# Supplementary data

**Table S1: Interventions and their study designs**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of intervention** | **Study design** | | | | |
| **Unknown evaluation** | **Qualitative** | **Descriptive and cross sectional** | **Randomised trials** | **Before-after comparison** |
| **STRUCTURAL** | | | | | |
| **Classifications** | * AWaRe Index |  |  |  |  |
| **Policy and commissioning** | * NHS Oversight Framework * NHS Standard Contract * O’Neill review * Hospital action plan to improve stewardship | * NAP68 * Quality Premium11 | * CQUINs9,69,70 * Pharmacy Quality Scheme16 * NAP71 |  | * Quality Premium1,8,10,72 |
| **Workforce & governance** | * Clinical pharmacists in primary care * NHSE Regional AMS leads * Pharmacy Infection professional network (UK Pharmacy Association) * Professional bodies e.g. Royal Colleges * APRHAI * NHS England AMS Regional Leads | * Community pharmacists roles119 | * Antimicrobial stewardship committees (in hospitals or primary care)39 * Antimicrobial pharmacists 39,77 * Community pharmacy antimicrobial stewardship intervention (PAMSI)58 * Pharmacist-led stewardship56 * Governance structures and processes in hospitals52 |  |  |
| **BEHAVIOURAL** | | | | | |
| **Guidance and toolkits** | * AMS Peer review tool * How to...? guides * Intravenous to oral switch * Managing common infections guidance (BNF, NICE, PHE) * Sepsis Action Plan * Specialist Pharmacy Service | * Antimicrobial Self-Assessment Toolkit73,74 * ARK-Hospital2 * TARGET23,24 * Community acquired UTI interventions67 * Local common infections guidance75 | * Antimicrobial Self-Assessment Toolkit76 * NICE guidelines28 * Primary care action plan39 * Secondary care Action Plan39,77 * Start Smart Then Focus 25,39,77,78 * TARGET 16,24–28,39,69,77,79,80 * Local common infections guidance75 | * ARK-Hospital30 * TARGET workshop29 | * NICE guidelines77,81 |
| **Monitoring and feedback** | * Building Rapid Interventions to reduce antibiotic resisTance (BRIT) * Care Quality Commission * NHSE AMS dashboard * NHSE RightCare UTI data packs * Point Prevalence Surveys * PresQIPP * QIPP * Unified Infection database | * CMO letter36 | * Auditing prescribing practices39,77 * Fingertips data69,80,82 * Self-reported tool (SAT)79 | * CMO letter3,83 * Feedback to clinicians 84,85 | * CMO letter37 |
| **Professional engagement & training** | * Continuing professional development courses * Health Education England Campaigns * NHSE education and training * RPS AMS training for pharmacists |  | * Antibiotic Guardian Campaign 6,38 * Conferences16,86 * Fleming Fund’s Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS)87 * GPs trained in integrated medicine88 * Primary & secondary care education strategies39 * Royal Colleges professional engagement39 * Undergraduate education89 * TARGET activities, including train the trainer, FutureLearn courses, webinars, campaigns6,16,77,79 | * Community pharmacy engagement40 * TARGET workshop 29 | * Conferences80 |
| **Public awareness** |  | * Games107 * Peer to peer education108 * Patient information109 | * Antibiotic Guardian Campaign and youth badge 6,16,28,43,44,69,80,82,110,111 * Antibiotic quiz112 * Keep antibiotics working campaign28 * Patient information6,109,113 * World Antibiotic Awareness Week / European Antibiotic Awareness Day28,80 * Fear messages114 | * Animated films for patients115 | * Debates in schools116 * Games (e-Bug)117,118 * Training educators (e-Bug)118 * The Mould that Changed the World theatre production47 |
| **TECHNOLOGICAL** | | | | | |
| **Prescriber tools** |  | * Point of Care CRP testing90–93 | * Delayed precribing94,95 | * Biomarker-guided stewardship96 * Clinical prediction scores97 * Computerised decision support tools4 * Delayed prescribing98 * Ear drops (children)99 * Probiotics 100,101 * Point of Care CRP Testing5,62 * Point of Care respiratory virus tests102 * Point of Care Urine tests103 | * Computerised decision support tool64 * Procalcitonin testing104 * Point of Care CRP testing63,105 * Delayed prescribing & point of care testing106 |
| **STUDIES COVERING MULTIPLE CATEGORIES** | | | | | |
| **Studies evaluating multiple types of interventions** |  | * Prescribing behaviour due to multiple interventions67 | * AMS education (face-to-face & e-learning), TARGET (patient information, prescriber checklists), Antibiotic Guardian campaign22 * Quality Premium, feedback of prescribing data, AMS audits, local incentive schemes, CMO letter, other AMS initiatives6 * Hospital structures & processes, including leadership models, AMS teams, policies, rapid testing, authorisation for some antibiotics, reviewing appropriateness, IVOS, automatic alerts feedback, education52 |  |  |
