nitrous oxide, killing the cells before they can become cancer. Sometimes there are side effects, including bleeding and mild cramping. In rare cases, women will experience a decrease in cervical mucus that can inhibit sperm. "VIA is not the most perfect screening," said Paulina Ospina, senior program manager with Direct Relief. "There's a higher degree of false positives. So you do have overtreatment." But proponents of "screen-and-treat" say it beats the alternative: undiagnosed cancer.

In September 2013, Pierre received a phone call from a Haitian doctor who worked on her biopsy. She needed Pierre

to come back to Klinik Manitane but wouldn't give her any straight answers over the phone. The most the doctor would say was, “You’ve had a cancer attack.”

When Pierre arrived, she met with Masch, who said, “I’m going to be frank. You have cancer.” Pierre cried. Masch let her sob for a little while, then explained what treatment would be like. There would be surgery. She would have to travel far from home to be bombarded with radiation and chemotherapy. “What do you think you want to do?” Masch asked.

“Well, I don’t have any more money,” Pierre said. She’d spent it all on other doctors and other hospitals that couldn’t get to the bottom of her illness. When Masch assured Pierre she wouldn’t have to pay anything, Pierre consented to undergo treatment.

St. Damien's Hospital in Haiti performs operations on women suffering from cervical cancer, such as Nanotte Pierre who went there for treatment after discovering she had cancer. Surgery is prohibitively expensive in Haiti, chemotherapy drugs are limited, and there isn’t a radiation center in the country. One typical treatment option is group prayer. Credit: Rebecca Arnold/Nos Petits Freres et Soeurs Haiti

Jesus Will Cure Her

Early the next year, Pierre was on the phone with her doctors again. It was important, they said, to remove Pierre's cervix, uterus, ovaries, part of her vagina and possibly several pelvic lymph nodes as quickly as possible. "When can you come in for surgery?" the doctor asked.

"Well, I have this money that I owe at the bank," Pierre said. She borrows money to buy food, accessories or various household items, which she sells at the market, then pays the money back after a month or two. She needed to keep working and pay the debt; she figured by April she could move into the black.

"You can't wait that long," the doctor said. "You need to have the surgery now." Pierre relented, and they scheduled the operation for February 2014.

For the next few months, Pierre felt shattered and overwhelmed. The pain still nagged at her, and her bank loan loomed. Her young brother couldn't bear to see her like this. In the past, when he couldn't find work or needed a roof, Pierre was there. She was the strong one who found the money, who held the family together.

Meanwhile, Masch called on two other doctors to volunteer to help her with Pierre's surgery. St. Damien Pediatric Hospital, a sister hospital to St. Luke, offered up a surgical suite. After some last-minute reluctance from Pierre's family—"You're not going to cure her!" one member told the hospital director, "Jesus is going to cure her!"—Pierre went on the table.

Masch, Ospina and others cast about the U.S., El Salvador, Cuba and the Dominican Republic for a facility that could provide chemo and radiation therapy. Direct Relief, which received more than $14 million that year, had set aside some money for cases like Pierre's. But the organization's worldwide mission and strict program budgets limited the resources it could devote to a single cancer patient—it was supposed to screen thousands of

women, not cure one. Pierre would require travel, lodging and weeks of therapy. She didn't even have a passport.

"Everybody went into this knowing that if we weren't able to find the treatment, then she would very likely die," Ospina said.

But through colleagues at the nonprofit Partners in Health, which would also pay for part of her care, they found a hospital on the other side of the island, in the Dominican Republic. Pierre secured a passport and a visa, and one day in August, she boarded a bus for Santiago in the Dominican Republic. The center there tried to make her feel comfortable, connecting her with the local Haitian community. But mostly she spent those four months feeling weak, sick and lonely. "I felt like I was exiled," she said.

A $10,000 Patient

When I met Pierre in late May, she had just learned she was cancer-free.

Direct Relief spent about $10,000 treating Pierre. That figure did not include donated care and the hundreds of volunteer hours and personal expenses of 50 people in at least five organizations who worked on her case. That year, 1,500 Haitians died of the same disease.

In developed countries like the U.S., cervical cancer screening is incorporated into the health infrastructure. When a woman sees her gynecologist, it's simple to add a Pap test or colposcopy exam (in which a doctor uses a magnifier to inspect the cervix). But in Haiti and other developing countries, primary care is almost nonexistent—which means screening is more or less absent too. One of the biggest problems is that most practitioners and facilities in Haiti are in the capital. Reaching women in rural areas would require establishing programs in clinics nationwide.

Representatives from the Ministry of Health did not respond to Newsweek's multiple attempts to reach them, but several people told me about government-driven plans in the

works for regional screening clinics to use HPV screening or Pap smears. “They want to see a national effort,” said Dr. David Walmer, who has been working on cervical cancer in Haiti since 1993 and is collaborating with the Haitian government through his organization, Family Health Ministries.

The barriers to adequate health care, though, are significant here. Dr. Josette Bijou, a public health expert and former presidential candidate, cites corruption, the centralization of resources in Port-au-Prince and, most important, the “lack of financial resources.” Haiti is a beneficiary of billions of dollars in foreign aid, of course, but so much of it is squandered through inefficiency and corruption. In addition, there is the difficulty of organizing efforts. I spoke with several organizations and individuals who are trying to solve this problem, and very few of them are working together to build a comprehensive plan.

The day I met Pierre at Klinik Manitane, her husband wandered over to me. There was no interpreter, but we exchanged a few words in broken French. I told him his wife is very lucky, but he disagreed. He said, “She’s favored by God.”

David Goldman/AP

THE CANCER EPIDEMIC IN CENTRAL APPALACHIA

AMERICA'S ENERGY ADDICTION IS KILLING KENTUCKY.

Seen from above, the Appalachian Mountains jut from the earth like a spine curving through the eastern U.S., reaching north into Canada and south into Mississippi. For most Americans, this lush region conjures the strum of a banjo, the songs of Loretta Lynn and the gentle twang of a thick mountain accent. A closer listen reveals other, more

disconcerting noises: the raspy voices, heavy wheezing and sighs of resignation that so frequently accompany a diagnosis of lung cancer.

One of those voices belongs to Charles McKinster. He and his wife live outside the small town of Louisa, Kentucky, in Spencer Branch; it's a hollow (“holler” in the local dialect), the term for the creek-bottomed central Appalachian valleys where family clans have lived since Scottish and Irish settlers first arrived in the region in the 1700s. Born a few miles away, McKinster has never left eastern Kentucky aside from some childhood years in Columbus, Ohio, and his drafted service in the Vietnam War. The noises of the coal mines scared him—he had “rabbit blood,” as he puts it—so instead of toiling in the region’s most important industry, he found steady work as a school bus mechanic. But after about 15 years, severe back pain from crushed vertebrae forced him into early retirement and disability payments. A pack-a-day smoker since he was 10 years old, he began seeing a pulmonologist four years ago because of breathing troubles. In February 2015, he was diagnosed with advanced lung cancer.

By June, McKinster had completed several rounds of chemotherapy and was about to start seven weeks of radiation treatment. His wife, who suffers from heart problems, lupus and fibromyalgia, is also unable to work, so the couple lives off their social security payments and small commission from a gas well installed on their land decades ago—totaling about $1,300 monthly—as well as food stamps. They have Medicaid coverage, but McKinster worries that the gas well earnings may inch their monthly income up too high to keep them qualified. In any case, if money ever runs out after paying for the essentials, “I’ll have to stop the treatments,” he says. He eats squirrels and groundhogs he shoots from his porch and skins himself because their budget is so tight. Although he understands his disease could go into remission, McKinster, 68, whose

brother died five years ago of lung cancer at 72, has a glum outlook. “I’m an old man,” he says. “Let’s be honest about it.”

Every hollow bears such stories. Kentucky has more cancer than any other state in the country. It has the highest rates of lung cancer and colorectal cancer—incidence and death—in the U.S. Several other cancers, including cervical, also occur at disproportionately high rates. The cases are heavily concentrated in the Appalachian counties and are accompanied by high instances of poverty and low educational attainment. The central Appalachian areas of West Virginia and Virginia are similarly plagued by malignancies.

Cancer in central Appalachia is itself like an invasive tumor, and restoring health to the region means excising a tangled knot of issues with roots that extend far beyond the mountain range and into the very heart and soul of America.

A West Virginia mountaintop is leveled after the removal of coal. Mines such as these are often near residential areas, leading some to question whether this close proximity is associated with health risks. Credit: Melissa Farlow/ National Geographic/Getty

Poverty Is a Carcinogen

Kentucky is the 45th poorest state in the country, with 18.8 percent of the population living below the federal poverty guidelines. Lower levels of education attainment often accompany poverty, and Kentucky has the third lowest percentage of people who have completed high school.

Escaping this poverty can be nearly impossible. When Angela McGuire, who works with Kentucky Homeplace, part of the University of Kentucky's Center for Excellence in Rural Health, makes home visits to ensure clients are following treatment recommendations, she frequently has to assist them with basic life needs. Steven Peterson, a 51-year-old southeastern Kentuckian, started smoking at age 7. Today, he is blind in one eye from an accident nearly 30 years ago, has suffered two heart attacks (he quit tobacco after the first, seven years ago) and myriad other health issues, and now supports his family on disability payments of $743 per month after insurance costs. McGuire recalls a recent phone message she received from Peterson saying, "I'm so embarrassed, but I need food." Unable to purchase basic appliances, the family rents them instead, and that consumes every spare dollar. "There's no way they can get out of it," says McGuire.

"Poverty is a carcinogen," former National Cancer Institute Director Samuel Broder said in 1989. Cancer rates are frequently higher where poverty is most concentrated, and eastern Kentucky is a case in point. Lung and bronchial cancers are diagnosed in about 98 of every 100,000 people annually in Kentucky, compared with an average of 59 per 100,000 nationwide. The trend persists across several other cancer types, leading to an annual cancer incidence in Kentucky of 513 per 100,000 people per year, far higher than the national average of 455 per 100,000. "There's not a family in eastern Kentucky that has not been touched by cancer," says Tom Collins, a native of the region who directs

projects with the Rural Cancer Prevention Center (RCPC), also part of the University of Kentucky.

Cigarettes play a huge role in this. Both poverty and low educational attainment are associated with smoking. Among the U.S. population with an annual income of less than $15,000, an estimated 33 percent are smokers; in Kentucky, that rate is about 48 percent. People who drop out of high school in Kentucky are also more likely to smoke than high school dropouts as a whole: 45 percent versus 33 percent. Smoking rates fall as income and educational attainment rise across the U.S., but in Kentucky the numbers at the bottom levels are disproportionately greater.

But smoking doesn’t account for all this devastation. Empty bank accounts cause much more fundamental problems; many people in Kentucky can’t even make it to a health clinic when they are sick. “They don’t have the gas money,” says McGuire. Medicaid provides transportation but not to people with a registered vehicle, “even if it’s on blocks in your driveway,” says McGuire, who has many clients with dirt floors in their kitchens.

Even those who do make it to the clinic often do not understand what they’re told. McGuire has clients with diabetes who were unaware of the dangers of skipping a meal when she first met them. Many people she knows with cancer do not believe treatment can help. To them, doctors speak what amounts to a foreign language. When Peterson had his first heart attack, he couldn’t understand what the doctors and nurses were telling him. “Those fancy doctor words, I don’t know what they are,” he says. “I just tell them, come out and tell me in my words.”

Blowing Up the Top of Mountains

Then there’s a problem unique to Appalachia that might be driving up cancer rates in the region: coal mining.

The coal extraction business has a been a fundamental part of central Appalachian life for decades. Although many

mines have closed recently, the industry still thrives. In 2013, more than 127 million tons of coal were extracted from 248 underground and 277 surface mines in central Appalachia, and the industry earned about $46 billion in revenue in 2014.

The long-standing concerns over the impact of the mines on the environment and human health have intensified in recent years with the advent of mountaintop mining. Begun in the 1970s, MTM, also called surface mining, escalated in the 1990s as a cheaper way to access the energy-rich bituminous coal beds lying beneath the Appalachian mountain forests. After a forest is cleared, explosives are used to blast away mountain peaks to expose seams of coal within. Debris from the blasts is deposited in the nearby valleys. Seen from above, MTM looks like brown rash splotches on a green body.

MTM is incredibly efficient. It also may be making people sick. A study of 403 counties in central Appalachia found that those with MTM have higher rates of cancers of the colon, liver, lung and cervix, as well as leukemia, compared with counties without mining. Cancer-related deaths were also more common in the MTM counties.

An explosive is detonated at an A&G Coal Corporation surface mining operation in the Appalachian Mountains on April 16, 2012 in Wise County, Virginia. Credit: Mario Tama/Getty

The mechanism connecting MTM to cancer is likely the release of carcinogens into the environment. A U.S. Geological Survey investigation of MTM regions in central Appalachia found high levels of aluminum and silica—two known carcinogens—in air samples from the region. The study also found traces of chromium, sulfate, selenium and magnesium in the air; research shows that these components of granite rock may be directly carcinogenic or may elevate the risk of cancer through respiratory damage. As Bill Orem, one of the USGS researchers involved in the work, notes, the findings were “what you would expect, since you’re blowing up the top of a mountain.” Another study found elevated levels of arsenic, also carcinogenic, in toenail samples from residents of Appalachian Kentucky.

