Paediatric Common Infections Pathways: Improving antimicrobial stewardship and promoting ambulation for children presenting with common infections to hospitals in the UK and Ireland

October 2020

Developed by: The British Society for Antimicrobial Chemotherapy (BSAC): 53 Regent Place, Birmingham, UK. Registered Charity 1093118. Registered as a company limited by guarantee in England & Wales No: 4443910.

Working Party Members (alphabetical): Sanjay Patel (Chair),[1] Robert Cunney,[2] Alicia Demirjian,[3] Conor Doherty,[4] Helen Green,[1] Mathew Mathai,[5] Paddy McMaster,[6] Alastair Munro,[1] Stéphane Paulus,[7] Andrew Taylor,[8] Damian Roland.[9]

BSAC Secretariat: Carolyne Horner

Affiliations

[1]Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, UK

[2]Temple Street Children's University Hospital, Dublin, Ireland

[3]Evelina London Children's Hospital, London, UK

[4]Yorkhill Children's Hospital, Glasgow, UK

[5]Bradford Teaching Hospitals NHS Trust, Bradford, UK

[6]North Manchester General Hospital, Manchester, UK

[7]Children's Hospital, John Radcliffe Hospital, Oxford, UK

[8]Alder Hey Children's Hospital, Liverpool, UK

[9]University of Leicester NHS Trust, Leicester, UK

Contents

68

69

Summary of Pathways

Common infection pathways have been developed on cellulitis, lymphadenitis & lymph node abscess, pneumonia & pleural empyema, pyelonephritis, tonsillitis / peritonsillar abscess, otitis media / mastoiditis, periorbital cellulitis/orbital cellulitis and meningitis, as well as the child presenting with a petechial rash and the baby under 3 months of age with fever. The focus of these pathways is guidance on presenting features, diagnostics, red-flags, choice and interpretation of investigations, management and guidance on safe ambulation for children presenting to hospital.

1. Introduction

1.1 Overview

In the UK about 41% of hospitalised children receive at least one antimicrobial agent during their admission.[1] Although antimicrobial stewardship (AMS) programmes have been implemented in the majority of UK children's hospital,[2] very little emphasis has been placed on paediatric antimicrobial stewardship (PAS) in secondary care settings. However, most children receiving intravenous (IV) antibiotics in the UK are being managed in secondary care centres. Bridging this implementation gap is the main justification for developing this series of Paediatric Common Infection Pathways.

The issue facing children is that the delivery of adult services and paediatric services is fundamentally different. Most patients in the UK (adults and children) are seen in district general hospitals (DGH), as opposed to teaching hospitals/tertiary centres. Whilst most DGHs have adult infection clinicians (infectious diseases or clinical microbiology), almost no DGHs have specialists in paediatric infectious diseases or paediatricians with a specific interest in infectious diseases. This explains why the quality of AMS for children in the UK is extremely variable, with paediatricians being reliant on advice from microbiologists, who themselves often have limited confidence with children and are often not familiar with the most recent

paediatric literature/practice. National paediatric infection guidelines would reduce variation in antibiotic prescribing in children across the UK as well as encouraging appropriate ambulation of children requiring IV antimicrobial agents.

There is an evolving evidence base negating the use of prolonged parenteral antimicrobial courses for specific pathologies in children, assuming the child can tolerate/absorb oral antimicrobials and adherence to oral treatment regimens without regular oversight is not a concern. There is also increasing evidence from the paediatric literature that for children with severe infections requiring IV antibiotics, earlier IV to oral switches and shorter total durations of antibiotic therapy are associated with equivalent outcomes.[3] There is a significant literature supporting this approach.[4]

Embedding paediatric antimicrobial stewardship principles within general paediatric services has been shown to reduce the duration of IV antimicrobials though earlier cessation of antimicrobial therapy or switching from IV to oral agents, compared with children being managed outside of services with PAS oversight.[5-7] This is especially relevant when children are being ambulated directly from the emergency department or paediatric assessment unit as part of an admission avoidance strategy.[8] Increasing evidence demonstrates that in the absence of PAS oversight, children have higher rates of bug/drug mismatches, drug dosing errors, readmission rates and less rigorous laboratory monitoring of drug side-effects.[9, 10]
Not only will these pathways provide an evidence based, practical approach to the antimicrobial management of children presenting to hospital with common infections, they will also provide clear guidance on when children can be safety ambulated (admission avoidance and reduced length of stay) and the clinical governance systems required to facilitate this.

1.2 Aims and Objectives

1.2.1 Aim

To develop pathways on the antimicrobial management of common infectious presentations in children presenting to hospital.

1.2.2 Objectives

1. To improve the quality of care provided to paediatric patients (<18 years old, male and female) presenting to hospital with common community acquired infections, including cellulitis, lymphadenitis & lymph node abscess, pneumonia & empyema, pyelonephritis, tonsillitis / peritonsillar abscess, otitis media / mastoiditis, periorbital cellulitis/orbital cellulitis and meningitis. In addition, guidance will be provided on the management of children presenting to hospital with petechial rashes and children under 3 months of age presenting with fever.
2. To provide an educational resource for all relevant healthcare professionals.
3. To promote a standardized approach to the diagnosis and management of common paediatric infections.
4. To advise on future research projects.
5. To provide an associated audit tool.

1.3 Potential health impact of the pathways

Successful implementation of the pathways will result in improved clinical management, which in many cases will result in shortened duration of antibiotic courses, earlier step down from IV to oral therapy and timely ambulation from hospital, with the ultimate goal being to slow the emergence of antimicrobial resistance.

2. Methodology

2.1 Scope

The scope of these pathways was approved by the RCPCH 21/02/19 (Mark Hannigan, Clinical Standards and Quality Improvement Manager (Appendix 1).

