

 Global Coalition on Aging

# Wonder Drugs

vs.

# Super- bugs:

The 21<sup>st</sup> Century Battle  
to Save 10 Million Lives  
a Year

## The Stakes

What if gasoline—or an electric charge—no longer powered your car? What if you opened the faucet, but no water came out? What if commonly used medicines no longer protected us from disease? What if you flipped the switch, but no lights came on? Modern life would be unthinkable.

Actually, one of these events is happening right now. In the coming decades, it could claim 10 million lives every year. That's more than double the current COVID-19 death toll.<sup>1</sup> Every year.

How did we arrive at this dystopian future? Simply put, the superbugs are overwhelming the wonder drugs—creating an urgent need to rebuild our arsenal of infection-fighting medicines.

In 1900, the leading causes of death in the U.S. were influenza/pneumonia, tuberculosis, and gastrointestinal infections like diarrhea.<sup>2</sup> Within a few decades, all were largely vanquished or turned into treatable conditions by antibiotics—an age of wonder drugs heralded by the discovery of penicillin in 1928.<sup>3</sup>

But these and other deadly infections are poised to make a comeback. Some already are.

Certain strains of pneumonia are once again defeating antibiotics. In Bangladesh, 77 percent of children under age 5 admitted to hospitals with pneumonia had a form that showed drug resistance.<sup>4</sup>

Drug-resistant tuberculosis is active in 100 countries.<sup>5</sup> Worldwide, nearly 500,000 people develop this highly dangerous form of TB each year, and

nearly a quarter million die.<sup>6,7</sup> About half live in India, China and Russia, which include many high-population areas where the disease can easily spread.

Few people understand the science—or its implications.

Beyond the revival of once-defeated diseases, germs constantly evolve to create new threats. This is inherent in their nature—a process of continual modification to survive and build greater resilience into future infections. As the use—and misuse—of antibiotics proliferates, germs adapt until they develop into superbugs capable of evading our current stockpile of tools to combat them.

Today, an estimated 2.8 million Americans get antibiotic-resistant infections from these superbugs every year;<sup>8</sup> over 160,000 die as a result, making it the fourth leading cause of death in the U.S.<sup>9</sup> Worldwide, drug-resistant infections kill 1.27 million people, an annual death toll set to expand to an estimated 10 million by 2050.<sup>10</sup>

This growing risk is as urgent and threatening to humanity as the COVID-19 pandemic or climate change.<sup>11</sup> Yet there are no public demonstrations or celebrity appearances calling on leaders to avert this looming crisis. No realiza-

tion among the broader public that a crisis even exists. No language even to frame the problem in a way that builds understanding and creates momentum for action. No emergency legislation or massive investment in solutions.

This problem *can* be solved. But faced with little pressure, governments have been slow to act.

## The Quarterback

On November 18, 2018, Alex Smith lay on the football field after suffering a gruesome compound fracture of his lower leg. The Washington Football Team quarterback—and millions of fans—wondered if his career was over. As he was carted off the field, no one knew his life was in jeopardy—not from his football injuries, but from a hidden killer lurking in the hospital where he was treated.<sup>12</sup>

Following surgery to reconstruct his leg, Smith was pumped with powerful antibiotics to prevent infection. Nevertheless, Smith quickly developed an infection that triggered sepsis, the body's toxic response to fight back.<sup>13</sup>

At that point, the conversation changed from "Will I play again" to "Can doctors save my leg. And my life?"

After 17 surgeries and a heroic rehabilitation, Alex Smith eventually recovered to return the football field. It's an inspiring story. But it conceals a larger, more deadly truth.

Every year, sepsis claims 11 million lives worldwide,<sup>14</sup> including 3 million children.<sup>15</sup> In the U.S., more children die each year from sepsis than from pediatric cancers.<sup>16</sup>

Sepsis is most common in people who are hospitalized or recently hospitalized—a setting where drug-resistant germs are easily spread. While any infection could lead to sepsis,<sup>17</sup> the widespread use of antibiotics in hospitals makes them a breeding ground for superbugs, resulting in millions of infections that, unlike Alex Smith's, don't have a happy ending.

# The Miracle of Longevity—At Risk

The 20th century saw the greatest leap in longevity in human history. In the U.S., life expectancy jumped from about 48 years in 1900 to nearly 79 years by 2020.<sup>18</sup> In Japan, lifespans have risen even more—from just over 38 years in 1900 to about 84 ½ by 2020.<sup>19</sup> Countries as diverse as Brazil, India and Saudi Arabia have also seen big increases.

Lives have not only become longer, they have become *better*.<sup>20</sup> Billions of people can remain more productive, more active, more fulfilled because they are more healthy. Retirement is now a jumping off point to a new, exciting phase, not the last, brief stop in life's journey.

This longevity miracle was built on three pillars.

