Investigating the ways in which health information technology can promote antimicrobial stewardship

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Investigating the ways in which health information technology can promote antimicrobial stewardship: A conceptual overview ~~and research agenda~~

Comment [KA1]: This was deleted in response to reviewer's comment: "However, the title also suggests that a research agenda will be presented. This is implied rather than specifically stated in the paper. The only real mentions of research are the final sentence of the introduction and the final sentence of the conclusion and neither really fall into what I would expect as a research agenda."

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~~Abstract~~Summary

Antimicrobial resistance is now recognised as a threat to health worldwide. Antimicrobial stewardship (AMS) aims to promote the responsible use of antibiotics and is high on international and national policy agendas. Health information technology (HIT) has the potential to support AMS in a number of ways, but this field is still poorly characterised and understood. Building on a recent systematic review and expert roundtable discussions, we take a lifecycle perspective of antibiotic use in hospitals and identify potential targets for HIT-based interventions to support AMS. We aim for this work to help chart a future research agenda in this critically important area.

Comment [AK2]: 'Abstract' replaced with 'Summary' in response to editorial comments 2 and 3: 2) Please provide a summary which is short and concise, ideally no longer than 250 words; 3) A formal abstract is not required.

Introduction

Antimicrobial resistance is now recognised as an urgent global threat to health.[1] The prevalence of single- and multi-drug resistant organisms is increasing[2] as is mortality due to infections caused by these organisms.[3] Across the European Union (EU) and the Unites States (US), antimicrobial-resistant infections are responsible for at least 50,000 deaths annually.[4, 5] Globally, these infections claim an estimated 700,000 lives each year.[6]

Antimicrobial Stewardship (AMS) is the international response to the threat of resistance. As the inappropriate use of antibiotics is a key contributor to resistance,[7] there is increasing policy and clinical interest to promote appropriate use of antibiotics[8] through a set of concerted interventions, including: health information technology (HIT),[9] guidelines and protocols,[10] education and training, and novel staffing structures in the form of antimicrobial committees and champions.[11] ~~Together,~~ Often used in combination, these interventions aim to optimise the use of antibiotic therapy,[12] reduce resistance, minimise hospital acquired infections, and improve clinical outcomes.[13]

Comment [KA3]: Added in response to reviewer's comment: "are the authors stating that all of these interventions should be used *together*, i.e. in combination, to optimise the use of antibiotics? This might need rewording."

HIT has much to offer the AMS agenda as can be seen by the increasing number of studies that have looked into the feasibility, effectiveness, and accessibility of various HIT-mediated AMS interventions.[9, 14, 15] There is however a lack of any comprehensive overview of the potential targets for HIT-based interventions. This may hamper progress in this still nascent, but critically important field.

The aim of this article is to highlight areas of the antibiotic lifecycle that are potentially most amenable to HIT interventions in hospital settings. This review also outlines HIT that has the potential to be deployed in relation to AMS, and is currently, or soon to be, available. We do not, however, make claims that this HIT is unequivocally helpful. Further, this review is not exhaustive but intends to invite discussion around which of these areas may be implementable and subsequently scalable in hospital AMS programmes in the UK and to identify areas for further research enquiry.

Methods

We began by developing a conceptual schema of all stages of an archetypal antibiotic lifecycle from the initial decision to prescribe an antibiotic for a patient with suspected infection, through to the review of treatment within a typical UK hospital setting (Figure 1). This antibiotic lifecycle was informed by a review of the published and grey literature, and multidisciplinary discussions involving patients, hospital clinicians and management staff undertaken as part of our ongoing programme grant of hospital electronic prescribing (ePrescribing) systems. More specifically, we drew on our recent systematic review[14] and expert multi-stakeholder roundtable discussion,[16] which highlighted the many ways in which HIT already supports, and could potentially support AMS by applying best practice technologies and procedures during the antibiotic lifecycle in UK hospital care. We conceptualised this work within the context of the UK policy framework for AMS: *Start smart - then focus*.[17]

