The Royal College of Pathologists
Pathology: the science behind the cure

National Medical Examiner's Good Practice Series No.9

Recording antimicrobial resistance on the Medical Certificate of Cause of Death

November 2022

Author: Dr Alan Fletcher, National Medical Examiner

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The Royal College of Pathologists
6 Alie Street
London E1 8QT
T: 020 7451 6700
F: 020 7451 6701
www.rcpath.org
Registered charity in England and Wales, no. 261035

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About the National Medical Examiner's Good Practice Series

Medical examiners – senior doctors providing independent scrutiny of non-coronial deaths in England and Wales – are a relatively recent development.

While there is extensive guidance available on a wide range of topics for NHS and public sector staff, the National Medical Examiner's Good Practice Series highlights how medical examiners and medical examiner officers can better meet the needs of local communities and work more effectively with colleagues and partners.

The Good Practice Series is a topical collection of focused summary documents, designed to be easily read and digested by busy front-line staff, with links to further reading, guidance and support.

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Introduction

One of the principal outputs of the Medical Examiner System is to improve the quality of Medical Certificates of Cause of Deaths (MCCDs).

The Royal College of Pathologists' *Cause of Death List*[1] specifies that infective organisms should be included in the MCCD, if known to have caused or contributed to the death. However, infections must be known to have or be suspected to have contributed to the death if they are to be included, not merely be a condition present at the time.

This good practice paper will help medical examiner offices to align with the wider *UK Antimicrobial Resistance National Action Plan*,[2] and to support surveillance of antimicrobial resistance (AMR). It asks medical examiners to encourage and educate those writing MCCDs to accurately record the organism responsible for the infection, whether it was resistant to microbial therapy, and whether the infection was hospital- or community-associated, where this is known. Medical examiners can make an important contribution to the understanding of the importance of AMR to patient deaths. In particular, the recording of relevant information in the MCCD would provide valuable insights.

During the development of this paper, subject matter experts advised that the term 'associated' is more appropriate than 'acquired'. For this reason, 'associated' has been used throughout this paper, apart from direct quotations from published material.

It is not intended that every organism resistant to one or two antimicrobials is recorded as AMR on the MCCD. The aim is to identify organisms of particular interest because they are resistant to a wide range of antimicrobials, and a list of these is included at Appendix 1.

[1] Royal College of Pathologists. *Cause of death list*. Published June 2020. Available at: www.rcpath.org/uploads/assets/c16ae453-6c63-47ff-8c45fd2c56521ab9/G199-Cause-of-death-list.pdf

[2] Department of Health and Social Care. *UK 5-year action plan for antimicrobial resistance 2019 to 2024*. Available at: https://www.gov.uk/government/publications/uk-5-year-action-plan-for-antimicrobial-resistance-2019-to-2024

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Recommendations for medical examiners

Where the organism that caused the infection (and whether it was resistant to antimicrobial therapy) is not known, the medical examiner should:

1. advise doctors to indicate this clearly on the MCCD.[3] The registrar will write to the certifying doctor, or to the patient's consultant for hospital deaths, with a form requesting further details to be returned to the Office for National Statistics (ONS). For example, this may occur when the clinical team are awaiting the results of laboratory investigations, and should not delay completion of the MCCD or registration of the death. Where investigations are ongoing, Box Part B on the reverse of the MCCD should be ticked.
2. seek the advice of the local medical microbiologist for further guidance if there is uncertainty about the relevance of a microbiological finding to a patient death, including AMR.

Where the organism that caused the infection is known and is resistant to antimicrobial therapy, medical examiners should:

1. assist doctors completing MCCDs to accurately record organisms responsible for infections if they directly led or contributed to death
2. where the infection caused or significantly contributed to the death and the organism was resistant to antimicrobials,[4] advise doctors to record this on the MCCD regardless of the antimicrobial treatment used. Where the infection was resistant to multiple antimicrobials, and antimicrobial treatment failure caused or contributed to death, the death may need to be notified to the coroner if not supported by another acceptable condition.[1]
3. where it is appropriate to notify the coroner, advise those making the notification to include any additional information that may help the coroner to decide whether they

[3] Indicating that investigation results will be available later is done by circling '2' on the front of the MCCD for autopsy information, or by ticking box 'B' on the back of the certificate for results of investigations initiated ante mortem.
[4] See Appendix 1 list.