Key principles that will be covered by the pathways:

a) Principles of antimicrobial management of children presenting to hospital with common infections

b) Guidance on deciding when children can be safely ambulated from hospital

c) Providing recommendations on clinical governance systems required to facilitate safe ambulation and robust antimicrobial stewardship in secondary care settings.

The choice of antimicrobial agent and doses of antimicrobials required to treat infections will not be covered. These require agreement at local level and in addition, guidance on choice of antimicrobial agents is provided within the recently developed NICE guidelines for common infections (https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines).

2.2 Development group

2.2.1 Pathway Development Group Membership

The British Society for Antimicrobial Chemotherapy (BSAC) was the host organization. Working Party membership comprised consultants in paediatric medicine, emergency medicine, infectious diseases, and medical microbiology, an antimicrobial pharmacist, and a clinical nurse specialist in paediatric infectious diseases (Table 1). Working Party members completed a Declaration of Interest (Appendix 3).

Individuals from speciality groups [British & Irish Paediatric Ophthalmology and Strabismus Association (BIPOSA), British Paediatric Allergy Immunology & Infection Group

(BPAIIG), British Society for Children's Orthopaedic Surgery (BSCOS), and ENT UK] contributed to the development of appropriate pathways.

Table 1: Working Party Members.

Title	Name	Job Role	Affiliation
Dr	Sanjay Patel	Chair of the Working Party. Consultant in Paediatric Infectious Diseases and Immunology	Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, UK
Dr	Alastair Munro	Clinical Research Fellow in Paediatric Infectious Diseases	Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, UK
Dr	Robert Cunney	Consultant Microbiologist	Temple Street Children's University Hospital, Dublin, Ireland
Dr	Alicia Demirjian	Consultant in Paediatric Infectious Diseases and Epidemiologist	Evelina London Children's Hospital, London, UK
Dr	Conor Doherty	Consultant in Paediatric Infectious Diseases	Yorkhill Children's Hospital, Glasgow, UK
Ms	Helen Green	Paediatric Infectious Diseases and OPAT Clinical Nurse Specialist	Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust, Southampton, UK
Dr	Mathew Mathai	Consultant Paediatrician	Bradford Teaching Hospitals NHS Trust, Bradford, UK
Dr	Paddy McMaster	Consultant Paediatrician in Infectious diseases	North Manchester General Hospital, Manchester, UK
Dr	Stéphane Paulus	RCPCH adviser. Representative from the British Paediatric Allergy Immunology & Infection Group (BPAIIG). Consultant in Paediatric Infectious Diseases	Children's Hospital, John Radcliffe Hospital, Oxford, UK
Mr	Andrew Taylor	Antimicrobial Pharmacist	Alder Hey Children's Hospital, Liverpool, UK
Dr	Damian Roland	Consultant in Paediatric Emergency Medicine	University of Leicester NHS Trust, Leicester, UK

2.2.2 Views and preferences of target population

Although users (parents, children or young people) were not directly involved in the development of the pathways, their views were captured through the literature review and consultation process.

2.2.3 Target users of the pathways

Clinical staff managing children presenting to hospital with common infections (secondary care or tertiary care settings). These staff could be based in Emergency Department settings, Paediatric Assessment Units / Short Stay Units / Ambulatory settings or inpatient settings. Staff groups include emergency medicine trainees / specialist nurses / specialists, paediatric trainees / specialist nurses / specialists and clinicians from other surgical specialities involved in the management of children.

2.3 Clinical questions

Infections in paediatric patients (<18 years old, male and female) presenting to hospital to be considered are cellulitis, lymphadenitis & lymph node abscess, pneumonia & empyema, pyelonephritis, tonsillitis / peritonsillar abscess, otitis media / mastoiditis, periorbital cellulitis/orbital cellulitis and meningitis. Children presenting with petechial rashes and children under 3 months of age presenting with fever are also considered.

Key principles that will be covered by the pathways:

a) Ensuring appropriate antimicrobial management of children presenting to hospital with common infections, including adherence with principles of antimicrobial stewardship

b) Guidance on deciding when children can be safely ambulated from hospital

c) Providing recommendations on clinical governance systems required to facilitate safe ambulation and robust antimicrobial stewardship in secondary care settings

Key questions for each infection:

(a) Which children require treatment with antimicrobial therapy?

(b) If antimicrobial therapy is required, would parenteral or oral therapy be more appropriate?

(c) If IV antimicrobials are required, does the child need to be admitted to hospital or can they be safely ambulated from ED / paediatric assessment unit?

(d) For children on IV antimicrobials, at which point can their antimicrobials be stopped / switched to oral antibiotics?

(e) What is the appropriate duration of antibiotic therapy for their infection?

(f) Is a different approach required in children with co-morbidities?

(g) What systems or mitigations need to put in place to ensure the safety and efficacy of antibiotics is preserved in this age group?

Review of the current evidence base on antimicrobial prescribing in children and areas for improvement was used to derive this list of questions.[6, 8, 9]

2.4 Evidence review (include details of the critical appraisal process)

2.4.1 Literature review

The Cochrane Database of Systematic Reviews (Issue 10 of 12, October 2019), CINAHL, EMBASE and MEDLINE databases were comprehensively searched from 1 January 2014 to 16 October 2019 using the search criteria of McMullan *et al*. (2016)[3] (Appendix 2.1). The same databases were searched using search criteria associated with paediatric outpatient parenteral therapy (pOPAT) (as published previously[11]) from 1 January 2018 to 16 October 2019.

2.4.2 Evidence selection criteria

Inclusion criteria

Children (<18 years old) presenting with common infectious presentations to hospital settings, including cellulitis, tonsillitis, otitis media, pneumonia (including empyema), periorbital

cellulitis, pyelonephritis, meningitis, mastoiditis, lymphadenitis, petechial rashes and fever in the young infant (<3 months).

Hospital settings include emergency departments, paediatric assessment units/short stay units and in-patient setting.