In one recent study, human lung cells in a lab were exposed to particulates found in air samples within a mile of an MTM in West Virginia. After three months of exposure —what would translate to about eight and a half years of breathing in body-bound lung cells—they started to act like

cancer cells, dividing more rapidly than normal. The same wasn't true for an accompanying group of cells exposed to air from another rural area in West Virginia not near a surface mine. "I can't definitely say yes, mountaintop removal causes lung cancer," says Indiana University public health professor Michael Hendryx, co-author of this 2014 study, published in Environmental Science and Technology, "but I believe that it does, based on the whole body of evidence."

Smoking increases lung cancer risk by up to 14 times—not enough to account for all the cases in the region. "It's not that smoking is not an issue," says Tom Tucker, an epidemiologist at the University of Kentucky and head of the Kentucky Cancer Registry. "It's just that there's something else going on along with it." The most likely explanation is that many carcinogens are mixing together: adding radon or asbestos to smoking pushes the risk up to 300 times higher than normal, and Tucker thinks the same is likely true for arsenic and chromium.

Coal mine economics may be increasing cancer risk and exacerbating the region's poverty. Wages for employees are typically high but the jobs are few, accounting for about 1 percent of all employment in Kentucky. Surface mines require less manpower, leading to a reduction in jobs, and the destruction of the landscape may be keeping other businesses away. Federal and state subsidies to the industry amount to billions of dollars. In 2008, Kentuckians paid on average more than $100 per month in taxes to the coal industry. Recent reports indicate the industry costs more than it earns and is mining beyond current demand, driving prices down. "The area needs to diversify and get away from coal as rapidly as possible if it wants to create a stronger economy," says Hendryx.

But it won't be easy to kill off the mining industry. Americans use more than 900 million tons of coal per year; it accounts for about 37 percent of all electric power fuel in

the country. The way we use electricity—every light switch, every phone charger—has turned central Appalachia into a "sacrifice zone," a term coined to describe Cold War nuclear fallout regions in the Soviet Union that has come to refer to areas where residents become victims of the pollution caused by an outside demand for their resources. "Mining communities are America's sacrifice zone," says Hendryx. Although recent reports indicate a decline in mountaintop mining, the damage already done has deeply scarred the land and its people.

Coal mine owner C.V. Bennett III smokes a cigarette while walking through an abandoned coal power plant in Lynch, Kentucky in October 2014. In the last few years, Bennett's workforce has dropped from more than 600 to fewer than 200. Credit: David Goldman/AP

Reaching People Where They Are

Local efforts to heal Appalachia are growing. Kate Eddens, who researches health behavior at the University of Kentucky, is developing touch-screen software for tablets that provides health information and collects data using visualizations and simple terms. "When you're expecting someone to read who can't read, how are you going to reach that person?" asks Eddens. Tablets and smartphones might

be the answer: The 2013 U.S. census shows that even among households where income is less than $25,000 a year, 40 percent have handheld computers. And across Kentucky, 75 percent of people live in a home with high-speed Internet. These devices can incorporate images, sound and video to help get messages across to those with substandard reading skills. For example, Edden hopes to create text-to-speech software in which health information can be provided in any regional accent or dialect, so that the user hears a familiar voice. Other researchers are focusing on “faith-placed” interventions, such as instituting smoking cessation and other programs at rural churches.

Smart clinical interventions may also thwart the epidemic. High mortality rates in the region indicate that cancer is only being diagnosed in its later stages, and early diagnosis is especially critical for colorectal and cervical cancer. The more advanced the cancer, the harder it is to treat, because the harmful cells have already burrowed deep in the body, multiplied beyond control or mutated into forms beyond the reach of current medications.

Colorectal cancer screening is recommended for everyone starting at age 50, and earlier for anyone with a family history. But many central Appalachians are reluctant to have a colonoscopy or other tests because taking time away from work is a hardship. That resistance is compounded by a lack of understanding about preventive medicine. McGuire frequently encounters clients who have not followed through on a doctor’s recommendation to have a mammogram or colonoscopy because they don’t have any pain. “You don’t want to wait until there’s pain,” she tells them. “Well, if it doesn’t hurt, why do it?” they ask.

To overcome these barriers, Collins and others at the RCPC are pushing fecal immunochemical testing, an at-home method to find early warning signs of cancer. Cheap and simple, an annual FIT test can serve as the basis for determining whether the more invasive and costly

colonoscopy is warranted. “If we are proactive and we get people to take a yearly test for colorectal cancer, dying from it is not even a possibility,” says Richard Crosby, director of RCPC, which also just completed a five-year campaign to encourage parents to have their children vaccinated for human papillomavirus, the underlying cause of most cases of cervical cancer.

Coal miners change in a locker room after working a shift underground at the Perkins Branch Coal Mine in Cumberland, Kentucky in October 2014. Most of what's still being mined in Harlan County is "met coal": the high-grade metallurgical coal used to make coke for steel production. As long-term contracts to supply "steam" coal to power companies expire, the mines that produced it are being shuttered. Credit: David Goldman/AP

But all these efforts are part of an uphill battle. A long history of poverty and disease in the region has led to a sense of resignation, a fatalistic belief about the inevitability of cancer and the death it brings. “Some of them are very despairing because every member of their family has had cancer, and they just knew it was going to happen to them,” says Susanne Arnold, who treats lung cancer patients at the University of Kentucky Markey Cancer Center. Many people who are diagnosed refuse treatment because they don’t see the point of going through the pain. “They accept it

and go on," says McGuire. "That's kind of the mentality of the elder generation here."

The hope, of course, is to change that fatalistic attitude. In the meantime, those involved in treatment and prevention are doing what they can to help. "It's such a terrible burden that this community bears in cancer disparity," says Arnold, an eighth-generation Kentuckian who stayed in the region because of the desperate need for medical care. With several studies under way to measure carcinogen levels among locals, gauge the benefits of routine screening and determine the efficacy of advance treatment, she says plenty of work remains to improve the desperate situation. The key, though, is "to try to give people hope," she says. "That is why we're here."

Follow Jessica Wapner on Twitter @jessicawapner

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THE HIGH COST OF CANCER CARE: YOUR MONEY OR YOUR LIFE?

NEW CANCER DRUGS CAN EXTEND LIFE FOR DAYS, MONTHS, EVEN YEARS. BUT THEY CAN ALSO PUSH YOU AND YOUR FAMILY INTO BANKRUPTCY.

In 2008, Hans Christensen received his death sentence.

He had a recurrence of melanoma, a sometimes deadly skin cancer he thought he had licked a decade before. It had spread to his lungs, invaded his intestines and eaten up

much of the bone in his left humerus, the long bone that runs from the shoulder to the elbow. Surgery and six debilitating rounds of chemo helped, but the treatments were only a temporary reprieve, and his chances of surviving more than a year were poor—until the Newhall, California, resident entered a clinical trial for an experimental treatment that rallies the immune system to vanquish cancers. After two years of infusions of the drug every three weeks, his cancer disappeared. “I’ve cheated death,” says the now-50-year-old electrician.

Great news for him, but the medicine that saved Christensen’s life, ipilimumab (brand name Yervoy), which came on the market in 2011, is probably out of reach for many Americans. The price for one injection is $30,000 (or $120,000 for a full course of treatment), and two other recently approved immunotherapies, pembrolizumab (Keytruda)# and nivolumab (Opdivo)#, carry similarly hefty price tags. While the new therapies work for only about 1 in 5 patients, for a lucky few like Christensen, they are lifesavers. Who wouldn’t jump at the chance to live long enough to walk a daughter down the aisle, attend a grandson’s college graduation or celebrate a 60th birthday—no matter how slim the odds or how high the cost? But that’s precisely the point, according to Dr. Hagop Kantarjian, chair of the leukemia department at the University of Texas MD Anderson Cancer Center. “The prices today are essentially extortion, and people are being taken hostage,” he says. “They’ll pay any price because life is precious.”

Oncologists like Kantarjian have become increasingly vocal about the financial strains for patients and the profits drug companies are making. This week, more than 100 of the nation’s leading cancer doctors, including several past presidents of the American Society of Clinical Oncology and James Allison, the scientist whose basic research led to the development of Yervoy, released a statement in the Mayo Clinic Proceedings that called for reforms to rein in costs,

including changing laws they believe have allowed prices to balloon.

Over the past decade, cancer drug prices have skyrocketed—going from $5,000 to $10,000 for a year's treatment before 2000 to more than $100,000 by 2012, according to another Mayo Clinic study. (Average household income in the U.S. dropped by about 8 percent during the same period.) While some patients are insulated from these price hikes by their insurers, many others, including those on Medicare, are on the hook for 20 percent copays for prescription drugs, which can translate to upward of $20,000 in yearly out-of-pocket costs. "Hardly anyone in this country can afford that," says Dr. Peter Bach, director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center in New York. "People are putting themselves into bankruptcy or trading the wealth they would pass on to their heirs for a few more months of life."

Little wonder that those diagnosed with cancer are more than 2.5 times more likely to declare bankruptcy than those without cancer, according to a 2013 study from the Fred Hutchinson Cancer Research Center in Seattle. And a 2014 survey conducted by the Cancer Support Community, a national nonprofit network, revealed that almost half of the 7,000 patients they polled were riddled with anxiety because of financial concerns, while about a third drained savings or tapped retirement accounts to pay for care. Jackie Farry, a 48-year-old former tour manager for rock bands, is a case in point. After being diagnosed with multiple myeloma 12 years ago, she depleted all her assets, including selling her co-op in Brooklyn, New York, and now lives on disability with her partner in Takoma Park, Maryland. She takes an arsenal of drugs to keep the incurable blood cancer in check, including Pomalyst, which costs $10,500 for a month's supply of 21 pills. "But they're keeping me alive,"

says Farry, who gets help with expenses though payment assistance programs.

Despite the growing backlash, prices continue to climb an average of 10 percent a year. What's fueling this trend, says Dr. S. Vincent Rajkumar, an oncologist at the Mayo Clinic Cancer Center in Rochester, Minnesota, "is a perfect storm of laws and regulations." For starters, the U.S. Food and Drug Administration greenlights drugs if they're proved safe and effective. But new isn't necessarily better. Zaltrap, which was approved in 2012 for metastatic colon cancers, is a notable example. Large clinical trials demonstrated it was no more beneficial than a drug already in use, but its $11,000 monthly price tag was more than double the cost—a fact that prompted oncologists at Memorial Sloan Kettering to refuse to stock it. Yet Medicare, the nation's largest insurer, with 54 million enrollees, is required to cover every cancer drug the FDA approves, and it is not allowed to negotiate drug prices. Essentially, these two provisions robbed Medicare of any cost-cutting leverage, because it can't bargain or threaten to drop a costly but only marginally effective medication.

Compounding this is the problem of treatment resistance. Conventional therapies—whether chemo or the newer biologics that target genetic mutations that prompt unchecked cell growth—eventually stop working once the cancer cells learn to outwit them. At which point, desperate patients move on to the next drug in the therapeutic arsenal, until they've exhausted all their options. Yet even if those treatments add only a few weeks of life, oncologists feel morally obligated to prescribe them to dying patients, which means that drugs with minimal benefits can become a bonanza for their makers. "Most patients are eternal optimists and are convinced they'll be the ones who are helped," says Dr. Deborah Schrag, a colon cancer specialist at Dana-Farber Cancer Institute in Boston.

Some cancer drugs can run into the six-figure range for a full treatment, putting a financial strain on patients and their families. Credit: Gallery Stock

In other industrialized nations, state-run health systems have the latitude to decide what drugs will be covered under their health plans, which enables them to negotiate deep discounts on pricey medications. But in the U.S., because the pharmaceutical industry is insulated from the natural price controls of a competitive free market, Americans pay 50 to 100 percent more for the same drugs than patients in other countries. “Essentially, we’re subsidizing their use in other parts of the world,” says Schrag, even though most of these medications were developed here.

Drugmakers justify the high price tags because development costs are staggering. Companies shell out more than $2.5 billion over the course of the decade it normally takes to shepherd a new treatment through the testing pipeline before it wins FDA approval, according to a 2014 study by the Tufts Center for the Study of Drug Development. “We’re trying to develop medications for really complex, life-threatening diseases,” says Robert Zirkelbach, senior vice president of communications with

Pharmaceutical Research and Manufacturers of America, the industry trade group. “Many of today’s drugs were the stuff of science fiction 15 years ago.”

However, critics counter that those development costs are artificially inflated because they factor in losses for dry holes. Only 11.8 percent of experimental therapies entering clinical tests eventually cross the finish line. For every potential blockbuster like Yervoy, there are dozens of costly disappointments. In the past 15 years, 10 new lung cancer drugs came on the market, but 167 promising compounds foundered in the development pipeline. Similarly, seven new melanoma treatments were approved, while 96 experimental therapies fell by the wayside. And drugmakers can burn through millions concocting these mind-bogglingly complicated meds.

