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Title: How Do Pharmacists Select Antimicrobials? A Model of Pharmacists' Therapeutic Reasoning Processes

Running Title: Pharmacists' Antimicrobial Reasoning

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Abstract

INTRODUCTION: Clinicians engage in clinical reasoning, comprised of both diagnostic and therapeutic components, when caring for patients. While diagnostic reasoning has been extensively investigated, relatively few studies have examined how clinicians make treatment decisions. Recent work has explored how physicians engage in therapeutic reasoning while selecting antimicrobials. However, understanding pharmacists' antimicrobial reasoning is equally important due to their role in ensuring appropriate antimicrobial use. Therefore, we aimed to further our understanding of antimicrobial reasoning in pharmacists and compare their reasoning processes to physicians.

METHODS: With a post-positivist orientation and using a general qualitative approach, we conducted semi-structured interviews with hospital-based pharmacists specializing in infectious diseases or other hospital-based specialties. Participants narrated their thought processes while selecting antimicrobials for three case vignettes. We analyzed transcripts iteratively using a code book from a prior study of antimicrobial reasoning in physicians as a sensitizing framework.

RESULTS: Participants included 11 pharmacists (5 infectious diseases and 6 non-infectious diseases pharmacists). Overall, participants' responses reflected a three-step reasoning process: *Naming the Syndrome*, *Delineating Pathogens*, and *Selecting the Antimicrobial*. Patient-, syndrome-, and system-based factors interacted with drug characteristics to influence the selection of specific antimicrobial regimens.

CONCLUSION: We identified a framework for pharmacists' antimicrobial therapeutic reasoning similar to physicians' reasoning, with some nuances that may be attributable to

the pharmacists' role in medication review and antimicrobial stewardship. Application of this framework has the potential to aid in teaching, improve multidisciplinary care, and provide a framework for interprofessional communication.

Keywords: decision making; clinical skills; pharmacology

Diagnostic and management reasoning are two interrelated cognitive processes underlying health professionals' work.[1] Diagnostic reasoning studies have produced several cognitive models[2,3] supporting design of instructional strategies, curricula, and interventions aimed at reducing diagnostic errors.[4-8] Conversely, the literature lacks robust models for therapeutic reasoning, the portion of management reasoning focused on treatment selection.[9,10] While some have theorized that therapeutic reasoning may resemble diagnostic reasoning[9,11], others[12] hypothesize that therapeutic reasoning is likely more complicated given the need to incorporate multiple, competing factors that rarely results in only one 'correct' approach.

Few studies have explored how therapeutic reasoning occurs in health professionals other than physicians. Pharmacists are trained to provide safe and effective patient-centered therapeutics. Yet studies of pharmacists' therapeutic reasoning focus primarily on the 'non-maleficent' roles of pharmacists (i.e., ensuring prescriptions do not harm patients), rather than 'beneficent' roles (i.e., developing efficacious therapeutic plans).[13,14] The pharmacist patient care process (PPCP) offers a framework for providing both safe and effective patient care using five steps: collecting, assessing, planning, implementing, and monitoring/evaluating effectiveness.[15] While the PPCP provides recommendations on *what* pharmacists should think about, this framework lacks guidance on *how* pharmacists should choose between therapeutic options.[16]

Decision-making around antimicrobial selection is particularly important because of the impact that individual prescribing choices have on antimicrobial resistance.[17,18] The general conceptual frameworks that exist in antimicrobial selection[19-21] do not consider the problem-solving inherent in expert practice, nor do they provide guidance about how antimicrobials should be chosen. Because effective antimicrobial stewardship practice requires close collaboration between physicians and pharmacists[22,23], understanding similarities and differences

in how physicians and pharmacists approach antimicrobial selection might promote more effective collaboration and improve patient care.

Previously, Abdoler and colleagues explored how internal medicine (IM) and infectious diseases (ID) physicians engage in therapeutic reasoning around antimicrobial selection (antimicrobial reasoning).[24] We aimed to further this line of inquiry in hospital-based pharmacists specializing in ID and other areas, to delineate their therapeutic reasoning approaches in comparison to what has been described in physicians.

METHODS

We explored antimicrobial reasoning of hospital pharmacists from a post-positivist orientation[25], and undertook a general qualitative approach.[26] From January through April 2019, we conducted semi-structured interviews of pharmacists practicing at the University of California, San Francisco Medical Center, a 600-bed academic medical center, and the Zuckerberg San Francisco General Hospital and Trauma Center, a 300-bed county hospital. The institutional review boards of both institutions granted our study exempt status.

Participants

We invited pharmacists with a range of experience practicing in ID, IM, critical care, and emergency medicine to participate using purposive sampling to ensure a range of experience in these areas. We chose to study ID pharmacists because they collaborate with physicians to select, manage, and optimize antimicrobial regimens for complex patients requiring ID consultation. We also included non-ID pharmacists because they work with prescribers to make antimicrobial decisions for less complex cases. Both groups of pharmacists assist with antimicrobial treatment

selection, evaluate physician-ordered therapies for appropriateness (order verification), and participate in formal and informal antimicrobial stewardship activities (e.g., intravenous to oral conversion of medications, streamlining spectrum of activity).