Randomised control trials (RCT), controlled clinical trials (CCTs), interrupted time series with at least three data points before and after implementation of the intervention (ITS), controlled before and after studies (CBA). Systematic reviews and meta-analyses, case-controlled studies, case series comprising >10 patients, and journal supplements will be considered. Articles in English language will be included, and full journal publication is required.

Exclusion criteria

Adult patients (>18 years old), infections managed exclusively in primary care or exclusively in tertiary centres, paediatric patients with cystic fibrosis, bronchiectasis, or post-operative infections were excluded.

References with no named author, case reports (defined as ≤3 patients), animal studies, abstract and conference proceedings, correspondence, and in a language other than English will be excluded.

2.4.3 Literature search results

A total of 1173 references were identified from the literature search (Appendix 2.2): 941 references based on the McMullan search strategy and 232 references using the pOPAT search strategy. An initial screen (CH) identified non-relevant references (n=690) (defined as references that only included adults, patients with cystic fibrosis, bronchiectasis or post-operative infections, other clinical conditions not within the scope of the pathways (such as melioidosis, tularaemia, *Burkholderia pseudomallei*), references not in English, without an author (blank or anon.), animal or *in vitro* studies, editorials, conference proceedings and duplicate references), which were removed from further appraisal. Titles and abstracts were reviewed; potentially eligible articles were identified independently by two reviewers (n= 483). There were 233 references selected for further appraisal and the full articles in the

English language were obtained and reviewed. Full text review and agreement on final inclusion was undertaken by two reviewers. Included references (n=109) were categorised into several key areas relating to the areas of the pathways (Appendix 2.2).

2.4.4 Strengths and limitations

The strength of this approach was the robust scientific process adopted to identify relevant literature, as well as using two reviewers to decide on the final list publications. In addition, the search strategy used mirrored that used by McMullen *et al.* (2016).[3] Their search covered the dates 1946 to Nov 21, 2014 and our search extended this to October 2019; however, it needs to be acknowledged that there is a paucity of high-quality data supporting many practices in paediatric infection management. For this reason, expert consultation forms an essential part of development of these pathways. All guidelines are produced in partnership with relevant national bodies followed by formal consultation. All comments will be addressed, and the pathways amended where appropriate.

2.5 Formulating recommendations

2.5.1 Pathway development

Pathways were written by individual working party members in collaboration with individuals from speciality groups [British & Irish Paediatric Ophthalmology and Strabismus Association (BIPOSA), British Paediatric Allergy Immunology & Infection Group (BPAIIG), British Society for Children's Orthopaedic Surgery (BSCOS), and ENT UK]. Pathways were drafted in partnership with the relevant national professional group prior to review by the wider steering group and executive committees of the national groups.

2.5.2 Consideration of health benefits, side effects and risks

Based on research evidence, successful implementation of the pathways will result in improved clinical management, which in many cases will result in shortened duration of antibiotic courses, earlier step down from IV to oral therapy and timely ambulation from

hospital, with the ultimate goal being to slow the emergence of antimicrobial resistance. Risks in terms of readmission to hospital for children being ambulated of failure of infection management will be monitored and benchmarking between centres conducted through the UK-PAS programme (http://uk-pas.co.uk/).

2.5.3 Pathway and supporting evidence

The evidence supporting specific recommendations within the pathways have been presented as a reference list for each pathway, with the citation added in superscript within the pathway.

2.6 External review

Draft pathways were circulated to all authors and speciality groups for agreement before wider consultation. In order to gather feedback and improve the quality of the content and format of the pathways, to assess applicability and feasibility, the draft pathways were sent to a comprehensive list of stakeholders (Appendix 4) (19.10.20), uploaded to the BSAC website (www.bsac.org.uk). Due to the COVID-19 pandemic situation, a formal two week consultation process was completed.

2.7 Update

Pathways will be reviewed after 24 months by the steering group.

2.8 Editorial independence

2.8.1 Funding

The Paediatric Common Infection Pathways were produced by a working group on behalf of the BSAC. BSAC provided administrative support for the working group's activities but had no involvement in the content of the pathways.

2.8.2 Transparency Declarations

Competing interests of Working Party members have been recorded and addressed (Appendix 3).

2.8.3 Acknowledgements

We thank Dr Vittoria Lutje for completing the literature searches and to colleagues who responded to the consultation and provided feedback about the pathways.

3. Implementation

3.1 Facilitators and barriers to application

Front-line clinicians (Emergency Medicine and Paediatricians) will be signposted to the clinical pathways through the RCPCH. The appetite for adopting them will be enhanced by the current COVID-19 situation, in terms of avoiding unnecessary admissions where possible. In addition, case-based education will be delivered to district general hospital staff based on the clinical pathways.

A barrier to application could be lack of agreement about choice of antimicrobial agent (conflicting with local/regional empirical antibiotic therapy guidelines). For this reason, these pathways will make no specific recommendations about choice of antimicrobial agent but will refer the user to local and national guidelines.

3.2 Resource implications

Implementation of these pathways is not anticipated to be associated with any additional costs in care provision or staffing resource. Implementation of the pathways may be associated with cost savings in terms of admission avoidance/reduced length of hospital stay and appropriate IV to oral switching of antibiotics.

3.3 Implementation tool and advice

The pathways will be freely available on a BSAC hosted website and an associated article with details of the methodology for pathway development will be published in the Journal of Antimicrobial Chemotherapy Antimicrobial Resistance journal (JAC-AMR).

The UK PAS network will be involved in local implementation of the pathways; each children's hospital will oversee the rollout of educational workshops on PAS across their clinical networks.

3.4 Audit tool and E-learning module

It is anticipated that an audit tool will be developed by BSAC to allow service providers to benchmark their services against pathways. This tool will be available online on the BSAC website and will facilitate benchmarking between centres. An associated E-Learning module may be developed to complement the pathways. Separate development plans will be written for the E-learning module.

