LEARNING OBJECTIVES

- To **understand** the concept of antibiotic resistance, how it develops and to identify driving factors of increasing resistance rates

- To **acknowledge** the threat of antibiotic resistance and the importance of antibiotic stewardship within primary care

- To **improve awareness** and **understanding** of when antibiotic use is appropriate for patients with upper respiratory tract infections (URTIs)

INTRODUCTION

- Antibiotic resistance is a **global threat to public health**.[1] High rates of resistance have been identified in all of the World Health Organization (WHO) regions[1]

- Inappropriate antibiotic use is the primary driver in the development of resistance.[2,3] Data show a direct correlation between the use of antibiotics and resistance. Countries where there is higher consumption of antibiotics show higher resistance rates[3,4]

- The risk of a post-antibiotic era, where everyday infections are **untreatable**, could be a very real possibility in the 21st century[1]

An estimated **33,110** people in Europe die each year as a result of resistant infections[5]

Two million antibiotic-resistant infections are reported annually in the USA; at least **23,000** are fatal[6]

Data shows antibiotic resistance is spreading **beyond** the hospital environment[7]

"Antimicrobial resistance (AMR) is a critical public health issue globally"
– WHO, 2018[8]

1. World Health Organization. Antimicrobial resistance global report on surveillance: 2014 summary. 2014. Available at: http://apps.who.int/iris/bitstream/10665/112647/1/WHO_HSE_PED_AIP_2014.2_eng.pdf?ua=1 (accessed April 2019); 2. Goossens H, et al. Lancet 2005;365:579–87; 3. World Health Organization. The evolving threat of antimicrobial resistance. Options for action. 2012. Available at: http://apps.who.int/iris/bitstream/handle/10665/44812/9789241503181_eng.pdf?sequence=1 (accessed April 2019); 4. Riedel S, et al. Eur J Clin Microbiol Infect Dis 2007;26:485–90; 5. Cassini A, et al. Lancet Infect Dis 2019;19:56–66; 6.Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013. Available at: https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf (accessed April 2019); 7. NCCID. Community-acquired antimicrobial resistance. Consultation notes. February 2010. Available at: https://nccid.ca/wp-content/uploads/sites/2/2015/04/caAMR_ConsultationNotes_final.pdf (accessed April 2019). 8. World Health Organization. Global antimicrobial resistance surveillance system (GLASS) report 2016–2017. 2018. Available at: https://www.who.int/glass/resources/publications/early-implementation-report/en/ (accessed April 2019)

Module 1: Understanding antibiotic resistance and the role of URTI management in primary care

HOW DOES ANTIBIOTIC RESISTANCE DEVELOP?

- Antibiotic resistance develops when potentially harmful bacteria mutate in a way that reduces or eliminates the effectiveness of antibiotics against them[1,2]

- Bacteria can mutate spontaneously[3,4] and those that develop a mutation conferring resistance to an antibiotic have a survival advantage over bacteria without the mutation and are therefore better able to multiply[4,5]

- The more exposure to antibiotics, the greater the rate of development of resistance[6,7] and the greater the risk of it spreading within communities

Antibiotic overuse can lead to the development of resistant bacteria[9,10]

ANTIBIOTIC RESISTANCE
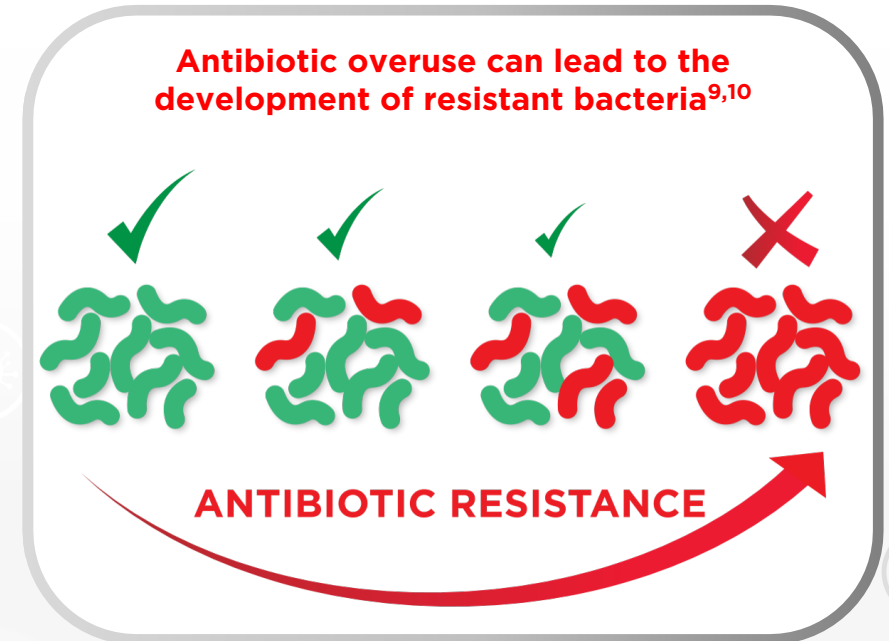
The immune system can usually clear a normal bacterial URTI within a few days without the need for antibiotics[8]

