

Antibiotic Stewardship: Choosing the right drug for the right bug

CLINICAL QUESTION

What are the environmental impacts of community antibiotic use and how can clinicians decrease these harms by practicing antimicrobial stewardship?

BOTTOM LINE

Antimicrobial resistance is rapidly becoming a global crisis, with 1.27 million deaths worldwide directly attributed to this phenomenon. Pollution of natural environments due to healthcare antimicrobial use contributes to antimicrobial resistance. Clinicians can reduce these harms by employing the following evidence-based approaches:

- Using lay language in informational posters and handouts to help patients better understand viral infections and their lack of response to antibiotics.
- Applying clinical scores in guiding management for common respiratory infections.
- Staying current on the recommended choice and duration of antibiotic prescriptions as per best practice guidelines for common bacterial infections (e.g. Bugs & Drugs)
- Considering delayed antibiotic prescriptions where appropriate.
- Verbally encouraging patients to dispose of their antimicrobial surplus properly.

EVIDENCE

- A USA RCT in 2014 showed that "nudging" techniques such as displaying posters in exam rooms
 highlighted their clinician's commitment to avoiding inappropriate antibiotic prescriptions which can be
 effective at reducing antibiotic prescription in adults with acute respiratory infection (Meeker et al. 2014).
- In a 2002 UK RCT of patients with symptoms of bronchitis, providing patients with informational handouts about indications for antibiotics was shown to reduce their use (MacFarlane et al. 2002).
- A 2005 USA study surveying healthy patients showed that using the word "chest cold" when referring to "acute bronchitis" when conversing with patients could reduce patient dissatisfaction when not prescribed antibiotics (Phillips & Hickner. 2005).
- At least three studies have established that delayed prescriptions decrease the use of antibiotics in uncomplicated respiratory tract infections both safely and effectively. Moreover, evidence suggests delayed antibiotic prescriptions have no significantly different outcomes in severity nor duration of symptoms compared to immediate prescriptions in children with uncomplicated respiratory infections. Additionally, they can decrease repeat visits as well as gastrointestinal side effects of antibiotics (Arrol et al. 2002; Little et al. 2017; Mas-Dalmau et al. 2020).
- Canada's Choosing Wisely guidelines as well as Canadian Pediatric Society guidelines recommend the use of the M-CENTOR criteria as a clinical score for the management of adults and children over 3 years of age presenting with pharyngitis. Additionally, Choosing Wisely guidelines recommend the use of PODS criteria for management of rhinosinusitis (Sauve et al. 2021; Desrosiers et al. 2011).

- Multiple studies have also shown shorter courses of antibiotics for symptomatic treatment of certain
 uncomplicated infections in adults and children to have comparable outcomes to longer courses of
 treatment (Milo et al. 2005; Agarwal et al. 2004; Tansarli and Mylonakis. 2018).
- Recently, in the UK, an educational, patient-facing campaign on proper medication disposal was
 provided by community pharmacies. It showed that providing patients verbal information regarding safe
 disposal of medication had a significant impact on the number of antibiotics returned, while posters
 alone did not (Hamilton et al. 2024).

CONTEXT

- Antimicrobial resistance is a global emergency. In 2019, 1.27 million deaths were directly attributed to by this crisis (Antimicrobial Resistance Collaborators. 2022).
- A 2020 study showed unnecessary antibiotic prescription in 15.4% of primary care encounters across Canada, most of which were attributed to viral upper respiratory and ear infections (Schwartz et al, 2020)
- Mortality rates related to Methicillin-Resistant Staphylococcus aureus bloodstream infections have increased from 16.3% in 2019 to 19.8% in 2022. During this time, nearly 1 in 5 (19.8%) patients hospitalized with a MRSA bloodstream infection have died within 30 days of diagnosis as documented in Canadian Nosocomial Infection Surveillance Program hospitals (CARSS, 2024).
- Many studies have confirmed the contamination of ground and surface waters with low concentrations
 of antibiotics. Though a big part of this problem continues to be agricultural use of antibiotics, the
 concentration of antibiotics in surface and ground waters tend to also be higher in wastewater from
 antibiotic production plants and healthcare facilities (Fick et al. 2009; Larsson et al. 2007).
- Antimicrobial resistant genes are widely present in the environment because of these contaminants, which are thought to contribute to the evolution of resistant bacteria in wastewater and aquatic sources downstream from antibiotic production plants (Liu et al. 2012; Guardabassi et al. 1998).
- There is contested information on how antibiotic resistance in our natural environment can contribute to the prevalence of antibiotic resistance from a human health perspective. However, many studies have isolated resistant bacteria from crops and livestock, as well as within local and imported foods commonly available to humans. It is suspected that antibiotic resistance genes can transfer between bacteria from the soil to livestock and human microbiome, respectively (Ole et al, 2009; Jans et al, 2018; Jorgensen et al, 2019; Hassan and Kassem, 2020)
- Particulate matter (microscopic solid and liquid particles in the air that cause pollution) has been shown
 to contain antibiotic-resistant bacteria as well as antimicrobial-resistant genes. Further evidence
 demonstrates that antimicrobial resistance is highly correlated with particulate matter and specifically air
 pollution, globally (Xie et al. 2019; Zhou et al. 2023).

