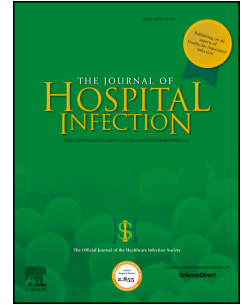# Accepted Manuscript

Critical points in the pathway of antibiotic prescribing in a children's hospital: the Antibiotic Mapping of Prescribing (ABMAP) study

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Critical points in the pathway of antibiotic prescribing in a children's hospital: the Antibiotic Mapping of Prescribing (ABMAP) study

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Background

The WHO has identified Antimicrobial Resistance (AMR) as one of the most significant global risks facing modern medicine. Interventions to improve antibiotic prescribing have so far had limited impact.

Aim

To understand the barriers to effective antibiotic prescribing.

Methods

Mixed methodologies were used to investigate prescribing behaviours to identify the critical points in the antibiotic prescribing pathway for hospital inpatients. We assessed knowledge, experience or empowerment of prescribers, organisational factors and use of the laboratory. Phase 1 was an online survey to map barriers and facilitators to antibiotic prescribing (56 participants). Phase 2 consisted of focus groups and interviews to gain more understanding of prescribing behaviours (10 participants). Phase 3 was an online survey to obtain opinions on possible solutions (22 participants).

Results

Barriers to prescribing were: laboratory factors 71.6%, resource issues 40%, time constraints 17.5%, pressure from others 52%. Ninety-three percent of prescribers were concerned about AMR. In three scenarios only 9% were confident not to prescribe antibiotics for a patient without bacterial infection; 53% would prescribe unnecessarily broad spectrum antibiotics for pneumonia. Only 5% would de-escalate antibiotics in a microbiologically-confirmed bacteraemia.

Despite concerns about AMR, prescribers did not perceive continuing antibiotics for individual patients might promote resistance. Prescribers were unwilling to change antibiotics out of hours and reported they preferred professional support for antibiotic prescribing.

Conclusions

There was a marked disparity between prescribers self-reporting of prescribing behaviour and responses to clinical scenarios. It was not clear whether training alone would change behaviours. Prescribers desired a directive mechanism to support antibiotic prescribing and stewardship.

Introduction

The emergence of extensively drug-resistant and pandrug-resistant bacteria has been identified by the World Health Organization as one of the most significant global risks facing modern medicine [1]. In the UK, annual antibiotic awareness campaigns have been promoted since 1999, and in 2011 the `Start Smart - Then Focus' antibiotic stewardship toolkit, that provided an outline of evidence-based antimicrobial stewardship in the secondary healthcare setting, was published [2]. Globally, there have been many other similar initiatives [1, 3]. However, this emphasis on antibiotic stewardship has so far had limited impact on reducing antibiotic use in hospitals. In England, the number of antibiotic prescriptions in secondary care increased by 6.5% between 2012 and 2016, with an increase of 2.6% since 2015 [4].

Antibiotic stewardship in hospitalized children presents a particular challenge. According to Gerber and co-workers, 60% of children may receive antibiotics during their hospitalization [5]. Not only are more children than adults prescribed antibiotics, but there have been fewer incentives to restrict antibiotic use in in children, for example to prevent *Clostridium difficile* infections. Another important consideration in paediatrics is parental expectations of antibiotic treatment for their children [6].

The barriers to effective antibiotic stewardship are substantial and complex. In 2015, a Department of Health report identified that few studies have addressed behaviours that support antibiotic stewardship, and encouraged research in this field to contribute to the fight against antimicrobial resistance [7]. More recently a systematic review of antimicrobial stewardship programmes in children found there is limited evidence for a reduction in

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antibiotic consumption and use of broad-spectrum/restricted agents following antibiotic stewardship programme implementation [8].

It is our opinion that a successful and sustainable antibiotic stewardship programme will require a bundle approach that addresses all the key processes involved in antibiotic prescribing [9]. However, whilst organisations such as the WHO [1], CDC [3] and the UK Department of Health [10] have published multi-point plans to address antibiotic stewardship, most research in antibiotic prescribing has focused on a single element, for example education-based interventions [11].

