Could better tests help reverse the rise of drug-resistant infections?

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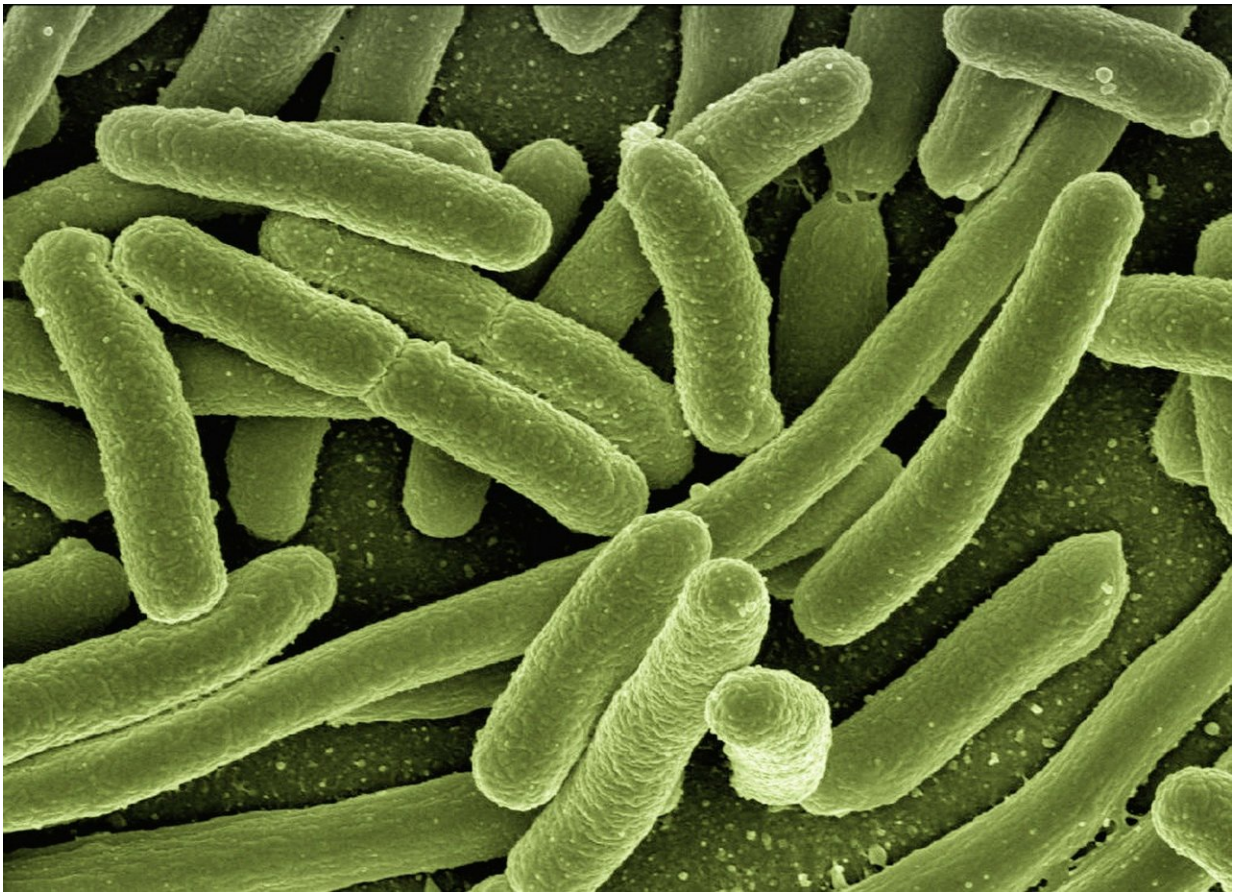

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A growing number of infections—such as pneumonia, gonorrhea and tuberculosis—are becoming harder to treat, as bacteria evolve defenses

against antibiotics faster than we can develop new drugs to replace them.

Duke University game theorist David McAdams says faster, more accurate tests for drug-resistant infections are being developed that could, at least in theory, change the game and turn the tables against some drug-resistant bacteria—but with a caveat.

