The Plan to Avert Our Post-Antibiotic Apocalypse - The Atlantic

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Science

Under instructions from U.K. Prime Minister David Cameron, economist Jim O'Neill has spent the last two years looking into the problem of drug-resistant infections—bacteria and other microbes that have become impervious to antibiotics. In that time, he estimates that a million people have died from such infections. By 2050, he thinks that ten million will die every year.

O'Neill is most famous for another prediction—that by 2050, the combined economies of Brazil, Russia, India, and China (BRIC), would eclipse those of the world's current richest countries. A former chairman of Goldman Sachs with no scientific training, he was an unorthodox choice to lead an international commission on drug-resistant infections. He was also an inspired one. The problem of drug-resistant microbes isn't just about biology and chemistry; it's an economic problem at heart, a catastrophic and long-bubbling mismatch between supply and demand. It's the result of the many incentives for misusing our drugs, and the dearth of incentives for developing new ones.

The scope of that problem is clear in O'Neill's final report, which launches today on the back of eight earlier interim publications. It is as thorough a review of the problem of drug-resistant infections as currently exists. "They've been extremely open-minded, and have sought opinion extensively across the world," says Laura Piddock, a microbiologist at the University of Birmingham and director of Antibiotic Action. "They've clearly recognized that this is a global issue and needs global solutions."

The report's language is sober but its numbers are apocalyptic. If antibiotics continue to lose their sting, resistant infections will sap $100 trillion from the world economy between now and 2050, equivalent to $10,000 for every person alive today. Ten million people will die every year, roughly one every three seconds, and more than currently die from cancer. These are conservative estimates: They don't account for procedures that are only safe or possible because of antibiotics, like hip and joint replacements, gut surgeries, C-sections, cancer chemotherapy, and organ transplants.

And yet, resistance is not futile. O'Neill's report includes ten steps to avert the crisis. Notably, only two address the problem of supply—the lack of new antibiotics. "When I first agreed to do this, the advisors presented it to me as a challenge of getting new drugs," says O'Neill. "But it dawned on me very quickly that there were just as many, if not more, important issues on the demand side." Indeed, seven of his recommendations focus on reducing the wanton and wasteful use of our existing arsenal. It's inevitable that microbes will evolve resistance, but we can delay that process by using drugs more sparingly.

The first step is to improve sanitation. Fewer infections means less need for antibiotics. For richer nations, the focus lies in reducing infections in hospital settings. For poorer countries, ensuring clean water and better sanitation is paramount; as O'Neill writes, resistance "is intrinsically an issue of economic development." In India, Nigeria, Indonesia, and Brazil alone, sanitation could save 300 million courses of antibiotics, currently used (often ineffectively) to treat diarrhea.

We also need a global surveillance network to understand the extent to which antibiotics are being used, the spread of resistant microbes and the genes behind their powers, and the effectiveness of different drug/bug combos. The World Health Organization has already planted the seeds of such a network, and following an earlier O'Neill report, the UK government launched the £195 million

Fleming Fund to build surveillance in poorer countries.

Even without such data, some remedial steps are already obvious. In the U.S. alone, 70 percent of antibiotics that are medically useful to humans are given to animals instead, and not just for treating disease but for promoting growth or compensating for poor farming practices. So O'Neill's report recommends that from 2018, countries should set ten-year reduction targets to reduce the unnecessary use of antibiotics in agriculture. It also argues for restrictions or bans on the agricultural use of any drug that's a last-line defense for humans. And it suggests that meat should be transparently labeled so consumers can make informed choices.

A lot of human antibiotic use is wasteful too. Of the 40 million people who get antibiotics in the U.S. every year, only 13 million actually need them; the rest

have viral infections that can't be treated with these drugs. One solution is to

develop better, faster, cheaper diagnostic tools, so doctors don't have to assess vague symptoms, or rely on slow, expensive tests based on centuries-old technology. "I sometimes think that if there was a single most important thing here it might be diagnostics," says O'Neill.

He thinks that rich countries should mandate that, by 2020, all prescriptions will be informed by "data and testing technology wherever available." That will create a market for developing better tests, and so boost innovation in this stagnant area. Meanwhile, a "diagnostic market stimulus" would provide top-up payments to poorer countries that buy diagnostic tests, in the same way that organizations like Gavi fund vaccine use in the developing world.

A large public-awareness campaign, with a yearly budget of $40 to 100 million, would also help. As I reported last year, people largely don't know how antibiotics work, don't distinguish between bacterial and viral infections, and assume that they, not microbes, are becoming resistant to antibiotics. These misconceptions lead people to pressure doctors for inappropriate prescriptions. Failing that, they can simply buy antibiotics online; the O'Neill report also recommends that countries should crack down on over-the-counter sales of antibiotics without prescriptions, and outrightly ban such sales online.

