Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI)

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Content

Chair's Foreword

The Department of Health and Social Care (DHSC) is committed to supporting the UK five year Antimicrobial Resistance (AMR) Strategy. The current programme focuses on delivery of the government ambitions as set out in four core programmes and three supporting work streams in England but with close links to work undertaken in the Devolved Administrations:

Programme 1: to reduce healthcare associated Gram-negative bloodstream infections in England by 50% by 2020/21; led by the Executive Director of Nursing, NHS Improvement.

Programme 2: to reduce inappropriate antibiotic prescribing by 50% with the aim of being a world leader in reducing antibiotic prescribing by 2020/21; led by the Chief Pharmaceutical Officer, NHS England.

Programme 3: to ensure that diagnostic tests or epidemiological data are used to support clinical decision making, implement our vision and delivering high quality diagnostics in the NHS in support of the other ambitions; led by the Chief Scientific Officer, NHS England.

Programme 4: to reduce use of antibiotics in livestock and fish farmed for food to a multispecies average of 50mg/kg by 2018; to agree sector specific targets for the animal sectors by the end of 2017, and to set agreed rules for use of antibiotics which are most critically important for human health; led by the Chief Executive of the Veterinary Medicines Directorate, an executive agency of Defra.

The supporting work streams address education and training, surveillance, behaviour change and evidence based interventions and work to promote the development of new technologies and the international response.

Since the launch of the current AMR Strategy in 2013, the surveillance and feedback of AMR data in England and the UK has changed dramatically. Creation of the ESPAUR (English Surveillance Programme for Antibiotic Utilisation and Resistance) programme and accompanying annual reports[i] has seen the generation of a single prescribing and resistance dataset across both primary and secondary care. The open-access, free publication of multiple AMR indicators on the Public Health England (PHE) Fingertips web portal has seen both local and national data on infection, AMR and prescribing made readily available to all[ii].

Launch of the Quality Premium and CQUIN (Commissioning for Quality and Innovation) financial incentives for improvements in performance measures has seen total antibiotic prescribing and proportional prescribing of broad-spectrum antibiotics lowered in England[iii, iv, v]. Awareness of AMR has, overall, increased among the general public[vi], through both the Antibiotic Guardian campaign[vii] and eBug[viii], and among healthcare professionals through publication of prescribing and stewardship competencies[ix].. Publication of the One Health report[x] saw animal and human antibiotic use data brought together and use of antibiotics in animals continues to fall[xi]

However, levels of healthcare-associated Gram-negative infection in community and hospital settings continue to rise[xii]. Outbreaks of carbapenem-resistant organisms (CRO) have increased[xiii], while the use of broad-spectrum antibiotics including meropenem and piperacillin-tazobactam continues to increase in our hospitals[xiv]. Clearly current infection prevention and control (IPC) practices are not adequately working to prevent such infections and outbreaks and our reliance on broad-spectrum antibiotics in a hospital setting must be tackled.

Following modelling work at PHE, APRHAI have put forward their recommended prescribing measures in both primary and secondary care[xv]. However, work needs to be done to improve data to enable more accurate determination of true levels of inappropriateness in antimicrobial prescribing. APRHAI also put forward recommendations for interventions to reduce Gram-negative infection[xvi], and work will be needed to measure their impact and consider which of these interventions have the most effect on infection levels. Furthermore, APRHAI recognises the importance of diagnostics and that more reliable data is needed to demonstrate the impact of diagnostic testing and what type of improvement has been made in this area. More needs to be done to ensure that the four countries are working to deliver the same ambitions and there is a means of monitoring progress across the UK.

The UK has played a key role in AMR work internationally and has committed funding via the Global AMR Innovation Fund and other key projects to support research and development to tackle AMR[xvi] .Much needs to be done to invigorate drug pipelines and innovation in IPC practices. Crucially work on repurposing of existing drugs should be undertaken and new economic models should be built to support the most effective interventions. Consideration should be taken of the changing political landscape around AMR and the role of the UK on the global stage.

This report covers the period between April 2016 and March 2017 and while it limits itself to activity in that period, it provides brief updates on some aspects of the work undertaken after March 2017 for the sake of presenting a complete picture.

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[i] https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report
[ii] https://fingertips.phe.org.uk/profile/amr-local-indicators

[iii] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf
[iv] https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/
[v] https://www.england.nhs.uk/wp-content/uploads/2013/12/qual-prem-guid.pdf

[vi] TARGET- training resources section: http://www.rcgp.org.uk/clinical-and-research/toolkits/target-antibiotic-toolkit.aspx

[vii] https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/
[viii] https://www.england.nhs.uk/wp-content/uploads/2013/12/qual-prem-guid.pdf
[ix] http://antibioticguardian.com/
[x] http://www.e-bug.eu/
[xi] https://www.gov.uk/government/publications/antimicrobial-prescribing-and-stewardship-competencies
[xii] https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals
[xiii] https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2015
[xiv] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf
[xv] https://www.gov.uk/government/news/phe-launches-toolkit-to-manage-hospital-infections-caused-by-antibiotic-resistant-bacteria
[xvi] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/575626/ESPAUR_Report_2016.pdf

Abbreviations

AMP	Antimicrobial Prescribing
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
APQM	Antimicrobial Prescribing Quality Measure
ASRIC	Antimicrobial Stewardship, Resistance and Infection Control
BSAC	British Society for Antimicrobial Chemotherapy
CAP	Community Acquired Pneumonia
CCG	Clinical Commissioning Group
CDI	*Clostridium difficile* infection
CoPSAC	Code of Practice for Scientific Advisory Committees
CQUIN	Commissioning for Quality and Innovation
DHSC	Department of Health and Social Care
DARC	Defra Antimicrobial Resistance Coordination group
DEFRA	Department for Environment, Food and Rural Affairs
E. Coli	*Escherichia Coli*
ESPAUR	English Surveillance Programme for Antimicrobial Utilisation and Resistance
GNHABSI	Gram-negative Healthcare-associated Bloodstream Infections
HAP	Hospital Acquired Pneumonia
HAI	Healthcare Associated Infections
HLSG	High Level Steering Group (for the UK 5 year AMR strategy)
HPRU	Health Protection Research Unit
ICU	Intensive Care Unit
IPC	Infection Prevention and Control
MDR	Multi-drug Resistant
MRSA	Meticillin-resistant *Staphylococcus aureus*
MSSA	Meticillin -susceptible *Staphylococcus aureus*
NHS	National Health Service
PHE	Public Health England
RTI	Respiratory Tract Infections
TDM	Therapeutic Drug Monitoring
VAP	Ventilator-acquired Pneumonia
WHO	World Health Organisation

Plain English Summary

APRHAI is the expert scientific advisory committee providing independent advice to the Department of Health and Social Care on antimicrobial prescribing, resistance and healthcare-associated infection. The committee provides advice on policies and guidance to minimise healthcare-associated infections, and to conserve the effectiveness of antibiotics by encouraging best practice in prescribing.