That's the take-home of a new modeling study led by McAdams and infectious disease expert Sam Brown of the Georgia Institute of Technology, to be published May 16 in the journal *PLOS Biology*.

The researchers used a type of mathematical model in epidemiology called a SIS model to predict the rate of spread of resistant and non-resistant strains of a given pathogen, with and without improved testing, to see which strains would take over.

Currently, a doctor who suspects a patient has a bacterial infection will often prescribe a "best guess" antibiotic, without knowing for sure whether that drug will be effective. But some bacterial strains may carry genetic mutations that help them survive the standard treatment. These survivors then continue to multiply and pass on their protective genes to their offspring. Over the generations, resistant bacteria eventually push out easier-to-treat ones.

A doctor can send a patient sample such as a throat swab or urine sample away for laboratory testing and adjust the prescription if necessary, but such tests can take days.

Armed with rapid tests for resistance, doctors could find the best treatment for a particular patient within minutes rather than days, on the patient's first doctor visit—before they take unnecessarily broad-spectrum drugs that are more likely to fuel resistance.

Knowing at the outset whether the standard first-line drug will work, doctors could prescribe that for patients when it's effective, or choose another when the traditional therapy is likely to fail. By doing so, bacteria resistant to first-line drugs lose the survival advantage they would otherwise have.

"It's like selectively targeting resistant infections with a sniper gun, instead of carpet-bombing every infection with the same one-size-fits-all treatment," McAdams said.

Not only that, doctors and others can take additional steps to reduce transmission of bacteria resistant to first-line antibiotics, such as keeping an infected child home from school longer. "Diagnostic-informed treatment and control is a one-two punch," McAdams said. "Targeted treatment takes away the survival advantage enjoyed by resistant strains, but it's the extra transmission control measures that can put these bacteria at an overall disadvantage relative to more-easily-treated strains."

"We can potentially turn the Darwinian tables on antibiotic-resistant bacteria," McAdams said.

But there's a catch, the researchers found. Many microbes live for some time on our skin or in our bodies peacefully, not causing trouble, during which time these "bystanders" are often incidentally exposed to multiple courses of antibiotics doled out for other infections.

Particularly for these types of bacteria, the team's models show, simply using rapid tests for patients who feel sick won't be enough to tip the scales.

To reduce or even reverse the spread of resistance, the team found, we must also screen for asymptomatic carriers who don't show signs and

usually go undetected—before they unwittingly contribute to the spread of drug-resistant germs.

The stakes are high, scientists say. As many as 50,000 lives are lost each year to drug-resistant infections in Europe and the United States alone, and that number is expected to grow in coming years. According to one recent estimate, antimicrobial resistance left unchecked could kill 10 million people worldwide a year by 2050. That's one person every three seconds—more than cancer.

Some experts warn of a grim future where even minor conditions such as urinary tract infections or scraped knees could turn lethal. Routine procedures such as cesarean sections and joint replacements could put patients at risk of contracting "superbugs" that existing drugs are unable to kill.

The team found that only by taking swift action to identify unsuspecting carriers, treat them and keep them away from others—such as by encouraging carriers to stay home until their infection has cleared—can we hope to turn the tide.

Results of their model also show that once enough infections become impervious to all the antibiotics that are available, rapid testing does little to control their spread, and new drugs are needed.

To be sure, the ability to identify resistant infections faster and treat them better makes rapid diagnostics worth the investment, McAdams said. But "our analysis implies that focusing on rapid diagnostics, while good, is not good enough" to preserve the power of existing antibiotics.

"We shouldn't settle for a post-antibiotic fate," McAdams said. "It's not just about discovering new antibiotics. It's about developing better diagnostic tools and intervention capabilities to preserve the antibiotics

we already have."

More information: "Resistance Diagnostics as a Public Health Tool to Combat Antibiotic Resistance: A Model-Based Evaluation," David McAdams, Kristofer Wollein Waldetoft, Christine Tedijanto, Marc Lipsitch and Sam P. Brown. *PLOS Biology*, May 16, 2019. DOI: 10.1371/journal.pbio.3000250

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