Lifecycle of hospital antibiotic use

The lifecycle of antibiotic management in hospital starts when a patient presents to hospital with or develops during their hospital stay a suspected infection. The lifecycle (Figure 1) proceeds through an initial differential (working) diagnosis from the initial presentation, obtaining specimens for microbiological cultures and sensitivity testing (where applicable), initial empirical treatment decision and generation of a prescription order, followed by timely review of treatment and subsequent amendment where applicable. This is far from a linear process; it typically involves many different 'actors' at different points in the care process, and each process is variable depending on patient demographics such as prior history and comorbidities. As such, to understand how the AMS agenda can be supported with HIT, it is important to consider the clinical situations that fall outside the lifecycle and how these too may be supported through appropriate HIT intervention. In the sections below we discuss the components that already are supported and those that can be supported by HIT to better align care with the AMS agenda. At present, some of these HIT interventions are commonly seen across hospitals in the UK, EU and US, while others have been employed by only a few benchmark hospitals.

Potential for HIT interventions to promote AMS

Health systems are moving towards digitisation.[18] The ability to store, share, access, and proactively use information at the point of care as well as through prospective and retrospective auditing and feedback is being used to drive forward efforts to enhance the safety, quality, and efficiency of healthcare.[19] HIT that supports AMS can come in many forms: electronic health records (EHRs) that record patient information such as diagnoses and previous medication sensitivities; ePrescribing systems, such as computerised physician order entry (CPOE) and/or clinical decision support (CDS) systems;[20] and monitoring systems that draw together information from disparate parts of the hospital, enabling, for example, the triaging of patients who require clinical intervention. These systems can make data accessible to support diagnosis, treatment decisions, and review of patients who may for example need the route of delivery of antibiotics to be changed (e.g. intravenous to oral) or those in whom treatment can be discontinued.[13]

In the subsequent sections, ~~W~~we describe particular points in the antibiotic lifecycle that may be supported by and optimised through HIT intervention (also delineated in Figure 2). These sections reflect the *Start smart – then focus*[17] framework as it is the recommended approach by Public Health England for all antibiotic prescribing. The ~~I~~interventions described mainly target clinical staff: doctors, pharmacists, and nurses at the point of care, as well as at the level of an AMS committee or hospital management. They may in the future also target patients/carers.

Comment [KA4]: Added in response to reviewer's comment: "it would be helpful to explain how/why the potential is going to be described using the "start smart, then focus" structure that comes in the next few sections"

Start Smart

(a) Patient presentation

At its simplest, the lifecycle of a hospital administered antibiotic starts when a patient presents with symptoms suggestive of an infection or develops a new infection whilst already in hospital. A clinician will take (or review) the patient's medical and drug history, undertake a physical examination, and perform relevant investigations, including blood tests. This process and information can be documented in the EHR alongside the patient's current regimen of medication and any known allergies to medications. Through the EHR, the clinician may also access the patient's previous microbiological results with any antimicrobial resistance data that may help inform assessment of the likely effectiveness of the antibiotic(s).

(b) Diagnosis

The clinician will make a differential diagnosis, and if an infectious process is suspected then a decision will be made whether to commence empirical treatment with a relevant antibiotic. Decisions can be documented in the EHR along with the suspected indication and proposed duration of any treatment. The diagnosis may also be documented in the ePrescribing system if this is separate to the EHR. As EHRs and ePrescribing systems are often integrated, the patient information and indication for treatment[21] can be easily accessed as is the ability to track the progress of the patient and the clinical decision making over time. However, not all information may be in a form that allows for this tracking of decision making processes over time – this is because the initial diagnosis may not be recorded or indications may not be reported in a structured way that can be used to drive reports. Further research using natural language processing (NLP) may prove helpful in such scenarios.

(c) Obtain cultures

An important step in the antibiotic prescribing process is, where appropriate, obtaining cultures to determine the organism responsible for the infection. Importantly, cultures should be obtained before starting treatment, although this should not delay the initiation of antibacterials in cases of suspected sepsis. ~~This~~ Culture results~~information~~ can confirm whether any empirical treatment commenced is appropriate to continue, or whether treatment needs to be changed for optimal management (or started if not done so previously). Through understanding local resistance patterns and susceptibility rates of particular organisms, clinicians can determine which antibiotics might work for the particular infection and also whether the chosen antibiotic(s) is likely to work in any individual patient.

Comment [AK5]: Added in response to reviewer's comment: "in this section mention could be made of the importance of obtaining cultures before starting treatment, which could be supported by linking culture orders, medication orders and administration records."