This report covers the period between April 2016 and March 2017, providing also brief updates on some aspects of the work undertaken after March 2017 for the sake of presenting a complete picture.

Resistance to antimicrobials (antibiotics, but also antifungals and antivirals) continues to increase. The threat that many common infections, as well as serious infections, will become increasingly difficult to treat is now being recognised worldwide, and there is increased public awareness of the danger of antibiotic resistance. Changes in prescribing behaviours are gradually taking place and the number of antibiotic prescriptions is decreasing, as shown by a report published in 2017 (ESPAUR report). There is, however, an ongoing clear need to educate the public about using antibiotics only when they are really needed, and a need to ensure that doctors always prescribe according to professional guidance.

In May 2016, a report by Lord Jim O'Neill presented recommendations on how to tackle antimicrobial resistance as a global threat. As a result, the government decided that two ambitions should be part of its strategy to combat antimicrobial resistance: 1) to halve the number of serious blood infections by 2020 and 2) to halve the number of antibiotic prescriptions by 2020-2021. Thus, in 2016-2017, much of the committee's work focused on supporting the Department of Health and Social Care, through its expert advice, to achieve these objectives and the overall strategy.

Examples of APRHAI's work in connection with the strategy and the two ambitions include:

- Recommendations on which specific types of resistance should be most closely monitored, i.e. resistance to which antibiotics being used for which bacteria: "drug-bug combinations".
- Goals to reduce prescribing of antibiotics both in primary care and in hospitals to specific levels, known as "prescribing quality measures".
- Recommendations to help reduce the number of inappropriate antimicrobial prescriptions, by defining what "appropriateness of antimicrobial prescribing" in primary care and in hospitals means and how to achieve it.

Turning to healthcare associated infections, the committee's work concentrated on infections caused by a group of bacteria called "gram negative". These bacteria include *E. coli*, a common bug in the gut which is becoming increasingly resistant to treatment. There was an overall fall in number of deaths associated with MRSA, MSSA, *E. coli* and *C. difficile* infection (CDI) from 2007/08 to 2015/16, however MSSA

infections showed to be on the rise and the Committee decided to study this increase in order to develop more effective future interventions to combat MSSA. In the next year, the committee will focus on supporting the development of the next strategy (2018-2023), including the reduction in inappropriate prescribing, the reduction in Gram negative infections, the issues arising from these two aims and monitoring and improving outcomes of patients admitted to hospital.

Introduction

Remit

APRHAI was established in April 2007 to provide practical and scientific advice to DHSC on strategies to minimise the incidence of Healthcare Associated Infections (HAI) and to maintain the effectiveness of antimicrobial agents in the treatment and prevention of microbial infections in man and animals. In making recommendations, the committee takes into account the relevant work of other expert groups in the human and veterinary fields.

From 2013, APRHAI has made recommendations to the High Level Steering Group (HLSG) for the UK 5 year AMR strategy and has formed a partnership with national bodies such as PHE and NHS England to enable pragmatic and effective implementation of APRHAI recommendations. Furthermore, the Committee's advice has national relevance and, as such, there is an effective ongoing communication between APRHAI and the Devolved Administrations. The D.A. are invited and represented at the Committee's meetings throughout the year.

Meetings

From 2015/16, APRHAI's meeting format reflected the main areas within the committee's remit: HAI; AMR; AMP. The committee holds three main meetings per year, focusing on these areas sequentially in spring, summer and autumn. Meetings commence with a focused session on the main theme, provided by external speakers, giving technical updates on for example current research, surveillance and epidemiology.

A further meeting, involving the Chair, deputy-chair, sponsor and secretariat, is held each winter to review the committee's work over the past year, consider current and upcoming outputs and determine the forthcoming years' work programme. APRHAI also meets with counterparts at the DARC to discuss cross-cutting "one health" aspects of infectious disease and antimicrobial resistance on an annual basis.

APRHAI Subgroups

Increasingly, the committee's work is carried forward by 'task and finish' subgroups; established to develop evidence-based guidance and other detailed pieces of work. Subgroups are chaired by a member of APRHAI and include co-opted experts relevant to the task. Subgroup reports and recommendations are considered at the main committee meetings. Following agreement, advice is provided to the DHSC sponsor for consideration and, where appropriate, implementation.

Openness and Transparency

APRHAI is an independent expert science advisory committee that operates in accordance with the Code of Practice for Scientific Advisory Committees, 2011.[1] As such the agenda open papers and minutes of meetings are published and accessible from the APRHAI webpage. [2,3]

Declarations of interest are posted on the APRHAI webpage and are updated annually. Members are invited to declare interests at the beginning of each meeting. Declarations of interest are dealt with on a case by case basis and in line with government guidance (Making and Managing Public Appointments - A Guide for Departments.[4])

Membership

The APRHAI membership list may be found on the APRHAI webpage, members present during the remit of this report may be found in Annex A. New members are appointed by the Department of Health and Social Cares Senior Responsible Officer and are accountable to the Chair for carrying out their duties and for their performance. Members are expected to demonstrate a commitment to and an understanding of the value and importance of the seven principles of public life and act in accordance to CoPSAC guidance. Representatives of the Devolved Administrations are invited as observers to all APRHAI meetings.

Public and Patient Information

APRHAI is dedicated to evolving and improving its engagement with the public. It strives to make its work better understood by the public and ensure that the work it undertakes is for the benefit of patients and the public. Inclusion of a lay summary is compulsory for all papers presented to the committee.

[1] http://www.bis.gov.uk/assets/goscience/docs/c/11-1382-code-of-practice-scientific-advisory-committees.pdf
[2] https://www.gov.uk/government/groups/advisory-committee-on-antimicrobial-resistance-and-healthcare-associated-infection
[3] http://webarchive.nationalarchives.gov.uk/20130402145952/http://transparency.dh.gov.uk/tag/arhai-minutes/
[4] http://www.civilservice.gov.uk/wp-content/uploads/2011/09/public_appt_guide-pdf_tcm6-3392.pdf

Healthcare associated infections (HAI)

HAIs are infections that occur following or during a healthcare intervention undertaken in a healthcare setting. HAIs remain a major cause of avoidable morbidity and mortality in patients admitted to hospital. The consequences of HAIs are frequently the most severe in patients with weakened immune systems for example the very young, the very elderly, patients within ICUs, patients on treatment for other diseases such as HIV and cancer, which suppress their immune systems.