Then there are the opportunity costs—in other words, the 10.6 percent in annual returns investors forgo during the lengthy gestation process, which amounts to nearly half, or $1.163 billion, of the total figure. Plus, more than half of the breakthrough drugs devised in recent decades—like Gleevec, a drug for leukemia, and the breast cancer treatment Herceptin, as well as Yervoy—were largely developed by taxpayer-supported researchers at academic institutions. “These figures incorporate a lot of hidden costs,” says MD Anderson’s Kantarjian, who calculates actual development expenses at about 10 percent of the oft-cited figure, or about $250 million per drug.

In a way, drugmakers are victims of their own success: The number of cancer survivors has risen steadily in the past decade. Today, there are nearly 14 million American cancer survivors, up from less than 3 million in 1971, the year President Richard Nixon declared war on cancer and signed the National Cancer Act. That’s attributable in large part to earlier detection and better treatments. And companies do have a right to recover their investment—if prices tumble once meds have been on the market for a while. But that’s

not what happens with these miracle drugs. Gleevec, the much-heralded leukemia cure, is a prime example.

Introduced in 2001, the drug was a miracle pill that transformed a lethal disease, chronic myeloid leukemia, into a manageable illness. Virtually overnight, five-year survival rates jumped from about 30 percent to nearly 90 percent—as long as patients took their daily doses. When Gleevec was introduced, its annual cost was $30,000, which even its maker, Novartis, acknowledged was steep. Yet 14 highly profitable years later, by which time the company presumably should have long since recouped costs, Gleevec now fetches an eye-popping $132,000 annually. Not surprisingly, about 1 in 5 CML patients who participated in the Cancer Support Community's registry reported missing a dose of medication at least once a month, 14 percent postponed filling their prescriptions, and 10 percent skipped doses.

"An accident in biology leads to a terrible illness and economic disaster—that's not the way a wealthy society should act," says Memorial Sloan Kettering's Bach. "We have to find a way to get out of the rat trap we've gotten ourselves into." To this end, oncologists, in their call to action in the upcoming Mayo Clinic Proceedings, propose removing bans on importing drugs for personal use from places such as Canada, where the meds are up to 50 percent cheaper; giving Medicare the clout to negotiate with Big Pharma; and setting costs based on how much benefit a patient will actually derive from the treatment—a trend called value pricing—rather than paying standard rates across the board. They suggest creating a follow-up mechanism for drugs that have received FDA approval to establish prices based on performance.

Not all meds work equally well for different types of cancer. Tarceva, for instance, a targeted biologic that thwarts growth factors that feed tumors, extends life for lung cancer patients by an average of five and a half months, but those

with pancreatic cancer will be lucky to gain an additional two weeks. Yet monthly costs for both types of cancer are identical: about $7,000. “Should you pay the same price for a drug that works only one-tenth as well?” wonders Dr. Steve Miller, chief medical officer of Express Scripts, a prescription benefits manager for U.S. employers and insurers that represents 85 million Americans. “Right now, we’re paying a premium price regardless of the response.” Express Scripts is now in talks with drug companies about rolling back prices, using the substantial leverage of its large patient base as a bargaining tool. It’s also working with the Institute for Clinical and Economic Review, a Boston nonprofit that examines cost benefits, to set prices based on effectiveness—similar to an approach proposed by oncology doctors in a 2014 JAMA article—and hopes to have some deals in place within the next year.

Because of the growing push for price cuts, industry observers are cautiously optimistic, and some drugmakers, like Eli Lilly and Co., have indicated a willingness to price drugs in ways that “better reflect treatment value” for different cancers. “There is a huge sense of frustration in the oncology community,” says Richard Evans, an analyst at SSR Health LLC. “Companies now realize it’s better to be part of the solution, and they’re beginning to make concessions. But it’s a game of inches, not of yards.”

BSIP/UIG/Getty

CHILDREN'S CANCER IS UNPROFITABLE AND IGNORED

EVERY YEAR, THE NUMBER OF KIDS DYING OF CANCER GROWS, YET NEW MEDICATIONS TO TREAT THEM ARE ACHINGLY SCARCE.

John London wanted to scream in frustration. Penelope, his 4-year-old bike-riding, cupcake-baking daughter, was dying. And the goddamn doctors had nothing left to offer. After three years of chemotherapy, radiation, surgery and a bone marrow transplant, they suggested that John and

his wife take Penelope home to enjoy their remaining time together. Instead, John began scanning hundreds of research abstracts from cancer conferences, seeking new treatments.

He spotted a case at the University of Vermont where a child with the same aggressive cancer as Penelope's—neuroblastoma, a cancer that originates in nerve tissue—went into remission after being treated with an anti-parasitic for an unrelated infection. The oncologist overseeing the case, Dr. Giselle Sholler, had followed up on the unexpected remission and had found that the anti-parasitic decreased tumor size in cell lines and mouse models by up to 75 percent.

John wanted the anti-parasitic for Penelope, but it was not approved for use in the U.S., and the manufacturer, Bayer, didn't have any: The U.S. Centers for Disease Control and Prevention (CDC) had stockpiled it for potential outbreaks of Chagas, a potentially deadly infectious disease mostly occurring in Latin America but increasingly seen in parts of the U.S.

Over two months, London enlisted a colleague to help him repeatedly call Bayer, the CDC and the U.S. Food and Drug Administration (FDA), which has the power to grant compassionate-use approval of unapproved drugs. Finally, he succeeded on all three fronts, and Sholler received the anti-parasitic to administer to Penelope. Six weeks later, she was running around a playground.

The Childhood Elephant

An estimated 2,000 children die of cancer each year, and the overall incidence of childhood cancer has been slowly increasing since 1975. Despite significant advances against certain pediatric cancers, including acute lymphoblastic leukemia, there are still some types of cancer for which there are few or no effective treatments. As John London found out, new drug development in the field is slow, often lagging way behind adult treatments, and few compounds are designed specifically for children. "I was on my own, as

many parents are," London says. "The medical community had no interest."

That is in large part due to a practical reason: Childhood cancers make up less than 1 percent of all cancers diagnosed each year, according to the American Cancer Society. That 1 percent is not much of a market for drugmakers, who rack up an estimated $1.4 billion in out-of-pocket costs while bringing a novel drug to market. They would never recoup that treating the 700 children diagnosed with neuroblastoma annually, or the 100 diagnosed with diffuse intrinsic pontine glioma, a deadly brain tumor.

"The big elephant in the room is the cost of this type of research," says Raphaël Rousseau, director of pediatric oncology drug development at pharmaceutical giant Roche. Combined with the small potential market, that's led very few pharmaceutical companies to invest in developing drugs for pediatric cancer. Merck has one ongoing pediatric oncology trial. Pfizer is testing preclinical therapies only. Novartis leads the pack, with seven drugs in clinical trials for children's cancer.

Where Big Pharma is absent, government has stepped in. Most pediatric clinical trials are operated by the National Cancer Institute's (NCI) Children's Oncology Group (COG), which runs approximately 40 to 50 therapeutic trials across the country at any one time, according to Peter Adamson, chairman of the organization and a pediatric oncologist at the Children's Hospital of Philadelphia. Yet even with federal funding, pediatric cancer research receives only a fraction of the money that adult cancer research gets, and it's decreasing. In 2013, the NCI invested $185.1 million from a $4.79 billion budget in pediatric cancer research, the lowest amount since 2009.

"The options we have now to be explored are really blossoming, but the funds available to do the studies that need to be done are shrinking," says Richard O'Reilly, chairman of pediatric oncology at Memorial Sloan Kettering

Cancer Center, in Manhattan. ‘We don’t want future generations to look back on this time and ask, ‘What the hell were they doing?’”

Still, many oncologists interviewed by Newsweek are optimistic. Numerous initiatives are underway to spur new drug development for children’s’ cancers, including small nonprofit companies identifying and funding clinical trials for early compounds, and industry- and government-led efforts to develop new clinical trial designs that are more cost-effective. Best of all, there are promising drug therapies, thanks to the breakneck speed of advancing scientific research. The challenge is to make those potential drugs available to children.

Challenge Anger

The antibiotic kept Penelope’s cancer at bay for six months before the disease came roaring back. With current therapies, less than 5 percent of children survive relapsed neuroblastoma. Penelope died just shy of her fifth birthday, in May 2007.

A month later, London walked into a dark, half-empty bar in Greenwich Village to meet another parent who had lost a child. The previous November, Scott Kennedy’s son Hazen had died at the age of 5 from the same cancer as Penelope. London recognized him by the expression on his face. “It was like looking into a mirror,” he says. Three beers later, the fathers had decided to solve children’s cancer. “We want to make this an urgent, faster process that cuts right to the chase of the best and most hopeful treatments children can benefit from,” Kennedy says.

Music instruments used to perform for cancer patients are left on empty chairs in the oncology ward of the JM de los Rios pediatric hospital, in Caracas on Sept. 26, 2013. Credit: Juan Barreto/AFP/Getty

Faster is a word often on the lips of parents of children with cancer. By some estimates, it takes an average of five years for promising laboratory results to move into clinical trials for pediatric cancer. Then there's an added delay: Drug development is not typically initiated for children until the drug has already made it into phase III clinical trials for adults.

For example, checkpoint inhibitors—drugs that activate the immune system to attack a tumor—are among the most promising cancer treatments. The first such drug, marketed by Merck, was approved to treat adult melanoma in September 2014. Yet clinical trials in children just began this May. It will be years before the same drug is approved for use in children. "It is one of our biggest challenges—getting access to high-priority drugs at an earlier time," says the COG's Adamson. "It has to do with risk aversion."

Companies want to measure the risks and the benefits of a drug in adults first, rather than exposing children to an

unknown entity, says Roy Baynes, senior vice president for global clinical development at Merck, who led development of the company's checkpoint inhibitor, Keytruda. So the delay is necessary for safety reasons, he argues.

But Roche's Rousseau points out that children receive and tolerate chemotherapy at much higher doses than adults, and neither adult trials nor mouse studies can tell whether a drug will have long-term side effects on them. Therefore, "there is really no reason to wait," he says. "Preventing children from accessing the drug is nonsense."

London and Kennedy agree, which is why they founded a nonprofit, Solving Kids Cancer—which London initially funded with more than $4 million of his money—to identify, fund and manage small pilot clinical trials to bring promising treatments to clinical trials quickly. Over the past eight years, Solving Kids Cancer has helped bring 19 new drugs into clinical trials that might have otherwise never seen the light of day.

The first study they funded was a phase I trial for Nifurtimox, the anti-parasitic that gave Penelope an extra six months. Led by Sholler, the drug successfully completed phase I safety trials and is now in phase II at 13 cancer centers in the U.S. and Canada. Not long after the Nifurtimox trial, Sholler founded her own clinical trials network, the Neuroblastoma and Medulloblastoma Translational Research Consortium, now 24 hospitals strong. It's part of a growing trend of small trial networks trying to move promising drugs into the clinic more quickly. "We're smaller groups that can get studies open faster, in about a year," says Sholler. "We're really trying to bring new research forward."

Carrot or Stick?

At Roche Pharmaceuticals, the third-largest pharmaceutical company in the world, with $39.5 billion in

revenue in 2014, Rousseau has another solution: Big Pharma needs to use its power for good.

If a drug shows promise in children while being developed for adults, companies typically pursue it in pediatrics for one of two reasons: the carrot or the stick. Under the Best Pharmaceuticals for Children Act of 2002 (reauthorized in 2007), drug companies that conduct FDA-requested pediatric studies can receive an additional six months of marketing exclusivity on an patented drug. For a drug that earns $1 billion per year, that's an extra $500 million—for a pediatric study that will cost just a fraction of that.

If that incentive doesn't work, there's the stick. Under the Pediatric Research Equity Act of 2003, the FDA can force a pharmaceutical company to test a new drug in a pediatric population. (However, many companies receive waivers if the condition they are treating is rare or not present in children, such as melanoma.)

Rousseau was a practicing pediatric oncologist and academic researcher for decades before joining Roche in 2009. Now he is trying to prove to large pharmaceutical companies that there is a sustainable model under which they can advance the development of drugs for children—and, though they won't make much money, they won't lose money.

The good news is that Roche is supporting him. In 2010, Rousseau formed a Pediatric Oncology Drug Development team there, which has since grown to 25 members. He's about to initiate a unique study design: a large, multinational, ongoing clinical trial that will test potential drugs in children with differing cancers at the same time, using the same facilities, rules and end points.

Rousseau has two Roche drugs ready to test in the trial. By doing the two together, instead of in two traditional, siloed clinical trials, he estimates the company will save $9 million. If he can reduce the cost of bringing a drug to

trial, the patent incentive offered in both the U.S. and Europe might be enough to justify investment in pediatrics. “I’m convinced there is a way forward,” he says. If he can prove it, he hopes other companies will follow suit.

