

Supporting Information for:

Classification: Medical Sciences

Title: Estimating the proportion of bystander selection for antibiotic resistance among potentially pathogenic bacterial flora

Short Title: Estimating bystander selection for resistance

Authors: Christine Tedijanto^a, Scott W. Olesen^b, Yonatan H. Grad^{b,c}, Marc Lipsitch^{a,b}

Author Affiliation: ^a Center for Communicable Disease Dynamics, Department of Epidemiology, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, Massachusetts, 02115, USA; ^b Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, 655 Huntington Avenue, Boston, Massachusetts, 02115, USA; ^c Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, 15 Francis Street, Boston, Massachusetts, 02115, USA

Corresponding Author: Christine Tedijanto
Harvard T.H. Chan School of Public Health
677 Huntington Ave, Suite 506
Boston, MA 02115
ctedijanto@g.harvard.edu

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Figure S1. Proportion of bystander exposures (with 95% confidence interval) by antibiotic class and species. “Overall” estimates reflect exposures to antibiotics in any of the included classes. Results for TMP/SMX and nitrofurantoin are for the individual drug instead of an antibiotic class.

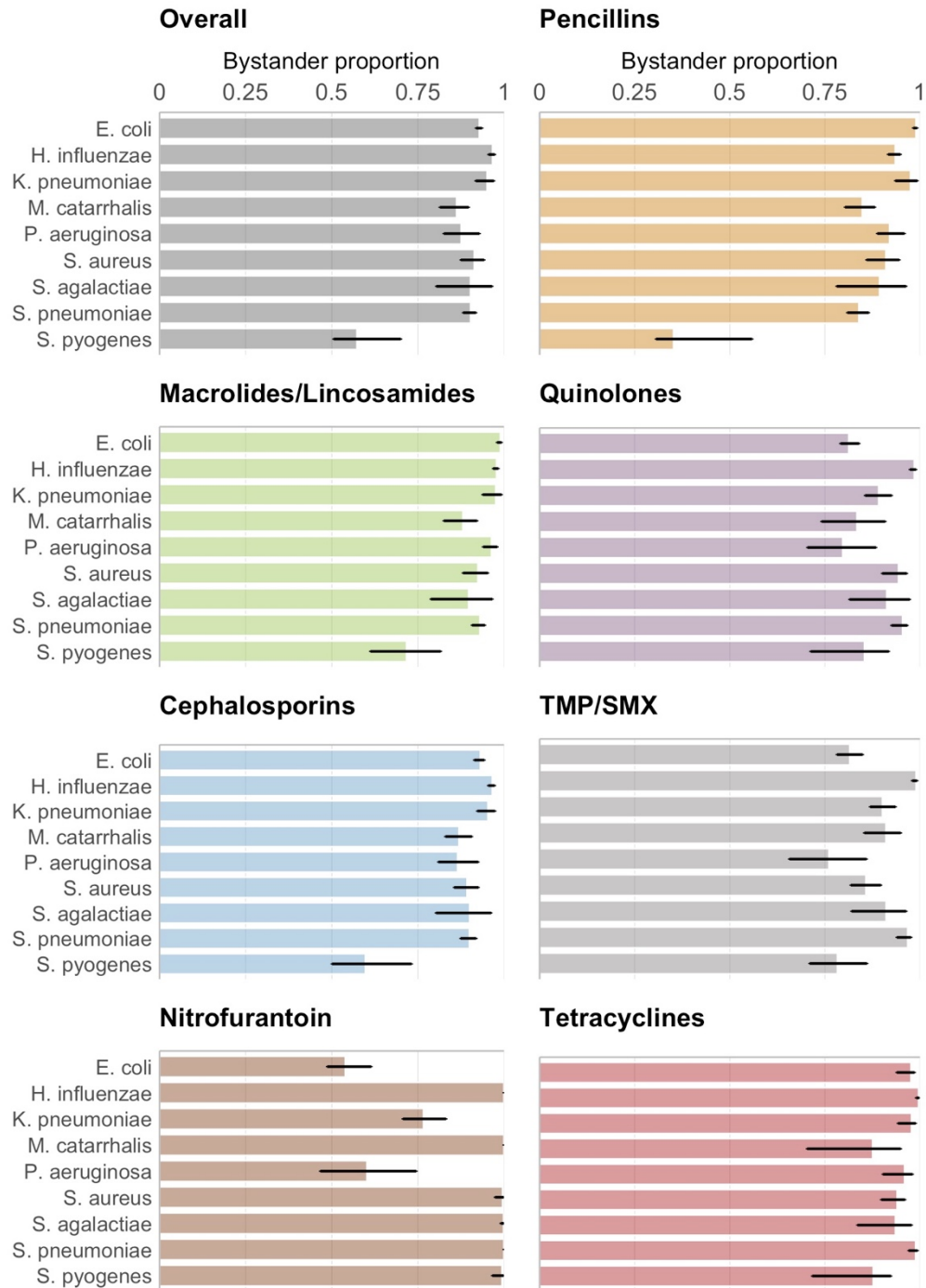


Figure S2. Number of sampled outpatient visits (unweighted) from NAMCS/NHAMCS 2010-2011 with given diagnosis and antibiotic prescription.

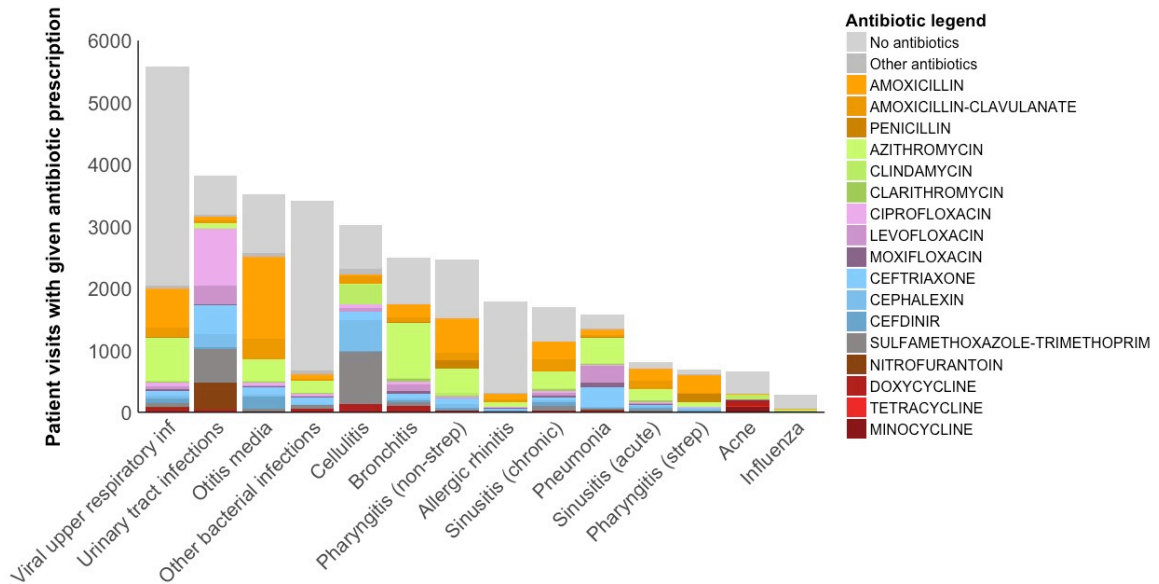


Figure S3. Heat map shading represents the proportion of visits (after weighting to be nationally representative) with a diagnosis of the specified condition, given that the visit resulted in a prescription of the specified antibiotic. Rows are not required to sum to 100% as only a subset of conditions are shown, and each visit may be associated with more than one condition.