1. Kapoor G, et al. J Anaesthesiol Clin Pharmacol 2017;33:300–5; 2. Munita JM, Arias CA. Microbiol Spectr 2016;4; 3. Hershberg R. Cold Spring Harb Perspect Biol 2015;7:a018077; 4. Smith RA, et al. Health Commun 2015;30:309–14; 5. Canton R, Morosini MI. FEMS Microbiol Rev 2011;35:977–91; 6. Goossens H, et al. Lancet 2005;365:579–87; 7. Riedel S, et al. Eur J Clin Microbiol Infect Dis 2007;26:485–90; 8. van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 9. World Health Organization. Global action plan on antimicrobial resistance, 2015. Available at: http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/ (accessed April 2019); 10. Zaman SB, et al. Cureus 2017;9:e1403

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FACTORS CONTRIBUTING TO ANTIBIOTIC RESISTANCE

- Driving factors for antibiotic resistance include:[1-6]

  - **Antibiotic use** (including overuse, inappropriate dosing and misuse, i.e. use as prophylaxis) in both human healthcare and agricultural settings (such as animal husbandry). There is a strong correlation between high levels of antibiotic use and antibiotic resistance

  - **Poor infection prevention** and infection control practices, which can increase the spread of drug-resistant infections. These include inadequate sanitation conditions, poor hand hygiene and inappropriate food handling (in the hospital, other healthcare facilities and at home)

  - The use of **counterfeit**, **sub-standard** or **poor-quality antibiotics**, often containing sub-optimal therapeutic doses that fail to fully eradicate bacteria

  - **Limited surveillance systems** to globally monitor antibiotic use and resistance

  - **Lack of investment** in the development of novel antibiotics, with few new antibiotics in development to replace existing antimicrobial agents

1. World Health Organization. Antimicrobial resistance. Factsheet 194. April 2014. Available at: http://www.who.int/mediacentre/factsheets/fs194/en/ (accessed April 2019); 2. World Health Organization. Ten facts on antimicrobial resistance. 2017. Available at: http://www.who.int/features/factfiles/antimicrobial_resistance/en/ (accessed April 2019); 3. Oxford J, et al. Educ Prim Care 2013;24:291–3; 4. ECDC/EMEA Joint Technical Report: The bacterial challenge: time to react. 2009. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2009/ 11/WC500008770.pdf (accessed April 2019); 5. IDSA. Facts about antibiotic resistance. April 2011. Available at: https://www.idsociety.org/public-health/antimicrobial-resistance/archive-antimicrobial-resistance/facts-about-antibiotic-resistance (accessed April 2019); 6. Del Mar C, et al. Aust Fam Physician 2012;41:839–40

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ANTIBIOTIC USE AND THE TREATMENT OF URTIs

- Acute URTIs are one of the most common diseases seen within primary care,[1] with symptoms including sore throat, blocked or runny nose, headache, cough and earache

- URTIs also account for a large proportion of antibiotic prescriptions, yet the majority of patients do not require antibiotics to recover. Antibiotics only modestly reduce severity or duration of symptoms, if at all[1–3]

URTI incidence: a global burden

Adults:
2–3
URTIs per year[4]