Comment [KA6]: Added in response to reviewer's comment: "specify whether this is local resistance patterns". We have specified resistance patterns as local, rather than personal as the latter is not a commonly utilised desription in practice.

HIT can play an important role here. By linking culture orders, medication orders and administration records, HIT ~~by~~ ~~mediating~~ supports ~~the~~ communication between the prescribers on the wards and the microbiologists in the laboratory. Further, ~~M~~microbiology results can be incorporated into the EHR and made available at the point of care. Systems can alert prescribers to results that have recently been made available, in order to prompt action for review. However, as these results often rely on free text data, the multiplicity of report formats mean that microbiology results are often not yet in a form that can be used to drive more specific alerts, such as when the organism causing a patient's infection is resistant to the antibiotic the patient has been prescribed. Coding for urgency in alerts prompted by available microbiology data is an important area of future HIT development.

Comment [KA7]: Added in response to reviewer's comment: "Page 4, line 26 – in this section mention could be made of the importance of obtaining cultures before starting treatment, which could be supported by linking culture orders, medication orders and administration records"

(d) Initial treatment decision

While awaiting the results of cultures and antibiotic sensitivity tests, clinicians will typically institute an empirical treatment plan based on the differential diagnosis. Minimising exposure to broad-spectrum antibiotics and maximising exposure to optimal therapies is an important component of AMS.[22] The initial treatment decision and prompt initiation for specific indications (e.g. ventilator-associated pneumonia)[23] and in specific hospital care contexts (e.g. critical care units)[24] is another strategic area for AMS, however, this may be in tension with the judicious use of antibiotics until culture results are available.[13]

ePrescribing systems can facilitate access to local antimicrobial prescribing guidelines designed to support practitioners in selecting the most appropriate first-line antibiotic, at a suitable route, dose, frequency, and duration for the specific patient and indication. Guidelines can be accessed via EHRs alongside updated formularies, supporting clinicians in selecting antibiotics that are locally approved and available. For certain clinical situations, such as surgical prophylaxis and post-operative care, HIT systems can also facilitate access to standardised local protocols via electronic order sets. These are aggregated collections of orders or steps to follow for a given condition or clinical situation that can support evidence-based practice for the judicious use of antibiotics. Procedures for prior authorisation of restricted antibiotics can also be built into the HIT-mediated prescription process. This may require the review and approval by a member of the AMS committee or specialist infectious disease (ID) doctors before a prescription can be ordered and thus prepared for administration. If a restricted agent is prescribed, the prescriber may be presented with a list of alternative options from the formulary and guidelines as well as the contact information for the person who can authorise the order. The HIT system can also alert relevant approving individuals that a restricted antibiotic has been ordered and can provide them with the relevant patient and prescription information to either accept or decline the prescription. For complex cases, the HIT system can support prompt communication between the patient care team and specialist ID doctors, facilitating shared prescription decisions as well as immediate authorisation for restricted agents. Treatment decisions can also be informed by antibiograms (Table 1) that provide practitioners with real-time, local profiles of antibiotic susceptibility and resistance patterns for specific organisms (Box 1, *Example 1*).

Comment [KA8]: Added in response to reviewer's comment: "the also seems to be the potential here to consider ways to speed up prescribing of restricted antibiotics where they have been explicitly recommended by infectious diseases specialists. The system described implies that the decision to prescribe a restricted antibiotic will always come from the team directly caring for the patient."

HIT can further support initial treatment decisions by enabling the clinician to document their decision including the drug name, route, dose and frequency in the EHR and/or ePrescribing systems. With this information, HIT can aid with indication-based prescribing, dose/frequency checking, as well as allergy, drug-disease interaction and drug-drug interaction checking. ePrescribing systems can also encourage the use of appropriate, evidence-based antibiotic therapies through behavioural nudges.[25] At the point of care, nudges can come in the form of 'accountable justification' and 'suggested alternatives', as described by Meeker et al (2016). Accountable justification, through prompts within the ePrescribing system, requires clinicians to explain their selection of antibiotics in a free text box that is ultimately included in the patient's EHR. Suggested alternatives, through pop-up alerts, are triggered when antibiotics are prescribed for conditions that may be treated through other therapeutic routes. These alerts can provide prescribers with a list of alternative therapies as well as easy access to electronic order sets for these therapies.