In our study, we used a novel mixed methodology approach to investigate antibiotic prescribing behaviours. The aim was to identify the critical points in the antibiotic prescribing pathway for inpatients in a paediatric hospital. Specifically, we sought to understand the extent to which antibiotic prescribing decisions are driven by matters such as lack of knowledge, experience or empowerment of prescribers, organisational factors, suboptimal access to, or use of, laboratory tests, and factors relating to the built environment. Understanding all stages of the antibiotic prescribing pathway should identify the key elements that need to be included in an antibiotic prescribing bundle for children.

Methods

Setting

Birmingham Children's Hospital is a 250-bed teaching hospital in the West Midlands (United Kingdom) that provides a wide range of secondary and tertiary paediatric services. The hospital has an onsite laboratory service (with online test requesting and results access) and an antibiotic pharmacist. There is no formal antimicrobial stewardship team outside routine working hours, but clinical teams can and do contact the on call microbiologist for antimicrobial prescribing advice. Medical records and drug prescriptions are paper-based. Antibiotic prescribing guidelines are available on the Trust intranet and via an app for Apple and Android users. Complex patients are treated across the hospital, and hence there is no restriction on use of broad spectrum antibiotics such as meropenem. However, a prescription of some antibiotics such as linezolid requires microbiology approval.

The study

The study was conducted in three phases. During Phase 1, a 20 item questionnaire was developed, which consisted of 9 demographic questions, 8 questions on prescribing behaviour and 3 scenario-based vignettes and open/closed questions. The aim was to develop a picture of the critical points in the pathway for antibiotic prescribing in the setting of a paediatric hospital. The questionnaire was piloted with staff from the hospital and the final version was distributed online through the hospital's internal mailing list. In Phase 2, focus groups and individual interviews were held to explore prescribers' views and experiences, in more depth. Phase 3 of the study was a 16 item questionnaire, which

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included the same 9 demographic questions as Phase 1 and 7 open/closed questions to obtain opinions on possible solutions that were devised using the findings of Phases 1 and 2.

The surveys used the Bristol Online Survey (BOS) platform (Jisc, Bristol, UK). Participation was anonymous and voluntary. The study was approved by the Aston University Research Ethics Committee (UREC).

Results

Phase 1

A total of 56 medical prescribers who regularly prescribed antibiotics completed the online survey. Of those, 25 participants had >10 years', 16 participants had 6-10 years' and 15 had ≤5 years' experience. 93% of prescribers were concerned about AMR and 64% were concerned about antibiotic related side effects.

Twenty-two (39.3%) participants reported being pressurised into prescribing antibiotics that they did not think were necessary in the preceding 12 months (Table I). Such pressure mainly came from senior medical colleagues and patients' families. There was a marked disparity between junior and senior staff with seventeen of the twenty-four (70.8%) junior staff reported having being pressurised compared with only five of thirty two (15.6%) consultants. The great majority (84%) of participants did not report that time constraints influenced their antibiotic prescribing (Figure 1). However, over half (59%) reported that laboratory factors were a regular barrier to antibiotic prescribing; the most common difficulty was results not being available when required.

Approximately a quarter (26%) of participants either had never had any antibiotic training or could not recall when they last received training; 77.3% were consultants. A further 21.4% last received training more than three years ago. However, only 23% of participants indicated they had a lack of antibiotic related training or knowledge; 80% of were junior prescribers. 40%, (n=27) of participants experienced a range of resource issues that

regularly (that is at least once a week) impacted on their decision whether or not to prescribe an antibiotic or to review an existing antibiotic prescription. The most common resource issue was inability to access antibiotic prescription guidelines.

Clinical scenarios

Scenario 1 was designed to assess prescribers' abilities to interpret positive microbiology results that may not be significant (Figure 2). Only 8.9% of respondents were confident autonomously to not treat unexpected bacteriuria in an asymptomatic child with no pyuria. Scenario 2 tested prescribers' willingness to prescribe narrow-spectrum antibiotics in a child with community-onset pneumonia, who was known to have gastrointestinal colonization with Extended Spectrum Beta Lactamase (ESBL) producing *Escherichia coli* (Figure 3). Almost half of prescribers were confident in selecting usual narrow spectrum antibiotics, although 16.4% indicated that they would prescribe meropenem. Scenario 3 tested prescribers' willingness to de-escalate antibiotic therapy in response to a positive microbiology result; only 5.5% were prepared to de-escalate broad-spectrum antibiotic therapy to benzyl penicillin to treat confirmed group A streptococcus sepsis (Figure 4).