Children:
up to 8
URTIs per year[4]
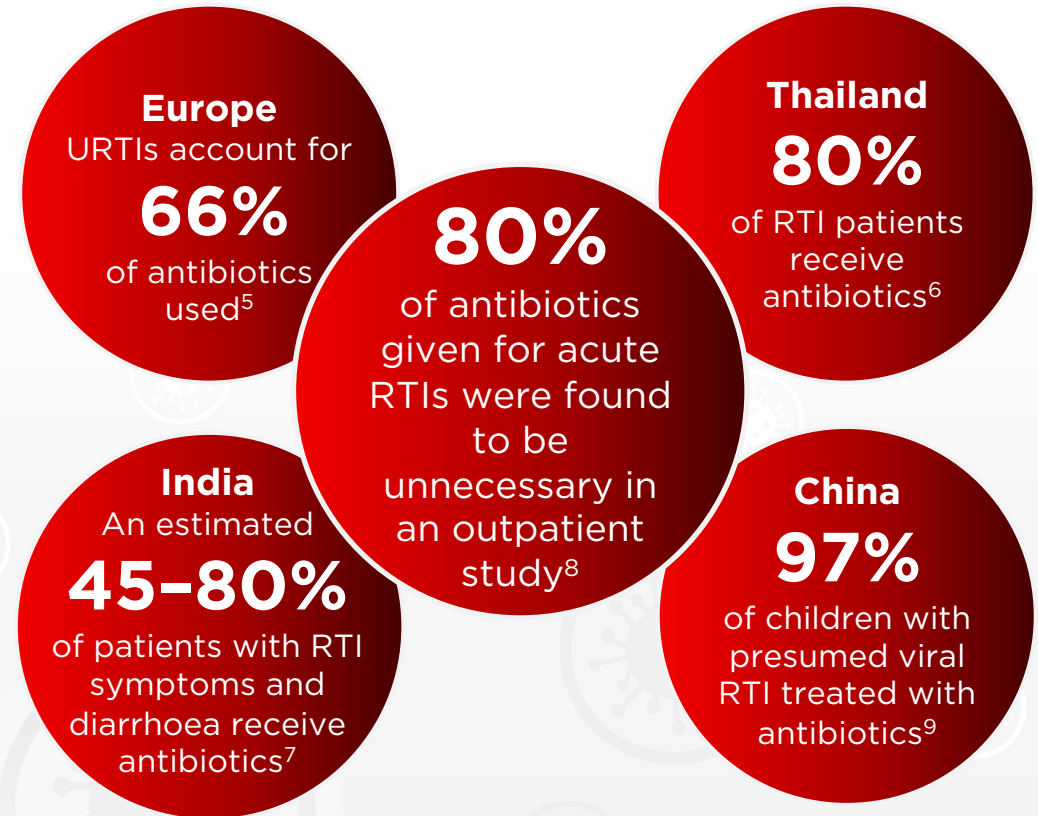
18.8 billion
global cases reported annually[5]

1. Francis NA, et al. BMJ 2009;339:b2885; 2. Van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 3. Kenealy T, Arroll B. Cochrane Database Syst Rev 2013;6:CD000247; 4. Thomas M, Bomar PA. Upper respiratory tract infection. 2018. Available at https://www.ncbi.nlm.nih.gov/books/NBK532961/ (accessed April 2019); 5. Global Burden of Disease Study 2013 Collaborators. Lancet 2015;386:743–800

ANTIBIOTIC USE AND THE TREATMENT OF URTIs

- Up to 8 out of 10 sore throats are caused by viral URTIs[1] (such as the common cold or flu) against which antibiotics do not work[2]

- Despite this, antibiotic use for respiratory tract infections (RTIs) or URTIs remains high globally, particularly for conditions like influenza, the common cold, sore throat and sinusitis[3]

- Overuse and misuse of antibiotics drives antibiotic resistance[4]

Europe
URTIs account for
66%
of antibiotics used[5]

80%
of antibiotics given for acute RTIs were found to be unnecessary in an outpatient study[8]

Thailand
80%
of RTI patients receive antibiotics[6]

India
An estimated
45–80%
of patients with RTI symptoms and diarrhoea receive antibiotics[7]

China
97%
of children with presumed viral RTI treated with antibiotics[9]