(e) Prompt initiation of effective treatment supported by EHR

The interoperability and automation of HIT systems aim to minimise the time from the diagnostic order to the patient receiving the first dose.[26] During prescription preparation, HIT can support pharmacists through a process of controls: checking whether the prescription is appropriate for the indication and the patient as well as facilitating contraindication checks such as allergies, drug-interactions and conditions such as renal impairment which may necessitate a modification of the antibiotic dose. EHR and ePrescribing systems can also support nurses during the administration of medication through reminders for timely administration as well as alerts for missed and delayed doses.

Then Focus

(a) Reviewing the clinical diagnosis and assessing the need for continuing antibiotics

The National Institute for Health and Care Excellence (NICE) recommends that prescriptions for antibiotics are reviewed 48 to 72 hours after initiation.[27] The purpose of the review is to determine:

- Whether the patient has an infection that will respond (or is responding) to antibiotics;
- Whether the patient is on the correct antibiotics (as well as if the therapy is at the right route and dose of administration);
- If a more targeted antibiotic can be used (especially if a narrower spectrum antibiotic will be sufficient);
- And, how long the patient should receive the antibiotic treatment.

Importantly, this review is performed alongside the culture and sensitivity data provided by the microbiology laboratory. These data will also provide information on drug resistance as well as the sensitivity of antibiotics to the isolated organism. If changes are deemed necessary following the review, there are several potential actions available: continuing treatment, stopping therapy, switching the route, changing the antibiotic, or discharging the patient with a continued course of antibiotics.

The review and subsequent changes to antibiotic treatment should occur in a timely manner, as soon as culture results are available or if the patient's condition is altering. HIT can support this process by alerting clinicians to view the results or by providing reminders that a review is required. HIT can further alert clinicians to ~~these~~ consider potential actions: for example, switching to an alternative therapy in the presence of a drug-organism mismatch, or switching from IV to oral antibiotics when the patient is eating/drinking/taking other treatments orally and appropriate treatments are available to take by mouth. These alerts can help to reduce the time between the availability of culture results and the review of antibiotic treatment. This is particularly important for AMS efforts as switching from initial therapy to a more optimal, appropriate therapy can minimise deleterious effects to patient health,[15] contribute to an earlier discharge,[9] minimise cost,[13] and reduce the risk of resistance.[13] HIT can further support review and subsequent therapeutic changes by facilitating access to relevant protocols: e.g. extended infusion of antibiotics, parenteral to oral switch or Out-Patient Antibiotic Therapy (OPAT). However, further research is needed to explore how HIT can support the behavioural components involved in reviews as healthcare professionals can be reluctant to revisit and change a decision previously made by a doctor.

Comment [KA9]: Amended in response to reviewer's comment: "it is unclear whether the authors mean that switching from IV to oral antibiotics would happen automatically when a record was made that the patient was able to eat or drink or whenever other treatments were given by mouth"

(b) Review by AMS champions

Alongside the work of individual practitioners in the medication process, AMS programmes are more effective when driven by a focused group of healthcare professionals.[13] Often termed the AMS Committee, or AMS Champions, this group supports many components of the AMS agenda (Figure 3) including the provision of face-to-face specialist review or support to clinical teams during complex patient cases. Important to the work of committees and champions is the ability to have oversight of all antibiotic prescriptions across the hospital. This oversight can be considerably enhanced through the use of monitoring systems (Box 1, *Example 2*). These systems can aggregate and organise data from many sources across the hospital into actionable alerts. Data can come in the form of resistance and susceptibility information, as well as information about patients, treatments, and indications. AMS committees can gain an overview of all patients on antibiotic therapy through these systems. The most urgent cases can also be made visible, enabling the prioritisation of patient review.

AMS committees also update antimicrobial guidelines and protocols, and inform the formularies that can be made available within the EHR. Further, committees can monitor adherence to guidelines and protocols with the help of HIT to identify wards, clinical teams or individual prescribers who may require further support as well as to inform the update of hospital policies.