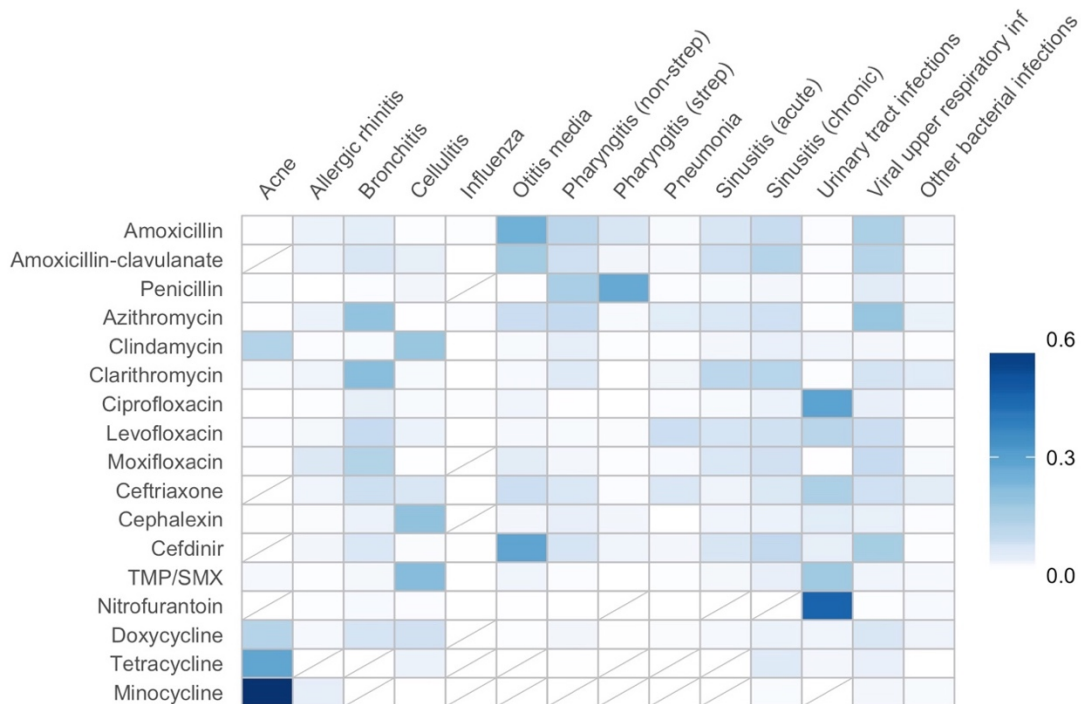


Figure S4. Proportion of bystander exposures (with 95% confidence interval) by antibiotic and species.