1. Ebell MH, et al. JAMA 2000;284:2912–8; 2. Hildreth CJ, et al. JAMA 2009;302:816; 3. Mazzaglia G, et al. Eur J Clin Pharmacol 2003;59:651–7; 4. World Health Organization. Global action plan on antimicrobial resistance, 2015. Available at: http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/ (accessed April 2019); 5. Special Eurobarometer 338. Antimicrobial resistance. Survey carried out by TNS Opinion & Social at the request of the Directorate-General for Health and Consumers. 2010. Available at: https://ec.europa.eu/health/sites/health/files/antimicrobial_resistance/docs/ebs_338_en.pdf (accessed April 2019); 6. Thamlikitkul V, Apisitwittaya W. Int J Infect Dis 2004;8:47–51; 7. Ganguly NK, et al. Indian J Med Res 2011;134:281–94; 8. Scott JG, et al. J Fam Pract 2001;50:853–8; 9. Hui L, et al. Pediatr Infect Dis J 1997;16:560–4

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ANTIBIOTIC USE AND THE TREATMENT OF URTIs

Antibiotic overuse can lead to the development of resistant bacteria[7,8]

- At the patient level, antibiotic use can result in the emergence of resistant bacteria which may persist in the body up to 12 months post-treatment,[1] increasing the use of second-line antibiotics[1] and affecting the wider community

  - The respiratory pathogen Streptococcus pneumoniae causes significant mortality around the globe.[2] Data from Asia show prevalence of multiple drug resistance at almost 60%, compared with 9–24% in the USA and 0–43% in Europe[2]

  - Consequently treatment is more difficult, illness is prolonged, and there is an increased mortality risk, contributing to increased healthcare costs[3]