Over longer timeframes (months to years), collecting and reusing data

As discussed above, HIT has much to offer the AMS process at the point of care. Many components of the AMS agenda can also provide benefits over longer timeframes, especially those supported by HIT. EHRs and ePrescribing systems can aggregate longitudinal prescribing data at multiple levels: individual clinicians, clinical teams, wards, and hospitals. This enables comparison of inappropriate prescribing rates (Box 1, *Example 3*). Meeker et al (2016) describe an intervention based on behavioural economics that contacted each prescriber via email reporting whether the prescriber was a "Top Performer" or "Not a Top Performer", as defined by their proportion of inappropriately prescribed antibiotics. Due to the positive reinforcement and social motivation behind this intervention, inappropriate antibiotic prescribing was significantly reduced.

Over longer timeframes, HIT can also enable further audit and feedback, monitoring, and benchmarking of antimicrobial prescribing practice. These functions can support clinicians, pharmacists, and AMS committees in further promoting the AMS agenda as well as lead to inter-hospital comparison. For example, in the UK there is a national benchmark indicator derived in many hospitals from HIT data to compare the total consumption of carbapenem antibiotics (a broad spectrum class agent) per 1,000 admissions as part of the NHS Commissioning for Quality and Innovation (CQUIN) targets in 2016/17.[28] Ultimately, data-driven surveillance can help to better define and direct effective AMS strategies, as well as continuously assess hospitals systematically at the local, regional, national, and international level.

These developments over longer timeframes can all feed back into HIT systems to further optimise future therapeutic decisions, improve outcomes, and reduce resistance to antibiotics.

The future of HIT-mediated AMS

There exist many further areas of HIT support that are either in the early stages of evaluation in pilot hospitals or are still in the development pipeline. Many of these involve the improvement of existing system design to more accurately transmit actionable information throughout the hospital (such as the potential for specific microbiology results to prompt urgent alerts, as discussed above).

Predictive modelling[29] is another emerging possibility for AMS support that has the potential to optimise the initial prescription of antibiotics. By bringing together information regarding an individual patient's risk factors for resistance and susceptibility to certain antibiotics, predictive modelling tools may aid in the selection of optimal antibiotic therapy at the level of the prescriber. Point-of-care diagnostic tests also offer the possibility of selecting optimal routes of care on the ward through the rapid identification of infectious agents.

HIT can also enable further data collection for audit and feedback. These data are important for benchmarking hospitals against others to evaluate AMS interventions and to better understand the barriers and facilitators to implementation.

Cloud-based EHRs are on the horizon which will raise the possibility of expanding HIT support from the antibiotic prescription and review lifecycle on the ward to an extended antibiotic lifecycle: one that follows patients through their hospital admission, discharge, and back into the community. Further support in the community is expected to come in the form of patient access to information and education about appropriate treatment and avoiding overuse of antibiotics. These approaches can also support those in the community who have different needs around antibiotics, such as expert patients with long-standing conditions (e.g. for a patient with cystic fibrosis, the timely administration of antibiotics is often more important than avoiding overuse of antibiotics). With the aim of empowering patients and involving them in the decision-making process around antibiotics, patients will soon be able to access information about their resistance patterns.[30]

Conclusions

AMS is a national and global priority being implemented to reduce the risk of antimicrobial resistance. HIT is both maturing and converging, and as a result offers considerable opportunities by supporting: access to relevant data (e.g. personal and local antibiotic resistance patterns) and antimicrobial guidelines, documentation of diagnoses, initial selection of empirical treatment, review, audit and feedback, and monitoring. The most effective HIT-enabled AMS interventions are likely to be multi-faceted, consisting of many of these different components in tandem with behavioural changes. Importantly, any implementation requires careful planning and integration with existing systems, as well as staff engagement and participation. HIT processes alongside education, training, and person-person interaction between staff as well as with patients will be most effective in comprehensively supporting AMS.

This paper provides a starting point for how these components may be conceptualised alongside the existing processes surrounding antibiotic prescription and review. Research in this area needs to be prioritised in order to ensure that the considerable potential offered by developments in HIT in relation to AMS are realised in a timely fashion.

Declarations

Competing interests

The authors declare that they have no competing interests.

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Guarantor

AK is the guarantor.