The incidence of HAIs within NHS hospitals in England is monitored by surveillance using both continuous surveillance and, less frequently, point prevalence ('snapshot') surveys. Data are collated and analysed by PHE and provide an indication of the prevalence of HAIs, the impact of infection prevention and control measures and emerging issues at both national and local levels.

Key Trends in HAI in England

The rate[5] of meticillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia remained steady in 2016/17 and over the last three financial years (2014/15 to 2016/17) (as shown in Figure 1, with counts and rates by source of bactaeremia shown in Table 1).

Figure 1: trends in the rate in MRSA bactaeremia in England

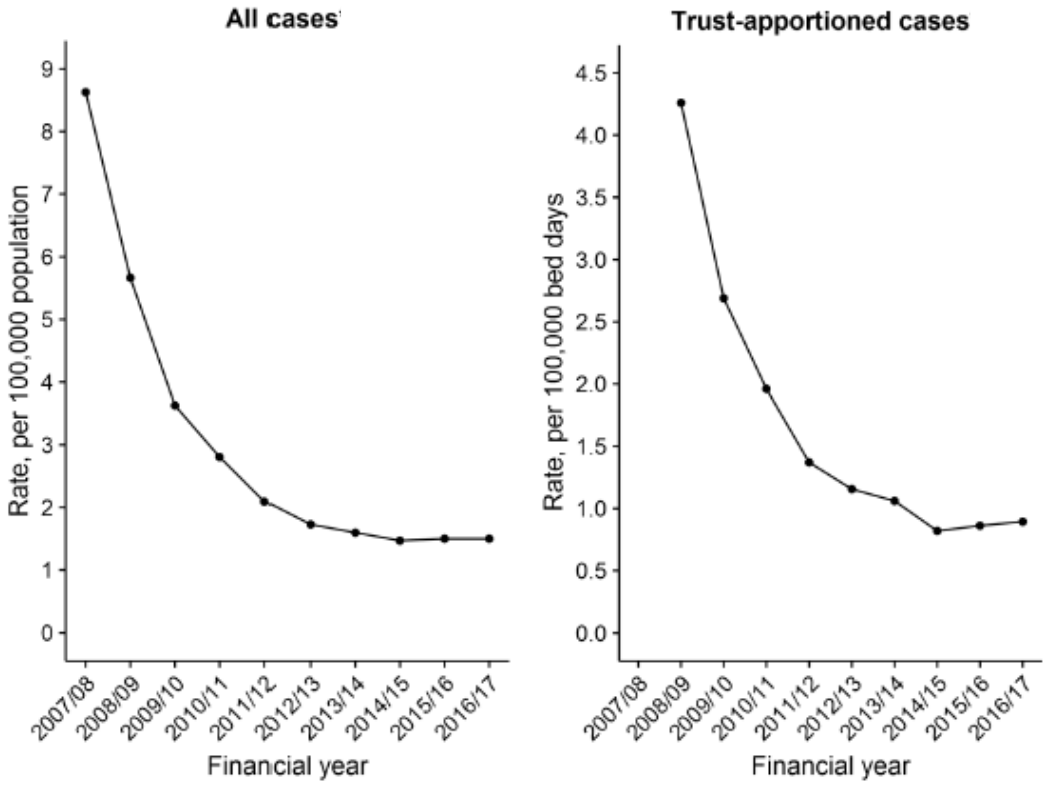


Table 1: MRSA counts and rates by source of bactaeremia, England:2016/17

Financial year	Catheters & lines n (%)	SSTI n (%)	Pneumonia n (%)	Other n (%)	Unknown source n (%)	Total n (%)
2007/08	617 (25.6)	395 (16.4)	160 (6.6)	705 (29.2)	537 (22.2)	2,414 (100.0)
2008/09	346 (22.5)	276 (17.9)	113 (7.3)	552 (35.8)	254 (16.5)	1,541 (100.0)
2009/10	178 (19.5)	191 (20.9)	63 (6.9)	328 (35.8)	155 (16.9)	915 (100.0)
2010/11	118 (17.5)	146 (21.6)	47 (7.0)	251 (37.1)	114 (16.9)	676 (100.0)
2011/12	71 (14.7)	98 (20.3)	41 (8.5)	177 (36.7)	95 (19.7)	482 (100.0)
2012/13	72 (18.3)	74 (18.8)	34 (8.6)	128 (32.5)	86 (21.8)	394 (100.0)
2013/14	39 (13.3)	57 (19.4)	33 (11.2)	100 (34.0)	65 (22.1)	294 (100.0)
2014/15	30 (11.9)	53 (20.9)	39 (15.4)	64 (25.3)	67 (26.5)	253 (100.0)
2015/16	38 (15.5)	56 (22.9)	25 (10.2)	89 (36.3)	37 (15.1)	245 (100.0)
2016/17	50 (19.7)	80 (31.5)	21 (8.3)	88 (34.6)	15 (5.9)	254 (100.0)

In contrast, rates[5] of meticillin-susceptible *S. aureus* (MSSA) increased between 2016/17.