But more than any other effort, it may be science—specifically, precision medicine—that will speedily identify effective drugs for children’s cancer. This month, the NCI opened the Molecular Analysis for Therapy Choice (MATCH) trial that will analyze patients’ tumors for mutations, and then match them with drugs targeting those mutations. As is typical, the MATCH trial has begun first in adults. But the pediatric version is not far behind, says Malcolm Smith, NCI associate branch chief for pediatric oncology. The NCI hopes to initiate it next year.

Many other teams around the country are working on similar efforts. Sholler, for example, now at Helen DeVos Children’s Hospital in Grand Rapids, Michigan, has been running trials matching genetic signatures to treatments over the past three years. Her team recently published results showing that the technique stabilized or reduced tumors in eight of 14 children with neuroblastoma.

“Our goal is to make the drugs available to patients,” Sholler says. “We try to give [families] more time with their children. Every year, every Christmas, every birthday, matters to a child.”

RJ Sangosti/The Denver Post

DON'T GET CANCER IF YOU'RE IN PRISON

IF YOU DO, CHANCES ARE THE CORRECTIONAL HEALTH CARE SYSTEM WILL HEM AND HAW UNTIL IT'S TOO LATE.

"I'm 76 years old. Please renew my wasting diet as soon as possible," Manfred Dehe begged health care workers at the Arizona State Prison Complex-Eyman on September 28, 2012.

Dehe stood at 5 feet 11 inches and weighed at least 200 pounds, boasting a considerable paunch and a head of thick,

white hair, when he entered Eyman in February 2012. But soon after, his weight began to plummet.

"My diet card [for the wasting diet, to help him put on weight] expired in September," he again pleaded on another request form, in December. "I have been trying to get it renewed ever since. I submitted HNR [a Health Needs Request form] requests on 9/28/2012 and 11/6/12. It's now 12/10/12, and my diet card is still not renewed. My weight continues to decline." By February 2013, his body weight had dropped to about 150 pounds.

"I started noticing his clothing looked very loose," says Dehe's son Mark, who visited him regularly at Eyman, in Florence, Arizona. "It looked like he had borrowed clothes from somebody else, because they were too big for him."

Dehe's weight loss wasn't a medical mystery. Almost immediately after he came to Eyman, a series of symptoms indicated he might have prostate cancer. Providers of Dehe's medical care—first, a private, for-profit prison health care company named Wexford Health Sources, followed by another private, for-profit prison health care company named Corizon—were well-aware of these symptoms, according to records provided to Newsweek.

Lab results dated March 31, 2012, indicated Dehe had a prostate-specific antigen (PSA) level of 23.3 nanograms per milliliter. The lab report flagged this level as "high"—the range listed there for a healthy individual was 0.0 ng/mL to 4.0 ng/mL—and according to the National Cancer Institute, "the higher a man's PSA level, the more likely it is that he has prostate cancer. Moreover, a sustained rise in a man's PSA level over time may also be a sign of prostate cancer." By June 2, Dehe's PSA had shot to 31.4 ng/mL.

Despite that alarming bloodwork, as well as multiple hospitalizations and Dehe's repeated requests for help, he didn't undergo a prostate biopsy until August 9, 2013. The results came back a month later: metastatic prostate cancer.

Cutting Corners & Pointing Fingers

There is little hard data on the quality of medical treatment behind bars, says Dr. Marc Stern, a correctional health care consultant and former health services director for the Washington State Department of Corrections. Nor is there much regulation of correctional facility health care.

No one disputes that prison care saves lives and often treats people who might not otherwise be treated. Many who end up imprisoned are too poor to get adequate health care on the outside. Hepatitis C is a useful case in point: An estimated one-third of those infected with hep C in the U.S. pass through the prison system. Outside of prison, this is a population that is unlikely to seek professional help when experiencing symptoms of a disease like hep C, and probably couldn't afford treatment ($25,000 to $189,000 for a full course of hep C drugs) if they did. In prisons with adequate health care services, these sick prisoners are more likely to be screened and diagnosed, and then are given the drugs at no cost to them.

However, after working in prisons across the country, Stern says his impression is that "the places that are excellent are more rare than the places that are not." The problems tend to stem from underlying financial issues: There is little public investment in correctional health care systems, and generally speaking neither public nor private providers can offer competitive salaries to prison health care workers.

"The problem is a structure that creates incentives to delay and deny care," says David Fathi, director of the National Prison Project at the American Civil Liberties Union (ACLU). "The reason to deny care is obvious—because you save money, particularly when you're talking about conditions like cancer, which can't be treated on-site by the prison doctor. Those patients have to be sent out to specialists. That gets very expensive. That's an area where we very often see private providers cutting corners."

Managers of correctional institutions typically have a background in criminal justice and don't have medical training, which exacerbates the situation, Stern says. "They don't keep an eye on things closely enough."

There are constitutional requirements for providing adequate health care to our incarcerated populations. In 1976, the U.S. Supreme Court decided in Estelle v. Gamble that "deliberate indifference to serious medical needs of prisoners constitutes the 'unnecessary and wanton infliction of pain'...proscribed by the Eighth Amendment," and ruled that correctional facilities must provide appropriate health care to prisoners. In 1993, in Helling v. McKinney, the court decided that prison officials cannot expose inmates to environments that "pose an unreasonable risk of serious damage" to their future health.

Since then, however, frequent reports and lawsuits charging negligent care of inmates—including numerous deaths—strongly suggest that many U.S. prisons and jails have ignored these rulings.

Allegations of subpar care in Arizona provide a good example of how correctional health care dysfunction puts cancer patients at extreme risk. In March 2012, the ACLU and allied prisoners' rights groups filed a lawsuit against the Arizona Department of Corrections (ADC) and several state officials, alleging that "grossly inadequate" health care puts "all prisoners to a substantial risk of serious harm, including unnecessary pain and suffering, preventable injury, amputation, disfigurement, and death." The suit points to several cases of what it describes as poorly treated, or untreated, cancer. (The ADC oversees the state's 16 prisons, six of which are privately run.)

A 73-year-old patient diagnosed with terminal colon cancer, takes his daily medication in the hospice care wing of California Medical Facility on December 17, 2013 in Vacaville, California. The prisoner, who asked to not be identified, is serving a 30 year sentence. He was diagnosed with cancer in April 2013; doctors currently expect him to live another three months.

Credit: Andrew Burton/Getty

For example, an inmate named Ferdinand Dix complained for two years of lung cancer symptoms such as chronic cough and shortness of breath, and tested positive for tuberculosis—but never received proper treatment. The cancer spread “to his liver, lymph nodes, and other major organs, causing sepsis, liver failure, and kidney failure,” according to the suit. Dix’s liver “was infested with tumors and grossly enlarged to four times normal size, pressing on other internal organs and impeding his ability to eat.” The suit claims medical staffers didn’t “even [perform] a simple palpation of his abdomen. Instead, medical staff told him to drink energy shakes.” In February 2011, Dix fell into a “non-responsive state,” and “his abdomen was distended to the size of that of a full-term pregnant woman.” The prison brought him to an outside hospital, where he died a few days later.

The American Friends Service Committee-Arizona released a report in October 2013 titled “Death Yards: Continuing Problems With Arizona’s Correctional Health Care.” The Quaker organization found that some 105 prisoners died in custody from March 2012 to June 2013. The AFSC studied 14 deaths in depth, and the report said that they “raise a number of ‘red flags’ regarding conditions that, if treated in a timely manner, might have been resolved.” Of these 14 deaths, six involved metastatic cancers. “This clearly indicates that the conditions were long-standing and suggests that these deaths might have been preventable had the individuals received more timely care,” the report charges.

Asked about allegations of subpar health care in general, and Dehe’s case specifically, the ADC directed Newsweek to a press release that states: “Arizona’s inmate mortality rates, including incidents of suicide, are within the national average for corrections departments. In 2012, the most recent year for which statistics are available, Arizona reported 215 deaths per 100,000 inmates, compared to the national average of 254 per 100,000.”

In 2013, the ADC terminated its contract with Wexford and handed over prison health care to Corizon. The state alleged that Wexford improperly dispensed medication and wasted state resources. Wexford, however, says the decision to end the partnership was mutual—while pointing fingers at the prison system. “Once it began operating the program, the company discovered the (now publicly documented) dysfunctional nature of the ADC system,” Wexford told Newsweek in a written statement.

‘I Don’t Feel Right’

The prison renewed Manfred Dehe’s wasting diet several days after his December 10, 2012, request, but it did not address his request for prostate treatment until months later. Meanwhile, he started needing to urinate constantly. Sometimes, he had to get up four or five times at night, and

each time it was a struggle to urinate. “I’m 77 years old & I don’t feel right,” he wrote in a Health Needs Request form.

By January 1, 2013, Dehe could barely pass urine. He was admitted to the hospital, where he was found to have a urinary tract infection and an enlarged prostate. The hospital staff inserted a catheter, prescribed a dose of antibiotics and then sent him back to Eyman.

But according to Dehe’s letters, his medication was cut off 10 days later and his catheter wasn’t changed for weeks. Finally, on March 19, Dehe was admitted to the hospital and diagnosed with urosepsis, a condition that develops when a urinary tract infection spreads into the bloodstream.

In May 2013, lab test results revealed that Dehe’s PSA had topped 100 ng/ml. By June 3, his PSA had soared to 174.4 ng/ml. “The patient needs a prostate biopsy,” an off-site urologist wrote on July 2. Dehe had his biopsy August 9. A month later, the doctor wrote in his report, “I am almost positive that he has widespread metastatic disease.” The urologist prescribed a testosterone suppressant injection every three months. (Male hormones encourage prostate cancer cell growth, according to the American Cancer Society.)

In February 2014, Mark visited his father. “He had to hold on to my arm for his support,” Mark recalls. “I knew he didn't have too much longer to live.” His care, Mark says, was consistently subpar. When Dehe went to the urologist on March 28, 2014, the doctor noted in his report, “His last known injection was 9/23/13.... His follow up injections should have been on 12/25/13 and 3/25/14.”

From April 2014 onward, Mark noticed that his father’s nose and ears had become overgrown with hair. He was too weak to take care of himself, and nobody was helping him groom. He had only two teeth and “ joked he looked like Bugs Bunny,” Mark says. His skin was blotchy and red with bruises, and bedsores had erupted on his feet and buttocks.

Dehe, who had always loved to walk, spent his days lying motionless, too sick to leave his bed.

“It was very, very painful to see that—to watch somebody deteriorate in front of you, to see the nurses not care, like he was an inconvenience,” Mark says. He adds that one infirmary staffer said to him, “Why don't you just throw a sheet over him? Because he already smells like he's dead.”

On October 14, 2014, the ACLU and the ADC reached a settlement requiring that the state improve prison health care in publicly managed facilities and comply with continued monitoring and oversight by the prisoners’ attorneys, to make sure the department abides by the agreement. That same day, Dehe died from “complications of metastatic prostate carcinoma.”

Corizon says it’s barred by federal privacy laws from commenting on Dehe’s treatment, but “can affirm” that his oncology “met medical standards of care and was appropriate for his condition.... As health care providers, we are deeply saddened by any negative medical outcome. We take providing care for our patients very seriously. We extend our sincere condolences to Mr. Dehe’s family.”

Guo Lei/Xinhua/eyevine/Redux

VIKINGS MIGHT SLAY CANCER

AN AGE-OLD FASCINATION WITH GENEALOGY HELPS ICELANDIC SCIENTISTS CHART THEIR NATION'S ENTIRE GENOME.

A nation known primarily for its stunning vistas and live volcanoes is poised to revolutionize global research on cancer and neurodegenerative disease. For that, the people of Iceland may credit the ingenuity of its researchers and the diligence of its historians, but above all they should applaud

the tenacity of the 435 Vikings who descended on the island 1,000 years ago.

In recent years, genetic profiling and personalized treatment have been hailed as the future of health care, promising targeted therapy and tailor-made drugs for a range of conditions. Yet the effort has been complicated by a few fundamental facts about human genetic material: There's a lot of it, coming from lots of us, hailing from a lot of different places. Establishing a database from which to draw general conclusions about the behavior of diseases like cancer and Alzheimer's disease requires massive amounts of data collecting and analysis.

In addition, a vault of information can only get you so far. In order to truly understand how a disease expresses itself in a population, you also need a handle on that population. "Knowing the genealogical links and distance between any two people is obviously crucial for much genetic work," says Gísli Pálsson, a professor of anthropology at the University of Iceland. Luckily, in Reykjavik the recording of family trees has been a national sport for centuries—and the history of the country has resulted in a, genetically speaking, rather close-knit population.

Early historical records indicate that the area was more or less uninhabited when the ninth century Nordic chieftain Ingólfur Arnarson, spurred by a lack of arable land and a blood feud in his native Norway, took to the sea in search of an island that, to date, had only figured in rumors and legends. His band of Vikings landed on the empty island and settled in. Scholars generally agree that by the end of the era known as the Age of Settlement (about 874 to 930 A.D.), the island was home to about 20,000 new inhabitants, and all the usable land had been claimed. "Farmland was fully settled fairly soon, and immigration slowed down," says Pálsson. "During later centuries the population shrank as a result of difficult conditions, including cooling of climate, eruptions

and plagues. Icelanders alive today mostly descend from the lineages that survived."

