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Population genomics of *Escherichia coli* in livestock-keeping households across a rapidly developing urban landscape

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Quantitative evidence for the risk of zoonoses and the spread of antimicrobial resistance remains lacking. Here, as part of the UrbanZoo project, we sampled *Escherichia coli* from humans, livestock and peri-domestic wildlife in 99 households across Nairobi, Kenya, to investigate its distribution among host species in this rapidly developing urban landscape. We performed whole-genome sequencing of 1,338 *E. coli* isolates and found that the diversity and sharing patterns of *E. coli* were heavily structured by household and strongly shaped by host type. We also found evidence for inter-household and inter-host sharing and, importantly, between humans and animals, although this occurs much less frequently. Residues similarly was differently distributed across host and household, consistent with being driven by shared exposure to antimicrobials. Our results indicate that a large, epidemiologically structured sampling framework combined with WGS is needed to uncover strain-sharing events among different host populations in complex environments and the major contributing pathways that could ultimately drive the emergence of zoonoses and the spread of antimicrobial resistance.

The spread of bacterial pathogens and antimicrobial resistance (AMR) across human and animal populations presents a substantial and growing threat to global health and economic development. Identifying risk factors for emergence and spread is one of epidemiology's most important challenges. Many recent pandemics and newly emergent infectious diseases have animal origins and are associated with rapidly urbanizing environments¹. The dynamic interfaces among humans, domestic livestock and wild animals act as conduits by which humans can be exposed to zoonotic pathogens and AMR in an environment with inadequate sanitation infrastructure, limited access to appropriate and effective drugs and emergent antimicrobial usage².

The importance of livestock to the transmission of bacteria and AMR remains unclear. The practice of keeping livestock, particularly in urban settings, has been described as a risk factor for the emergence and spread of zoonoses³. Antimicrobial agents used

in human medicine are also used for growth promotion, disease prevention and disease treatment in livestock, enhancing selection pressures on bacterial pathogens for AMR emergence and spread⁴.

Wild birds and mammals have also been documented to carry and exchange drug resistant bacteria with livestock and humans^{5–7}. The rapid expansion of urban environments into previously pristine or sparsely populated natural landscapes also increases the potential for greater contact among wildlife, humans and livestock, which can provide conduits for microbe sharing⁸.

Fundamental to whole-genome sequencing (WGS) studies is the availability of systematically sampled bacterial isolates obtained from humans, livestock and wildlife across overlapping geographical regions and time frames, yet data are lacking⁹. In this study, we sampled the bacterium *Escherichia coli* from humans, livestock and peri-domestic wildlife in 99 households and their environs across 33 subdivisions in Nairobi, Kenya, in an epidemiologically

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