- Rising childhood immunizations defeated killers like measles, hepatitis, polio, rubella and whooping cough.<sup>21</sup>
- Improved sanitation dramatically curtailed the spread of disease.<sup>22</sup>
- Antibiotics enabled doctors to treat once-deadly infections and make progress against life-threatening diseases and conditions.

Medical experts believe antibiotics add 20 years to global life expectancy.<sup>23</sup> Yet the rise of drug-resistant infections threatens a century of progress by knocking out this pillar of longevity.

Superbugs are engaged in a life-or-death battle with the wonder drugs. And the miracle of longevity hangs in the balance.

Without antibiotics, doctors and patients lose one of the most powerful tools modern medicine has developed to fight infections. In previous decades, new antibiotics were developed to meet new threats. This is no longer the case.

# The Pipeline is Empty

The period from the 1950s to the 1970s is often called the “golden era” of antibiotics. Since then, no new classes of antibiotics have been discovered.<sup>24</sup>

Between 2000 and 2020, FDA approvals of new antibiotics dropped nearly 75 percent compared to the previous two decades. Today, only 9 out of 138 new medicines in the pipeline offer a lower risk of resistance.<sup>25</sup>

**The bottom line: Innovation in antibiotics has nearly ground to a halt.**

Resistance is a natural process. But it is aided and abetted by human actions and choices. When bacteria survives a dose of antibiotics, it passes along this resistance to the next generation—a process which continues until it can no longer be defeated by the drugs in our current arsenal.<sup>26</sup>

The more antibiotics are prescribed, the faster this process works. The misuse and abuse of antibiotics by doctors and patients is rampant—making it one of the main accelerators in superbug development, along with antibiotics in the environment among other factors.<sup>27</sup>

At least 30 percent of antibiotics prescribed in the U.S. are unnecessary—a stunning 47 million excess prescriptions.<sup>28</sup> Half of outpatient

prescriptions are unnecessary.<sup>29</sup> In Italy, the percentage of inappropriate use of antibiotics ranges from 33 percent for people under 45 to 51 percent for people between 66 and 75.<sup>30</sup> In Greece, daily consumption of antibiotics is more than double that of the EU as a whole.<sup>31</sup>

It's a global challenge. Some 84 percent of pharmacies in China hand out antibiotics without prescriptions.<sup>32</sup> On our current trajectory, antibiotic use will increase 200 percent worldwide by 2030.<sup>33</sup> In many parts of the world, patients too poor to see a doctor buy antibiotics from street vendors.<sup>34</sup>

Until the last 20–30 years, medical science defeated new resistant strains with new drugs. But new discoveries have been slowed as incentives for

antibiotic innovation have gone from weak to almost non-existent. Now, perversely, marketplace incentives are stacked *against* innovation.

A properly functioning market should reward the development of new antibiotic innovations. Sales should grow to reflect the value delivered by new medications, jumpstarting a virtuous cycle of innovation. Yet due to the threat of ever-evolving superbug resistance, health authorities advise doctors not to prescribe new antibiotics. When a new innovation arrives, our first instinct is to lock it in the medicine cupboard to safeguard its efficacy.

Instead of simply *locking* the cupboard, the goal should also be to constantly *replenish* the cupboard. The problem must be attacked from both the demand and supply side.

Doctors and patients need to reduce antibiotic demand by limiting prescriptions to those infections where they can have a benefit. And governments worldwide, pharmaceutical companies and all stakeholders need to work together to create a far more robust supply of new treatments.

The rapid development of highly effective COVID-19 vaccines shows that drug innovation *can* be accelerated. Dramatically. By March—just months after the first outbreak—80 vaccine candidates were in development.<sup>35</sup>

When the stakes are high enough and incentives strong enough, the public and private sectors can be impelled to action. Well, the stakes are that high today.

# The Future Without Antibiotics?

In 2017, a Nevada woman died from an incurable infection that could defeat 26 different antibiotics—every treatment in the U.S. arsenal. She had broken her leg and was hospitalized with a bone infection.<sup>36</sup>

In 2012, high school senior Meredith Littlejohn was diagnosed with leukemia. One year later, she died—not from cancer, but from an infection antibiotics couldn't beat.<sup>37</sup>

George Semakula was flown back to the U.S. from Tanzania with a severely broken ankle—and an infection that nearly killed him. After four months on antibiotics—including a Japanese experimental drug that hadn't been approved in the U.S.—George survived.<sup>38</sup>

These cases provide a window into a possible future—a future where antibiotics stop working and routine medical procedures become potentially deadly. Who is most likely to be impacted?