Today, the Icelandic government describes its 329,000 citizens as 93 percent ethnically Icelandic. To get an idea of how deeply ingrained Iceland's close-knit family tree is in the population's cultural and social consciousness, consider that there's an Icelandic dating app that allows users to cross-check potential connections against the nation's comprehensive genealogy records, so as to avoid going out for cocktails with a second cousin. "Bump the phone before you bump in bed," says Hakón Thrastar Björnsson, one of the creators of IslendingaAPP, which is basically Tinder fitted with what the developers call an "incest-alarm."

But 1,000 years of slow-to-nonexistent migration may soon become much more than a nuisance for Reykjavik's singles. Beginning in 1998, when Iceland's parliament passed a law allowing the sale of encrypted medical records to private companies, Dr. Kári Stefánsson and his colleagues at Reykjavik-based deCODE Genetics have been working on one of the most ambitious genetics-based research projects to date: compiling a database of the Icelandic population's entire genome.

Visitors sit in the geothermal waters at the Blue Lagoon close to the Icelandic capital of Reykjavik on April 7, 2014. The country's gene pool is not very diverse, making it an ideal population to study in hopes of discovering how cancer grows in the body. Credit: Matt Cardy/Getty

"There's an Orwellian flavor to this," admits Stefánsson, a celebrated neurologist who has been pioneering genetic research for decades. At its most basic level, deCODE's study resembles a 21st century version of national documents like the Islendingabòk, an iconic, meticulous study of Iceland's early lineages dating back to the Middle Ages. DeCODE's Islendingabok.is, named after its 12th century ancestor and developed in collaboration with programmer Fridrik Skúlason, illuminates new variations and details about the nation's genetic blueprint while continuing a thousand-year-old tradition. Many can now trace their lineage back to the time of the settlement.

"Not only have we taken advantage of the records, but we have also expanded them and put them into user-friendly format in a computer," Stefánsson explains. He and his team have now sequenced the genome of 2,636 Icelanders and studied genetic information collected from another 104,220, meaning that a third of the country's population is directly involved in the project. This dataset has been combined

with the nation's extensive medical records and detailed genealogies found in documents like the Islendingabòk. The results, which were detailed earlier this year in four articles published in the journal Nature, amount to a stunning picture of an entire nation.

These articles shed new light on the genetic workings of a range of serious conditions. For example, the discovery of a new gene variation that appears to protect against Alzheimer's disease could be used to derive a new treatment model for neurodegeneration and disease progression.

But the most significant feature of deCODE's research effort may be its capacity to yield insights into cancer epidemiology and biomarker discovery. Stefánsson gives the example of a mutation discovered in a gene called BRCA2: About 2,000 Icelandic men and women, or 0.6 percent of the nation's population, carry a nefarious gene variation in BRCA2 that results in a 4.6-fold increase in the lifetime risk of developing cancer. For men, at least 360 of the carriers will develop prostate cancer and can expect to die about seven years short of the national average for life expectancy. For women who carry this mutation, the health risks are even more dire: They are at an 86 percent probability of developing either breast cancer or ovarian cancer. Their life expectancy is 12 years fewer than noncarriers.

These insights can be applied to other populations, as well. DeCODE researchers, in a 2011 study of a gene linked to ovarian cancer among Icelanders, found that a rare "frameshift" mutation in the same gene was associated with an elevated risk of both ovarian cancer and breast cancer in a Spanish population sample. While 0.7 percent of Spanish ovarian cancer patients carried the gene variant, only 0.06 percent of control subjects did.

Preventive surgeries like mastectomies and hysterectomies can decrease that cancer risk significantly —and in Iceland, deCODE could theoretically notify all at-risk men and women. Although the personal records are

currently encrypted, the Icelandic state holds the key to turn anonymous number sequences into names of real people. An invasion of privacy, some charge—but for many Icelanders, such an invasion could be the difference between life and death. “Here we have this insight into the genome of an entire nation,” Stefánsson says. “Should we take advantage of this?”

For now, the information will remain a theoretical research tool. But experts agree that there will come a time when the world has to find a way to balance privacy and the greater good. Within five years, most nations in the Western world could be in the same position as Iceland, says Stefánsson, who reasons that deCODE’s capacity to transform preventive care and personalized health care will inspire other nations to pursue similar population-wide research efforts. What we do with all this information is up to us. “Knowledge is never evil in and of itself,” Stefánsson says. “You can use it for good, and you can use it for bad.”

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THE 'LINKEDIN' FOR CANCER

‘SUPER RESPONDERS’—PATIENTS WHOSE RECOVERY IS SO REMARKABLE IT DEFIES EXPECTATION—ARE BEING USED TO HELP DESIGN BETTER-TARGETED CANCER TREATMENTS.

Marty Tenenbaum shouldn’t be here today. Almost 20 years ago, the computer scientist and e-commerce pioneer was diagnosed with metastatic melanoma, an aggressive cancer that, at the time, had no effective treatments. Told he should measure the rest of his life in months, not years,

Tenenbaum scoured the Web for a clinical trial that might buy him more time.

He decided to bet his life on a Phase III trial of Canvaxin, an investigational vaccine designed to stimulate the immune system to combat tumors. In an earlier phase of clinical testing, the vaccine had been shown to extend the lives of people with the deadliest form of skin cancer. But in the trial Tenenbaum got into, Canvaxin failed to demonstrate that kind of survival benefit in enough people, so it was abruptly halted. The vaccine, deemed a flop, was destroyed.

A few outlier patients, however, responded remarkably to Canvaxin before the trial was closed. Tenenbaum, now 72 and cancer-free, was one of them.

The history of oncology is peppered with similarly curious (or miraculous) anecdotes about one or two patients, like Tenenbaum, who had recoveries so spectacular they defied explanation. Often these patients failed to respond to multiple courses of therapy and eventually sought treatment in a clinical trial as a last resort.

Until recently, such dramatic outcomes have left patients thanking some higher power for their Lazarus-like recovery, and physicians and researchers scratching their heads. Not enough was known about cancer's basic biology, and the technology did not exist to understand why someone fared so well on a drug that provided little to no help for most patients.

But today, thanks to powerful new genome-sequencing technologies, which are getting faster and cheaper every day, it's increasingly possible to pinpoint genetic mutations and other molecular abnormalities that play a role in some patients' astounding recoveries. By studying these patients—known as "super responders" or "exceptional responders"—a growing number of researchers hope to not only learn how and why a patient responded to a specific treatment but to

identify other patients who could benefit from the same regimen.

Dr. David Carbone, a lung cancer specialist and genetics expert at Ohio State University's (OSU) Comprehensive Cancer Center, says he's seen a "fair share" of super responders come through his clinic, but one in particular stands out: a 66-year-old woman with advanced lung cancer. Neither surgery nor chemotherapy could help her, and within six months of her diagnosis, she was admitted to a hospice. However, her health remained stable, and she sought a second opinion.

"For her, it was a shot in the dark," says Carbone. "She had no expectations." He enrolled her in a clinical trial for sorafenib, a drug that blocks the function of certain enzymes that play a role in the development of tumor formation. It is approved in the U.S. for advanced forms of liver, kidney and thyroid cancers, but not for lung cancer.

The woman's tumors began to shrink almost immediately. Within two months, they had disappeared entirely, and her disease was kept at bay for another five years. Only nine others among the 306 patients in the trial responded to the drug, says Carbone, but she "by far had the best and longest-lasting response of them all."

Although she eventually relapsed and succumbed to her disease years later, her off-the-charts response to sorafenib prompted Carbone to take a deeper, more intensive look at the genetics of her tumor. He and his team performed whole-genome sequencing to look for genetic mutations in the DNA of the patient's cancer cells before her use of sorafenib. They also sequenced RNA—molecules that carry genetic messages within the cell—from the woman's tumor and healthy cells.

Their analyses revealed more than 100 genetic abnormalities in her cancer cells, compared with her healthy cells, but one stood out: a mutation in a gene called ARAF that had never been linked to cancer. Further research

demonstrated that the abnormal ARAF gene formed tumors and that these tumors were inhibited by sorafenib.

OSU has since added ARAF to the panel of cancer-causing genes it routinely screens in patients with all cancers, in the hopes of identifying others with the rare mutation who may respond to targeted therapy. “If we can show that a particular gene mutation is making one person’s tumor vulnerable to a drug, there’s a chance that other patients with the mutation—including those with different kinds of cancers—may benefit from the same treatment,” Carbone says.

Muting the Mutations

Decades of cancer research have shown that cancer is a remarkably diverse disease. Even cancers that begin in the same part of the body are radically different at the DNA level. Lung cancer, for example, is now understood not as one disease but as a collection of subtypes—each characterized by a spectrum of mutated genes and other abnormalities—that require different treatment approaches.

Because several known cancer-causing mutations occur in multiple types of tumors, cancer is increasingly defined not just by the organ in which it originated but by the mutations that drive its growth. “These mutations can sometimes be targeted with the same drug, but it’s unfortunately not a given,” Carbone says. Melanoma patients who have a mutation in a gene called BRAF respond well to drugs that block the activity of the BRAF protein. Lung cancer patients with the BRAF mutation also respond well to the drug, but colorectal cancer patients with that same mutation do not. Still, Carbone says, “knowing which mutations are present in an individual patient is the first step in helping to precisely tailor a patient’s treatment to the genetic features present in his or her cancer cells.”

Dr. Glen Weiss, director of clinical research and Phase I and Phase II clinical trials at Cancer Treatment Centers of America and a clinical associate professor at the

Translational Genomics Research Institute in Phoenix, has also treated patients whose cancer took an unexpected trajectory. One of them was a 54-year-old woman who was dying of ovarian cancer. “She had exhausted all other treatment options. She came to me already having started to get her affairs in order,” he says.

On a hunch, Weiss treated her with an experimental drug called a PARP inhibitor as part of a clinical trial. In earlier studies, PARP inhibitors had been shown to be effective in ovarian cancer patients who had a mutation in the BRCA gene, which the woman had.

Weiss was stunned to find that she was cancer-free six weeks after beginning treatment. “Rather than just having some tumor shrinkage or disease control for a period of time—as is usually the best case for that particular class of drugs—she recently celebrated four years with no sign of disease,” he says.

Late last year, the Food and Drug Administration approved the first medication of this type, olaparib, for the treatment of women with ovarian cancer who no longer respond to other treatments and who are likely or suspected to have BRCA mutations. PARP inhibitors are also under study for patients with other cancers who harbor BRCA mutations, such as breast, pancreatic and prostate cancers.

Cancer Commons

But what about those patients who’ve had an exceptional response outside a clinical trial? After all, only about 3 percent of the 1.7 million people diagnosed with cancer each year in the U.S. take part in one. “Surely there are other super responders, but unless these cases are published in medical journals or shared at medical meetings, we just are not hearing about them,” Carbone says. It is not uncommon for research data to be published years after being generated.

This is where Tenenbaum re-enters the picture. He drew on his experience as a super responder to start Cancer

Commons. The nonprofit organization, based in Palo Alto, California, aims to place data relating to exceptional responders in a free, searchable online database. “If there was another patient who had similar mutations as me and who had a miraculous response to a drug, I’d want to know before I made any decisions about my treatment. Wouldn’t you?” he says.