- There are growing calls from the WHO and the European Centre for Disease Prevention and Control to tackle antibiotic resistance.[4,5] Re-evaluating antibiotic use for URTIs is one area where primary care can make a difference
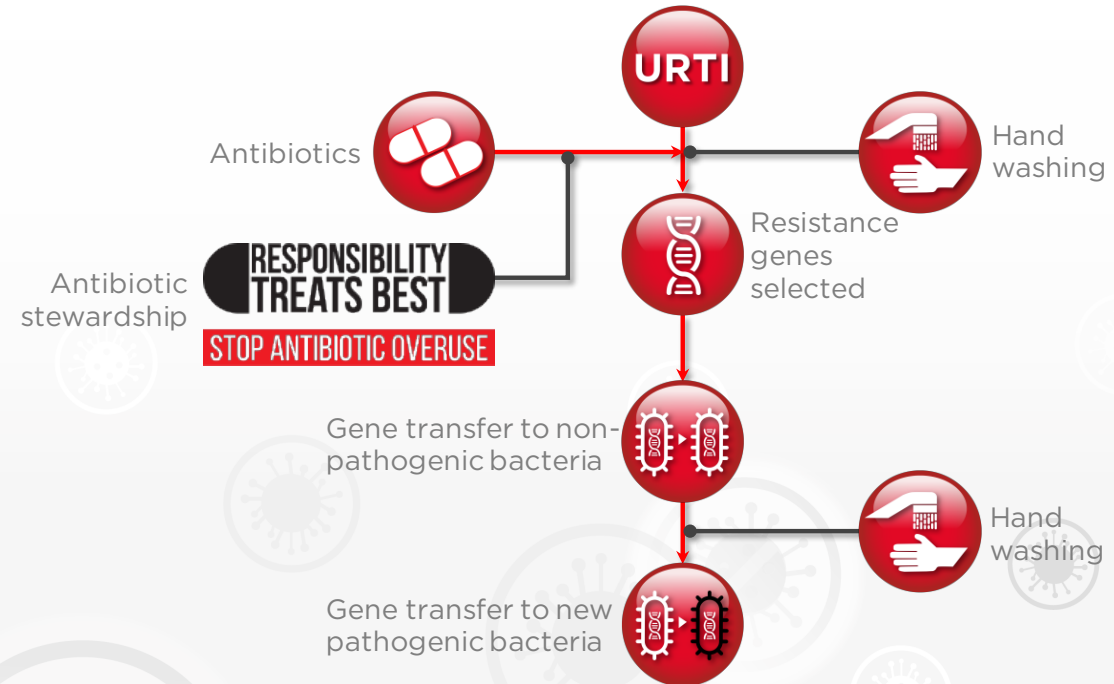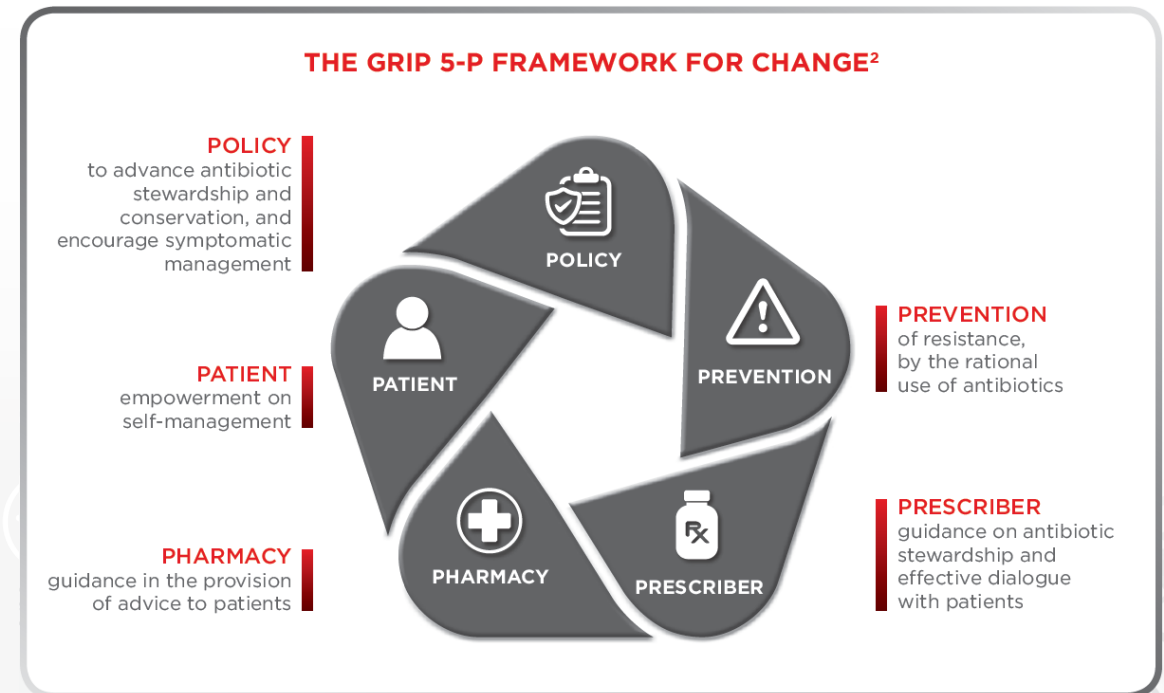

For URTIs, symptomatic relief is often all that is necessary and antibiotics only have a modest effect, if any, on the duration of symptoms[6]

1. Costelloe C, et al. BMJ 2010;340:c2096; 2. Kim SH, et al. Antimicrob Agents Chemother 2012;56:1418–26; 3. World Health Organization. Antimicrobial resistance. Factsheet 194 Available at: http://www.who.int/mediacentre/factsheets/fs194/en/ (accessed April 2019); 4. World Health Organization. The evolving threat of antimicrobial resistance. Options for action. 2012. Available at: http://apps.who.int/iris/bitstream/handle/10665/44812/9789241503181_eng.pdf?sequence=1 (accessed April 2019); 5. ECDC/EMEA Joint Technical Report: The bacterial challenge: time to react. 2009. Available at: https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf (accessed April 2019); 6. van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 7. World Health Organization. Global action plan on antimicrobial resistance, 2015. Available at: http://www.who.int/antimicrobial-resistance/publications/global-action-plan/en/ (accessed April 2019); 8. Zaman SB, et al. Cureus 2017;9:e1403

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ANTIBIOTIC USE AND THE TREATMENT OF URTIs

- Tackling antibiotic resistance requires a cohesive, consistent approach across primary care to restrict antibiotic prescribing, in alignment with evidence-based guidelines[1]

- Primary healthcare professionals (HCPs) are vital in ensuring such national policies are implemented, while also playing an important role in facilitating patient education[1]

- Promoting behaviour change is at the core of GRIP's mission, based on a pentagonal (5-P) framework[2]