| Qualitative studies used interviews and focus groups methods. Descriptive and cross sectional studies were ones conducted at a single point in time, usually through a single survey to gain feedback but also quantitative observational analysis of data (e.g. to track webpage usage). Randomised trials all utilised designs based on RCTs, e.g. cluster randomised trials, pragmatic, open randomised trials, (open adaptive pragmatic parallel group RCT). Before-after comparison used a mix of interrupted time series analyses (often with a controlled or comparative element), or surveys conducted at multiple time points. | | | | | |

**Table S2: Interventions and outcomes evaluated**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Type of intervention** | **Focus of evaluation** | | | | | | |
| **Cost-effectiveness** | **Clinical** | **Microbiological** | **Antibiotic use or prescribing** | **Sustainability** | **Implementation or process** | **Knowledge or**  **behaviour** |
| ***STRUCTURAL*** | | | | | | | |
| **Classifications** |  |  |  |  |  |  |  |
| **Policy and commissioning** |  | * Quality premium10 | * Quality premium1 | * CQUINs9,70 * Quality premium1,8,10 | * Quality premium1,8 | * CQUINs 9,69 * NAP67,68 * Pharmacy quality scheme7,16 * Quality premium6,11,72 |  |
| **Workforce & governance** |  |  |  | * Community pharmacy antimicrobial stewardship intervention (PAMSI) 57 * Structures and processes for AMS in hospitals52 |  | * Antimicrobial pharmacists 39,56,77 * Community pharmacists roles119 * Community pharmacy antimicrobial stewardship intervention (PAMSI)58 * Antimicrobial stewardship committees (in hospitals or primary care)39 * Structures and processes for AMS in hospitals52 |  |
| ***BEHAVIOURAL*** | | | | | | | |
| **Guidance and toolkits** |  | * Antibiotic review kit (ARK-hospital) 30 * NICE guidelines81 |  | * Antibiotic review kit (ARK-hospital) 30 * NICE guidelines77,81 | * TARGET toolkit23–27,39,69,79,80,82 * Start Smart Then Focus25,39,77 | * Antimicrobial self-assessment tollkit74 * antibiotic review kit (ARK-Hospital)2 * Secondary care Action Plan39,77 * Local common infections guidance75 * Local use of national strategies 6,39,77 * Primary care action plan39 * Start Smart Then Focus25,39,77 * TARGET toolkit22–27,39,67,69,79,80,82 | * Start smart then focus 78 * TARGET toolkit26,67 * NICE guidelines28,67,77,81 |
| **Monitoring and feedback** |  |  |  | * CMO letter3,37,79,83 * Feedback to clinicians 84,85 | * CMO letter 3,37,79,83 | * Auditing prescribing practices6,39,77 * CMO letter22,36,67 * Fingertips data67,69,80,82 * Self-reported tool (SAT)79 * Benchmarking and feedback of prescribing data22,52 | * Fingertips data67,69,80,82 * CMO letter67 |
| **Professional engagement & training** |  | * Community pharmacy engagement40 |  | * GPs trained in integrated medicine88 * TARGET workshop 29 |  | * Antibiotic Guardian Campaign67 * Community pharmacy engagement40 * Primary & secondary care education strategies39 * TARGET activities, including train the trainer, FutureLearn courses, webinars, campaigns6,16,77,79 * Undergraduate education89 | * Antibiotic guardian campaign 38,67 * Conference86 * Fleming Fund’s Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS)87 |
| **Public awareness** |  |  |  | * Patient information113 | * Antibiotic guardian campaign69 | * Antibiotic quiz112 * Games107 * Patient information22,109 * Peer to peer education108 * World Antibiotic Awareness Week / European Antibiotic Awareness Day28,80 | * Debates in schools116 * Animated films for patients115 * Antibiotic guardian campaign43,44,69 * Games (e-Bug)117,118 * Fear messages114 * Keep antibiotics working campaign28 * Patient information109 * The Mould that Changed the World theatre production47 |
| ***TECHNOLOGICAL*** | | | | | | | |
| **Prescriber**  **tools** | * Point of Care CRP Testing120 * Point of Care Urine tests103 * Outpatient parenteral antimicrobial therapy (OPAT)121 | * Computerised decision support tools4,64,106 * Delayed prescribing98 * Point of Care CRP Testing120 * Point of Care respiratory virus tests102 | * Biomarker-guided stewardship96 * Clinical prediction scores97 * Electronic health records to guide AMS106 * Point of Care Urine tests103 | * Biomarker-guided stewardship96 * Computerised decision support tools4,64,106 * Delayed prescribing98 * Point of Care CRP Testing5,62,105,120 * Delayed prescribing & point of care testing combined66 * Point of Care respiratory virus tests102 * Point of Care Urine tests103 * Probiotics 100,101 * Procalcitonin testing104 | * Computerised decision support tools4,64 * Delayed prescribing98 * Outpatient parenteral antimicrobial therapy (OPAT)121 * Point of Care CRP Testing120 | * Computerised decision support tools4,64,106 * Clinical algorithm122 * Delayed prescribing & point of care testing combined66 * Point of Care CRP testing62,90–93,105 * FeverPAIN clinical score67 * Centor clinical score67 | * FeverPAIN clinical score67 * Centor clinical score67 |