Phase 2

Three main themes surfaced in the focus group discussions: despite concerns about AMR, prescribers did not associate continuing antibiotics for individual patients with a societal risk of antibiotic resistance; prescribers working out of hours were unwilling to change

antibiotics; prescribers of all grades reported they needed a clear decision-making mechanism to change current practice.

Phase 3

Phase 3 of the study was completed by 22 medical prescribers. Of those, 7 participants had >10 years', 7 participants had 6-10 years', and 8 participants had up to 5 years' experience. Prescribers expressed a strong preference for direct instruction on antibiotic prescribing, rather than being given data upon which to base their own decisions. Professional advice was preferred to electronic support (Table IIa). Where prescribers were offered options for electronic support, they preferred didactic algorithms to any other solution (Table IIb). Most prescribers (95%) indicated that it would be useful to have a single direct access portal to access antibiotic prescribing advice; 12 (57%) favoured this being telephone-based, 7 (33.3%) preferred an online system, and only 2 (9.5%) wanted a SMS-based system. Only a third of prescribers felt that they needed support on an out of hours basis. To obtain earlier laboratory results, respondents preferred these to be available on ward-based PCs; there was little support for the concept of dedicated electronic information points to access laboratory results (Table III). When asked about the content of any future training on antibiotic stewardship, prescribers indicated that a broad range of subjects needed to be covered (Table IV).

Discussion

At least two of the five strategic objectives in the WHO Global Action Plan on Antimicrobial Resistance relate directly to the everyday prescribing practice, that is improving awareness and understanding of antimicrobial resistance through effective communication, education and training, and optimizing use of antimicrobials in human and animal health [1]. Likewise, the UK Five Year Antimicrobial Resistance Strategy includes objectives of optimising prescribing practice and improving professional education and training [10].

In recent years, many papers have been published on measures to improve antibiotic stewardship. However, these have mostly addressed only one element underpinning antibiotic prescribing. Moreover, it has been noted that most antibiotic stewardship programmes have encountered significant barriers to success [12]. The challenge of successfully implementing an antibiotic stewardship campaign is underlined by our observation of the contradiction between prescribers' understanding and practice. Whilst 95% of prescribers responded that they were concerned about AMR, when their practice was tested in clinical vignettes, most of them were inclined to over treat with antibiotics.

Education is widely held to be one of the cornerstones of antibiotic stewardship programmes [11, 13] and in England, the Health and Social Care Act requires that all prescribers receive induction and training in prudent antimicrobial use (14). However, almost half the participants in our study did not recall receiving any training in at least the last three years. Given that the volunteer participants in the study were likely to be amongst

the most motivated of antibiotic prescribers, this was surprising. However, during the focus groups it became clear that most senior doctors did not perceive that they required further training on antibiotic stewardship.

A recent review of antimicrobial stewardship training noted that although almost all studies of antibiotic stewardship training have reported positive results, there is a lack of rigorous evaluation of the true effectiveness of education programmes [15]. There is also no clarity on how training should be delivered. Although e-learning has become widely used as a means of delivering training on antibiotic stewardship [11], a recent Cochrane review of e-learning for health professionals concluded that compared to traditional learning, e-learning may make little or no difference in patient outcomes or health professionals' behaviours, skills or knowledge [16]. Guidelines have identified that an extensive curriculum of antibiotic stewardship training is required, and our results show that prescribers themselves recognise that.

It is possible that the lack of comprehensive education on antibiotic prescribing influenced participants' responses to questions about the support they needed for antibiotic stewardship. Prescribers of all degrees of seniority expressed a strong preference for direct support in antibiotic decision making. Their preference was for professional support from an infection team member, which fits with the observations by Doernberg *et al.,* that each 0.50 increase in pharmacist and physician full-time equivalent support, predicted a 1.48-fold increase in the odds of demonstrating effectiveness of antibiotic stewardship programmes [15]. The preference for didactic support was also expressed when prescribers were asked

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about IT-based solutions in more detail in phase 3, in that they preferred a support tool that gave instruction, rather than information to help them make their own decisions. This reflected the earlier opinions in the focus groups, that prescribers would be unwilling to change antibiotics on an out of hour's basis, whatever support was available to them at that time.