3.5 Research Recommendations

No specific research recommendations were generated during the development of these pathways. The main objective of the pathways was to translate evidence (and expert opinion) into practice. The nature of the output (clinical pathways) did not lend itself to the insertion of research recommendations.

4. References

1. Gharbi M, Doerholt K, Vergnano S *et al.* Using a simple point-prevalence survey to define appropriate antibiotic prescribing in hospitalised children across the UK. *BMJ Open* 2016; **6**: e012675.

2. Vergnano S, Bamford A, Bandi S *et al.* Paediatric antimicrobial stewardship programmes in the UK's regional children's hospitals. *J Hosp Infect* 2020; **105**: 736-40.

3. McMullan BJ, Andresen D, Blyth CC *et al.* Antibiotic duration and timing of the switch from intravenous to oral route for bacterial infections in children: systematic review and guidelines. *Lancet Infect Dis* 2016; **16**: e139-52.

4. Patel S, Abrahamson E, Goldring S *et al.* Good practice recommendations for paediatric outpatient parenteral antibiotic therapy (p-OPAT) in the UK: a consensus statement. *J Antimicrob Chemother* 2015; **70**: 360-73.

5. Hersh AL, Olson J, Stockmann C *et al.* Impact of Antimicrobial Stewardship for Pediatric Outpatient Parenteral Antibiotic Therapy. *J Pediatric Infect Dis Soc* 2018; **7**: e34-e6.

6. Knackstedt ED, Stockmann C, Davis CR *et al.* Outpatient parenteral antimicrobial therapy in pediatrics: an opportunity to expand antimicrobial stewardship. *Infect Control Hosp Epidemiol* 2015; **36**: 222-4.

7. Tanner E, Munro APS, Gray J *et al.* Improving paediatric antimicrobial stewardship in hospital-based settings: why, where and how? *JAC-Antimicrobial Resistance* 2020; **2**.

8. Xu M, Doan Q. Outpatient Parenteral Antimicrobial Therapy and Judicious Use of Pediatric Emergency Resources. *Pediatric Emergency Care* 2020; **36**: e247-e53.

9. Akar A, Singh N, Hyun DY. Appropriateness and safety of outpatient parenteral antimicrobial therapy in children: opportunities for pediatric antimicrobial stewardship. *Clin Pediatr (Phila)* 2014; **53**: 1000-3.

10. Mace AO, McLeod C, Yeoh DK *et al.* Dedicated paediatric Outpatient Parenteral Antimicrobial Therapy medical support: a pre-post observational study. *Arch Dis Child* 2018; **103**: 165-9.

11. Chapman ALN, Patel S, Horner C *et al.* Updated good practice recommendations for outpatient parenteral antimicrobial therapy (OPAT) in adults and children in the UK. *JAC-Antimicrobial Resistance* 2019; **1**.

5. Appendices

Appendix 1: Scope

The scope was approved by the RCPCH 21/02/19 (Mark Hannigan, Clinical Standards and Quality Improvement Manager).

1 Guidance title

UK AND IRELAND GOOD PRACTICE RECOMMENDATIONS FOR IMPROVING ANTIMICROBIAL STEWARDSHIP AND PROMOTING SAFE AMBULATION OF CHILDREN PRESENTING WITH COMMON INFECTIONS TO SECONDARY CARE HOSPITALS

1.1 Short title

Good practice recommendations for managing common infections in hospital settings

2 The remit

The British Society for Antimicrobial Stewardship (BSAC) in collaboration with key partners will be undertaking a project to develop good practice recommendations (GPRs) for improving antimicrobial prescribing in District General Hospitals (DGHs).

3 Clinical need for the guideline

3.1 Current practice

In the UK up to 41% of hospitalised children receive at least one antimicrobial agent during their admission (1). Although antimicrobial stewardship programmes have been implemented in the majority of UK children's hospitals, very little emphasis has

been placed on paediatric antimicrobial stewardship (PAS) in secondary care settings. However, most children receiving intravenous (IV) antibiotics in the UK are being managed in secondary care centres. Bridging this implementation gap is the main justification for developing these good practice recommendations (GPRs).

The issue facing children is that the delivery of adult services and paediatric services is fundamentally different. Most patients in the UK (adults and children) are seen in DGHs, as opposed to teaching hospitals/tertiary centres. Whilst most DGHs have adult infection clinicians (infectious diseases or clinical microbiology), almost no DGHs have specialists in paediatric infectious diseases or paediatricians with a specific interest in this field. This explains why the quality of antimicrobial prescribing for children in the UK is extremely variable, with paediatricians being reliant on advice from microbiologists, who themselves often have limited confidence with children and are often not familiar with the most recent paediatric literature/practice. National paediatric infection GPRs would reduce variation in antibiotic prescribing in children across the UK, as well as encouraging safe ambulation of children requiring IV antibiotics.

Embedding PAS principles within general paediatric services has been shown to reduce the duration of IV antibiotics through earlier cessation of antibiotics or switching from IV to oral antibiotics, compared to children being managed outside of services with PAS oversight (2, 3). This is especially relevant when children are being ambulated directly from the emergency department or paediatric assessment unit as part of an admission avoidance strategy (4). Increasing evidence demonstrates that in the absence of PAS oversight, children have higher rates of “bug/drug” mismatches, drug dosing errors, readmission rates and less rigorous laboratory monitoring of drug side-effects (5, 6).

There is an evolving evidence base negating the use of prolonged parenteral antimicrobial courses for specific pathologies in children, assuming the child can tolerate/absorb oral antimicrobials and adherence to oral treatment regimens (without regular oversight) is not a concern. There is also increasing evidence from the paediatric literature that for children with severe infections requiring IV antibiotics, earlier IV to oral switches and shorter total duration of antibiotic therapy are associated with equivalent outcomes (7). There is a significant literature supporting this approach (8), with a large number of in the past 12 months.