Figure 2: Trends in the rate of MSSA bactaeremia in England

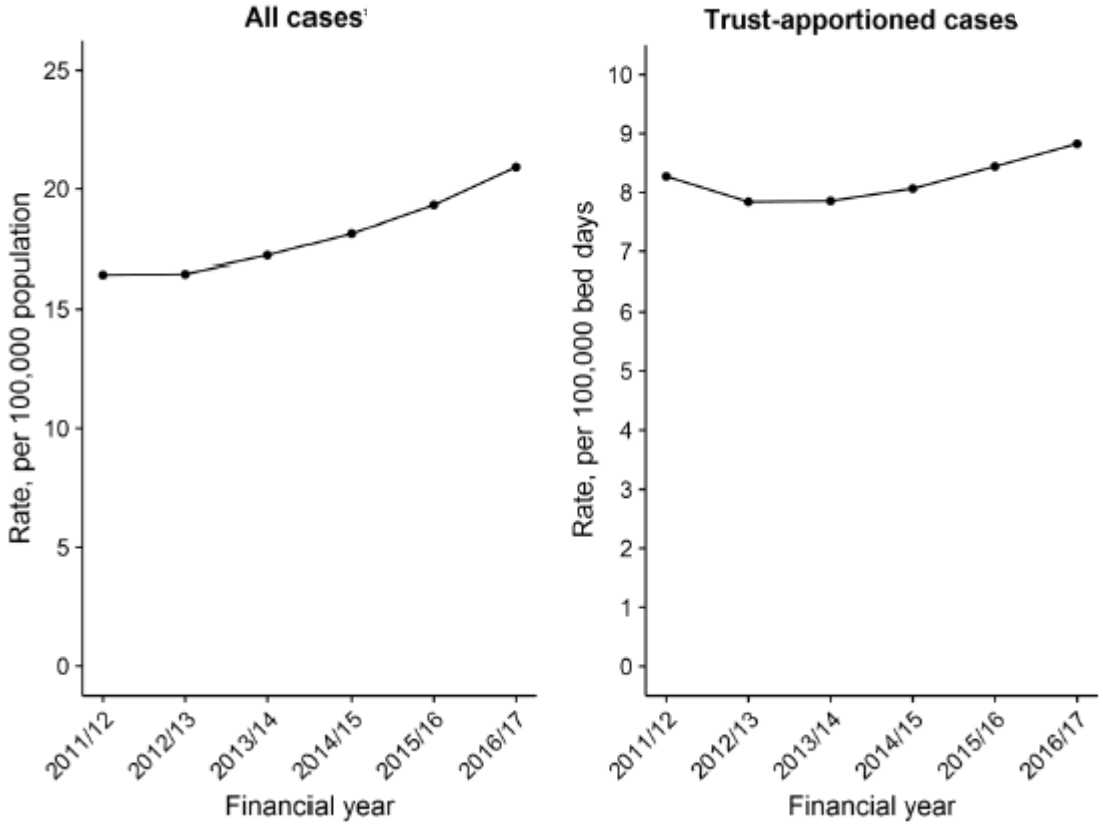


Table 2: MSSA counts and rates by source of bactaeremia, England: 2016/17

Financial year	Catheters & lines n (%)	SSTI n (%)	Pneumonia n (%)	Other n (%)	Unknown n (%)	Total n (%)
2011/12	565 (17.1)	670 (20.3)	197 (6.0)	1,093 (33.1)	780 (23.6)	3,305 (100.0)
2012/13	492 (15.1)	699 (21.4)	232 (7.1)	1,088 (33.3)	755 (23.1)	3,266 (100.0)
2013/14	435 (13.4)	684 (21.1)	218 (6.7)	1,124 (34.7)	775 (23.9)	3,236 (100.0)
2014/15	445 (13.1)	705 (20.8)	305 (9.0)	1,087 (32.0)	855 (25.2)	3,397 (100.0)
2015/16	493 (15.3)	769 (23.9)	306 (9.5)	1,168 (36.2)	487 (15.1)	3,223 (100.0)
2016/17	495 (15.7)	869 (27.5)	362 (11.5)	1,266 (40.1)	168 (5.3)	3,160 (100.0)

Also rates of *Escherichia coli* (*E.coli*) bacteraemia[5] both increased between 2015/16 and 2016/17.

Figure 3: Trends in the rate of E. Coli bactaeremia in comparison to S. aureus bactaeremia for context. England, 2012/13 to 2016/17

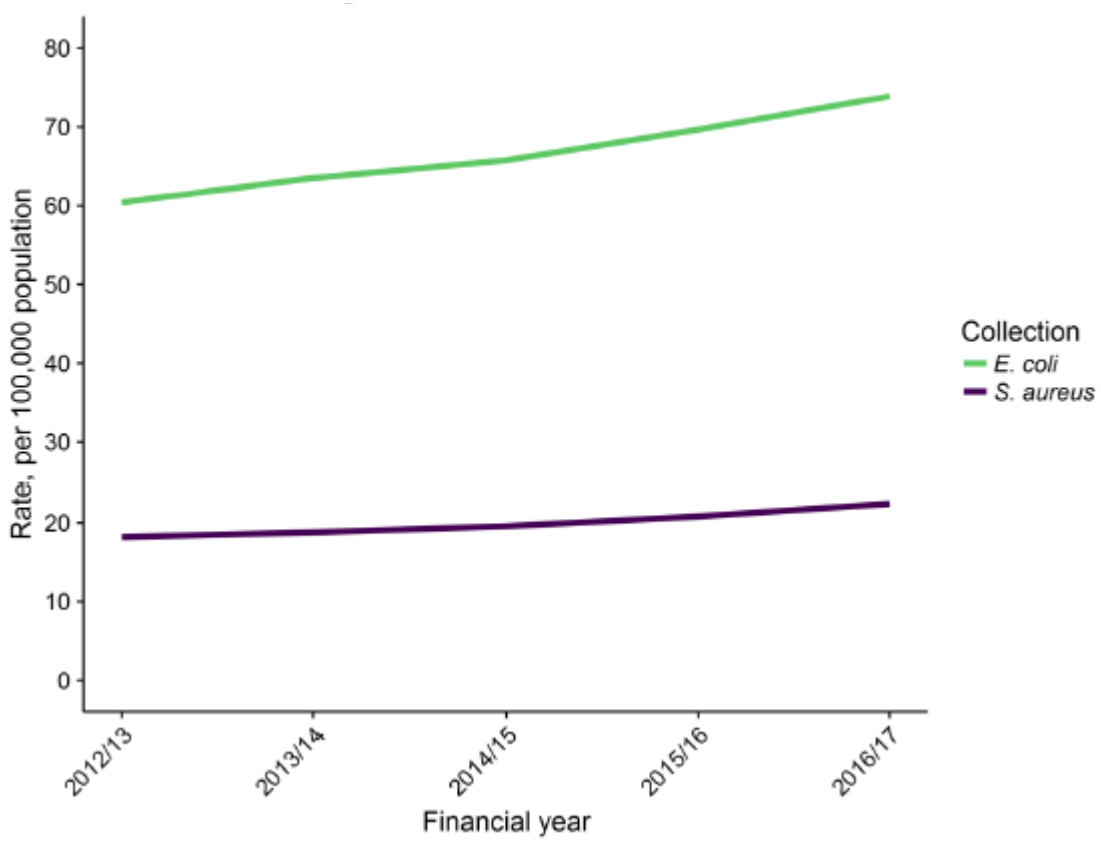
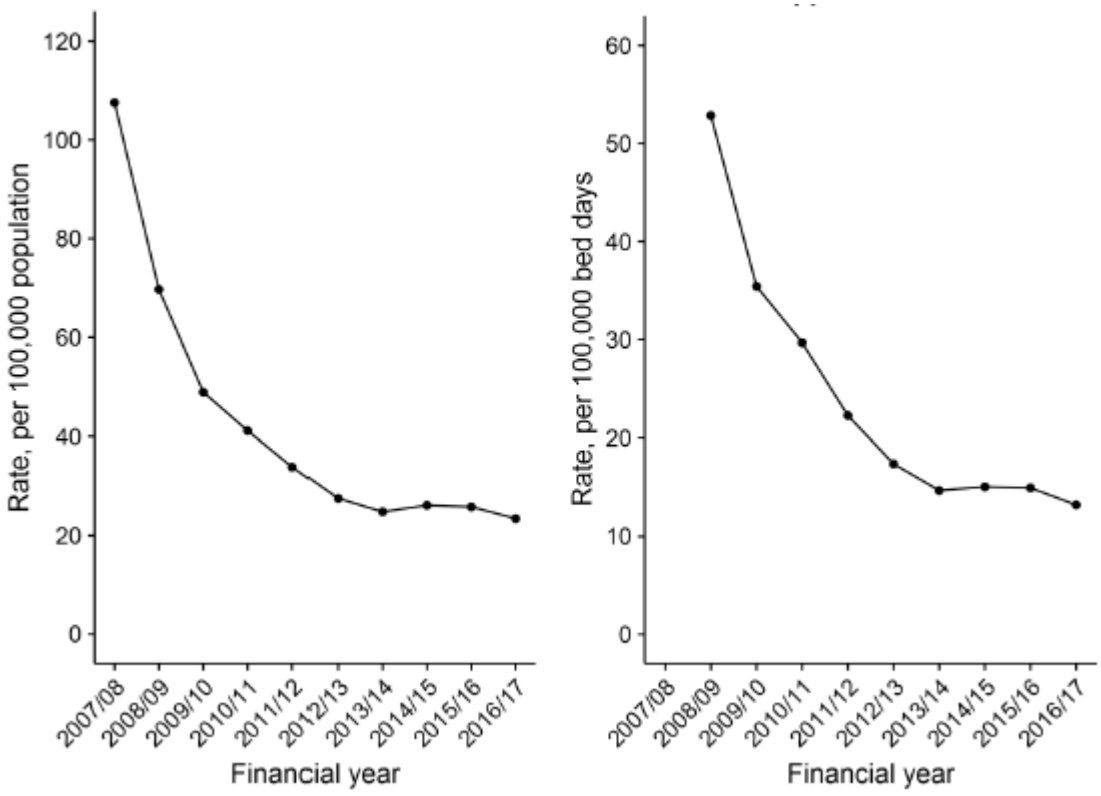