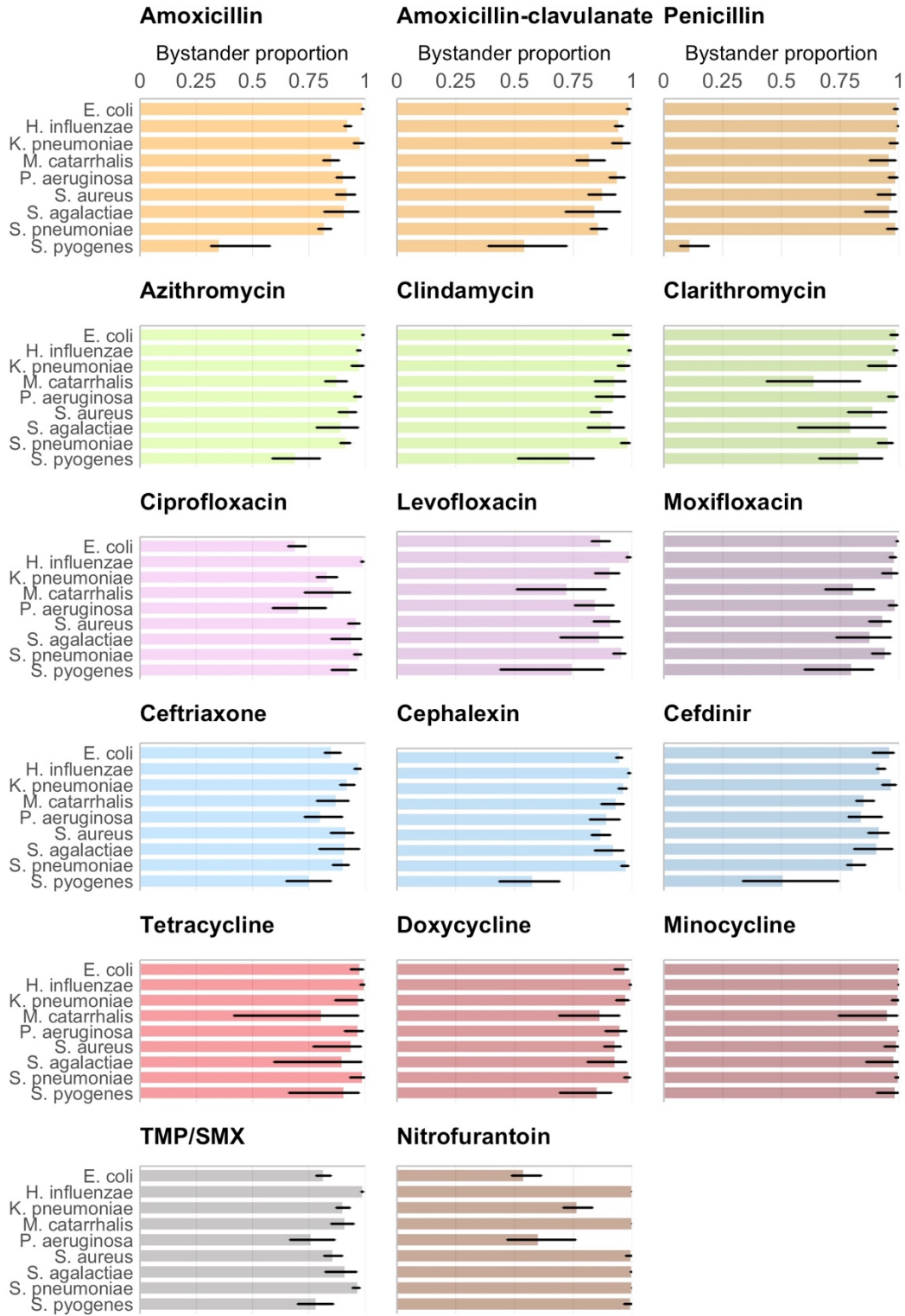


Table S1. Carriage studies used to characterize microbial prevalences for which HMP data was unavailable. In addition to prevalences among children <5 years old, additional carriage studies were also used for *S. pyogenes* and *S. pneumoniae* in the >5-year-old age group as taxonomic profiling of HMP data via MetaPhlan2 does not distinguish between these and similar species. Specific studies were not identified for *P. aeruginosa* and *S. agalactiae* for children from 1 to 5 years old; the prevalences among children under 1 year old were imputed in these cases.