4 The good practice recommendations (GPRs):

a) Will be developed according to RCPCH standards for guideline development, which is NICE accredited.

b) This document is the scope. It defines exactly what these GPRs will (and will not) examine, and what the GPR developers will consider.

c) The areas to be addressed by the GPRs are in the following sections.

4.1 Populations

4.1.1 Groups that will be covered

Children presenting with common infectious presentations to secondary care settings, including cellulitis, tonsillitis, otitis media, pneumonia (including empyema), periorbital cellulitis, pyelonephritis, meningitis, mastoiditis, lymphadenitis, petechial rashes and fever in the young infant (<3 months).

4.1.2 Groups that will not be covered

Infections managed exclusively in primary care or exclusively in tertiary centres. The management of cystic fibrosis and bronchiectasis will not be addressed in these

GRPs. The management of post-operative infections will not be addressed within these GRPs.

4.2 Healthcare setting

Secondary care settings including emergency departments, paediatric assessment units/short stay units and in-patient setting.

4.3 Clinical management

4.3.1 Key issues that will be covered

a) Principles of antimicrobial management of children presenting to hospital with common infections

b) Guidance on deciding when children can be safely ambulated from hospital

c) Providing recommendations on clinical governance systems required to facilitate safe ambulation and robust antimicrobial stewardship in secondary care settings.

4.3.2 Clinical issues that will not be covered

The choice of antimicrobial agent and doses of antimicrobials required to treat infections. These require agreement at local level and in addition, guidance on choice of antimicrobial agents is provided within the recently developed NICE guidelines for common infections ((https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines).

4.4 Main outcomes

The output of this work will be a series of evidence based clinical pathways on common infections. These pathways (one for each condition) will articulate the approaches to antimicrobial management, stewardship and ambulation which can be embedded within local antimicrobial guidelines.

Successful implementation of the GPRs will result in improved clinical management, which in many cases will result in shortened duration of antibiotic courses, earlier step down from IV to oral therapy and timely ambulation from hospital, with the ultimate goal being to slow the emergence of antimicrobial resistance.

4.5 Key questions for each infection

(a) Which children require treatment with antimicrobial therapy?

(b) If antimicrobial therapy is required, would parenteral or oral therapy be more appropriate?

(c) If IV antimicrobials are required, does the child need to be admitted to hospital or can they be safely ambulated from ED / paediatric assessment unit?

(d) For children on IV antimicrobials, at which point can their antimicrobials be stopped / switched to oral antibiotics?

(e) What is the appropriate duration of antibiotic therapy for their infection?

(f) Is a different approach required in children with co-morbidities?

(g) What systems or mitigations need to put in place to ensure the safety and efficacy of antibiotics is preserved in this age group?

4.6 Status

4.6.1 Scope

This is the final scope agreed by the working group.

4.6.2 Timing

The development of these good practice recommendations will begin in September 2019.

5 Related guidance

The authors will ensure that the GPRs are aligned with the NICE antimicrobial guidelines (https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/antimicrobial-prescribing-guidelines) and will signpost readers to these guidelines in terms of choice of antimicrobial agent.

6 References

(1) Gharbi M, Doerholt K, Vergnano S, Bielicki JA, Paulus S, Menson E, et al. Using a simple point-prevalence survey to define appropriate antibiotic prescribing in hospitalised children across the UK. BMJ Open. 2016;6(11):e012675.

(2) Hersh AL, Olson J, Stockmann C, Thorell EA, Knackstedt ED, Esquibel L, et al. Impact of Antimicrobial Stewardship for Pediatric Outpatient Parenteral Antibiotic Therapy. J Pediatric Infect Dis Soc. 2018;7(2):e34-e6.

(3) Knackstedt ED, Stockmann C, Davis CR, Thorell EA, Pavia AT, Hersh AL. Outpatient parenteral antimicrobial therapy in pediatrics: an opportunity to expand antimicrobial stewardship. Infect Control Hosp Epidemiol. 2015;36(2):222-4.

(4) Xu M, Doan Q. Outpatient Parenteral Antimicrobial Therapy and Judicious Use of Pediatric Emergency Resources. Pediatr Emerg Care. 2017.

(5) Akar A, Singh N, Hyun DY. Appropriateness and safety of outpatient parenteral antimicrobial therapy in children: opportunities for pediatric antimicrobial stewardship. Clin Pediatr (Phila). 2014;53(10):1000-3.

(6) Mace AO, McLeod C, Yeoh DK, Vine J, Chen YP, Martin AC, et al. Dedicated paediatric Outpatient Parenteral Antimicrobial Therapy medical

support: a pre-post observational study. Arch Dis Child. 2018;103(2):165-9.

(7) McMullan BJ, Andresen D, Blyth CC, Avent ML, Bowen AC, Britton PN, et al. Antibiotic duration and timing of the switch from intravenous to oral route for bacterial infections in children: systematic review and guidelines. Lancet Infect Dis. 2016;16(8):e139-52.

(8) Patel S, Abrahamson E, Goldring S, Green H, Wickens H, Laundy M. Good practice recommendations for paediatric outpatient parenteral antibiotic therapy (p-OPAT) in the UK: a consensus statement. J Antimicrob Chemother. 2015;70(2):360-73.