Contributorship

Comment [KA10]: Added in response to reviewer's comment: "Support can also be given by cloud-based EHRs for expert patients with long-standing problems, who have specific needs in the community (e.g. people with cystic fibrosis) and who may need more timely antibiotics rather than avoiding overuse of antibiotics"

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Comment [AK11]: Added in response to editorial comment 1: Provide a competing interests statement for all authors.

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Comment [AK12]: Full details of funding and sponsorship have been included in response to editorial comment #6: Please provide full details of funding and sponsorship of the paper.

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Comment [AK13]: AK has been nominated as a guarantor of the work in response to editorial comment #7 (Please nominate an author as a guarantor for the work. The guarantor accepts full responsibility for the work and/or the conduct of the work, had access to the data, and controlled the decision to publish). AK accepts full responsibility for the work and the conduct of the work, had access to the data, and controlled the decision to publish.

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AK wrote the first draft of the paper. All authors contributed to further drafts and all approved the final version.

Comment [AK14]: This statement has been added in response to editorial comment #8: Please provide a contributorship statement.

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References

1. World Health Organization. Antimicrobial resistance: 2014 global report on surveillance. World Health Organization. 2014

2. Levy SB. The antibiotic paradox: how the misuse of antibiotics destroys their curative powers. Da Capo Press, 2002.

3. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. Clinical Infectious Diseases. 2006; 42: S82-S9.

4. Centres for Disease Control and Prevention (US). Antibiotic resistance threats in the United States, 2013. Centres for Disease Control and Prevention, US Department of Health and Human Services. 2013.

5. World Health Organization. Global action plan on antimicrobial resistance. 2015

6. O'Neill J. Review on antimicrobial resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations Available online: http://amr-review org/sites/default/files/AMR% 20Review% 20 Paper. 2014.

7. Goldmann DA, Weinstein RA, Wenzel RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals: a challenge to hospital leadership. Jama. 1996; 275: 234-40.

8. Fishman N. Antimicrobial stewardship. American journal of infection control. 2006; 34: S55-S63.

9. Evans RS, Pestotnik SL, Classen DC, et al. A computer-assisted management program for antibiotics and other antiinfective agents. New England Journal of Medicine. 1998; 338: 232-8.

10. Braxton CC, Gerstenberger PA and Cox GG. Improving antibiotic stewardship: order set implementation to improve prophylactic antimicrobial prescribing in the outpatient surgical setting. The Journal of ambulatory care management. 2010; 33: 131-40.

11. Srinivasan A. Engaging hospitalists in antimicrobial stewardship: the CDC perspective. Journal of hospital medicine. 2011; 6: S31-S3.

12. Shlaes DM, Gerding DN, John JF, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. Clinical infectious diseases. 1997; 25: 584-99.

13. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clinical infectious diseases. 2007; 44: 159-77.

14. Cresswell K, Mozaffar H, Shah S and Sheikh A. A systematic assessment of review to promoting the appropriate use of antibiotics through hospital electronic prescribing systems. International Journal of Pharmacy Practice. 2016.

15. Evans RS, Pestotnik SL, Classen DC and Burke JP. Evaluation of a computer-assisted antibiotic-dose monitor. Annals of Pharmacotherapy. 1999; 33: 1026-31.

16. Cresswell K, Smith P, Swainson C, Timoney A and Sheikh A. Establishing data-intensive healthcare: the case of Hospital Electronic Prescribing and Medicines Administration systems in Scotland. Journal of Innovation in Health Informatics. 2016; 23: 572-9.

17. Public Health England. Start Smart - Then Focus. Antimicrobial Stewardship Toolkit for English Hospitals March 2015.

18. Cresswell K, Bates DW and Sheikh A. Six ways for governments to get value from health information technology.

19. Shojania KG, Jennings A, Mayhew A, Ramsay C, Eccles M and Grimshaw J. Effect of point-of-care computer reminders on physician behaviour: a systematic review. Canadian Medical Association Journal. 2010; 182: E216-E25.

20. Bates DW, Leape LL, Cullen DJ, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. Jama. 1998; 280: 1311-6.

21. Schiff GD, Vazquez ES and Wright A. Incorporating Indications into Medication Ordering—Time to Enter the Age of Reason. 2016.

22. Eliopoulos GM, Paterson DL and Rice LB. Empirical antibiotic choice for the seriously ill patient: are minimization of selection of resistant organisms and maximization of individual outcome mutually exclusive? Clinical infectious diseases. 2003; 36: 1006-12.