REFERENCES

Agarwal G, Awasthi S, Kabra SK, Kaul A, Singhi S, Walter SD; ISCAP Study Group. Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial. BMJ. 2004 Apr 3;328(7443):791. doi: 10.1136/bmj.38049.490255.DE. Epub 2004 Mar 16. Erratum in: BMJ. 2004 May 1;328(7447):1066. PMID: 15070633; PMCID: PMC383371.

Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022 Feb 12;399(10325):629-655. doi: 10.1016/S0140-6736(21)02724-0. Epub 2022 Jan 19. Erratum in: Lancet. 2022 Oct 1;400(10358):1102. doi: 10.1016/S0140-6736(21)02653-2. PMID: 35065702; PMCID: PMC8841637.

Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. J Fam Pract. 2002 Apr;51(4):324-8. PMID: 11978254.

Canadian Antimicrobial Resistance Surveillance System (2024). https://health-infobase.canada.ca/carss/amr/results.html?ind=14.

- Desrosiers, M., Evans, G.A., Keith, P.K. et al. Canadian clinical practice guidelines for acute and chronic rhinosinusitis. All Asth Clin Immun 7, 2 (2011). https://doi.org/10.1186/1710-1492-7-2.
- Fick J, Söderström H, Lindberg RH, Phan C, Tysklind M, Larsson DG. Contamination of surface, ground, and drinking water from pharmaceutical production. Environ Toxicol Chem. 2009 Dec;28(12):2522-7. doi: 10.1897/09-073.1. Epub 2009 May 18. PMID: 19449981.
- Guardabassi L, Petersen A, Olsen JE, Dalsgaard A. Antibiotic resistance in Acinetobacter spp. isolated from sewers receiving waste effluent from a hospital and a pharmaceutical plant. Appl Environ Microbiol. 1998 Sep;64(9):3499-502. doi: 10.1128/AEM.64.9.3499-3502.1998. PMID: 9726904; PMCID: PMC106754.
- Hamilton RA, Ercolani MG, Aggarwal R, Cooper D, Kelly S, Root H, Pabari K, Jamieson C. Evaluation of antibiotics returned for safe disposal during and after a community pharmacy antibiotic amnesty campaign. JAC Antimicrob Resist. 2024 Oct 24;6(5):dlae172. doi: 10.1093/jacamr/dlae172. PMID: 39464859; PMCID: PMC11503646.
- Hassan J, Kassem II. Audacious Hitchhikers: The Role of Travel and the International Food Trade in the Global Dissemination of Mobile Colistin-Resistance (mcr) Genes. Antibiotics (Basel). 2020 Jul 1;9(7):370. doi: 10.3390/antibiotics9070370. PMID: 32630272; PMCID: PMC7400688.
- Jans C, Sarno E, Collineau L, Meile L, Stärk KDC, Stephan R. Consumer Exposure to Antimicrobial Resistant Bacteria From Food at Swiss Retail Level. Front Microbiol. 2018 Mar 6;9:362. doi: 10.3389/fmicb.2018.00362. PMID: 29559960; PMCID: PMC5845543.
- Jorgensen J, Waite-Cusic J, Kovacevic J. Prevalence of Listeria spp. in produce handling and processing facilities in the Pacific Northwest. Food Microbiol. 2020 Sep;90:103468. doi: 10.1016/j.fm.2020.103468. Epub 2020 Feb 28. Erratum in: Food Microbiol. 2022 Aug;105:104027. doi: 10.1016/j.fm.2022.104027. PMID: 32336359.
- Larsson DG, de Pedro C, Paxeus N. Effluent from drug manufactures contains extremely high levels of pharmaceuticals. J Hazard Mater. 2007 Sep 30;148(3):751-5. doi: 10.1016/j.jhazmat.2007.07.008. Epub 2007 Jul 6. PMID: 17706342.
- Little P, Stuart B, Smith S, Thompson MJ, Knox K, van den Bruel A, Lown M, Moore M, Mant D. Antibiotic prescription strategies and adverse outcome for uncomplicated lower respiratory tract infections: prospective cough complication cohort (3C) study. BMJ. 2017 May 22;357:j2148. doi: 10.1136/bmj.j2148. PMID: 28533265; PMCID: PMC5439222.
- Liu M, Zhang Y, Yang M, Tian Z, Ren L, Zhang S. Abundance and distribution of tetracycline resistance genes and mobile elements in an oxytetracycline production wastewater treatment system. Environ Sci Technol. 2012 Jul 17;46(14):7551-7. doi: 10.1021/es301145m. Epub 2012 Jul 2. PMID: 22709269.