Prescribers expressed a very clear preference for the most expensive solution to antibiotic stewardship that is hiring additional specialists for support. However we speculate that one of the reasons for the negative attitude towards decision support tools in phase 3, may be that prescribers cannot envisage the degree of support that a properly designed tool may offer. Recognising this we propose future research on a support tool prototype.

Prescribers were also critical of laboratory services, with around 25% of participants saying that delays in laboratory results reporting impacted on their antibiotic prescribing. The apparent dichotomy between prescribers' unwillingness to take individual responsibility for actions in response to laboratory test results, and their desire for more rapid laboratory test results needs to be addressed in any support tool and if new or improved rapid and/or point-of-care diagnostic tests are to become an effective element of stewardship strategies.

The strength of our study is that it provides a comprehensive assessment of the experiences and opinions of a good number of medical antibiotic prescribers in a children's hospital. Because most of the research team were unaffiliated to the hospital, it is likely that the

opinions expressed by participants were unbiased. However, this was a single centre study, performed in a specialist children's hospital, where there are no IT-based solutions to antibiotic prescribing and there is no formal provision of an antibiotic stewardship team over the whole 24 hours, 7 days a week. As such, the findings of this study may not be generalizable to all hospital settings.

Conclusions

Our study showed that whilst there was general awareness of the importance of antibiotic stewardship, prescribers at all levels of seniority indicated that they lacked confidence to manage antibiotic treatment optimally. Whilst in the longer term a comprehensive education programme beginning at undergraduate level, and continuing throughout prescribers' careers, may change antibiotic prescribing behaviours, our study suggests that in the shorter term, prescribers will require considerable support, preferably in the form of specialist personnel, if antibiotic stewardship goals are going to be met.

Acknowledgements

Transparency declarations

None to declare

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Table I: Influences on prescribing antibiotics that the prescriber did not think were necessary (Respondents were permitted to select more than one option).

Number (%) of 56 prescribers who indicated that they had been pressured into prescribing antibiotics that they did not think were necessary because of influence from:						
Senior Medical colleagues	Medical colleagues at same grade as you	Nurses	The patient, or their carer/parents	Time of day when you are prescribing	Other	I have not experienced this
12 (21.4)	3 (5.4)	1 (1.8)	9 (16.1)	5 (8.9)	4 (7.1)	34 (60.7)

Table IIa: Ranking of factors that may provide prescribers with reassurance that it is safe to stop or change an antibiotic prescription on the basis of preliminary microbiology results (1 = most confidence, 3 = least confidence)

Factors	Number (%) of responses		
	1	**2**	**3**
Daily report of the progress of laboratory tests	8 (36.4)	5 (22.7)	9 (40.9)
Electronic guidance in addition to daily reports of the progress of laboratory tests	2 (9.1)	8 (36.4)	12 (54.5)
Antibiotic professional support in addition to the daily reports of the progress of laboratory tests	12 (54.5)	5 (22.7)	5 (22.7)