THE GRIP 5-P FRAMEWORK FOR CHANGE[2]

POLICY to advance antibiotic stewardship and conservation, and encourage symptomatic management

PATIENT empowerment on self-management

PHARMACY guidance in the provision of advice to patients

PREVENTION of resistance, by the rational use of antibiotics

PRESCRIBER guidance on antibiotic stewardship and effective dialogue with patients

POLICY · PREVENTION · PRESCRIBER · PHARMACY · PATIENT

Optimising the HCP–patient interaction during an URTI consultation is key

1. der Velden AW, et al. Int J Clin Pract Suppl 2013;10–6; 2. Essack S, Pignatari AC. Int J Clin Pract 2013;67(Suppl 180):4–9

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ANTIBIOTIC USE AND THE TREATMENT OF URTIs

- Antibiotics are not recommended for the treatment of most URTIs because:

  - URTIs are self-limiting and only symptomatic relief products are generally needed for the patient to feel better. Antibiotics only modestly shorten the duration or severity of URTI symptoms, if at all[1,2]
  - The majority of URTIs are viral, with up to 8 out of 10 sore throats caused by a virus.[3] As antibiotics only target bacterial infections, they are not effective in most patients[2,4]
  - Antibiotics may do more harm than good; side effects include diarrhoea, skin rash and thrush.[5,6] For example, the incidence of antibiotic-associated diarrhoea can be up to 25%[7]
  - Antibiotic-resistant bacteria can remain in the body for up to 12 months[8]

1. The vast majority of URTIs are caused by	● Bacteria		● Viruses
2. Antibiotics are not recommended for most URTIs	● True		● False
3. Antibiotic-resistant bacteria can remain in the body for up to how many months?	● 3	● 6	● 12

1. Van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 2. Kenealy T, Arroll B. Cochrane Database Syst Rev 2013;6:CD000247; 3. Ebell MH, et al. JAMA 2000;284:2912–8; 4. Hildreth CJ, et al. JAMA 2009;302:816; 5. Spinks A, et al. Cochrane Database Syst Rev 2013;11:CD000023; 6. Wilton L, et al. Drug Saf 2003;26:589–97; 7. Bergogne-Bérèzin E. Int J Antimicrob Agents 2000;16:521–6; 8. Costelloe C, et al. BMJ 2010;340:c2096

ANSWERS: 1=Viruses, 2=True, 3=12

URTI CONSULTATIONS IN PRIMARY CARE

- **Primary care** has an important role in ensuring appropriate antibiotic use in the community. Effective communication is required to give clear messages to the public on why antibiotics are not recommended for the majority of URTIs, and to educate people around appropriate antibiotic use

- There are many opportunities to speak to patients about appropriate URTI management, such as when a URTI is being diagnosed, during treatment decisions, at the point of dispensing and when advising on self-care

- Physicians, nurses, pharmacists and pharmacy assistants may all be involved in a patient dialogue on antibiotic stewardship throughout the patient journey

DIAGNOSING URTIs

- When **evaluating a URTI**, the following factors should be considered:

  - **Patient history** (immunocompromised, chronic illness, age)
  - **Symptoms** (duration and severity)
  - **Red flags** (severe symptoms indicating immediate GP referral or antibiotic treatment)
  - **Patient concerns** and **expectations**

- **Effective communication** is an opportunity for primary care teams to engage patients in a dialogue, allowing patients to identify reasons for consulting and explain their symptoms. Understanding their expectations allows HCPs to directly address a patient's concerns and provide the most appropriate advice[1]

For more information on effective communication and diagnosing URTIs
go to **Module 2** and **Module 3** of this series

1. Van der Velden AW, et al. Int J Clin Pract 2013;67(Suppl 180):10–6

TREATMENT DECISIONS

- **Involving the patient** in a shared decision-making process provides an ideal opportunity to engage patients in appropriate treatment of URTIs and to explain why antibiotics are only required on rare occasions, as well as the potential impact of antibiotic resistance on public health[1]

- Time should be taken to clearly **explain the benefits and risks** of each treatment option so that the patient can better understand why treatments are recommended and partake in an informed discussion about what products will best meet their needs (which will be symptomatic in the majority of cases)[1]