- **Expectant Mothers:** Nearly 1/3<sup>rd</sup> of the 4 million babies born in the U.S. in 2019 were delivered by cesarean.<sup>39</sup> Worldwide, about 30 million babies are born by C-section every year.<sup>40</sup> Antibiotics protect mothers during this procedure and recovery.<sup>41</sup> Yet as antibiotics become less effective, expectant mothers and their babies are put at risk—and childbirth becomes a potentially deadly event.
- **Joint Replacement Patients:** About 1 million hip and knee replacement surgeries are performed every year in the U.S.<sup>42</sup> By 2030, a projected 3.5 million knee joints will be replaced annually,<sup>43</sup> providing freedom from pain and promising a more active lifestyle. Or will they? Already, doctors are advising some patients to avoid joint replacements for fear of developing an infection that can't be treated.<sup>44</sup>
- **Women Everywhere:** Urinary tract infections (UTIs) will impact 50 to 60 percent of adult women in the U.S.<sup>45</sup> Once commonly treated with a pill, these infections often require IV-delivered antibiotics now that resistance has grown.<sup>46</sup> A common illness can now mean a hospital stay—and the risk of further infection grows far more dangerous.
- **Cancer Patients:** Around 10 million people worldwide receive chemotherapy to treat various forms of cancer.<sup>47</sup> Chemotherapy kills cancer cells and has dramatically boosted cancer survival rates. But it also wipes out patient immune systems, raising the threat of infections resistant to antibiotics. The result: growing ranks of patients who beat cancer only to be killed by an infection that can't be treated.<sup>48</sup>



From newborn babies to the elderly and everyone in between, people with once-treatable conditions will run a far greater risk of deadly infections. Routine procedures that millions of

people undergo every day—removing a wisdom tooth, a heart valve replacement, treating pneumonia—will all be transformed from routine procedures into potentially life-or-death situations.

## The Way We Live

A proliferation of antibiotic-evading infections won't just raise the global death toll, it will impose sweeping changes in the way we work, socialize and live our lives. Ask anyone who spent the last year living through the COVID-19 pandemic.

When deadly conditions can be spread person-to-person, our lives change.

To “flatten the curve” on COVID-19's spread, millions of businesses closed and jobs were lost. Children suffered through lost education and socialization. Personal contact with family, friends and loved ones was curtailed. Masks and social distancing replaced handshakes and hugs. Depression, drug and alcohol abuse, and suicide rose dramatically.<sup>49</sup>

Think back to the leading causes of death before the age of antibiotics. Back in 1900, a sick family member, neighbor or coworker represented a potentially mortal threat. Sound familiar?

Since 1900, U.S. influenza/pneumonia deaths dropped by 92 percent.<sup>50</sup> Deaths from tuberculosis have fallen

98 percent.<sup>51</sup> What happens when our antibiotic defenses start to fail for these and other diseases that spread relatively easily from person to person? Will we allow influenza or pneumonia to become a primary killer, as it was in 1900?

“When highly resistant bacteria crop up in one part of the world, they eventually crop up everywhere,” said Dr. Jason Harris of Massachusetts General Hospital and Harvard Medical School, co-author on a study on pneumonia among Bangladeshi children. “If COVID-19 was a tsunami, then emerging antibiotic resistance is like a rising flood water.”<sup>52</sup>

# The Innovation Solution

In the late 1960s, a book called *The Population Bomb* sounded the alarm about the potential dangers of over-population, the collapse of society's ability to feed humanity, and the resulting famines that would soon kill hundreds of millions of people. It became an international best-seller and a cultural phenomenon—a driver of public discussion, a motivator of public policy, a launching point for academic seminars, think tank symposiums and legislative hearings. It was also wrong, largely because its author, Paul Ehrlich, could not appreciate the power of innovation to change the dynamic, transform progress and the future. His problem, like so many others, was assuming a straight line to the future.

He could not imagine the Green Revolution and other profound impacts over the next decades. But as wrong as he was on the facts and how innovation and science can work to change the future, his attention getting predictions should be lessons for our challenge today on the threat of antibiotic extinction.<sup>53</sup>

In the 2020s, the battle between the superbugs and the wonder drugs deserves the same attention and impact.

So, yes, the crisis predicted in *The Population Bomb* was averted. In the 1960s and 1970s, the world experienced a "Green Revolution"—a surge in innovation across the agricultural spectrum. The power of science and technology produced innovations like high-yield, disease resistant crops; high-tech precision farming; more effective and efficient irrigation; improved fertilization.<sup>54</sup> Nobel prizes were awarded.<sup>55</sup> Literally billions of people were saved.<sup>56</sup>

Today, the world needs an equivalent leap forward in antibiotic innovation. But on our current path, we will not achieve it. Several steps need to be taken.

**Reinvent and reimagine AMR:**

AMR—anti-microbial resistance—is the commonly used term for the rise of superbugs that can defeat current antibiotics. The problem is, if you stop 100 people on the street, 99 of them won't be able to tell you what it is or why it's a threat. The language around AMR needs to generate an uprising, not a yawn.