-End-

Appendix 2: Search Strategy and Selection Criteria

Appendix 2.1: Search Strategy

Search No.	Date	Databases searched (limits: 2014-present; English language)	Search results (before duplicate removal)
1	16/10/2019	Medline (OVID)	451
2	16/10/2019	Embase (OVID)	478
3	16/10/2019	Cinahl (EBSCOHost)	58
4	16/10/2019	Cochrane Library issue 10 2019	123
Total number results			1110
Total number results in Endnote after removing duplicates			941

a. Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to October 15, 2019>

Indexed Citations, Daily and Versions(R) <1946 to October 15, 2019>

1	exp Anti-Bacterial Agents/
2	exp Administration, Oral/
3	(oral$ or per os or po).tw.
4	2 or 3
5	Infusions, Intravenous/
6	Injections, Intravenous/
7	(intra-venous$ or intravenous$ or iv or parenteral$).tw.
8	5 or 6 or 7
9	1 and 4 and 8
10	Time Factors/
11	((short* or long*) adj3 (length or period or duration)).tw.
12	((one or two or three or four or five or six or seven or eight or nine or ten) adj (day or days)).tw.
13	(("1" or "2" or "3" or "4" or "5" or "6" or "7" or "8" or "9" or "10") adj (day or days)).tw.
14	((one or "1" or two or "2") adj (week or weeks)).tw.
15	11 or 12 or 13 or 14
16	1 and 10
17	1 and 15
18	16 or 17
19	exp Infant/ or exp Child/ or Adolescent/
20	(child* or infant* or newborn* or babies or boys or girls or adolescen* or paediatric* or pediatric*).tw.
21	19 or 20
22	9 or 18
23	21 and 22
24	limit 23 to (english language and yr="2014 -Current")
25	Cellulitis/ or cellulitis.mp.
26	Tonsillitis.mp. or Tonsillitis/

27	Otitis media.mp. or Otitis Media/
28	exp Pneumonia/
29	empyema.mp. or exp Empyema/
30	Orbital Cellulitis/ or Periorbital cellulitis.mp.
31	Pyelonephritis/ or Pyelonephritis.mp.
32	Meningitis.mp. or exp Meningitis/
33	Mastoiditis.mp. or Mastoiditis/
34	Lymphadenitis.mp. or exp Lymphadenitis/
35	Osteoarthritis/ or Osteomyelitis/ or Arthritis, Infectious/ or Osteoarticular infections.mp.
36	Petechial rashes.mp.
37	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
38	24 and 37

b. Embase <1996 to 2019 Week 41>

1	(oral$ or per os or po).tw.
2	(intra-venous$ or intravenous$ or iv or parenteral$).tw.
3	((short* or long*) adj3 (length or period or duration)).tw.
4	((one or two or three or four or five or six or seven or eight or nine or ten) adj (day or days)).tw.
5	(("1" or "2" or "3" or "4" or "5" or "6" or "7" or "8" or "9" or "10") adj (day or days)).tw.
6	((one or "1" or two or "2") adj (week or weeks)).tw.
7	3 or 4 or 5 or 6
8	exp Infant/ or exp Child/ or Adolescent/
9	(child* or infant* or newborn* or babies or boys or girls or adolescen* or paediatric* or pediatric*).tw.
10	8 or 9
11	Cellulitis/ or cellulitis.mp.
12	Tonsillitis.mp. or Tonsillitis/
13	Otitis media.mp. or Otitis Media/
14	exp Pneumonia/
15	empyema.mp. or exp Empyema/
16	Orbital Cellulitis/ or Periorbital cellulitis.mp.
17	Pyelonephritis/ or Pyelonephritis.mp.
18	Meningitis.mp. or exp Meningitis/
19	Mastoiditis.mp. or Mastoiditis/
20	Lymphadenitis.mp. or exp Lymphadenitis/
21	Osteoarthritis/ or Osteomyelitis/ or Arthritis, Infectious/ or Osteoarticular infections.mp.
22	Petechial rashes.mp.
23	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	anti-bacterial agents.mp. or exp antiinfective agent/
25	oral drug administration/
26	intravenous drug administration/
27	intravenous drug administration/
28	1 or 25
29	2 or 26 or 27

30	24 and 28 and 29
31	time factor/
32	30 and 31
33	7 and 30
34	32 or 33
35	30 or 34
36	10 and 35
37	limit 36 to (english language and yr="2014 -Current")
38	23 and 37

c. Cochrane Database of Systematic Reviews (Issue 10 of 12, October 2019)

ID	Search Hits
#1	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#2	MeSH descriptor: [Administration, Oral] explode all trees
#3	(oral$ or per os or po)
#4	#2 or #3
#5	MeSH descriptor: [Infusions, Intravenous] explode all trees
#6	MeSH descriptor: [Injections, Intravenous] explode all trees
#7	(intra-venous$ or intravenous$ or iv or parenteral$)
#8	#5 or #6 or #7
#9	#1 and #4 and #8
#10	MeSH descriptor: [Time Factors] explode all trees
#11	((short* or long*) adj3 (length or period or duration))
#12	((one or two or three or four or five or six or seven or eight or nine or ten) adj (day or days)
#13	(("1" or "2" or "3" or "4" or "5" or "6" or "7" or "8" or "9" or "10") adj (day or days))
#14	((one or "1" or two or "2") adj (week or weeks))
#15	#11 or #12 or #13 or #14
#16	#1 and #10
#17	#1 and #15
#18	#16 or #17
#19	MeSH descriptor: [Infant] explode all trees
#20	MeSH descriptor: [Child] explode all trees
#21	MeSH descriptor: [Adolescent] explode all trees
#22	#19 or #20 or #21
#23	(child* or infant* or newborn* or babies or boys or girls or adolescen* or paediatric* or pediatric*)
#24	#22 or #23
#25	#9 or #18
#26	#24 and #25
#27	cellulitis
#28	tonsillitis
#29	otitis media
#30	pneumonia
#31	empyema

#32	periorbital cellulitis
#33	Pyelonephritis
#34	meningitis
#35	mastoiditis
#36	Lymphadenitis
#37	Osteoarthritis or Osteomyelitis or " Osteoarticular infections"
#38	Petechial rash*
#39	#27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38
#40	#26 and #39

d. Cinahl (EbscoHost)