Table 3: *E. coli* counts and rates by primary focus of bacteraemia, England: 2016/17

Financial year	Gastro-intestinal (not hepatobiliary) n (%)	Hepatobiliary n (%)	UTI n (%)	Other* n (%)	Unknown n (%)	Total n (%)
2012/13	1,782 (6.5)	3,756 (13.6)	13,501 (48.9)	2,986 (10.8)	5,585 (20.2)	27,610 (100.0)
2013/14	1,711 (6.0)	3,855 (13.6)	13,393 (47.3)	2,889 (10.2)	6,452 (22.8)	28,300 (100.0)
2014/15	1,640 (5.7)	3,818 (13.3)	13,086 (45.6)	2,950 (10.3)	7,233 (25.2)	28,727 (100.0)
2015/16	1,489 (5.6)	3,554 (13.4)	12,213 (46.2)	2,769 (10.5)	6,407 (24.2)	26,432 (100.0)
2016/17	1,218 (5.4)	3,236 (14.3)	10,606 (47.0)	2,542 (11.3)	4,957 (22.0)	22,559 (100.0)

The rate[5] of *C. difficile* infection (CDI) has declined slightly from 2015/16 to 2016/17.

Figure 4: Trends in the rate of C. *difficile* infection in England



[5]https://www.gov.uk/government/statistics/mrsa-mssa-and-e-coli-bacteraemia-and-c-difficile-infection-annual-epidemiological-commentary

Future delivery of IPC in the NHS to meet the Gram-negative ambition

Responsibility of delivery of the Government's Gram-negative reduction ambition now lies with NHS Improvement, working closely with NHS England and PHE. The 2016/17 data of *E. coli* bloodstream infections would be the baseline against which progress

would be measured, with *Klebsiella* and *P. aeruginosa* baselines being set following the mandated data collection. The committee strongly endorsed published guidance on reducing MRSA screening in Trusts and emphasised the approx. £1 million savings each Trust could make by adhering to the guidance, some of which could be utilised to reduce Gram-negative infection.

National HAI point prevalence survey

In order to perform and collect data on the 2016 point prevalence study (PPS), PHE trained approximately 350 individuals face to face, and 150 by webinar. The data system to collect the data was developed with the British Society for Antimicrobial Chemotherapy (BSAC) with hospital reports sent to all organisations within 4 weeks following submission and validation. Of concern, results had shown a 29% increase in Pneumonia infections. The Committee agreed to the formation of a subgroup to look at the reasons for these increases in hospital-acquired (HAP), ventilator-acquired (VAP) and community-acquired (CAP) pneumonia, if they are related to the change in definitions of these conditions and what interventions can reduce their incidence. The recommendations of this group will be presented to APRHAI in 2018.

Defining quality measures to reduce Gram-negative bloodstream infections

Following the Government's announcement, at the G7 meeting in 2016, that actions were to be implemented to halve the number of healthcare-associated bloodstream infections that pose the biggest risk to health by 2020, the APRHAI 'GNHABSI quality measures' subgroup produced a report with recommendations.

The recommendations included reduction of Gram-negative bloodstream infections by 50% over three years, which were endorsed by the Committee in June 2016. A key goal of the quality measures was to move the primary focus away from MRSA and *C. difficile* infections to better reflect where the greatest burden of infection now lay. The Committee also agreed that it would review the quality measures annually and that they would evolve over time to better reflect the importance of a whole healthcare economy approach and that further work would be carried out to clarify policy messaging, as a way of improving understanding on how these infections arise in the patient care pathway and to improve knowledge of the importance and implications of these infections in community care.

Interventions to reduce Gram-negative bloodstream infections

At the APRHAI meeting in June 2016, it was proposed that the nationwide actions that led to significant reductions achieved in MRSA and *C. difficile* infections should be applied to Gram-negative infections. APRHAI and NHS England agreed to discuss ways by which the burden of monitoring and reporting MRSA and *C. difficile* infections could be re-focussed to Gram-negative infections without increasing the burden of NHS colleagues. APRHAI had previously made recommendations regarding MRSA screening which could ease this burden but were not being applied nationally. The Committee endorsed the intervention recommendations and proposed that further

work would be carried out to clarify IPC expectations for RTIs, dehydration and implementation systems for interventions in the community.