*How can we create a new way of speaking about AMR that connects with ordinary people, alerts them to the dangers they themselves now face, and generates demand for the public policies and market-based incentives needed to find a solution?*

**Broaden the Audience:**

The problem of antibiotic-resistant infection was declared a public health crisis by the U.S. CDC and WHO in 2013. Yet this must be the lowest profile public health crisis in modern history. In recent decades, deadly health threats like HIV/AIDS and many forms of cancer have become treatable conditions by capturing public attention and spurring advocacy for treatments.

*What will it take to broaden understanding of the superbug threat beyond the specialized healthcare community to win attention among global policymakers and demands for action by key opinion influencers and the wider public?*

**Right-size Incentives:**

Antibiotic-resistant infections cost the U.S. \$20 billion per year in direct costs and \$35 billion in lost productivity.<sup>57</sup> Globally, the economic cost is projected at \$100 trillion per year if we keep following the same course. Avoiding that economic threat certainly justifies significant public and private investment.

*How can we create a marketplace with sustained incentives for antibiotic research, development, testing and distribution that are equal to the economic threat we face?*

**Adapt the COVID-19 Model:**

The race for treatments and vaccines to fight the COVID-19 pandemic created new models of collaboration and cooperation between government regulators and private pharmaceutical companies.

*What lessons did we learn from COVID-19 about how to accelerate innovation, and how can we adapt those lessons to the fight against superbugs?*

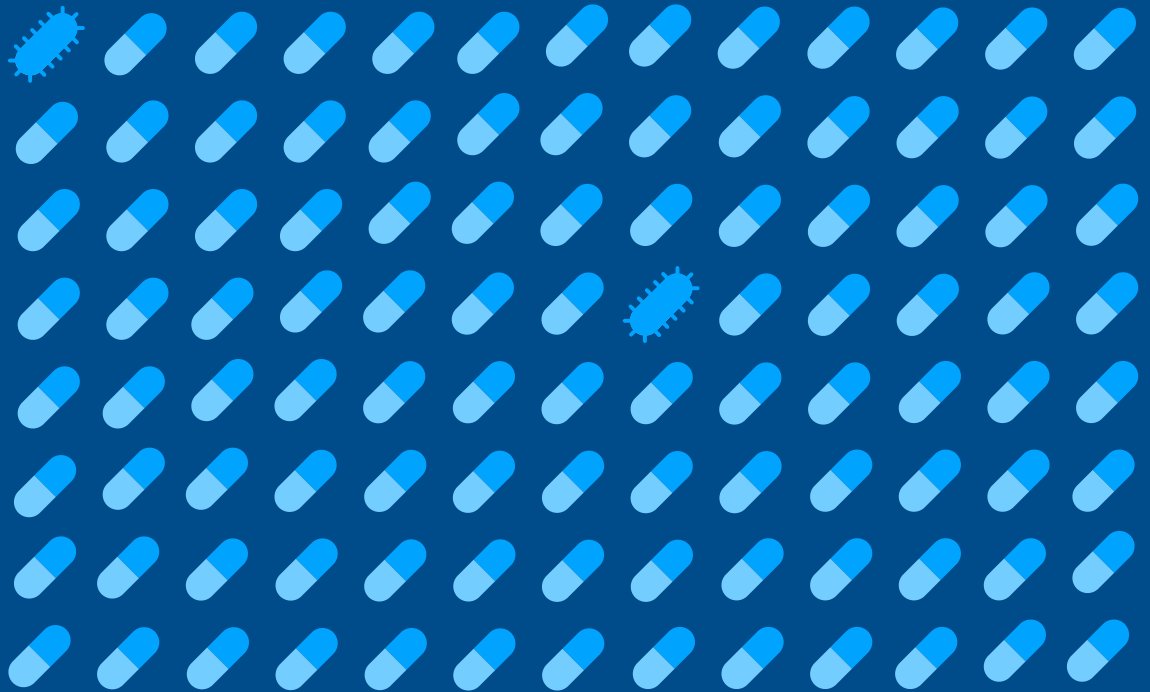
The battle between wonder drugs  
and superbugs can be won.  
Innovation can deliver the  
treatments we need.  
Millions of lives can be saved.  
The time to start is now.

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### **About the Global Coalition on Aging**

The Global Coalition on Aging aims to reshape how global leaders approach and prepare for the 21st century's profound shift in population aging. GCOA uniquely brings together global corporations across industry sectors with common strategic interests in aging populations, a comprehensive and systemic understanding of aging, and an optimistic view of its impact. Through research, public policy analysis, advocacy, and strategic communications, GCOA is advancing innovative solutions and working to ensure global aging is a path to health, productivity and economic growth.

### **For more information contact**

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