#	Query	Limiters/Expanders
S28	S23 AND S26	Limiters - Published Date: 20140101-20191231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S27	S23 AND S26	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S26	S24 OR S25	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S25	TX meningitis or mastoiditis or or Lymphadenitis or Osteoarthritis or Osteomyelitis or " Osteoarticular infections" or "Petechial rash*"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S24	TX cellulitis or tonsillitis or "otitis media" or pneumonia or empyema or "periorbital cellulitis" or Pyelonephritis	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S23	S21 AND S22	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S22	S11 OR S20	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S21	TX (child* or infant* or newborn* or babies or boys or girls or adolescen* or paediatric* or pediatric*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

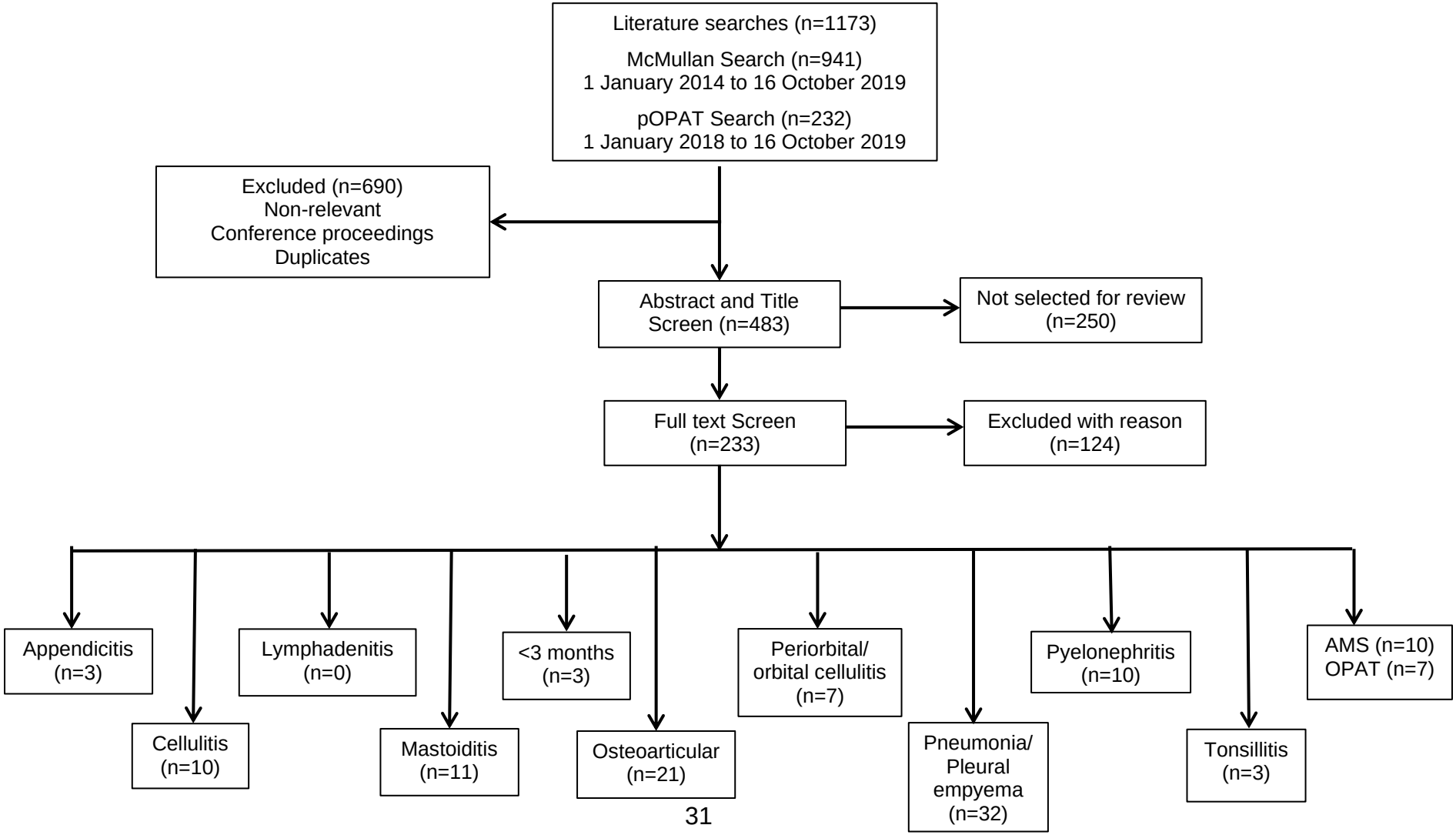
S20	S17 OR S19	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S19	S8 AND S18	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S18	TX treatment duration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S17	S8 AND S16	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S16	S12 OR S13 OR S14 OR S15	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S15	"((one or "1" or two or "2") and (week or weeks))"	Expanders - Apply equivalent subjects Search modes - SmartText Searching
S14	"((one or two or three or four or five or six or seven or eight or nine or ten) and (day or days))"	Expanders - Apply equivalent subjects Search modes - SmartText Searching
S13	"((short* or long*) and (length or period or duration))"	Expanders - Apply equivalent subjects Search modes - SmartText Searching
S12	(MM "Time Factors")	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S11	S9 AND S10	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S10	S7 AND S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S9	S3 AND S8	Expanders - Apply equivalent subjects

		Search modes - Boolean/Phrase
S8	"antibacterial agents"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S7	S4 OR S5 OR S6	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S6	TX (intra-venous$ or intravenous$ or iv or parenteral$)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S5	MW intravenous injection	Expanders - Apply equivalent subjects Search modes - SmartText Searching
S4	MW intravenous infusion	Expanders - Apply equivalent subjects Search modes - SmartText Searching
S3	S1 OR S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S2	TX (oral$ or per os or po)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase
S1	MW oral administration	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase

-End-

Appendix 2.2: Selection Criteria

Flow diagram illustrating process of the literature search (some papers may have covered more than one subject).