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need to investigate the death. This should include specific concerns the relatives may have expressed about AMR.

4. where it is possible to identify whether the infection was hospital-associated or community-associated, support the doctor completing the MCCD to record this where appropriate and not to appear to apportion responsibility for infection acquisition, in line with guidance for doctors completing medical certificates of cause of death[5]
5. ensure they or the delegated medical examiner officer (MEO) can explain terminology used on the MCCD to bereaved people in a way they can understand, and consider how information about AMR may be perceived and interpreted. Definitions and simple explanatory phrase that may be helpful are included at Appendix 2.
6. where scrutiny indicates that further review of the care is appropriate, refer the case to established clinical governance processes.

Context and background

Antimicrobial resistance

The World Health Organization (WHO) states that AMR occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness and death.[6] As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective, and infections become increasingly difficult or impossible to treat.

The rise of AMR

AMR is a natural phenomenon. Resistance to antibiotics was recorded even before the first clinical use of penicillin in the early 1940s. Since then, increased use of antibiotics has led to the evolution and spread of bacterial resistance to all routinely used antibiotics. Antibiotic resistance has become prevalent in environmental and pathogenic bacteria alike. Use of antibiotics within healthcare, veterinary and agricultural sectors has created a strong selection pressure for resistant bacteria. Human use of antibiotics has also resulted

[5] Ministry of Justice. *Notification of Deaths Regulations 2019 guidance*. Available at: www.gov.uk/government/publications/notification-of-deaths-regulations-2019-guidance
[5] World Health Organization. *Antimicrobial resistance*. Available at: www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

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in an accumulation of these drugs in many environments, where antibiotic-resistant bacteria can flourish. This has also resulted in selection and spread of bacteria that are resistant to several different antibiotics.[7]

Causes and effects of AMR in healthcare

AMR is a global threat. The cost of AMR to the economy is significant. In addition to death and disability, prolonged illness results in longer hospital stays, the need for more expensive medicines and financial challenges for those affected. AMR is increasing, with few new effective antimicrobial medicines coming to market. Without effective antimicrobials, the success of modern medicine in treating infections, including during major surgery and cancer chemotherapy, is at risk.[8]

According to the *Health and Social Care Committee Eleventh Report*[9] published in October 2018, misuse and overuse of antimicrobials and poor infection prevention are the main drivers in the development of drug-resistant pathogens. Through processes of spontaneous genetic mutation and natural selection current antimicrobial treatments are becoming less effective, because bacteria and other pathogens have evolved resistance to the medicines used to treat them. The development of AMR is inevitable, but the speed at which it develops is accelerated by excessive, inappropriate and unnecessary use of antimicrobial treatments.

Administering antimicrobials when they are not needed and prescribing an overlong course are common misuses. Another factor said to have contributed to over-prescribing antibiotics is patients' expectations. Studies have indicated that clinicians consider patients' requests for antibiotics as one of the major barriers to adhering to standard guidelines for antibiotic prescriptions.[10] In any particular case where the development of a fatal infection is linked to the use of a specific antimicrobial, it would meet the requirements

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[6] ReAct. *How did we end up here*. Available at: www.reactgroup.org/toolbox/understand/how-did-we-end-up-here/

[8] World Health Organization. *Antimicrobial resistance*. Available at: www.who.int/health-topics/antimicrobial-resistance

[9] Health and Social Care Committee. *Antimicrobial resistance*. Available at: https://publications.parliament.uk/pa/cm201719/cmselect/cmhealth/962/962.pdf

[10] Public Health England, Department of Health. *Behaviour change and antibiotic prescribing in healthcare settings. Literature review and behavioural analysis*. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/774129/Behaviour_Change_for_Antibiotic_Prescribing_-_FINAL.pdf

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to refer to the coroner (cause to suspect the death is linked to the use of a medicinal product). Full information regarding the appropriateness, dose and duration of the antimicrobial should be provided to allow an informed coroner decision.