Article	Age group	Body site	Organisms
Bäckhed et al. 2015 (1)	<1 year old	Gastrointestinal	<i>P. aeruginosa</i> <i>S. agalactiae</i>
Bogaert et al. 2011 (2)	1-5 years old	Nasopharyngeal	<i>H. influenzae</i>
Mainous et al. 2006 (3)	1-5 years old	Nasopharyngeal	<i>S. aureus</i>
Regev-Yochay et al. 2004 (4)	<1 year old 1-5 years old	Nasopharyngeal	<i>S. aureus</i> <i>S. pneumoniae</i>
Verhaegh et al. 2010 (5)	<1 year old 1-5 years old	Nasopharyngeal	<i>M. catarrhalis</i>
Pettigrew et al. 2012 (6)	<1 year old 1-5 years old	Upper respiratory tract	<i>H. influenzae</i> <i>M. catarrhalis</i> <i>S. pneumoniae</i>
Holgerson et al. 2015 (7)	<1 year old 1-5 years old	Oral	<i>E. coli</i> <i>H. influenzae</i> <i>K. pneumoniae</i> <i>S. aureus</i> <i>S. pyogenes</i>
Yassour et al. 2016 (8) (DIABIMMUNE cohort)	<1 year old 1-5 years old	Gastrointestinal	<i>E. coli</i> <i>H. influenzae</i> <i>K. pneumoniae</i> <i>S. aureus</i>
Ginsburg et al. 1985 (9)	All	Throat	<i>S. pyogenes</i>
Gunnarsson et al. 1997 (10)	All	Throat	<i>S. pyogenes</i>
Hammitt et al. 2006 (11)	All	Nasopharyngeal	<i>S. pneumoniae</i>
Huang et al. 2009 (12)	All	Nasopharyngeal	<i>S. pneumoniae</i>

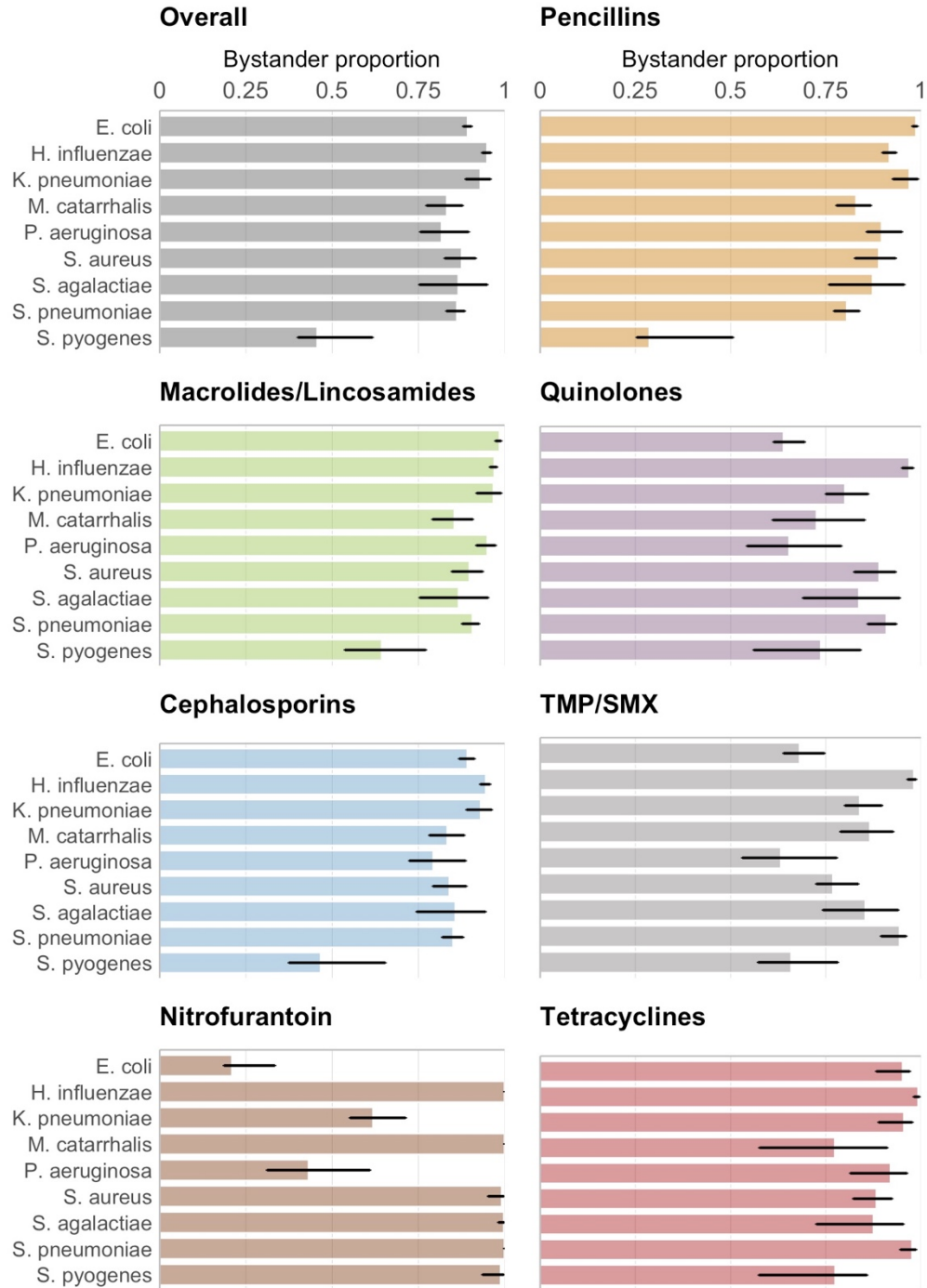
Table S2. Carriage prevalence estimates by age group and species from the Human Microbiome Project (HMP) and carriage studies.