Appendix 3: Conflicts of Interest

Title	Name	Job Role	Declaration
Dr	Sanjay Patel	Chair of the Working Party. Consultant in Paediatric Infectious Diseases and Immunology	Chaired Paediatric Infections advisory board for Pfizer, Dubai – 19/11/19. Delivered lecture (online) on Management of complicated infections in paediatrics, Pfizer – September 2020 Recorded AMS podcast for MSD "The Steward Podcast Series" Sept 2020
Dr	Alastair Munro	Clinical Research Fellow in Paediatric Infectious Diseases	None to declare
Dr	Robert Cunney	Consultant Microbiologist	Awaiting declaration
Dr	Alicia Demirjian	Consultant in Paediatric Infectious Diseases & Epidemiologist	None to declare
Dr	Conor Doherty	Consultant in Paediatric Infectious Diseases and Immunology	None to declare
Ms	Helen Green	Paediatric Infectious Diseases and OPAT Clinical Nurse Specialist	None to declare
Dr	Mathew Mathai	Consultant Paediatrician	None to declare
Dr	Paddy McMaster	Consultant Paediatrician in Infectious diseases	NICE Managing Common Infections Committee member
Dr	Stéphane Paulus	RCPCH adviser. Representative from the British Paediatric Allergy Immunology & Infection Group (BPAIIG). Consultant in Paediatric Infectious Diseases	Awaiting declaration
Mr	Andrew Taylor	Antimicrobial Pharmacist	Paid by Vygon to provide Educatic Training for sales representatives on Antimicrobial Stewardship
Dr	Damian Roland	Consultant in Paediatric Emergency Medicine	Chair of Paediatric Emergency Re United Kingdom and Ireland. Clinical Lead for National PEWS programme board.
Dr	Carolyne Horner	BSAC Guideline Development Coordinator	None to declare

-End-

Appendix 4: Consultation Stakeholders

List of stakeholders to whom the pathways were sent for consultation. Those with a paediatric speciality are shown in **bold**.

	Consultation Group
A	Academy of Medical Royal Colleges
	Academic Paediatrics Association of Great Britain and Ireland
	Association of Paediatric Emergency Medicine
	Association for Prescribers
	Association of Surgeons of Great Britain & Ireland
	Association of the British Pharmaceutical Industry
B	**British Association of General Paediatrics**
	British Association of Paediatric Nephrology
	British Association of Paediatric Surgeons
	British Cardiac Patients Association
	British Dental Association
	British HIV Association
	British & Irish Paediatric Ophthalmology and Strabismus Association
	British Infection Association
	British Medical Association
	British Orthopaedic Association
	British Paediatric Allergy, Immunology & Infection Group
	British Paediatric Respiratory Society
	British Pharmacological Society
	British Society for Children's Orthopaedic Surgery
	British Society for Medical Mycology

	British Society for Paediatric Gastroenterology, Hepatology and Nutrition
C	**Children's Cancer and Leukaemia Group**
	Children's HIV Association
	Community Pharmacy Scotland (formerly Scottish Pharmaceutical General Council)
D	**Department of Health and Children (Ireland)**
	Department of Health Social Services & Public Safety (NHS Northern Ireland)
E	European Society of Clinical Microbiology and Infectious Disease
	ENT UK
F	Faculty of Accident and Emergency Medicine
	Faculty of Intensive Care Medicine
	Faculty of Pharmaceutical Medicine
	Faculty of Public Health Medicine
G	General Dental Council
	General Medical Council
	General Pharmaceutical Council
	Generation R: Young People's Advisory Group
	Guild of Healthcare Pharmacists
H	Health and Safety Executive
	Health Protection Scotland
	Healthcare Improvement Scotland (NHS)
	Healthcare Infection Society
I	Infection Prevention Society
	Institute of Decontamination Sciences
	Irish Paediatric Association

M	Medical Defence Union
	Medical Protection Society
	Medical Research Council
	Microbiology Society (formerly Society for General Microbiology)
	MRSA Action UK
N	National Institute for Health and Clinical Excellence
	National Institute for Health Research
	National Patient Safety Agency
	National Pharmaceutical Association
	Neonatal and Paediatric Pharmacy Group
	NHS Confederation
	Nursing and Midwifery Council
P	**Paediatric Intensive Care Society**
	Patients Association
	Pharmaceutical Quality Group
	Pharmaceutical Society of Northern Ireland
	Public Health England
Q	Quality Improvement Scotland (NHS)
R	Research Quality Association
	(formerly the British Association of Research Quality Assurance)
	Royal College of Anaesthetists
	Royal College of General Practitioners
	Royal College of Midwives
	Royal College of Nursing
	Royal College of Obstetricians & Gynaecologists
	Royal College of Ophthalmologists
	Royal College of Paediatrics and Child Health

	Royal College of Pathologists
	Royal College of Physicians & Surgeons
	Royal College of Physicians of London
	Royal College of Psychiatrists
	Royal College of Radiologists
	Royal College of Surgeons
	Royal College of Surgeons (Edinburgh)
	Royal Pharmaceutical Society
	Royal Society for Public Health
	Royal Society of Tropical Medicine and Hygiene
S	Scottish Association of Health Councils
	Scottish Intercollegiate Guidelines Network
	Society for Acute Medicine
	Standards for Microbiology Investigations
	UK Sepsis Trust
T	The British Society for Allergy & Clinical Immunology
	The British Thoracic Society
	The Consumers' Association (Which?)
	The Parliamentary and Health Service Ombudsman
	The Royal Institute of Public Health
U	UK Clinical Pharmacy Association
W	Welsh Assembly Government
	Welsh Microbiological Association
	Welsh Paediatric Society

-End-