- Macfarlane J, Holmes W, Gard P, Thornhill D, Macfarlane R, Hubbard R. Reducing antibiotic use for acute bronchitis in primary care: blinded, randomised controlled trial of patient information leaflet. BMJ. 2002 Jan 12;324(7329):91-4. doi: 10.1136/bmj.324.7329.91. PMID: 11786454; PMCID: PMC64506.
- Mas-Dalmau G, Villanueva López C, Gorrotxategi Gorrotxategi P, Argüelles Prendes E, Espinazo Ramos O, Valls Duran T, Gonzalo Alonso ME, Cortés Viana MP, Menéndez Bada T, Vázquez Fernández ME, Pérez Hernández Al, Muñoz Ortiz L, Little P, de la Poza Abad M, Alonso-Coello P; DAP PEDIATRICS GROUP*. Delayed Antibiotic Prescription for Children with Respiratory Infections: A Randomized Trial. Pediatrics. 2021 Mar;147(3):e20201323. doi: 10.1542/peds.2020-1323. Epub 2021 Feb 11. PMID: 33574163.
- Meeker D, Knight TK, Friedberg MW, Linder JA, Goldstein NJ, Fox CR, Rothfeld A, Diaz G, Doctor JN. Nudging guideline-concordant antibiotic prescribing: a randomized clinical trial. JAMA Intern Med. 2014 Mar;174(3):425-31. doi: 10.1001/jamainternmed.2013.14191. PMID: 24474434; PMCID: PMC4648560.
- Milo G, Katchman EA, Paul M, Christiaens T, Baerheim A, Leibovici L. Duration of antibacterial treatment for uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD004682. doi: 10.1002/14651858.CD004682.pub2. PMID: 15846726.
- Ole E. Heuer, Hilde Kruse, Kari Grave, P. Collignon, Iddya Karunasagar, Frederick J. Angulo, Human Health Consequences of Use of Antimicrobial Agents in Aquaculture, Clinical Infectious Diseases, Volume 49, Issue 8, 15 October 2009, Pages 1248–1253, https://doi.org/10.1086/605667
- Phillips TG, Hickner J. Calling acute bronchitis a chest cold may improve patient satisfaction with appropriate antibiotic use. J Am Board Fam Pract. 2005 Nov-Dec;18(6):459-63. doi: 10.3122/jabfm.18.6.459. PMID: 16322409.
- Sauve L, Forrester AM, Top KA. Group A streptococcal pharyngitis: A practical guide to diagnosis and treatment. Paediatr Child Health. 2021 Jul 28;26(5):319-320. doi: 10.1093/pch/pxab025. PMID: 34336062; PMCID: PMC8318536.
- Schwartz KL, Langford BJ, Daneman N, Chen B, Brown KA, McIsaac W, Tu K, Candido E, Johnstone J, Leung V, Hwee J, Silverman M, Wu JHC, Garber G. Unnecessary antibiotic prescribing in a Canadian primary care setting: a descriptive analysis using routinely collected electronic medical record data. CMAJ Open. 2020 May 7;8(2):E360-E369. doi: 10.9778/cmajo.20190175. PMID: 32381687; PMCID: PMC7207032.

- Tansarli GS, Mylonakis E. Systematic Review and Meta-analysis of the Efficacy of Short-Course Antibiotic Treatments for Community-Acquired Pneumonia in Adults. Antimicrob Agents Chemother. 2018 Aug 27;62(9):e00635-18. doi: 10.1128/AAC.00635-18. PMID: 29987137; PMCID: PMC6125522.
- Xie J, Jin L, He T, Chen B, Luo X, Feng B, Huang W, Li J, Fu P, Li X. Bacteria and Antibiotic Resistance Genes (ARGs) in PM2.5 from China: Implications for Human Exposure. Environ Sci Technol. 2019 Jan 15;53(2):963-972. doi: 10.1021/acs.est.8b04630. Epub 2018 Dec 26. PMID: 30525504.
- Zhou Z, Shuai X, Lin Z, Yu X, Ba X, Holmes MA, Xiao Y, Gu B, Chen H. Association between particulate matter (PM)2-5 air pollution and clinical antibiotic resistance: a global analysis. Lancet Planet Health. 2023 Aug;7(8):e649-e659. doi: 10.1016/S2542-5196(23)00135-3. PMID: 37558346.

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