Antimicrobial resistance

One of seven key aims of the UK five year AMR strategy is better access to and use of surveillance data. This can be achieved through greater consistency and standardisation of data collected and improved data linkage. APRHAI was commissioned by the DH to determine the critically important antibiotic resistances and specific bacterial infections, so called drug/bug combinations, to be included in surveillance with reference to the best available evidence. The list of key drug/bug combinations was created in 2014/15 and is reviewed annually by APRHAI on the basis of the latest evidence.

Table 4. Key drug/bug combinations to be the initial focus of national surveillance (NS, non-susceptible)[6]

Bacteria	Antibiotic class	Metric
E. coli	Fluoroquinolones	% NS to ciprofloxacin
E. coli	Cephalosporin	% NS to cefotaxime and/or ceftazidime
E. coli	Aminoglycosides	% NS to gentamicin
E. coli	Carbapenem	% NS to imipenem and/or meropenem
E. coli	β-lactam	% NS to co-amoxiclav
E. coli	β-lactam	% NS to piperacillin/tazobactam
K. pneumoniae	Fluoroquinolones	% NS to ciprofloxacin
K. pneumoniae	Cephalosporin	% NS to cefotaxime and/or ceftazidime
K. pneumoniae	Aminoglycosides	% NS to gentamicin
K. pneumoniae	Carbapenem	% NS to imipenem and/or meropenem
K. pneumoniae	β-lactam	% NS to piperacillin/tazobactam
Pseudomonas spp.	Cephalosporin	% NS to ceftazidime
Pseudomonas spp.	Carbapenem	% NS to imipenem and/or meropenem
S. pneumoniae	β-lactam	% NS to penicillin
N. gonorrhoeae	Cephalosporin	% NS to ceftriaxone
N. gonorrhoeae	Macrolide	% NS to azithromycin

[6]https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/553496/2nd_UK_AMR_annual_report.pdf

AMR Trends

The UK 5 year AMR strategy had clearly set out how success would be judged in tackling AMR. At this halfway point in the strategy the Committee looked to both review current data and consider if any additional appropriate metrics for measuring success were required.

The decline seen in ciprofloxacin-resistant *E. coli* from 2007/08 showed correlation with a decline in use of ciprofloxacin and third-generation cephalosporins, prompted by the need to reduce *C. difficile* infections. This demonstrated the effects possible from rigorous antimicrobial stewardship programmes; however vigilance for a rise in

ciprofloxacin prescribing as an unintended consequence of the 2016/17 CQUIN to reduce total and broad spectrum prescribing is required.

While the proportion of *E. coli* and other Gram-negative bacteria resistant to ciprofloxacin and third-generation cephalosporins declined, the increasing incidence of *E. coli* and other Gram-negative bloodstream infections continued to rise. Thus the burden of AMR as measured by the numbers of antibiotic-resistant infections continued to increase. In light of this APRHAI recommended a renewed emphasis on infection prevention and control measures. It was suggested that the future burden of AMR should be projected and the impact of specific interventions on this burden be monitored; APRHAI agreed to advise PHE on this work.

Lack of standardisation of susceptibility testing and incompleteness of susceptibility of data reported centrally (for example where data had been supressed to clinicians) had been obstacles to monitoring the burden of AMR until recently. Data concerning multi-drug resistance was complex and hard to display; however data visualisations were being developed by the HAI and AMR department at PHE with the aim of being published in the 2016 report from the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR).

Surveillance of Gram-negative healthcare associated bloodstream infections

Data demonstrated an overall fall in mortality associated with MRSA, MSSA, *E. coli* and *C. difficile* infection (CDI) from 2007/08 to 2015/16. The Committee cautioned that a myriad of factors could influence this drop in mortality, not just the virulence of the pathogen or the treatment a patient had received for that specific infection. Data on CDI demonstrated the increase in community-onset, healthcare-associated infections over time, with a significant reduction in hospital-onset, healthcare-associated infection also seen. Data also demonstrated a marked increase in MSSA, with a decrease in MRSA. The committee expressed concern regarding the continued rise in MSSA bloodstream infections and at the meeting in March 2017 agreed to the formation of a new subgroup to investigate the continued rise in MSSA bloodstream infections and determine future interventions to combat this increase. The group considered underlying infections that may lead onto bacteraemia. A quarter of bacteraemia originated as skin and soft tissue infections. In order to identify underlying risk factors the subgroup also looked at the THIN dataset and cross-validate with patient level data at a local level. The subgroup was also intent on uncovering the underlying epidemiology of these infections and thus begin to formulate recommendations for interventions to combat them. A report is due back to the Committee in March 2018.

Local AMR Indicators- Fingertips

APRHAI and the HLSG endorsed recommendations on concept and data to inform the content of a data portal that could be used to develop local ASRIC action plans in Autumn 2015 and the local AMR Indicators were launched on the Fingertips website in April 2016. The data is held centrally by PHE and is open access. At the end of the period that this report addresses, there were 81 indicators across the AMR domains,

with local data at Acute trust, CCG and GP practice level available, which can benchmarked against the national picture. The committee discussed the importance of CCG engagement with Fingertips to aid progress of the ambitions and the Chair asked the Fingertips team to consider revisiting the idea of a composite indicator, potentially for use in the new/refreshed AMR strategy.

Health Economic Burden of AMR

Knowledge of the health economic burden of AMR is important to drive investment and to focus resource and interventions appropriately. It has been estimated that infections caused by resistant organisms can cost up to £20,000 more compared to infections that can be treated with common antimicrobials. However, there are many different causative organisms and resistance types, leading to different types of infections, meaning that exactly what was being estimated varied.

The recent AMR review conducted by Lord Jim O'Neill had provided a macro-economic estimate of AMR, which was now widely quoted. PHE and the Imperial HPRU were developing methods to more accurately estimate attributable length of stay and attributable mortality for drug-resistant infections, initially focussing on *E. coli*. A model to estimate the cost of *E. coli* and drug-resistant *E. coli* to the NHS was being developed by combining these more sophisticated methods and infection prevalence data.

Modelling work estimating the future cost burden of AMR, which had been used to inform the joint strategic risk register was being strengthened. It was hoped that this would aid cost effectiveness analyses to justify clinical interventions to tackle AMR and so avoid future costs.

Antimicrobial prescribing and stewardship

There is strong evidence to suggest that the inappropriate prescribing of antibiotics drives antimicrobial resistance, which can persist for at least 12 months.[7] Optimisation of prescribing practice was identified as one of seven key areas in the UK 5 year AMR strategy, with the aim of conserving the effectiveness of available antimicrobials.

