next generation of more powerful and expensive antibiotics, and are setting the stage for a time when antibiotics might no longer be effective for many infections.

Another major reason for antibiotic resistance is the use of antibiotics in animals (eg, tetracycline in chicken feed) in subtherapeutic doses to promote growth. This important point was also highlighted very clearly in the article.[1]

As mentioned, many high-income countries have enacted laws to curb the practice of adding antibiotics to animal feed, even as early as 1971, to avoid antibiotic resistance in people. It is therefore time for countries like India and Nepal, and other low-income countries, to use antibiotics in animals only for the treatment of infections. Indiscriminate, subtherapeutic use of antibiotics for animal growth promotion must be stopped by governments; by increasing awareness in the general population about drug resistance, and by enacting laws so that antibiotics for saving human lives will continue to be effective, and the likelihood of resistance will decrease.

If India takes the lead in this venture, it will probably be easier for smaller countries in the vicinity like Nepal to follow suit, because its pharmaceutical commerce is closely linked with India.

I declare no competing interests.

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1 Laxminarayan R, Duse A, Chand W, et al. Antibiotic resistance—the need for global solutions. *Lancet Infect Dis* 2013; **13:** 1057–98.

I read with interest Simon Howard and colleagues' Comment[1] on the increasing threat of antibiotic resistance and the necessity for a strong global response. That antibiotic use results in selective pressure favouring resistant bacteria is beyond dispute, and this is certainly a large part of the story, but not the entire one.

Antibiotic resistance is probably ancient.[2] Researchers analysing sediment samples obtained from deep below the earth's surface at two sites in the USA found a diverse array of bacteria with resistance to 13 different antibiotics, and 90% of samples were resistant to at least one antibiotic. Perhaps most surprising, some of the bacterial strains were thought to be completely isolated from past human exposure, which raises the likelihood that they developed novel antibiotic resistance.[2]

In another study,[3] 30 000-year-old ice cores from the Beringian permafrost in Canada were collected. DNA segments from flora and fauna characteristic of the Arctic Pleistocene epoch were extracted and analysed. Metagenomic analysis revealed a highly diverse array of genes encoding resistance to multiple antibiotics such as β-lactams, tetracyclines, and glycopeptide antibiotics, including the *VanA* gene that confers the highest resistance to vancomycin.[3]

That antibiotic resistance pre-dates the anthropogenic antibiotic era might seem surprising, but it should not be. Bacteria are estimated to have originated more than 3·8 billion years ago, and antibiotics might be at least hundreds of millions of years old.[4] In an effort to survive in competitive environments, bacteria and other pathogens have developed mechanisms to compete with other species, which include the production of antibiotics. As Howard and colleagues note,[1] in one of history's most famous examples, the mould *Penicillium chrysogenum* produces a substance that inhibits the growth of Gram-positive bacteria, which led to the discovery of the antibiotic penicillin.[5]

The widespread use of antibiotics has certainly accelerated the pace of antibiotic resistance that occurs naturally. The degree of resistance that exists, and the extensive head start that bacteria already have, increases the threat of antibiotic resistance even more. The pace of new antibiotic discovery and licensing has certainly slowed in recent years, which threatens our ability in the future to fight off life-threatening infections.

But somewhere out there is probably a gene yet to be expressed that encodes a resistance mechanism to an antibiotic yet to be invented. Perhaps somewhere in the Beringian permafrost or the bathroom sink of a hospital near you…

I declare no competing interests.

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3 D'Costa VM, King CE, Kalan L, et al. Antibiotic resistance is ancient. *Nature* 2011; **477:** 457–61.
4 Wright DG, Poinar H. Antibiotic resistance is ancient: implications for drug discovery. *Trends Microbiol* 2012; **20:** 157–59.
5 Rifkind D, Freeman G. The Nobel prize winning discoveries in infectious diseases. London: Academic Press, 2005.

We agree with Ramanan Laxminarayan and colleagues[1] that antimicrobial resistance (AMR) in bacteria that cause community and health-care-associated infections (HAI) in low-income countries poses a serious threat to global health. In the first 60 years of antibiotic use, resistance predominantly emerged from hospitals in high-income countries; now, health-care environments in low-income countries have also become an important crucible for the evolution of resistance. The increased resistance is eroding the effectiveness of local management strategies for life-threatening diseases such as pneumonia and meningitis. Increased interconnectedness means that resistance genes emerging in one place rapidly become a global threat.

AMR and HAI are tightly related issues that are both poorly described in low-income settings, and basic data on the burden of disease are extremely scarce.[2] The Global Burden of Disease studies have never estimated the effect of either HAI or AMR, but this is hardly surprising, in view of the