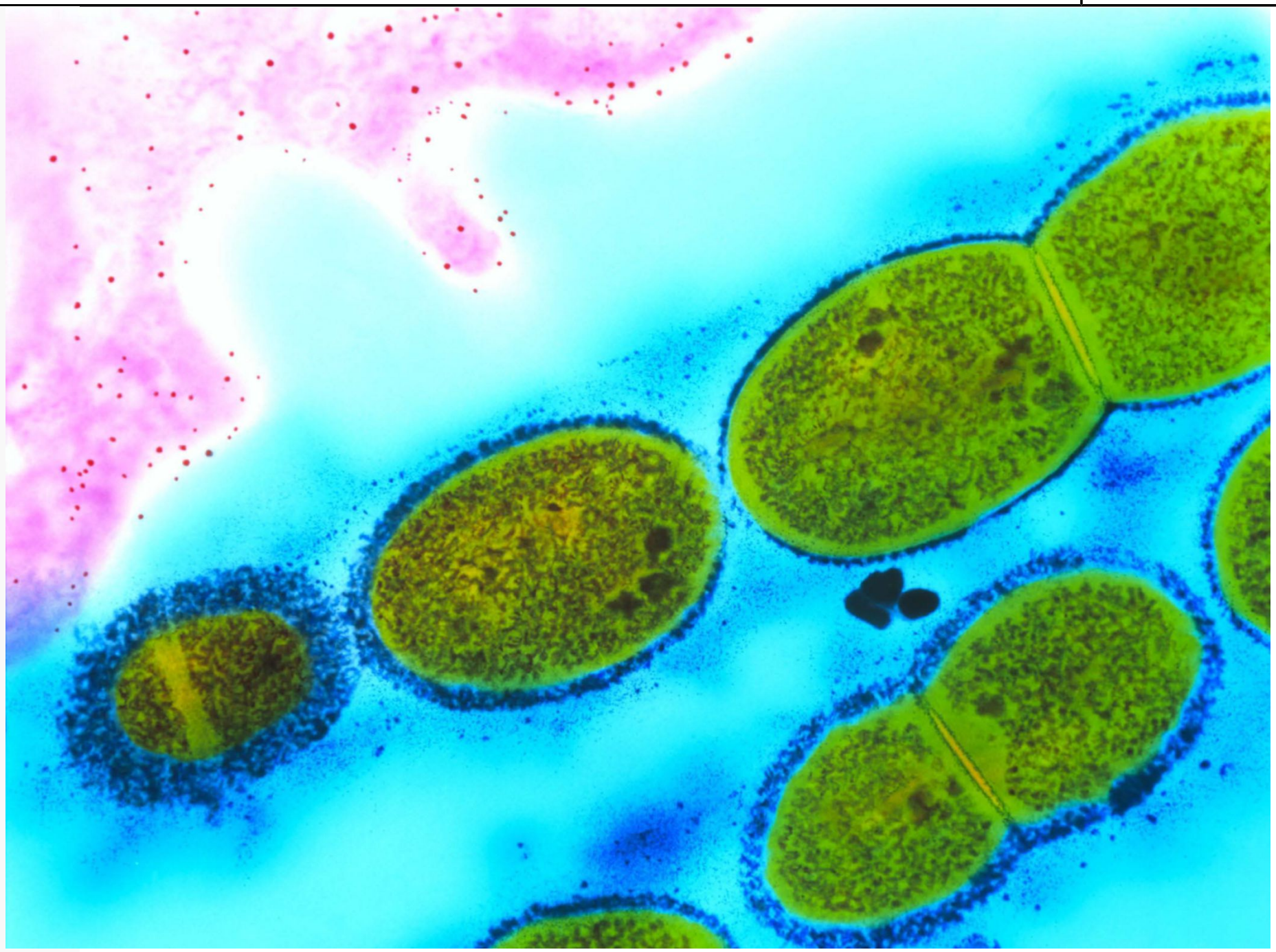
Both health care providers and patients can contribute via smartphone data that is immediately rendered anonymous. Powerful analytics then sift through that data, along with information from other sources, like physicians' notes, clinical guidelines and journal articles, to provide treatment recommendations. “As more data are added, patterns emerge that you could not have seen in just one patient or even in bigger clinical trials where positive responses from one or two patients get lost in the rest of the data,” Tenenbaum explains.

In theory, doctors would tap the database for insights into how to treat a patient based on the experiences of super responders and other patients who share the same genetic mutations and other genomic characteristics. Patients can also query the database. Together, doctors and patients will form a knowledge network around certain genetic mutations that Tenenbaum envisions as “similar to LinkedIn.”

Others groups are also seeking to tap into patient experiences—the good, the bad, the spectacular—that are not captured by clinical trials. The American Society of Clinical Oncology’s CancerLinQ and health care technology company Flatiron Health, both of which aim to cull data from millions of electronic health records, will allow physicians to base their treatment choices on the experiences of similar patients. And cancer institutes such as the Dana-Farber Cancer Institute in Boston and Memorial Sloan Kettering Cancer Center and the Icahn School of Medicine at Mount Sinai, both in New York City, have created their own

databases in the hopes of helping doctors match the right treatment to the right patient.

Says Tenenbaum, “You could say we’re hoping to make the exception routine.”



Dr. Kari Lounatmaa/Science Source

PROGRAMMING BACTERIA TO KILL CANCER CELLS

NEW IMMUNOTHERAPY RESEARCH HOLDS PROMISES OF TREATING CANCER AND PROVIDING LONG-TERM PROTECTION FROM RECURRENCE.

In the late 1800s, Dr. William Coley—a bone surgeon and cancer researcher at New York Cancer Hospital—observed something peculiar. A patient named Fred Stein was suffering from a tumor growing in his cheek—until he became infected by Streptococcus pyogenes bacteria (which

causes strep throat). Shortly after his infection, the cancer began disappearing, as though the fever had burned it away.

Afterward, Coley began to notice that several other cancer patients who had recently undergone tumor-removal surgery were more likely to recover from their cancer if they developed a post-surgical infection. In an effort to figure out why, Coley began injecting inoperable cancer patients with streptococcal bacteria. These came to be known as "Coley toxins." In one case, Coley treated a 21-year-old man with a mix of bacteria and bacterial lysates—natural secretions of bacteria that keep the immune system on alert—who then had a complete remission.

Coley injected over 1,000 patients with his toxins—and many recovered. But he never properly documented all his cases or followed up with enough patients, and after his death in 1936, general medical opinion dismissed his methods in favor of radiation and chemotherapy. It wasn't until much later, when several pioneering cancer researchers revisited his work, that the medical community began to realize that Coley—sometimes called the "father of immunotherapy"—had been onto something.

In the fall of 2014, the FDA approved an immunotherapy drug known as Anti-PD1 for melanoma, the most serious type of skin cancer. Soon after, Anti-PD1 became the standard of care for melanoma. It's so effective, in fact, that it's used completely alone, without the need for chemotherapy or radiation. "I have not given chemotherapy to a person with melanoma for the past two years," says Dr. Antoni Ribas, a medical oncologist at UCLA who treats mainly melanoma patients. "The days of chemotherapy for these diseases are over."

Anti-PD1, like all immunotherapies, works by hacking your immune system—essentially, teaching it how to attack cancer cells, which it would otherwise ignore. There are huge advantages to immunotherapy compared with traditional cancer treatments. When patients undergo

chemotherapy, the side effects are often debilitating, including extreme pain and fatigue, nausea, diarrhea, hair loss, poor appetite and a risk for life-threatening infections, as well as long-term health consequences like heart and lung disease. In addition, chemotherapy and radiation generally don't guarantee lasting protection from recurrence.

Immunotherapy, on the other hand, "would get the immune system to impact cancer long-term, because the immune system has the ability to remember," says Ribas. "So if you develop a therapy that turns on the immune system correctly, it will continue to remember that the bad guy is the tumor and should be attacked."

That's why the field of immunotherapy research has exploded in recent years. And one of the most promising areas of cancer immunotherapy goes all the way back to Coley: Controlled bacteria might be the best tool yet to turn the immune system into a cancer-fighting machine.

We know Salmonella bacteria as a sickening bug, lurking in undercooked meat or buckets of cookie dough and making its way into our system if we don't prepare our food properly. When it does, it wreaks havoc on us in the form of nausea, fever, diarrhea, vomiting and chills. But there's another side of Salmonella.

Roy Curtiss, a professor who runs a lab at the Arizona State University's Biodesign Institute has been studying the bacteria's cancer-killing properties for some time now. He's found that certain strains of Salmonella, when genetically modified to become safer, have the ability to enter cancer cells and take over. It's different from anti-PD1 therapy, where the immune system is taught to recognize cancer cells that were previously "hidden"—with Salmonella, the bacteria itself can exert its toxic effects on individual tumor cells.

But there's been one major challenge in introducing the Salmonella cure to humans: The bacteria are toxic and can cause infections and even sepsis, especially if the person's

immune system is compromised. “You kill the tumors, but then you kill the patient,” says Curtiss. “It’s a struggle to find a balance between the bacteria’s ability to reach a solid tumor and multiply profusely there in the manner that ultimately kills most of the tumor cells—and the ability to prevent damage to healthy tissues.”

Curtiss’s most recent project involved genetically modifying Salmonella to lower the toxicity of the bacteria while maintaining its efficacy. To do so, Curtiss and his research team altered its lipopolysaccharide structure, or outer membrane, which is the primary culprit in causing sepsis. They fine-tuned a little more, then injected the bacteria into mice with tumors. It turned out to be a rousing success, killing the tumors without harming the healthy cells nearby. This proved, for the first time, that bacteria could fight cancer without any serious side effects.

Salmonella is one of the few strains of bacteria, along with Listeria and Clostridia, that have shown potential in entering, colonizing and ultimately destroying cancer cells. One member of the Clostridia group, Clostridium novyi, is particularly promising. In 2014, researchers at Johns Hopkins University injected a modified version of the bacteria, called C. novyi-NT, into cancer-stricken dogs and found it could reduce their tumors. They even tried it out, successfully, on one human patient with advanced leiomyosarcoma—a rare form of smooth muscle cancer.

C. novyi-NT is unique because it thrives in a low-oxygen environment—and the centers of tumors, it turns out, have very little oxygen. Once injected into the tumor, the bacteria are “in a low-oxygen environment, where they germinate, begin to divide and grow, and in the process consume cancer cells,” says David Chao, president and CEO of BioMed Valley Discoveries, which is collaborating with Johns Hopkins. The bacteria then stop growing at the rim of the tumor, where there is more oxygen to be found—preventing them from going any further into healthy cells.

Larger clinical trials of C. novyi-NT on humans are now in the works. It's difficult, of course, to predict how well treatments that have been successful in animal trials will translate to people. Dr. Mario Sznol, at Yale University, worked on Salmonella research for five years only to find that exciting results in rats and dogs didn't occur in tests on human tissue. "What we learned is that we don't see the same kind of tissue colonization [in humans] that we did in mice and rats," says Sznol. "There's something really different about the biology of human tumors." If this obstacle is overcome, he says, bacteria can truly become "nifty" vehicles of tumor destruction.

After Coley died, his daughter, Helen Coley Nauts, fought for years to bring his work to the attention of the medical community. And for years, she was shunned; her father's results were dismissed as lacking in evidence. But she worked tirelessly to organize his data and track down patients who had been treated with Coley's toxins. Even though she wasn't trained as a scientist and hadn't even graduated from college, Coley Nauts ultimately laid the basis for a field of research that now spans across countless labs and pharmaceutical companies, and is flying forward. There are projects developing immune-triggering therapies for lung, breast, colon, head and neck, skin and pretty much every other type of cancer out there.

"In the future," Sznol says, "I think we're going to get so good at it, we're going to actually be able to give patients very limited therapy and cure them of their cancer."

This article is one in a series from Newsweek's 2015 Cancer issue, exploring challenges and innovations in cancer treatment and research. The complete issue will be available in newsstands and on digital platforms from July 24.

John B. Carnett/Bonnier Corporation/Getty

KANZIUS CANCER MACHINE GETS ITS FIRST HUMAN TRIAL

THE GROWTH OF NANOTECHNOLOGY IS REVITALIZING HOPE IN THE RADIO WAVE CANCER CURE MANY THOUGHT TO BE BUNK SCIENCE.

His body ravaged by chemotherapy treatments, retired radio engineer John Kanzius spent months in his basement in 2003 cobbling together a makeshift tumor-killing machine. Kanzius had no medical background. He had been a ham

radio operator and the owner of a television and radio station company. But he had leukemia, and he did not want to die.

He was also sharp, dogged and a quick learner. He immersed himself in scientific studies, poring over the latest cancer research. Radio waves heated metal, and he wondered if they could be safely transmitted into humans to destroy tumors. He did not know it then, but the John Kanzius's Noninvasive Radiowave Cancer Device that evolved from this thought experiment would eventually make the pages of respected medical journals and attract the support of leading cancer researchers, as well as a Nobel Prize winner. When I interviewed him in his Erie, Pennsylvania, home in 2007, he vowed to live to see the day that his device would treat humans. He also desperately wanted to cure himself.

Dr. Steven A. Curley, an oncologist then at MD Anderson Cancer Center in Houston who launched Kanzius’s research into the national spotlight and devoted his career to the project, visited him in the hospital in 2008. Curley had treated many cancer patients, but over the previous five years he had grown particularly close with Kanzius. “I don’t think I’ve got long to go,” Kanzius told Curley. “I just want you to promise me that you won’t give up. You will get this to human trials.”

Curley promised he would. “I believe in this,” he said. “It has unbelievable potential.”

In 2009, Kanzius died at 64 from pneumonia while undergoing chemotherapy. Many thought the Kanzius machine would die with him.

But this May, Curley filed protocols with the Italian Ministry of Health to test the radio wave machine on humans diagnosed with pancreatic and liver cancer. Pending approval in the fall, human clinical trials will begin in the spring of next year in Naples, Italy.

Burning Red Meat

The device Curley will use for clinical trials looks much different from the first one Kanzius built. He's now on the sixth-generation version. Looking back at the original machine, "it was very basic," Curley says. "But it got the job done."

It began with some antennas, copper wires and copper sulfate solid that Kanzius hunted down. He combined them —along with some of his wife's pie pans—into a radio wave transmitter device. With it, Kanzius proved that when stabbed with metal prongs and zapped with radio waves, areas of hot dogs and slabs of liver and steak would burn while the rest of the meat remained unaffected.