- Information on treatment from pharmacists is important to consumers, whether spoken, written, or a combination of both.[2] A tailored approach is needed to ascertain preference so that appropriate information is provided. Consider providing a patient leaflet to reinforce advice and reassure them about their symptomatic treatment

GRIP patient leaflet 2018

1. van der Velden AW, et al. Int J Clin Pract 2013;67(Suppl 180):10–6; 2. Hamrosi KK, et al. BMC Health Serv Res 2014;14:183

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DISPENSING ANTIBIOTICS

- A further opportunity to engage with the patient about appropriate treatment is during the dispensing and collection of antibiotics. Advice provided during this brief interaction can help ensure correct adherence to treatment and help to prevent development of antibiotic resistance

- It is also an opportunity to offer products for symptomatic relief, as antibiotics only modestly reduce symptom severity or duration, if at all,[1,2] and even when appropriate may take up to 72 hours to have an effect[3]

- Patient advice should include:
  - Complete the full course of antibiotics
  - Clarify dose and number of doses per day
  - Use the antibiotics for the current infection only – do not store antibiotics to treat future infections

- Mention potential side effects of the drug
- Do not give any unused tablets to friends/family
- Offer symptomatic relief options

! Clarify the expected symptom duration and highlight signs or symptoms that require further medical advice. Give recommendations on how to best treat symptoms, if appropriate

See **Module 2** and **Module 3** for more information on symptom duration, red flags and high-risk groups

1. van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 2. Kenealy T, Arroll B. Cochrane Database Syst Rev 2013;6:CD000247; 3. Spinks A, et al. Cochrane Database Syst Rev 2013;11:CD000023

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ADVISING PATIENTS

- Healthcare professionals should aim to provide the optimum symptomatic relief for patients with URTIs. Many different types of products are available to quickly relieve symptoms and address patients' individual preferences[1]

- Patients should be reassured that treatment of symptoms will make them feel better quickly while the body recovers from the infection[2]

  - Using sore throat as an example, a survey of 2040 people investigating general expectations, knowledge and attitudes concerning prescription of antibiotics showed that 83% of respondents expected symptomatic treatment for sore throat, while only 54% expected antibiotics[3]

  - Studies have shown that other key reasons for visiting a doctor for a sore throat are to explain how serious the problem is, to establish the cause and duration, and discuss possible treatments[3,4]
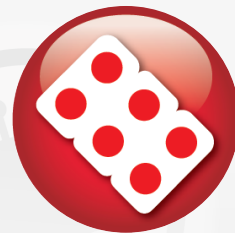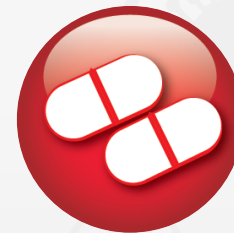
| Solubles | Drops | Syrups | Gargles | Lozenges | Tablets | Sprays |

1. Van Duijn HJ, et al. Br J Gen Pract 2007;57:561–8; 2.National Institute for Health and Care Excellence. Respiratory tract infections (self-limiting): prescribing antibiotics. Clinical guideline 69. July 2008. Available at: https://www.nice.org.uk/guidance/cg69 (accessed April 2019);7. 3 van der Velden A, et al. Poster presented at the International Conference on One Health Antimicrobial Resistance (ICOHAR), Utrecht, The Netherlands, 16–18 April 2019; 4. van Driel, ML, et al. Ann Fam Med 2006;4:494–9

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ASSESSMENT

Question 1: What is the correct definition of antibiotic resistance?

A.   Antibiotic resistance develops when a bacterium evolves to withstand antibiotics

B.   Antibiotic resistance is when an antibiotic develops resistance against the bacteria that causes URTIs

C.   Antibiotic resistance is when a person develops resistance to antibiotics

Question 2: Which of these is NOT a driver of antibiotic resistance?

A.   Poor infection control

B.   Poor quality assurance in antibiotic manufacturing

C.   Effective infection prevention practices

Question 3: Which opportunities are appropriate to engage in a patient discussion about the correct use of antibiotics in URTIs and antibiotic resistance?

A.   At the point of diagnosis

B.   When making a treatment decision

C.   At the point of antibiotic dispensing

D.   All of the above

ANSWERS: 1=A, 2=C, 3=D

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