| * *Clinical outcomes include: antibiotic-free days following a procedure, infection incidence, symptom or disease severity (e.g. CURB-65 score for pneumonia, COPD status), symptom or infection duration, length of therapy, length of hospital stay, reattendance to primary care, diagnostic tests results (CRP, prolactin), IVOS, antiviral use, use of X-rays, self-reported referral to GP or pharmacist* * *Microbiological outcomes include: blood cultures sampled before antibiotic initiation, detection of resistant Enterobacterales cultured from stool samples, number of isolates tested against antibiotic during antimicrobial susceptibility testing, resistance to at least one antibiotic,* * *Antibiotic use outcomes include: number of antibiotics prescribed (e.g. per GP practice, per month, per STAR-PU), any antibiotic prescribed (yes/no), defined daily doses (e.g. total, per bed days), patient-reported antibiotic use, duration of antibiotic use, antibiotic days for infections over 1-year, diagnostic accuracy of prediction scores compared to microbiological cultures, achieving antibiotic use targets, percentage of antibiotics prescribed by each AWaRe category* * *Implementation includes: quantitative outcomes (such as adherence to guidelines, use of intervention materials, perceptions of interventions from surveys, AMS-specific job roles present) as well as qualitative studies (e.g. perceptions of interventions from interviews, barriers and facilitators of implementing interventions) and process evaluation* * *Knowledge and behaviour change outcomes include: self-reported change in knowledge, children’s change in knowledge of AMR* | | | | | | | |

**Table S3: Effectiveness of interventions aimed at optimising antibiotic use**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Type** | **Study details (intervention name, design, outcomes)** | | **High quality** | **Effect size** |
|  | | ***Primary care*** | | |
| Guidance & toolkit | **TARGET workshop, RCT over 32 months in 152 general practices, outcomes: Total ABU (oral antibiotic items dispensed per 1000 patients) & ABU by antibiotic** 123 | | **Yes** | **Total ABU reduced 2.7%.**  Amoxicillin/ampicillin reduced 4.4%, Trimethoprim reduced 5.6%, nitrofurantoin no effect |
| Monitoring & feedback | CMO letter, RCT over 6 months in 1909 general practices, outcome: total ABU (antibiotic items prescribed per STAR-PU) and broad spectrum ABU (percentage of broad spectrum items prescribed per STAR-PU)83 | | Yes | Total ABU no effect |
| **CMO letter, RCT over 5 months in 1581 GP practices (high prescribing practices), outcome: total ABU (antibiotics dispensed per 1000 weighted population, controlling for pas prescribing)**3 | | **Yes** | **Total ABU reduced 3.3%** |
| **CMO letter, controlled before-after study over 6 months in 7425 GP practices, outcome: total ABU (average STAR-PU-adjusted rate of antibiotic items dispensed)** 37 | | **Yes** | **Total ABU reduced 3.69%** |
| **Feedback to clinicians, RCT over 12 months in 9 GP practices (RTI patients), outcome: total ABU (rate of antibiotic prescribing for RTI per 1000 patient years over 12 months)**85 | | **Yes** | **Total ABU for RTIs reduced 12%** |
| Feedback to clinicians, RCT over 5 months in 1401 general practices, outcome: broad spectrum use (proportion of antibiotics which were broad-spectrum)84 | | Yes | No effect broad spectrum ABU |
| Policy & commissioning | **Quality premium, before-after study (ITS) over 47 months in primary care, outcome: total ABU (number of antibiotic items prescribed; number of antibiotics prescribed per STAR-PU), broad spectrum ABU (number of broad-spectrum antibiotic items prescribed; and as a percentage of total antibiotics prescribed)**8 | | **Yes** | **Total ABU reduced 8.2%** |
| **Quality premium, before-after study (ITS) over 72 months in 6882 general practices, outcomes: total ABU (change in rate of antibiotics prescribed per 1000 patients in general practitioner practices)**1 | | **Yes** | **Total ABU reduced 57%** |
| Prescriber tools | Computerised decision support tool, RCT over 12 months in 79 GP practices, outcome: total ABU (antibiotic prescriptions for self-limiting RTIs over 12 months), also adult ABU, children ABU, elderly ABU4 | | Yes | **Total ABU reduced 12%** |