Invigorated, Kanzius secured a patent and tracked down Curley, who specialized in radiofrequency ablation (which involves inserting needles into tumors and zapping them with electrodes—a method that heats and kills them, but can't reach all tumor sites and sometimes damages surrounding cells). Curley recalls: "His physician called me and said, 'Look, I've got this patient who has read your work. He thinks he's got a better idea for curing cancer, and he won't leave me alone. Would you talk to him?'"

Doctors perform a radiofrequency ablation of a liver tumor in a hospital in Lyon, France on August 13, 2012. Radiofrequency ablation involves inserting a needle into a tumor in order to heat and kill it; Kanzius sought out Dr. Steven Curley based on his expertise with the technique to help develop his own method—which is both less invasive and capable of targeting smaller tumors than radio frequency ablation. Credit: BSIP/UIG/Getty

Curley gave Kanzius a call, and after listening to him explain his invention, told him he needed to find a substance that could attach to cancer cells and would burn when blasted with radio waves, so as not to damage nearby cells. Nanoparticles, Kanzius replied. They are so tiny that 100,000 of them lined up are about the width of sewing thread. More than 2,000 nanoparticles could fit inside of a red blood cell. Kanzius didn't know how he could get some nanoparticles, and no one actually knew if they would burn, but it was worth a try.

"It was the start of a beautiful friendship," Curley says. He put Kanzius in touch with a Nobel Prize–winning chemist, Richard Smalley, who specialized in nanoscience and was on his deathbed from cancer. Smalley gave Curley two vials of carbon nanotubes, a kind of nanoparticle that is hollow, with a cylinder structure. In June 2005, with

Kanzius' encouragement, Curley put them in the machine, which used a pair of antennas with copper coils at each end to send high-voltage radio waves through the nanoparticles. "They heated at a remarkable rate."

To Curley, this meant the machine had the potential to treat cancer without needles, debilitating chemo or invasive surgeries. Combined with nanoscience, it could possibly one day detect and kill the most microscopic of cancer cells, which current machines cannot even find. "It blew my mind," he says. "I started putting together research proposals."

Researchers from the University of Pittsburgh, the MD Anderson Cancer Center and Rice University tested the technology. Curley's team injected nanoparticles into human cancer cells in petri dishes, as well as into tumors in mice, rats, rabbits and pigs. Using the Kanzius machine, they were able to heat the nanoparticles and, as a result, kill all those cancerous cells. Results were published in the oncology medical journal Cancer, as well as Nano Research. They were publicized around the world and featured on 60 Minutes. Over and over again, after being injected with nanoparticles and heated with radio waves, cancer cells died while surrounding healthy areas remained intact.

"We've treated pigs with far higher doses than I would ever use in a human being," Curley says. "We found that animals we treated were fine; their blood tests were fine. It really did nothing in terms of damage to other cells."

Enough to Fight for

Though he had become thinner with his illness, Kanzius still enjoyed expensive fine dining out on the town. Curley accompanied him on some of those drives about town, as residents waved and shouted, "Mr. Kanzius!" He says the locals treated Kanzius like a rock star.

An unabashed optimist, Kanzius sometimes made overreaching claims about his device, telling audiences and

fans: “I think I’ve found a cure for cancer.” This always made Curley cringe. He had to explain to Kanzius that it was dangerous to get people’s hopes up too high. “I don't tell patients they are cured until eight, nine, 10 years down road —and after proving they don't have microscopic cancer cells hiding somewhere.” If the machine led to a more effective, less toxic treatment for cancer, he told Kanzius, then that was a huge accomplishment. That was enough to fight for.

As publicity grew, Curley began receiving hundreds of calls and emails a week from cancer patients and their families. Curley had to tell people, many of whom were on their deathbeds, that the treatment was not yet ready. Still, they persisted. “I will sign a waiver. I will do whatever it takes,” they pleaded. Patients promised that if they could come to Curley’s lab as secret test subjects, they wouldn't tell anybody. Curley would again say no with apologies. “I get it,” Curley says now. “Cancer scares the hell out of people.” Other people tried to figure out how to build their own Kanzius machine. “One guy sent a video of himself standing between two antennas,” Curley says.

Kanzius finally stopped telling people he had a cure when cancer patients began showing up at his house asking for impromptu treatments. He couldn’t actually help; he didn’t have any spare nanoparticles. And even if he could get ahold of the nanoparticles, he didn’t have a way to get them into the cancer cells. Kanzius knew this, because he tried to treat himself in the summer of 2008. He called Curley and told him he was using the device to channel radio waves into his own body. “I just wanted to see what happened,” Kanzius told him. But, of course, radio waves alone didn't seem to make a difference.

Into the Lab

Since Kanzius first built his machine, there have been tremendous scientific advances in both nanotechnology and cancer research. Researchers have shown that nanoparticles can be used to create supersensitive biosensors able to

detect cancer cells and even identify molecules that indicate someone is at increased risk for cancer.

Google's life sciences division, for example, has been working on combining nanoparticles with a wearable device to create the ultimate cancer detector. The theory is that nanoparticles could be ingested in a pill, for example, and then enter the bloodstream, where they would bind to a cancer cell. Since the core of the nanoparticles can be magnetic, the wearable device would detect and lure these cells toward it, where they would be counted using light and possibly even radio waves.

Recently, Abhilash Sasidharan at India's Amrita Centre for Nanoscience and Molecular Medicine was so inspired by the work of Kanzius and Curley that he decided to test a similar technique using nanoparticles called graphene—honeycomb sheets of carbon atoms that make up the thinnest solid ever discovered. Graphene is flexible, transparent, highly electrically conductive and stronger than steel.

Sasidharan's team has used radio waves to destroy advanced-stage cancer cells that are highly resistant to other treatments, and found that graphene could heat at higher levels than other nanoparticles—which makes for a more efficient tumor-killing machine. In addition, in comparison to carbon nanotubes or gold nanoparticles—another material currently being investigated for cancer-curing potential—which may be toxic and hard for the body to break down, graphene, Sasidharan says, "is biodegradable; it can be safely used for human applications."

Curley has 20 researchers with expertise in nanomaterials, radiofrequency, immune function and drug delivery functions working in his lab at the Dan L. Duncan Cancer Center at Baylor College of Medicine in Houston, Texas. But he's also been doing clinical research in Italy since 1982—the regulatory processes for human trials there, he says, are not as arduous as they are in the U.S. He did initial clinical trials for his early radiofrequency ablation

research in Italy in 1997, which were followed by successful clinical trials in the U.S. a year later.

The first round of clinical trials for the new Kanzius machine design will involve exposing 15 to 20 pancreatic and liver cancer patients to radio waves in the Kanzius machine, primarily to prove the process will not harm them, and to study the impact on their cancer cells. Tests will also examine how effectively radio wave treatments work when used along with known chemo drugs.

The treatment, of course, would need to be approved by the Food and Drug Administration before it could treat patients in the U.S. Curley is hopeful, but more cautious than Kanzius was, pointing out: “A whole bunch of us have been able to cure cancer in animals. You go to humans, and sometimes there are opposite results,” he says. “You never know.” But like he told Kanzius before he died, Curley deeply believes in the potential. He made a promise to his friend, and he intends to keep it.

Matthew Staver/Bloomberg/Getty

MARIJUANA IS A WONDER DRUG WHEN IT COMES TO THE HORRORS OF CHEMO

"I WOULD GET BLASTED ON THE STUFF AND BE HAPPY AS A CLAM, NO PROBLEMS," SAID FORMER CANCER PATIENT JEFF MOROSO.

After a successful surgery to remove a cancer-ridden section of Jeff Moroso's large intestine in the spring of 2013, the oncologist sat down with his patient to prepare

him for what would come next: 12 rounds of punishing chemotherapy, once every two weeks for six months—standard practice for the treatment of colon cancer.

Moroso's oncologist spent most of that appointment writing prescriptions for medications he said would minimize the debilitating side effects of chemotherapy. He gave Moroso scripts for ondansetron (Zofran) and prochlorperazine (Compazine) for nausea, and lorazepam (Ativan) for anxiety and insomnia. Because the nausea drugs are known to cause gastrointestinal problems and headaches, he also recommended three over-the-counter medications for constipation and one for diarrhea, as well as ibuprofen for pain. In total, he instructed Moroso to take more than a dozen prescription and nonprescription drugs and supplements.

Moroso says the first three rounds of treatment were more awful than he could have ever imagined. After chemotherapy, he felt so ill and weak that he could barely stand up, and it took him days to rebound. And the prescription drugs just made him feel worse. "I felt real sick, incapable of doing anything except for lying there and trying to hang on," says Moroso, who is 70 and now cancer-free.

Moroso couldn't afford to lose days of work while he was doing his chemo. He'd heard from friends and read in the paper that cannabis can help a patient through chemotherapy, so he got a letter from his oncologist that allowed him to obtain medical marijuana. (He chose coffee beans infused with 5 milligrams of cannabis, a low dose that he took when he felt he had to.) By the seventh round of chemotherapy, Moroso had dumped his prescription pills. "I would get blasted on the stuff and be happy as a clam, no problems," he says.

A growing number of cancer patients and oncologists view the drug as a viable alternative for managing chemotherapy's effects, as well as some of the physical and emotional health consequences of cancer, such as bone pain,

anxiety and depression. State legislatures are following suit; medical cannabis is legal in 23 states and the District of Columbia, and more than a dozen other states allow some patients access to certain potency levels of the drug if a physician documents that it's medically necessary, or if the sick person has exhausted other options. A large number of these patients have cancer, and many who gain access to medical marijuana report that it works.

"A day doesn't go by where I don't see a cancer patient who has nausea, vomiting, loss of appetite, pain, depression and insomnia," says Dr. Donald Abrams, chief of hematology-oncology at San Francisco General Hospital and a professor of clinical medicine at the University of California, San Francisco. Marijuana, he says, "is the only anti-nausea medicine that increases appetite."

It also helps patients sleep and elevates their mood—no easy feat when someone is facing a life-threatening illness. "I could write six different prescriptions, all of which may interact with each other or the chemotherapy that the patient has been prescribed. Or I could just recommend trying one medicine," Abrams says.

A 2014 poll conducted by Medscape and WebMD found that more than three-quarters of U.S. physicians think cannabis provides real therapeutic benefits. And those working with cancer patients were the strongest supporters: 82 percent of oncologists agreed that cannabis should be offered as a treatment option.

Dr. Benjamin Kligler, associate professor of family and social medicine at Albert Einstein College of Medicine, says there has been enough research to prove that at a bare minimum cannabis won't actually harm a person. In addition, "given what we've seen anecdotally in practice I think there's no reason we shouldn't see more integration of cannabis in the long run as a strategy," he says. "We have this extremely safe, extremely useful medicine that could potentially benefits a huge population."

Some years ago, Dr. Gil Bar-Sela, director of the integrated oncology and palliative care unit at the Rambam Health Care Campus in Haifa, Israel conducted two rounds of phone interviews with 131 cancer patients who used cannabis while in chemotherapy; just less than 4 percent of participants reported that they experienced a worsening of symptoms when they started using cannabis and the majority said it helped, according to the resulting paper published, in Evidence-Based Complementary and Alternative Medicine in 2013.

But self-reported data like this is limited when it comes to proving the clinical impact of cannabis. Patients may be biased in their opinions that cannabis is effective, may not accurately document their use of the drug, or may confuse the effects with those of the cancer treatment. In addition, symptoms such as pain are subjective and difficult for a physician to measure.

A paper published recently in JAMA analyzed the findings of 79 studies on cannabinoids for a variety of indications, including nausea and vomiting from chemotherapy, appetite stimulation for patients with HIV/AIDS, chronic pain and multiple sclerosis, among other conditions. This review, which accounted for 6,462 patients, found most who used cannabinoids reported improvements to symptoms compared with patients in placebo groups. However, the researchers say these improvements were not statistically significant. The analysis also indicated that cannabinoids had limited impact on symptoms of nausea and vomiting, and a number of patients reported adverse effects from the drug, including dizziness, disorientation, confusion and hallucinations.

Perhaps the biggest challenge in understanding marijuana stems from the fact that it is not a bespoke drug designed to act in a specific way on the body — it's a complex plant that appears to provide a wealth of health benefits. The cannabis sativa plant contains more than 85 cannabinoids, a variety

of chemical compounds that also exist in the body. Just as opioid pills activate the opioid receptors (and limit a person's perception of pain), cannabinoids in marijuana activate the cannabinoid receptors, located throughout the body, including in the brain, liver and immune system.

To date, we really know about only two of these cannabinoids: tetrahydrocannabinol and cannabidiol. Research into THC and CBD has led to the development of drugs such as dronabinol (Marinol), a synthetic cannabinoid approved by the U.S. Food and Drug Administration for nausea and vomiting from chemotherapy and as an appetite stimulant, anti-nausea and anti-pain medication for AIDS patients. Nabiximols (Sativex), another cannabinoid drug, is THC and CBD that is derived from the plant and delivered as a mouth spray. It's available in Europe and several other countries—but not yet FDA-approved—for multiple sclerosis patients to treat neurological pain and spasticity. One study on nabiximols for the treatment of cancer-related pain produced disappointing results. However, the GW Pharmaceutical Company, the maker of Sativex, is pushing through with further trials to evaluate the drug as a potential adjunctive therapy for opioids for pain management in patients with advanced cancer.