Antimicrobial Prescribing Appropriateness Measures

The UK's ambition to reduce inappropriate antimicrobial prescribing by 50% by 2020 is to date the most ambitious antimicrobial prescribing ambition of any country worldwide.
To ensure a clear method to measure inappropriate prescribing to support the Government ambition, APRHAI agreed to the formation of the new APAM (antimicrobial prescribing appropriateness measures) subgroup. The programme of work for the subgroup was planned in December 2016 and it was agreed that both primary and secondary care should be discussed together. In March 2017, the APAM subgroup hosted a workshop at DH with attendees from across healthcare to discuss defining appropriateness of antimicrobial prescribing in Primary and Secondary care and to agree on the first targets by which to reduce prescribing. This work would then influence the content of the future QP/CQUINs.

Different definitions of inappropriate prescribing are applied worldwide and no consensus has been reached. For the purpose of delivering the ambition of halving inappropriate prescribing in the UK, inappropriate prescribing is defined as;

- Prescribing an antibiotic for a patient in the absence of (documented) evidence of bacterial infection.
- Prescribing a critical broad-spectrum antibiotic (piperacillin-tazobactam or carbapenems in secondary care; co-amoxiclav, cephalosporins and quinolones in primary care) to patients in the absence of a (documented) rationale.
- Continuing an antibiotic prescription beyond the course length recommended in local or national guidelines, in the absence of a (documented) rationale.

PHE undertook a project to model the level of inappropriate prescribing in England in Primary Care. Results from this modelling have been to presented to APRHAI and have informed the development of suggested measures of reduction. On the basis of this modelling work, recommendations were produced in May 2017 and presented to APRHAI, these recommendations were revised and subsequently endorsed in December 2017 before submission to the DHSC.

NHS England Quality Premium

In September 2016, APRHAI discussed updates on the NHS Quality Premium. Two new prescribing measures have been included in the CCG Improvement Assessment Framework meaning CCG's will continue to be assessed against these.

CQUIN

The CQUIN was implemented in April 2016 to run in 2016/17 and APRHAI had recommended aspirations of a reduction in total antibiotic prescribing in hospitals of 1% and reduction in carbapenems and piperacillin/tazobactam of 1% each.

Establishing optimal quantity measures in primary care

In September 2016, the Committee discussed the low levels of prescribing in Sweden and the Netherlands and how the UK could approach achieving similar levels. APRHAI agreed it should give the Government clear guidelines on targeted reduction and whether the net benefit of resistance outcomes are achievable. For example, the Committee discussed pneumonia and periodontal abscesses, where if prescribing were to be reduced by 10%, one additional case of pneumonia per year could be expected and one periodontal abscess every 10 years in a practice could be expected. These conditions are treatable, and therefore increasing infection rate can be offset by the vital savings made to antibiotics. APRHAI also discussed how obtaining data at patient level would allow direct comparisons between high and low prescribing countries. Data could be used to show the probability of a patient with a respiratory tract infection in the UK being prescribed an antibiotic versus the same patient in the Netherlands.

PHE worked on modelling inappropriate prescribing in primary care in 2017. This work is completed and results have been evaluated and endorsed by APRHAI in 2017 and used to inform national prescribing ambitions. Furthermore, PHE has worked on variability in prescribing practices and comorbidities and, as a result of this work, four peer reviewed papers have been published in March 2018 [7].

Infection in Critical Care Quality Improvement Programme (ICCQIP)

In November 2016, a letter was circulated to Chief Executives to encourage hospital trusts to participate in ICCQIP. To date, 183 hospital Trusts have registered interest and 48 are entering data. The Committee raised concerns surrounding the small number of Trusts entering data and suggested contacting the Trusts to query why they were not contributing. The Committee also noted that Trusts would be more likely to participate once others start submitted their data.

Monitoring for unintended consequences of reduction in antimicrobial prescribing

In 2015, APRHAI had endorsed a research proposal and the work is now being carried out at the Imperial College Health Protection Research Unit (HPRU). The project looked at prescribing, admissions, length of stay, readmission, mortality rates and primary care consultation data to determine the impact of reduced prescribing on infection rates. National prescribing data and primary care data from the clinical practice research datalink are used. Hospital episode statistics (HES) and ICD-10 codes were used to pull together read codes for primary care data. Current data showed increased admissions in particular for rheumatic fever, scarlet fever and sepsis with community-acquired pneumonia (CAP) showing a steady increase. However, the quality of the information held for CAP and sepsis is questionable due to the likely sub-optimal coding for these diagnoses in HES.
Hospital-acquired pneumonia (HAP) cases (around 20,000 per year) are derived from using a secondary code. Future work will look at length of hospital stay. CAP and HAP admissions have been rising in parallel for the last 10 years.

Long stays have remained stable and there has been a decline in mortality rates. Sepsis data shows a slight increase for readmissions and this may be due to coding. The relationship between causation and association is complex. Reporting has become more complete in recent years with possible variation in blood culture and practice.

In sepsis, mortality has gone down, but more incidences are being coded as sepsis than previously. Work has been done on comparing administrative data with clinical data and the administrative data appears to be more accurate than some of the risk prediction models. Admissions data shows comprehensive coverage.

The project was due to end in October 2017, when it was hoped to have two years of hospital admissions data and the committee requested to see this data once a year.

Therapeutic drug monitoring (TDM) in antimicrobials

The group was formed following a paper presented by William Hope (University of Liverpool, Infectious Diseases) at APRHAI in September 2016. This looked at the potentially growing need for therapeutic drug monitoring (TDM) in respect of antibiotics. His argument was predicated upon individualised therapy being increasingly sought for difficult infections, and on the issues surrounding the current and future availability of antibiotic TDM in the UK.
The TDM subgroup met in February 2017 to work on recommendation which have been presented to APRHAI in the September meeting.

Anti-microbial Resistance (AMR) Strategy

Following on from the announcement of the Government ambitions and in anticipation of the development of a refreshed strategy in 2018 following the close of the current AMR strategy, the Department of Health and Social Care (DHSC) had revised the governance of the UK AMR Strategy implementation programme. This change to governance was approved by the DH High Level Steering Group, the oversight committee for the Programme, and was brought to APRHAI for information. APRHAI met in September 2016 and agreed to the formation of a 'Strategy refresh' subgroup to discuss and decide on recommendations on the scientific content of the strategy, with input from National experts and representation from the devolved administrations. The subgroup organised an AMR refresh strategy workshop, which took place in April 2017, to discuss progress to date, lessons learnt and challenges still to be overcome, in line with the five objectives set out in WHO Global Action Plan. Recommendations were developed and presented at the APRHAI meeting in June 2017.