In developing countries, there are a number of other issues contributing to the misuse of antibiotics. Insufficient regulation and poor-quality antimicrobials sold over the counter make it easy for patients to self-medicate for conditions that may not need antibiotics. There are deficiencies in proper diagnostic tools, and doctors must manage patient care with a degree of uncertainty, resulting in the over-prescription of medication, particularly antibiotics. Variations in medical training of doctors lead to diverse educational understanding and knowledge. Moreover, financial incentives can play an important factor in over-prescribing of antibiotics.

Research on the impact of AMR

AMR remains a serious threat to people's health. In England alone during 2019:[11]

- there were 178 antimicrobial-resistant infections diagnosed each day
- there were an estimated 65,162 antimicrobial-resistant infections diagnosed – an increase from 61,946 in 2018
- *Escherichia coli* remained the most common bloodstream infection and incidence rose by 14% from 68.3 cases per 100,000 population in 2015 to 77.5 in 2019
- antimicrobial-resistant bloodstream infections increased by a third (32%) from 2015 to 2022 with AMR linked to one in five people with a key bacterial bloodstream infection.

AMR is a problem across the world and a British Medical Association publication estimated that the cost of drug-resistant infections to the global economy could be as high as $100 trillion by 2050 without effective preventative interventions.[12]

[11] Public Health England. Press release: *New antibiotic-resistant infections rise to 178 per day in England*. Available at: www.gov.uk/government/news/new-antibiotic-resistant-infections-rise-to-178-per-day-in-england

[12] British Medical Association. *Antimicrobial resistance*. Available at: www.bma.org.uk/what-we-do/population-health/protecting-people-from-threats-to-health/antimicrobial-resistance

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A study published by Global Research on Antimicrobial Resistance[13] (GRAM) estimated that in 2019, antimicrobial-resistant infections:

- directly caused 1.27 million deaths worldwide
- played a role in 4.95 million deaths.

Researchers concluded that improving data collection worldwide will lead to more accurate measures of AMR, and better health treatments.

Remedial actions to tackle AMR in the UK

Over the last decade there have been multiple antimicrobial stewardship programmes and resources launched in England and Wales.[14,15] Many interventions aimed at preventing AMR focus on preventing infection in the first place. These include vaccination and the general implementation of infection prevention and control methods, such as a range of precautions (e.g. hand hygiene, gloving, gowning, use of masks), patient isolation, active screening of patients, decontamination of devices and environmental cleaning. Alongside these are policies regarding the use and care of invasive devices. Infection prevention and control strategies influence the development and spread of all infections, irrespective of their resistance pattern.

Antimicrobial stewardship has a specific role in slowing AMR which is to optimise clinical outcomes while minimising unintended consequences of antimicrobial use, including toxicity, the selection of opportunistic pathogens and the emergence of AMR.[16]

Patients can contribute to the understanding of misuse of antibiotics by being briefed properly by healthcare professionals so that the full impact of longer-term risks and effects can be appreciated. This activity can form a key part of antimicrobial management.

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[13] Global Research on Antimicrobial Resistance (GRAM). *Antibiotic resistance caused more than 1.2M deaths in 2019, according to landmark GRAM study*. Available at: www.tropicalmedicine.ox.ac.uk/gram/news/global-burden-of-bacterial-antimicrobial-resistance

[14] Public Health Wales. *Antimicrobial resistance and prescribing guidance and resources*. Available at: https://phw.nhs.wales/services-and-teams/harp/antimicrobial-resistance-and-prescribing-guidance-and-resources/

[15] NHS England. *Fighting antimicrobial resistance*. Available at: www.england.nhs.uk/patient-safety/fighting-antimicrobial-resistance/

[16] Cambridge University Press. *Challenges to Tackling Antimicrobial Resistance*. Available at: www.cambridge.org/core/books/challenges-to-tackling-antimicrobial-resistance/challenges-to-tackling-antimicrobial-resistance/2643DE8E3B21DFD8E2F6008E5CC850F4#

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Current strategy to tackle AMR

The *UK 5-Year Antimicrobial Resistance National Action Plan*[2] focuses on three key strategies to slow the growth of AMR:

1. reducing the need for, and unintentional exposure to, antimicrobials
2. optimising the use of antimicrobials
3. investing in innovation, supply and access.