Table IIb: If a tool was available to guide your antibiotic prescribing decisions (either before or after preliminary microbiology results were available) which of the following would give you confidence to use this tool? Please rank the options (1 = most confidence, 3 = least confidence)
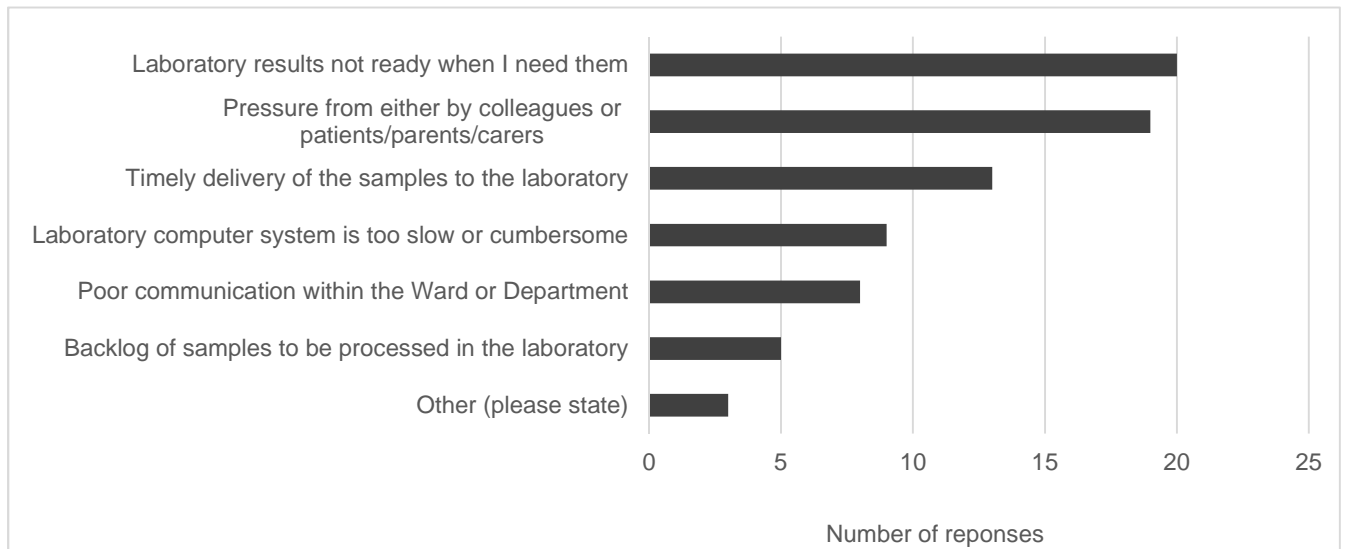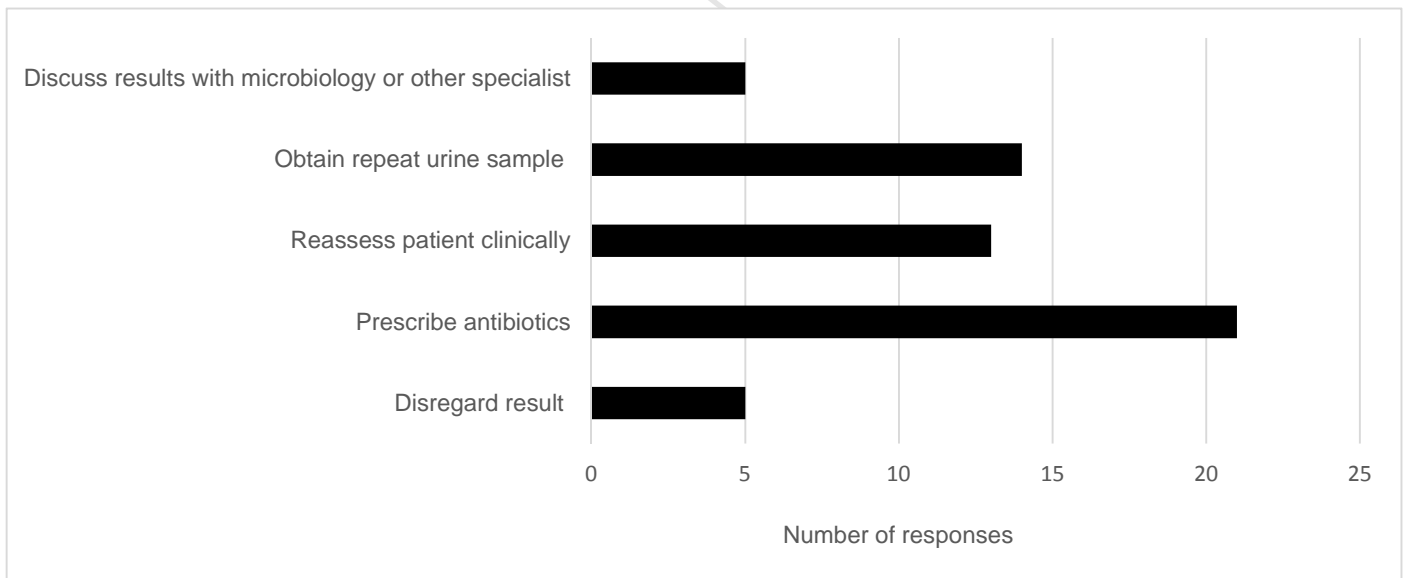
Format of decision making tools	Number (%) of responses		
	1	**2**	**3**
An algorithm to aid appropriate antibiotic prescription, based on risk factors for antibiotic resistance in the individual patient	18 (81.8)	3 (13.6)	1 (4.5)
Statistical data to allow you to understand the likelihood of patients having infection with antibiotic-resistant bacteria. This might include data showing the overall risk of any patient having infection with an antibiotic-resistant bacterium, &/or the risk of a patient colonised with an antibiotic-resistant bacterium becoming infected with the same organism	3 (13.6)	11 (50)	8 (36.4)
Data on how similar patients were treated, and their outcomes	1 (4.5)	8 (36.4)	13 (59.1)