23. Meehan TP, Fine MJ, Krumholz HM, et al. Quality of care, process, and outcomes in elderly patients with pneumonia. Jama. 1997; 278: 2080-4.

24. Jensen JU, Hein L, Lundgren B, et al. Procalcitonin-guided interventions against infections to increase early appropriate antibiotics and improve survival in the intensive care unit: a randomized trial. Critical care medicine. 2011; 39: 2048-58.

25. Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. Jama. 2016; 315: 562-70.

26. Brooks H, Hodson J, Richardson S, Stezhka L, Gill M and Coleman J. Improving the timeliness of meticillin-resistant Staphylococcus aureus antimicrobial decolonization therapy administration: a descriptive account. Journal of Hospital Infection. 2014; 86: 209-15.

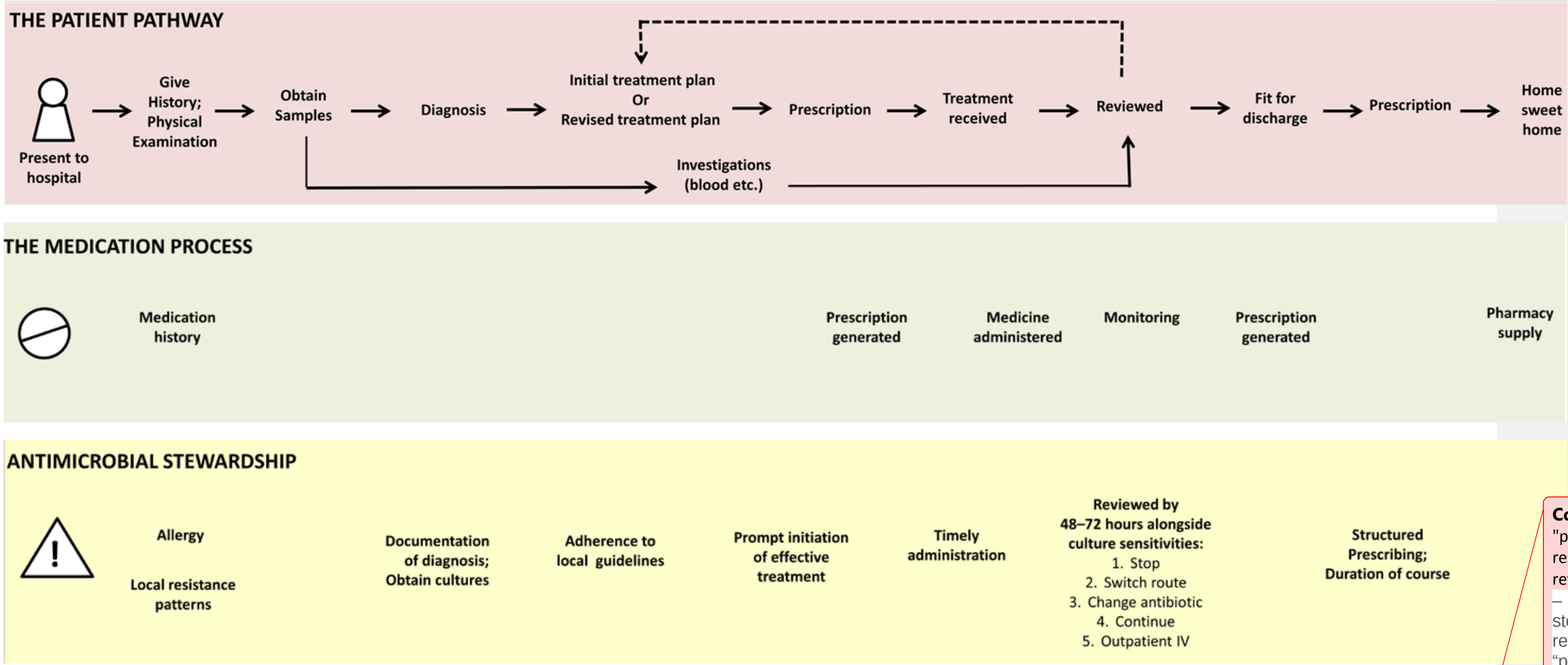
27. National Institute for Health and Care Excellence (NICE). Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. NICE guideline [NG15]. 2015.