| Delayed prescribing or clinical scores or antigen tests, RCT over 24 months in 1760 patients with acute sore throat presenting at general practices, outcome: total ABU (patient-reported antibiotic use)98 | | Yes | Total ABU 29% lower in clinical score group. Total ABU 27% in antigen test group. Comparator group was delayed prescribing. |
| Delayed prescribing & point of care CRP tests, before-after study over 12 months in 9 general practices, outcome total ABU (total antibiotic prescriptions per general practitioner practice)66 | | No | Total ABU no effect |
| Point of care CRP testing, RCT over 6 months in 8 general practices, outcome patient-reported total ABU (binary outcome of whether antibiotic dispensed or not) 62 | | Yes | Total ABU for RTI no effect |
| **Point of care CRP testing, RCT over 6 months in 653 participants with COPD (86 general practices), outcome: total ABU (patient reported antibiotic use)**5 | | **Yes** | **Total ABU for COPD patients 22% fewer participants in the CRP POCT arm were prescribed antibiotics** |
| Point of care urine tests, RCT over 3 months in 329 female patients in primary care, outcome: total ABU (concordant antibiotic use corresponding to laboratory culture results) 103 | | Yes | Total ABU in females with UTI no effect |
| Probiotics, RCT over 12 months in 310 care home residents, outcome total ABU (cumulative antibiotic administration)100 | | Yes | Total ABU no effect |
| Probiotics, RCT over 6 months in 1302 asthmatic patients with RTIs in primary care, outcome: total ABU (proportion of patients prescribed antibiotics for RTIs) 101 | | Yes | Total ABU asthmatic patients with RTI no effect |
| Professional engagement & training | GP training, observational study over 12 months in 7283 general practices (only 9 with the intervention), outcome: total ABU (antibiotic prescribing rates per STAR-PU, total and for RTIs and UTIs)88 | | No | Total ABU reduced 22%. RTI ABU reduced 26%. No effect UTI. |
|  | |  | | |
|  | | ***Secondary care*** | | |
| Guidance & toolkit | **ARK-hospital, RCT over 14 months in 39 hospitals (acute general admission patients), outcome: total ABU (monthly antibiotic consumption as defined daily doses per adult acute general medical admission)** 30 | | **Yes** | **Total ABU reduced 4.8% per year** |
| NICE guidelines, before-after study over 24 months in 101 hospital patients (paediatrics), outcome: total ABU (proportion of patients prescribed antibiotics) 81 | | No | Total ABU in paediatrics reduced 16% |
| Policy & commissioning | CQUINs, Before-after study over 24 months in 116 hospitals, outcome: total ABU (antibiotic consumption in hospital trusts)9 | | No | Total ABU no effect.  Carbapenem 8.0% reduction. piperacillin/tazobactam 4.8% reduction |
| Prescriber tools | Biomarker-guided stewardship, RCT over 34 months with 214 patients (in ICU), outcome: total ABU (antibiotic free days over 7 days)96 | | Yes | Total ABU no effect |
| Computerised decision support tool, before-after study over 48 months in 1 hospital, outcome: total ABU (antibiotic consumption as defined daily doses per 1000 occupied bed-days)64 | | No | Total ABU higher without computerised decision support tool. (mean difference − 110.14 defined daily doses/1000 bed day) |
| Point of care respiratory virus testing, RCT over 6 months in 720 hospital patients, outcome: total ABU (proportion of patients receiving antibiotic whilst hospitalised)102 | | Yes | Total ABU (proportion patients receiving ABU, duration) not changed, over 6 months, hospital |
| Procalcitonin testing, controlled before-after study (ITS) over 12 months in 105 hospitals, outcome: total ABU (antibiotic consumption as defined daily doses of antibiotic per admission per week per hospital trust)104 | | Yes | Total ABU during COVID-19 no effect |
| Workforce & governance | Structures and processes in hospitals, cross-sectional, outcomes: total ABU and ABU by AWaRe category (antibiotic consumption as defined daily doses per 1000 hospital admission)52 | | No | Total ABU no effect |

*Intervention highlighted in bold if it had higher quality evidence & reported reductions in antibiotic use. Higher quality evidence are those which were either RCTs or which utilised an appropriate quasi-experimental design such as interrupted time series analyses.*

*Acronyms: ABU: Antibiotic use. ARK-Hospital: Antibiotic Review Kit-Hospital. AWaRe: Access Watch Reserve. CMO: Chief Medical Officer. CRP: C-Reactive Protein. GP: General Practitioner. ITS: Interrupted Time Series. NICE: National Institute for Health and Care Excellence. RCT: Randomised Controlled Trial. RTI: Respiratory Tract Infection. TARGET: Treat Antibiotics Responsibly, Guidance, Education and Tools.*

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