Table III: Ranking of electronic means of delivery of early laboratory results (1 = most preferred, 3 = least preferred)

| Electronic format	Number (%) of responses		
	1	**2**	**3**
Portable electronic devices	4 (19)	14 (66.7)	3 (14.3)
Dedicated electronic information points	4 (19)	5 (23.8)	12 (57.1)
Availability on the ward PC to check results	13 (61.9)	2 (9.5)	6 (28.6)

Table IV: Which of the following do you think antibiotic training and education should cover? Please tick all of the options which apply.

Option	*n*
Data relating to antibiotic resistance at the local, regional, national and international level	18
Risks of inappropriate antibiotic use	19
Wider impact of individual antibiotic prescribing decisions for example the risk to other patients from commencing a patient on broad spectrum antibiotics	19
Factors which guide reviewing and stopping antibiotic treatment	20
Factors which guide antibiotic prescribing decisions	21

Figure 1: laboratory factors influencing antibiotic prescribing

Laboratory results not ready when I need them
Pressure from either by colleagues or patients/parents/carers
Timely delivery of the samples to the laboratory
Laboratory computer system is too slow or cumbersome
Poor communication within the Ward or Department
Backlog of samples to be processed in the laboratory
Other (please state)

Number of reponses

Figure 2: responses to clinical scenario 1 (patient with unexpected asymptomatic bacteriuria)

Discuss results with microbiology or other specialist
Obtain repeat urine sample
Reassess patient clinically
Prescribe antibiotics
Disregard result

Number of responses

Figure 3: responses to clinical scenario 2 (patient with community acquired pneumonia and carriage of ESBL producing *E.coli*)
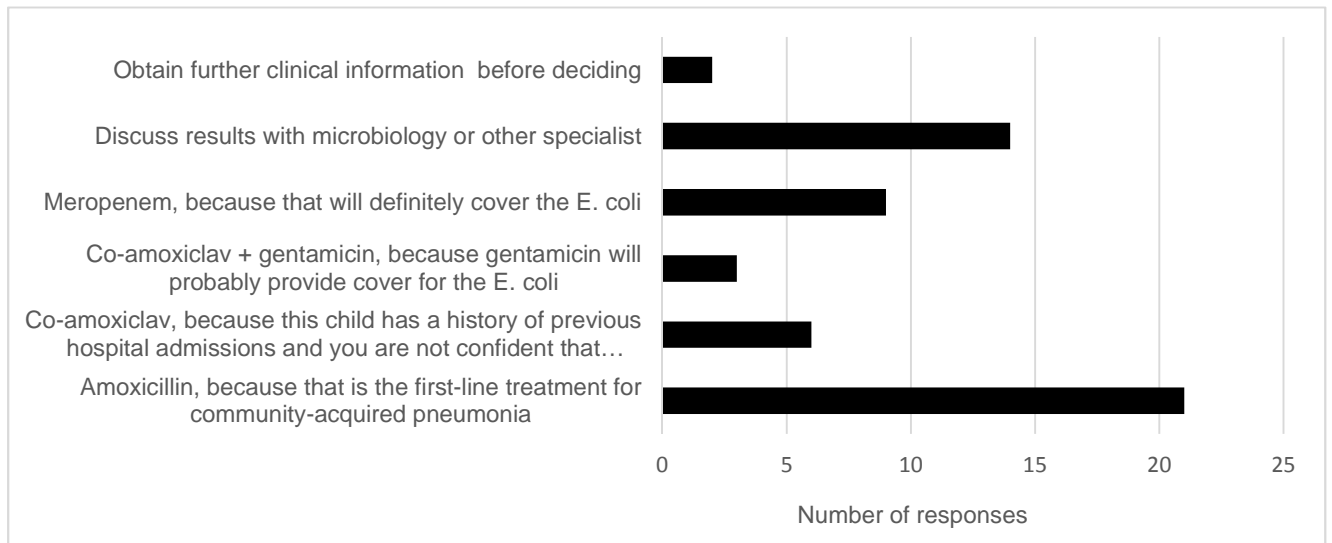
Figure 4: responses to clinical scenario 3 (patient with Group A streptococcus)