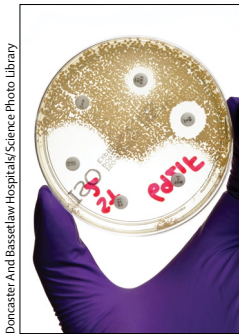


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Is it time for an antibiotic prenuptial agreement?



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Antimicrobial resistance threatens many of modern medicine's greatest achievements.¹ Although antimicrobial resistance occurs naturally or can be acquired through gene transfer, antimicrobial use promotes the selection of resistant microbes. Any inappropriately or incorrectly prescribed antimicrobial drives this selection pressure. Frontline antimicrobial stewards see the consequences of inappropriate antimicrobial use every day, which range from the development of *Clostridium difficile* infection to fatal infection with multidrug-resistant pathogens against which there is no effective antimicrobial therapy.

On Sept 20, 2014, a report from the US President's Council of Advisors on Science and Technology described the present state of antimicrobial resistance as "a crisis that is growing at an alarming rate and requires urgent attention".²

In *The Lancet Infectious Diseases*, Nikolay Braykov and colleagues³ report how physicians from six US hospitals prescribed empirical antimicrobials and modified therapy within the first 5 days of treatment. The results are startling. Antimicrobial use was prevalent (60% of patients on each study day), two-thirds of patients started on empirical antimicrobials did not have a fever, and one-third had neither fever nor elevated white blood cells. By the 5th day of therapy most regimens (66%) remained unchanged. Culture and imaging studies were often not obtained. In cases with negative urine or blood cultures only 37% and 50% discontinued or narrowed therapy, respectively. When culture and imaging studies were done, this was associated with narrowing or earlier cessation of antimicrobials.

The study results show yet again that antimicrobials are misused. This finding is consistent with those from other US and non-US investigators,^{4–6} bringing to mind

Albert Einstein's remark "Insanity is doing the same thing over and over again and expecting different results". What will it take to fix this? We believe the findings from this study promote the need for drastic measures in response.

First, who should prescribe antibiotics? Consider why chemotherapy is only prescribed by oncologists. If the wrong chemotherapy is prescribed at the wrong dose for the wrong duration it can kill a patient. The same applies to antimicrobials, which have the added potential of negatively affecting people other than the patient, by increasing the pool of resistance in the population. The ability of antimicrobials to cause collateral damage is vastly underappreciated. Unfortunately, only allowing infectious disease physicians to prescribe antimicrobials is unrealistic. However, other options can be considered. A mandatory qualification such as an antimicrobial prescribing license renewed every 2 years could be implemented by hospitals. Similar to infection control standards, prescribers who consistently breach policy and negatively affect patient care, ultimately lose their admitting privileges. It is the antimicrobial prenuptial agreement between the physician and the hospital. Misuse of antimicrobials, leads to divorce—ie, the physician loses admitting rights.

Second, as Braykov and colleagues³ show, having an antimicrobial stewardship programme in and of itself, does not always ensure appropriate antimicrobial use. Three of the hospitals included in the study had active stewardship programmes. In the real world, reviewing all antimicrobials ordered in a hospital setting is beyond the scope of a stewardship physician or pharmacist. Guidelines with consequences for non-compliance should be used.

Third, prolonged, inappropriate use of empirical antibiotics must be prevented. Implementation of automatic stop orders at days 3–5, forcing an antimicrobial timeout to reassess therapy should be applied across the board. Development and use of more rapid diagnostic tests with stewardship interventions to enable early rationalisation of antimicrobial choice, have been shown to be game changing and improve patient outcomes.^{7,8}

Fourth, we need to seriously decide how we promote appropriate antimicrobial use. How do we get the message into the hands of non-infectious diseases oriented prescribers such as surgeons, oncologists, and other high users of antimicrobials who we are failing to reach? One option would be to publish more in their journals. It is unlikely that infectious diseases guidelines are on their top ten must-read list, and it is clear from the present study that the message is not resonating with this cadre of prescribers. Additionally, it is time that we got patients and the public involved. Long-term, global social media campaigns by WHO, US Centers for Disease and Control, and others, using Twitter and Facebook should be employed. Continued antimicrobial misuse in hospitals is unacceptable, and a direct threat to patient safety.

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Influenza vaccine effectiveness in elderly people

In *The Lancet Infectious Diseases*, Maryam Darvishian and colleagues¹ present the results of their meta-analysis to estimate influenza vaccine effectiveness in people aged 60 years or older. Many countries have implemented annual influenza vaccination programmes^{2,3} with the goal of reducing serious illnesses and deaths from seasonal influenza, particularly in susceptible populations. Most influenza-related deaths occur in elderly people,⁴ who are a high priority for influenza vaccination. Previous attempts to estimate influenza vaccine effectiveness in elderly people have either been strongly biased (because of the use of outcomes not specific to influenza and inadequate control of differences between vaccinees and non-vaccinees)⁵ or have included too few participants to estimate vaccine effectiveness with any meaningful precision.^{6,7}

Darvishian and colleagues reduce the limitation of small sample sizes by undertaking a meta-analysis

of nearly 30 different vaccine effectiveness studies in elderly people. They also reduce problems of bias by restricting their meta-analysis to test-negative studies, which only include laboratory-confirmed illnesses in the outcomes, and which reduce confounding due to differential use of health care between vaccinated and unvaccinated elderly people.⁸ Averaged across countries and years, Darvishian and colleagues estimate that influenza vaccination reduces the risk of medically attended influenza infection in elderly people by 28%, to 58%.¹ The range depends on the intensity of influenza circulation and the apparent antigenic match between the vaccine strains and the circulating influenza strains. The results suggest to policy makers that influenza vaccination programmes provide slight to moderate benefits for elderly populations.

Now that estimates of average vaccine effectiveness in elderly people have been calculated, what is next



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