But how other cannabinoids work together is still much of mystery, says Dr. David Casarett, a professor of medicine at the University of Pennsylvania's Perelman School of Medicine and the author of Stoned: A Doctor's Case for Medical Marijuana. This means researchers aren't entirely sure why the plant could help people manage symptoms like nausea and pain. "Marijuana is not as much of a science as it should be," he says.

In large part, says Casarett, that's because medical marijuana has proved to be most effective in palliative care, the medical specialty that focuses on managing symptoms of disease and improving a patient's quality of life—and there is very little funding for palliative care in this country.

“That's changing slowly,” he says, “but it's still much easier to get funding to test disease-modifying treatments than it is to develop and test palliative therapies, including cannabis.”

We are starting to get some idea of the palliative power of cannabis, Abrams says. “The reason we think we have this whole pathway of the receptors and the endocannabinoids is to get us to forget things, and particularly to get us to forget pain,” he says. In addition, cannabinoids relieve symptoms of nausea because that’s also a physiological reaction stemming from the central nervous system.

With the public perception of marijuana changing rapidly, barriers to studying the plant’s medicinal potential are beginning to fall. Earlier this spring, for example, the Obama administration announced it would remove some of the restrictions on medical marijuana research. In the meantime, though, it is clear that marijuana has a unique and important role to play in cancer care.

“People are realizing that even when patients do well in terms of survival, there’s a lot of suffering along the way that needs to be addressed,” says Casarett. “For many patients, [marijuana] is an opportunity to take control over their disease and symptom management when they can't get the relief they need from the health care system.”

Sait Serkan Gurbuz/The St. Joseph News-Press/AP

CHILDHOOD CANCER SURVIVORS FACE LIFELONG CHALLENGES

THE CHANCES OF SURVIVING CHILDHOOD CANCER ARE RISING, BUT SO ARE THE LONG-TERM EFFECTS OF TOXIC TREATMENTS.

Her 7-year-old daughter Lexi returned from softball practice complaining of a pain in her chest along the breastbone, and though the most natural thing in the world

would have been to assume this was some minor ballgame injury, Kayci Wilson sensed something much worse.

“My mother's intuition said something's really, really wrong here,” she says. Instead of waiting to see how things developed, Wilson took Lexi to and urgent care clinic the next morning. The normally reserved Lexi piped up to say she was tired, and Wilson felt a twinge of maternal dread. After examining Lexi and drawing blood for tests, the doctor said she had a viral infection and sent Wilson home with the usual advice: rest and liquids.

But less than two weeks later, Lexi was hospitalized at Children's Mercy Hospital in Kansas City, Missouri, where doctors diagnosed her with anaplastic large-cell lymphoma, a rare form of non-Hodgkin lymphoma that affects white blood cells. The diseased cells then travel to other parts of the body, including the lymph nodes, spleen, bone marrow, blood or organs. It’s often an aggressive cancer. With treatment, many stricken children survive. Still, in just 12 days, Lexi had gone from a rough-and-tumble softball player to a child so thin and weak her parents had to carry her out of the house and into the hospital.

The next few months were a whirlwind: chemotherapy, radiation treatment, a diagnosis of remission, a recurrence, a bone marrow transplant from Lexi’s 4-year-old sister Audrey and then, finally, recovery.

The all-clear sign was far from the end, though. Lexi suffered an infection shortly after her bone marrow transplant, and she spent almost the entire next year in bed. “We were unprepared for how long it would take,” says Wilson. Even now, Lexi still cannot run the way she used to —her hips are too weak. But with the help of tutors, she’s managed not to fall behind at school. She even won an award for reading this year.

Though the specter of lymphoma is gone, the doctors gave Wilson some more bad news during a recent checkup: At the age of 9, Lexi received a diagnosis of primary ovarian

failure. “She’s basically not going to have children when she’s older,” Wilson says, her voice breaking. “I didn’t realize it would happen that fast. I was heartbroken.”

Despite their persistence in the face of disease, survivors of childhood cancer like Lexi are at high risk for what doctors refer to as “late effects.” Chemotherapy drugs and radiation not only destroy cancer cells but also cause undetected damage to the DNA of normal cells nearby. The resulting late effects can include infertility, heart and other cardiovascular problems, neurocognitive effects, growth problems and even secondary cancers—not a metastasis but an entirely new tumor.

“By 30 years from diagnosis of the original cancer, 22 percent of [surviving] children will have developed a second neoplasm; that includes both malignant and benign tumors,” says Dr. Gregory Armstrong, principal investigator of the Childhood Cancer Survivor Study, which contains data on more than 34,000 survivors nationwide. There are 400,000 childhood cancer survivors alive today; by 2020, that number will grow to half a million. Based on the current data, malignant tumors will strike about 11 percent of these survivors, most when they are still young adults. “These are people who are still in their 30s and 40s," says Armstrong, whose research shows that childhood cancer survivors are 15 times more likely to die from a second cancer than the general population dying from any cancer.

Roberto Martinez reflects on his experience battling germ cell (testicular) cancer at age 17, at his home in Los Angeles, May 09, 2008. In his 20s and cancer free, Martinez is heading into a career in health care, armed with deeper knowledge of cancer treatments. He worries about the late health effects on childhood cancer survivors. Credit: Richard Hartog/Los Angeles Times/Getty

To a large extent, this is a result of a necessary balancing act. Over recent years, the success rates for curing childhood cancers have inched up, and today survival rates are astounding. Dedicated doctors and nurses in pediatric oncology wards across the nation cure 80 percent of their patients. For many childhood cancers, the survival rate tops 90 percent. More important, “we have children who could survive not just six months, not just three years, five years, but for 60 years and 70 years,” says Dr. Andrew L. Kung, professor of pediatrics at Columbia University and chief of the Department of Pediatrics’ Division of Hematology, Oncology and Stem Cell Transplantation.

Unfortunately, that also means there are many children who, as adults, get secondary illnesses. Most of the late effects of cancer are due to exposure to radiation and some chemotherapy agents, including anthracyclines, which are

"classic" and important drugs used to treat many different types of cancer, including breast and lung cancers and leukemia, says Armstrong. It is well-known that the higher the dose of radiation, the higher the risk of a second cancer —and much of the recent improvements in survival rates in children have been driven by oncologists using stronger doses to fight childhood cancer.

Research also shows that chest-directed radiation increases the risk for cardiac disease and cardiac death. Anthracyclines also affect heart function, says Kung, while another chemotherapy drug, etoposide, can cause genetic mutations leading to a second unrelated cancer.

Today, oncologists are working to limit the long-term health impacts of these cancer-killers by, for example, avoiding the use of radiation when treating some leukemias and lowering radiation doses used to treat Hodgkin lymphoma. Newer technologies, such as proton beam irradiation, will be able to treat the tumor while sparing nearby normal tissue from high doses of radiation. Future generations of survivors will not be exposed to quite so much radiation as generations past. And with the recent advent of precision medicine, the war chest of chemo drugs has increased, allowing doctors not only a greater choice of drugs but also the ability to use lower doses, which means fewer late effects for survivors.

"The good news is, 20, 30, 40 years down the road, those kids have lower mortality rates due to second cancers and heart disease," says Armstrong.

The other key to long-term health is ongoing "survivor care," designed specifically to address the fear, anxiety, nutritional challenges, physical disability and financial burdens that can come with the late effects of cancer survival. Ashley Dado was treated for brain cancer at the age of 10. At the age of 18, she transitioned to the Survive and Thrive Clinic, part of the University of Kansas Cancer Center for adult survivors of childhood cancers. Recently,

Dado, now 22, graduated from MidAmerica Nazarene University with a degree in health and exercise science, yet she still makes yearly visits to monitor her late effects—hand-eye coordination, trouble concentrating and adrenal insufficiency, which requires her to take a growth hormone.

Gaps in survivor care still exist for some, says Carol Bush, an oncology nurse navigator with the Midwest Cancer Alliance and the University of Kansas Cancer Center. Addressing psychological problems can be particularly challenging. For example, though terminally ill patients often create strong networks and support groups among themselves, when one of them makes unusual progress—a long remission or becoming cured—they can develop survivor guilt, says Bush, and they feel isolated. There is no built-in support to address these types of difficulties.

In fact, between 13 and 17 percent of childhood cancer survivors experience mental health problems, pain or anxiety, with high levels of psychological distress, says Siobhan M. Phillips, assistant professor of preventive and behavioral medicine at the Northwestern University Feinberg School of Medicine in Chicago. These can lead to serious cognitive decline: Just over one-third of childhood cancer survivors between 20 and 49 have more trouble remembering things, solving problems and prioritizing tasks than their same-age peers, her most recent research suggests. “What’s really striking is when you put this in context of how old these survivors are,” Phillips says. “You wouldn’t expect these conditions to develop until much older ages, yet everyone [in her recent study] was under the age of 50.”

That’s a major part of the problem, of course. While Bush favors addressing survivor problems immediately following a diagnosis, so that cancer patients and their families will know what to expect, she says that “all of those late effects don't really resonate because you're concerned about living.”

The fallout of cancer treatment often becomes clear long after the fact. “I don’t think Lexi’s battle is necessarily over just because we don’t have cancer,” says Wilson. “Maybe the scary part is over, but we still have so many tough life situations ahead of us. There’s probably many unshed tears.”

Newsweek

TOP CANCER DOCTORS 2015

'NEWSWEEK,' IN CONJUNCTION WITH CASTLE CONNOLLY MEDICAL LTD. IS PROUD TO PRESENT THE LIST OF THE 'TOP CANCER DOCTORS 2015' FOR THE UNITED STATES.

According to the National Cancer Institute, in 2015 an estimated 1,658,370 new cases of cancer will be diagnosed in the United States, and 589,430 people will die from the disease.

Newsweek , in conjunction with Castle Connolly Medical Ltd., the well-respected publisher of America's Top Doctors, is proud to present the list of the “Top Cancer Doctors 2015” for the United States.

This list was compiled through peer nominations and extensive research that Castle Connolly Medical Ltd. has conducted for more than two decades. The Castle Connolly physician-led research team makes tens of thousands of phone calls each year, talking with leading specialists, chairs of clinical departments and vice presidents of medical affairs, seeking to gather further information regarding the top specialists for most diseases and procedures. Each year, Castle Connolly receives nearly 100,000 nominations via this process. Read the list of physicians who, after a careful review of credentials, have been selected to be a part of the Newsweek “Top Cancer Doctors 2015” list.

Newsweek Health: Top Cancer Doctors 2015

01

COCKTAIL HOUR

Athens, Greece—Riot police face Molotov cocktails thrown by a small group of anti-establishment demonstrators in front of Parliament after the approval of a 7.16 billion euro bailout deal that includes tough austerity measures, July 15. Prime Minister Alexis Tsipras lobbied for a deal with the country's creditors in an abrupt about-face after a July 5 referendum in which 61 percent of voters rejected a bailout with similar conditions. Under the terms of the nation’s third bailout since 2010, Greece remains on the euro and can use the funds to repay loans from the International Monetary Fund and European banks, but it must also cut pensions, raise taxes and take other unpopular steps to improve its budget.

Yannis Behrakis/Reuters

02

PEACE FIGHT

Tehran, Iran—Iranians celebrate in the streets after the signing of a nuclear accord under which Iran accepted strict curbs on its nuclear program in return for sanctions relief, July 14. U.S. President Barack Obama has championed the deal as the best way to stop Iran from acquiring nuclear weapons, but he faces a tough job convincing Republican critics and U.S. allies in the Middle East, including Israel and Saudi Arabia. The deal is not universally popular in Iran either: Hard-liners are worried that international inspectors may get access to sensitive military installations.

Mostafa Bazri/Demotix/Corbis

03

FROM WHITE HOUSE TO BIG HOUSE

Oklahoma City—President Barack Obama walks away after speaking with reporters on July 16 during his visit to the El Reno Federal Correctional Institution. Obama, the first sitting president to visit a federal prison, said it was time to re-examine mandatory federal sentences for nonviolent and low-level drug offenses, arguing that there are cheaper and more effective alternatives. At a cost of $80 billion, the U.S. has the world's most expensive and crowded criminal justice system. Since 1980, the number of people incarcerated has quadrupled, to 2.2 million.

Kevin Lamarque/Reuters

04

BATTLEGROUND

Chattanooga, Tennessee—Marine Corps veteran Joshua Blea pays his respects at a memorial to four Marines and a Navy seaman who were killed on July 16 when Kuwaiti-born gunman Mohammod Abdulazeez opened fire at a military recruiting station and a naval reserve facility. Police shot and killed the attacker, a 24-year-old naturalized U.S. citizen who grew up and went to college in Chattanooga. Authorities are treating the attack as an act of terrorism and investigating a trip Abdulazeez made to Jordan last year.

Joe Raedle/Getty