28. NHS England/ Contracting and Incentives Team. NHS England: Commissioning for Quality and Innovation (CQUIN) - Guidance Technical Annex for 2016/17. 2016.

29. Martínez JL, Baquero F and Andersson DI. Predicting antibiotic resistance. Nature Reviews Microbiology. 2007; 5: 958-65.

30. Wachter RM. Making IT Work: Harnessing the power of health information technology to improve care in England. Department of Health, London, 2016.

Figure 1. Conceptual schema of an archetypal antibiotic lifecycle through prescription and review within a UK hospital setting.



Comment [KA15]: Changed "previous resistance" to "local resistance patterns in response to reviewers comment: Figures 1 and 2 – in the section on antimicrobial stewardship, the phrase "previous resistance" should be written as "personal resistance patterns" as described in the text, as I initially thought that this referred to local resistance patterns.
We have added "local" to the text to qualify the resistance patterns rather than "personal" as the latter is not a commonly utilised description in practice.

Figure 2. HIT support of the antimicrobial stewardship agenda.

Table 1. Hypothetical antibiogram of Gram negative and Gram positive isolates from urine cultures.

Antibiograms summarise antibiotic susceptibilities in order to facilitate the selection of appropriate antibiotic therapy. In the past, antibiograms were updated annually. Presently, through the help of HIT, antibiograms are updated continually as new susceptibility data becomes available. Antibiograms can be filtered to show prescribers susceptibility patterns for the region, the institution, and the ward.

Organism Group	ampicillin	amoxycillin	cefazolin / cephalexin	gentamicin	ceftriaxone	piperacillin + tazobactam
Escherichia coli	46%	78%	57%	96%	97%	S
	n=415	414	415	415	416	
Klebsiella species	R	89%	68%	96%	98%	S
		55	56	56	56	
Proteus mirabilis	91%	94%	76%	100%	100%	S
	33	33	33	33	33	
Pseudomonas aeruginosa	R	R	R	93%	R	97%
				43		38
Staphylococcus saphrophyticus	100%	S	S	n/a		S
	38					
Enterococcus faecalis	98%	S	R	R		S
	145					

Gram negative organism	
Gram positive organism	

n/a	not available (not routinely tested in local laboratory)
S	Susceptible by extrapolation
R	Instrinsically resistant
%	% isolates susceptible
n=	number of strains tested

Box 1: Clinical examples of inappropriate use of antibiotics targeted and remedied by HIT intervention

Examples draw on preliminary explorative work investigating HIT-enabled AMS strategies in international benchmark hospitals.

Example 1: Antibiogram

Antibiograms are available on smart phones and accessible to prescribers at the point of care. Clinicians at one large, city hospital use antibiograms to look up antimicrobials and infectious organisms to get a real time sense of resistance patterns, either within the whole hospital or specifically on a single unit. Antibiograms also provide clinicians at this hospital with sensitivity data of specific vectors in their health system to specific antibiotics. This is helpful when selecting initial antibiotic treatment for a patient whilst awaiting cultures and sensitivities.

Example 2: HIT enables a focused review of patients on antimicrobials

At one academic medical centre, a monitoring system organises microbiology results alongside prescription, diagnosis, and patient data. This system alerts members of the stewardship team to situations where antimicrobials have the potential to be optimised. This robust system of alerts can capture most concerns related to AMS by organising information and focusing AMS efforts to where they are most needed. Before the implementation of this monitoring system, pharmacists at this hospital had to review all antibiotic prescriptions to find an intervention. This took a great amount of time and resulted in the absence of review for some of the most complex and high risk cases. With the HIT system in place, pharmacists gain an overview of all patients on antimicrobials as well as knowledge of which patients need to be prioritised.

Example 3: HIT enables reporting of antimicrobial usage

At one of the pioneer hospitals in AMS, HIT enables intervention on the level of the user by reporting antimicrobial usage of individual prescribers and wards. Prescribing statistics are reported to individual clinicians, benchmarking them against their peers. Reporting encourages personnel to become engaged in the stewardship process and to expand the reach of the AMS programme.

Figure 3. Support of the antimicrobial stewardship agenda through AMS committees and champions.