Species	<1 year old	1-5 years old	>5 years old
<i>E. coli</i>	94.9%	100%	66.3%
<i>H. influenzae</i>	100%	95.9%	68.6%
<i>K. pneumoniae</i>	39.1%	15.0%	7.4%
<i>M. catarrhalis</i>	45.5%	50.8%	2.3%
<i>P. aeruginosa</i>	1.4%	1.4%	1.9%
<i>S. aureus</i>	35.0%	19.1%	12.4%
<i>S. agalactiae</i>	8.2%	8.2%	2.7%
<i>S. pneumoniae</i>	64.3%	64.6%	25.2%
<i>S. pyogenes</i>	1.1%	4.4%	4.7%

Table S3. Estimated etiologies by condition. Conditions in which none of our species of interest are causative agents are excluded. If two numbers are shown, the number to the left was applied to children under 5 years old, and the number to the right was applied to individuals over 5. Diagnoses with etiology specified by ICD-9CM code (e.g. 481: pneumococcal pneumonia) were attributed to the appropriate organism.

Species	Cellulitis (13)	Pneumonia (unidentified cause) (14, 15)	Sinusitis (acute) (16)	Sinusitis (chronic) (17)	Strep throat	Otitis media (suppurative) (18, 19)	UTI (20, 21)
<i>E. coli</i>	0.4%	-	-	2.9%	-	-	75% 78.5%
<i>H. influenzae</i>	0.1%	- 0.6%	0.7%	4.4%	-	23% 26%	-
<i>K. pneumoniae</i>	-	-	-	2.9%	-	-	4.7% 4.8%
<i>M. catarrhalis</i>	-	-	0.1%	11.8%	-	14% 3%	-
<i>P. aeruginosa</i>	0.5%	- 0.4%	-	-	-	-	2.3% 2.7%
<i>S. aureus</i>	8%	- 1.6%	0.1%	11.8%	-	1% 3%	-
<i>S. agalactiae</i>	0.5%	-	-	5.9%	-	-	-
<i>S. pneumoniae</i>	-	27% 5.1%	0.8%	5.9%	-	35% 21%	-
<i>S. pyogenes</i>	4.3%	- 0.3%	-	7.4%	100%	3% 3%	-

Figure S5. Proportion of bystander exposures (with 95% confidence interval) by antibiotic class and species, excluding the term $\sum_{g=1}^G d_{acg} \times p_{sg}$ from the denominator. “Overall” estimates reflect exposures to antibiotics in any of the included classes. Results for TMP/SMX and nitrofurantoin are for the individual drug instead of an antibiotic class.



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