Summary

During 2016/17, APRHAI made several recommendations and undertook work in several subgroups across a wide range of priorities in AMR. The Committee has also continued to monitor and horizon scan for current and emerging research issues, scientific advances and development and availability of drugs. APRHAI continues to work in support of the 'UK 5 Year Antimicrobial Resistance Strategy' with priorities going forward into 2017/18 being; reduction in inappropriate prescribing, reduction in Gram negative infections, the issues arising from these two aims, monitoring and improving clinical outcomes of patients with MDR infections and the role of diagnostic testing in supporting the ambitions in the next UK AMR strategy. APRHAI will also support further work to inform a risk based approach to combating AMR in the development of the next UK AMR Strategy.

[7] https://academic.oup.com/jac/issue/73/suppl_2

Annex A

APRHAI membership

Member	Profession	Organisation
Professor Mike Sharland (Chair)	Professor of Paediatric Infectious Diseases	St George's Hospital
Professor Mark Wilcox (Deputy Chair)	Professor of Medical Microbiology	Leeds Royal Infirmary
Ms Jane Binyon	Lay Member	
Nicholas Fox	Lay Member	
Dr Nicholas Brown	Consultant Medical Microbiologist	Addenbrooke Hospital, Cambridge
Dr Carmen Lefevre	Research Lead at the Centre for Behaviour Change	University College, London
Dr Kieran Hand	Consultant Pharmacist of anti-infectives	University Hospital Southampton
Professor Alastair Hay	Professor of Primary Care	University of Bristol
Ms Judy Potter	Lead Nurse for Infection Control & Tissue Viability Service and Joint Director of Infection Prevention & Control	NHS
Professor Alan Johnson	Head of HCAI & AMR (Healthcare Associated Infections & Antimicrobial Resistance) Department	Public Health England
Mr Martin Kiernan	Nurse Consultant	Southport and Ormskirk Hospital NHS Trust
Professor David Livermore	Professor of Medical Microbiology	University of East Anglia
Professor Michael Moore	Professor in Primary Health Care Research	University of Southampton
Professor Peter Moss	Consultant in Infectious diseases	Hull & East Yorkshire Hospitals NHS Trust
Professor Andrew Peter Wilson	Professor of Microbiology & Consultant Microbiologist	UCLH NHS Foundation Trust
Dr Sarah Tonkin-Crine	Chartered Psychologist, Health Psychologist	Nuffield Department of Primary Care Health Sciences, University of Oxford
Professor Neil Woodford	Molecular Microbiologist, Head of H Antimicrobial Resistance and Healthcare Associated Infections Reference Unit (AMRHAI)	Public Health England

Department of Health and Social Care

Dr Mike DeSilva
Dr Ailsa Wight (Sponsor)
Ms Tracy Parker (Sponsor)
Ms Jane Robinson (Sponsor)
Ms Sally Wellsteed (Sponsor)
Dr Cathleen Schulte (Sponsor)

Pharmacist Lead to APRHAI

Dr Diane Ashiru-Oredope (September 2010 - Present)

Public Health England Secretariat

Ms Viviana Finistrella (October 2017- present)
Ms Caroline Purslow (June 2016 – October 2017)
Dr Emma Budd (September 2013 – June 2016)
Mrs Carol Huygebaert

Observers

Prof Paul Cosford (Director for Health Protection & Medical Director, PHE)
Dr Matthew Fogarty (NHS England)
Mrs Carole Fry (Public Health England)
Mrs Tracey Gauci (Welsh Government)
Mr Paul Green (Veterinary Medicines Directorate)
Dr Katherine Healey (Veterinary Medicines Directorate)
Professor Anthony Kessel (Public Health England)
Dr Anne Kilgallen (Department of Health, Northern Ireland)
Mr Philip Howard (NHS Improvement)
Dr Elizabeth Beech (NHS England)
Dr Emma Cramp (NHS Improvement)
Dr Sarah McAleer (Department of Health and Social Care)
Professor Alistair Leonard (Health Protection Scotland)
Ms Thara Raj (Public Health England)
Dr Elizabeth Reaney (Department of Health, Northern Ireland)
Dr Andrew Riley (Welsh Government)
Ms Jenny Thorne (NHS Wales)
Dr Bruce Warner (NHS England)
Professor John Watson (Deputy Chief Medical Officer)
Dr Susan Howard (Public Health England)
Dr Susan Hopkins (Public Health England)
Dr Naresh Chada (Department of Health, Social Care and Public Safety, Northern Ireland)

Annex B

Glossary

Antibiotic A drug that destroys or inhibits the growth of bacteria. The action of the drug may be selective against certain bacteria.

Antimicrobial stewardship Antimicrobial stewardship is a key component of a multifaceted approach to preventing emergence of antimicrobial resistance. Good antimicrobial stewardship involves selecting an appropriate drug and optimising its dose and duration to cure an infection while minimising toxicity and conditions for selection of resistant bacterial strains.

Antimicrobials An antimicrobial is a drug that selectively destroys or inhibits the growth of micro-organisms.

Bacteraemia The presence of bacteria in the bloodstream.

Catheter A tubular flexible device passed through body channels (e.g. artery, vein, or urethra) for the withdrawal or introduction of fluids.

Clostridium difficile A toxin producing bacterium which can cause severe diarrhoea or enterocolitis. This most commonly occurs following a course of antibiotics which has disturbed the normal bacterial flora of the patient's gut.

Enterobacteriaceae A family of Gram negative bacilli that contains many species of bacteria that normally inhabit the intestines. Enterobacteriaceae, that are commonly part of the normal intestinal tract flora, are referred to as coliforms.

Epidemiology The study of the incidence, spread, causes, and effects of diseases in defined populations. Epidemiology forms an evidence base which may inform policy decisions and targets for preventive healthcare.

HAI An infection that was neither present nor incubating at the time of the patient's admission (normally seen more than 48 hours after admission to hospital).

Incidence The number of new events/episodes of a disease that occur in a population in a given time period.

Infection Invasion and multiplication of harmful microorganisms in body tissues.

One Health Collaborative multi-disciplinary work at local and national levels to attain optimal health for people, animals and the environment.

Pathogenic organisms Microorganisms that can cause disease in a host.

Surveillance Systematic collection of data from the population at risk, identification of infections using consistent definitions, analysis of these data and dissemination of the results to those responsible for the care of the patients and to those responsible for implementation of prevention and central measures.