The plan also sets out measures of success. Those relevant to healthcare include targets to:

- halve healthcare-associated Gram-negative bloodstream infections (GNBSIs)
- reduce the number of specific drug-resistant infections in people by 10% by 2025
- reduce UK antimicrobial use in humans by 15% by 2024
- be able to report on the percentage of relevant prescriptions supported by a diagnostic test or decision support tool by 2024.

Relevance to medical examiners

The *UK 5-Year Antimicrobial Resistance National Action Plan* notes the need to increase training to ensure death certification correctly records AMR. Medical examiners are well-placed to support the national plan and increase available surveillance intelligence of AMR by ensuring the accuracy of MCCD completion. Recording AMR is addressed in guidance for doctors completing MCCDs, [2] which advises:

“In deaths from infectious disease, you should state the manifestation or body site, for example pneumonia, pyelonephritis, hepatitis, meningitis, septicaemia or wound infection. You should also specify, giving as much detail as is available:

- the infecting organism, such as pneumococcus, influenza A virus, meningococcus
- antibiotic resistance, if relevant, for example methicillin-resistant *Staphylococcus aureus* (MRSA), or multiple drug-resistant *Mycobacterium tuberculosis*
- the source and/or route of infection, if known, such as food poisoning, needle sharing, contaminated blood products, post-operative, community or hospital acquired, or healthcare-associated infection”.

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Identifying hospital- and community-associated infections

The pressures of the COVID-19 pandemic may have led to less consistent recording of the likely source of infections on MCCDs.[17] It is important this practice does not become established, and that MCCDs record the infection source where it is known. This will inform strategies to combat AMR developments depending on whether they are community- or hospital-associated.

Public knowledge and understanding of antimicrobial medication

Research indicates that misunderstandings persist in a substantial minority of the public.[18] Unsurprisingly, many appear uncertain about the carriage of resistant bacteria, whether resistance was caused by taking antibiotics, and whether all resistant bacteria were harmful. However, other surveys noted public support increased significantly for delaying antibiotic prescribing for respiratory tract infections, and for urinary, ear or throat infections.[19]

[17] Office for National Statistics. *Quality of mortality data during the coronavirus pandemic, England and Wales: 2020*. Available at: www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/qualityofmortalitydataduringthecoronaviruspandemicenglandandwales

[18] Public Health England. *Antibiotic use and resistance: what the public know*. Available at: www.gov.uk/government/publications/antibiotic-use-and-resistance-what-the-public-know

[19] UK Health Security Agency. *English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2021 to 2022*. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1069632/espaur-report-2020-to-2021-16-Nov-FINAL-v2.pdf

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Find out more

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Acknowledgments

This document was drafted following circulation to and input from the following people. The National Medical Examiner is grateful to all for their participation and support:

- Dr Alan Fletcher, National Medical Examiner (Chair)
- Anne Marie Aherne, Deputy Head of the Chief Coroner's Office
- Stuart Cella, Death Registration Lead, Civil Registration Directorate, General Register Office
- Catherine Cody, Senior Policy Advisor, Welsh Government
- Jane Crossley, Team Leader – Death Certification Reform, Department of Health and Social Care
- Nick Day, Policy and Programme Lead, Medical Examiner System, NHS England
- Jeff Featherstone, Head of Antimicrobial Resistance, NHS England
- Professor Angharad Davies, Vice President for Learning, Royal College of Pathologists
- Dr Eleri Davies, Deputy Medical Director and Head of Healthcare Associated Infection, Antimicrobial Resistance and Prescribing Programme, Public Health Wales
- Ginny Fieldsend, Senior Programme Manager – Infection and Antimicrobial Resistance, NHS England
- Douglas Findlay, lay representative
- Myer Glickman, Head of Methods, Quality and International, Health Analysis and Life Events Division, Office for National Statistics
- Tracey Guise, Chief Executive Officer, British Society for Antimicrobial Chemotherapy
- Natalie Harris, Healthcare Standards and Governance Lead, Welsh Government
- Austin Hayes, Death Registration Senior Advisor, Civil Registration Directorate, General Register Office
- Dr Matthew Inada-Kim, National Clinical Director – Infection, Antimicrobial Resistance & Deterioration, NHS England

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- Dr David Jenkins, Consultant in Medical Microbiology and Virology, Lead Infection Control Doctor, University Hospitals of Leicester NHS Trust and Honorary Associate Professor University of Leicester
- Dr Suzy Lishman, Royal College of Pathologists
- Amanda Martin, South East Regional Medical Examiner Officer, NHS England
- Eric Powell, Deputy Registrar General for England and Wales, Deputy Director Civil Registration, General Register Office
- Graham Prestwich, lay representative
- Ian Thomas, Welsh Government
- Professor Mark Wilcox, Professor of Medical Microbiology, University of Leeds.