We can also lift some of the pressure on our antibiotic supply by promoting effective alternatives like vaccines, for both humans and animals. This means encouraging the use of existing vaccines (say, against pneumonococcal infections) and developing new ones against increasingly resistant threats like Clostridium difficile and Pseudomonas aeruginosa. It also means looking into other lines of treatment like probiotics (beneficial bacteria), phages (bacteria-killing viruses), and immunotherapies (substances that stimulate the immune system). It's noteworthy that these alternatives, often lauded by the media as incipient solutions to the antibiotic crisis, are just small and underplayed parts of O'Neill's strategy.

These measures depend on scientists and doctors who specialize in infectious disease. Unfortunately, of the 25 main medical specialities in the US, infectious disease is the lowest paid and among the most unpopular. Its publications receive markedly fewer citations than most other biomedical fields.

"I was unaware of that myself and I'm a microbiologist," says Piddock. "Clearly you need scientists to do the basic science that will underpin new treatments,

and you need physicians for leadership in using antimicrobials. If you don't have that, the drugs get used by everyone." To fix the "exodus of expertise", the O'Neill report calls for funding and training schemes to improve the numbers, pay and recognition of people working in infectious disease.

That covers the demand. Now for the supply.

No new classes of antibiotics have emerged for decades and barely 40 new drugs are in development. Just three are potentially effective against carbapenem-resistant bacteria, which have already reached worryingly high levels

in some countries. Simply put, we are not developing enough new medicines to make up for those that are being defanged by resistant microbes.

We were too successful too early. The golden age of antibiotic discovery between

the 1940s and 1970s allowed us to wage a very successful war against infectious disease. But just as new drugs became harder to find, we grew overconfident, shifting our attention and investment to other bogeymen like cancer. Of the $38

billion that went into pharmaceutical research and development between 2003 and 2013, just $1.8 billion was spent on antibiotics.

From a business standpoint, this disinvestment makes perfect sense. Pharmaceutical companies want a breakthrough drug to arrive with a splash, capture a large market share, and sell as well as possible while it's still on patent. But we actually want to restrict the use of new antibiotics to prolong their usefulness. That creates a terrible market, which will only get worse if the first seven of O'Neill's measures come to pass.

His solution is to set up market-entry rewards—billion-dollar payments for any company that takes new antibiotics to market (and sells and promotes them responsibly). Such payments ensure that companies are rewarded for developing drugs rather than just selling them—or even instead of selling them. "We need a couple of drugs against the most serious pathogens ready, but we hope not to buy

them or use them," says Kevin Outterson, who co-directs Boston University's Health Law Program. "That's what we're doing here. "You need to build the fire station and sprinklers years before you need them, but you don't only pay the contractor when a fire breaks out."

To complement this, the report recommends creating a global innovation fund for early-stage research. A lot of the basic science that underpins the discovery of

new drugs is not sexy and has poor commercial returns. Consequently, with a few exceptions, it's underfunded. It will take a pooled fund of $2 billion over five

years to support such work, and the U.K. and China have already pledged $145 million each.

How much will all this cost? Roughly $40 billion over a decade, O'Neill estimates. That includes roughly $18 for the two measures designed to stimulate drug development, £10 to 20 billion for developing and rolling out diagnostics and vaccines, and up to $1 billion for improving public awareness. The G20 countries could raise this sum on their own by repurposing just 0.05 percent of their healthcare budget. It may be possible to supplement this by taxing antibiotic use (especially in animals), or levying an investment charge on companies that sell health-care products, many of which rely on antibiotics.

"It's not a major financial challenge," says O'Neill. "It's the attitude.

Everybody has got to get out of their comfort zone in order to get a solution to this multi-faceted challenge.” That’s why his final recommendation is to build a global coalition—an international entity that can turn plans into actions, protect funds from the vagaries of political cycles, and ensure that new drugs and diagnostics are accessible and affordable to poorer countries.

The coming months will be crucial. The WHO’s World Health Assembly in taking place in Geneva next week, as is a G7 meeting in Japan. In September, the G20 is convening in China and the UN General Assembly is meeting in New York; antibiotic resistance will be discussed at both. “I am cautiously optimistic,” says O’Neill. “We have a lot of intellectual buy-in for the spirit of what we’re recommending.”

“The time for arguing over the broad strokes is over,” adds Outterson. “This is a good report. We need to move forward.”