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Appendix 1: Infective organisms of particular interest

These should be recorded on MCCDs where they are known to have been caused or more than minimally contributed to the death.

Gram-positive bacteria

- Methicillin-resistant *Staphylococcus aureus*
- Vancomycin-resistant enterococci
- Penicillin-tolerant *Streptococcus pneumoniae*

Gram-negative bacteria

- Enterobacterales[20] resistant to any member of one or more of the following antibiotic classes:
  - fluoroquinolones
  - third-, fourth- or fifth-generation cephalosporins
  - carbapenems (meropenem, imipenem, ertapenem).[21]
- Carbapenem-resistant *Acinetobacter baumanii*
- Carbapenem-resistant *Pseudomonas aeruginosa* if known to be carbapenemase producing. (Note: in the UK, most carbapenem-resistant *P. aeruginosa* strains are not carbapenemase producing.)

Other bacteria

Mycobacterium tuberculosis resistant to one or more of the following drugs:

- isoniazid
- rifampicin
- fluoroquinolones

[20] Enterobacterales is an order of bacteria that includes *Escherichia coli* and *Klebsiella pneumoniae*.
[21] Carbapenem resistance in Enterobacterales may be due to acquired carbapenemase production. Where available, the type of carbapenemase should be included (e.g. OXA-48, KPC, NDM).

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- an injectable antituberculosis drug (amikacin, capreomycin, kanamycin)
- bedaquiline
- linezolid.

Fungi

Candida species (including *Candida auris*) resistant to one or more of the following drug classes:

- azoles
- echinocandins.

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Appendix 2: Definitions and explanatory phrases

Antimicrobials

Antimicrobials are medications like antibiotics or antivirals used to treat or prevent some types of infection. They work by killing microorganisms or preventing them from spreading.

Antimicrobial resistance

Antimicrobial resistance is the ability of microorganisms to withstand antimicrobial treatments such as antibiotics. This resistance occurs as bacteria, for example, adapt and find ways to survive the effects of an antibiotic, meaning the drug no longer works to fight the infection it was previously used to treat.[22]

Antimicrobial resistance happens when germs like bacteria and fungi develop the ability to defeat the medicines designed to kill them. That means the germs are not killed and continue to grow.[23]

Multidrug-resistant infections

Multidrug-resistant organisms cause infections that are resistant to several medications used to treat the infection and are often adapted to spread easily. These are sometimes also called 'superbugs'.[24]

Healthcare-associated infections

Healthcare-associated infections develop either as a direct result of healthcare interventions such as medical or surgical treatment, or from being in contact with a healthcare setting.[25]

[22] NHS England. *Fighting antimicrobial resistance*. Available at: www.england.nhs.uk/patient-safety/fighting-antimicrobial-resistance/
[23] Centers of Disease Control and Prevention (CDC). About Antimicrobial Resistance. Available at: www.cdc.gov/drugresistance/about.html
[24] Great Ormond Street Hospital. Available at: www.gosh.nhs.uk/conditions-and-treatments/general-medical-conditions/resistant-bugs-antibiotic-resistance-and-multidrug-resistant-organisms/
[25] NHS England. *Healthcare-associated infections*. Available at: www.england.nhs.uk/patient-safety/healthcare-associated-infections/

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Healthcare-associated infection refers to infections that occur as a result of contact with the healthcare system in its widest sense – from care provided in your own home, to primary care, nursing home care and care in acute hospitals.[26]

Community-associated infection

Community-associated infection is any infection which a patient is suffering from when they come into hospital or occurs within the first couple of days of admission. In this latter case, it is assumed that the patient was already incubating the infection, which they picked up in the community prior to admission.[26]

[26] NHS Wales. *Healthcare-associated infections*. Available at: www.wales.nhs.uk/sites3/documents/379/FAQ.pdf

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