Vignettes and interview guide development

We made minor adaptations to the semi-structured interview guide developed by Abdoler and colleagues[24] to reflect pharmacists' scope of practice. Our interview guide (Appendix) included the same three clinical vignettes involving antimicrobial selection for community-acquired pneumonia, cellulitis, and urinary tract infection with bacteremia. Vignette prompts and probes garnered detailed responses about participants' reasoning processes. Participants also wrote out the steps of their reasoning process on note cards, arranging them in order and placing simultaneous steps side-by-side. Participants did not have access to informational resources during the interview. Finally, we asked participants questions about resources they use to support their antimicrobial selection decisions.

Procedure

Participants meeting the criteria described above were invited to participate in the study via email. Participants were told the purpose of the study was to better understand how pharmacists make recommendations about antibiotic use in treating infections. Interested individuals were scheduled for a 60-minute interview based on their availability. Three investigators conducted and recorded interviews (E.A., K.G., C.M.) in-person. One investigator (E.A.) trained the other two investigators prior to starting the interviews. This investigator also led the first two

interviews, while the other investigators (K.G. and C.M.) observed. The three investigators then proceeded to conduct all interviews individually.

Analytic Approach

A professional service transcribed recorded interviews. Dedoose 8.2.14 (SocioCultural Research Consultants, LLC, Los Angles, California) was used for coding. Two investigators (E.A., K.G.) began analyzing transcripts after the first interview, using the codebook developed by Abdoler and colleagues[24] as a sensitizing framework[27] for thematic analysis. Interviews continued alongside data analysis until multiple examples were identified for each code and no new codes emerged. Another investigator (C.M.) evaluated the updated codebook for clarity and refinement. E.A. and K.G used the updated codebook to independently code each interview and then met seven times to compare code applications and resolve discrepancies, which were arbitrated by C.M.

These three investigators then used the same codebook to analyze the note card exercise, with each participant's response independently analyzed by two investigators. The three investigators met to compare their analyses, add new codes as needed, and then re-review the interview transcripts for evidence of new codes. The investigators then used the coded sequence data to generate an overall antimicrobial reasoning process and finalize the resulting themes.

Reflexivity

The majority of our research team's members have expertise in ID and these professional identities influenced our interpretation of participants' responses in ways that both deepen our understanding and also may result in assumptions differing from participants' intent. Including

pharmacists (K.G. and C.M.), physicians (E.A. and B.S.), and non-clinicians (B.O'B.) on our team provided a way to check our interpretations and minimize the risk of inferring beyond the data.

RESULTS

Participants

We interviewed 11 pharmacists, 5 ID pharmacists and 6 non-ID pharmacists representing a range of postgraduate clinical experience between less than 1 to over 15 years. Both groups of participants reported similar amounts of time dedicated to clinical care, with two participants in each group attributing less than 30% of their time to clinical care and the remainder spending more than 50% of their time providing clinical care. Three of the five ID pharmacists engaged in formal antimicrobial stewardship activities as part of their clinical time.

Antimicrobial Reasoning Process

Pharmacists' antimicrobial reasoning encompassed three steps: *Naming the Syndrome*, *Delineating Pathogens*, and *Antimicrobial (Therapy Script) Selection*. *Naming the Syndrome* involved specifying or exploring the diagnosis. For many participants, this involved confirming the physician's diagnosis and ensuring an infection was present. *Delineating Pathogens* involved identifying or seeking to identify the microbes responsible for the clinical presentation, either specifically or by general organism classes. In *Antimicrobial (Therapy Script) Selection*, participants stated a therapeutic choice or range of choices, which included varying degrees of explanation. These steps were nearly ubiquitous in participants' descriptions of their reasoning

processes across vignettes. While a few participants did not mention a particular step in any given vignette, all participants described each step at least once across the three vignettes and all participants selected an antimicrobial in every case.

Factors impacting antimicrobial reasoning

Participants mentioned 23 different factors influencing their antimicrobial reasoning process across four groups: preexisting patient characteristics, current case features, provider and health system factors, and treatment principles (Table 1). Different factors impacted the reasoning process to varying degrees and frequencies, depending upon the participant and vignette.

Preexisting patient characteristics

Participants considered how a patient's past medical history and social situation can affect the pathogens involved and/or antimicrobial choice. *Past infections* and patient *exposures* broadened or narrowed a participant's list of potential pathogens, often raising the specter of more resistant or atypical organisms. Participants described how patient factors (e.g., *age*) made certain antibiotic regimens more or less desirable, while others, such as a patient's *ability to take oral medications* or *financial factors* influenced how participants anticipated administration and cost issues, respectively. Some factors, like *comorbidities* and *past exposure to antimicrobials*, influenced both pathogen determination and antimicrobial selection.

Current case features

Participants also described how the clinical case affected their antimicrobial reasoning. *Differentiating features of the case* – such as exam findings or laboratory data – influenced

which pathogens and antimicrobials participants considered. *Microbiologic data* (e.g., cultures) helped participants define causative organisms and choose antimicrobials. The *severity of illness* led some participants to consider certain pathogens, while for others it influenced the route or antimicrobial classes they considered for treatment. In terms of *illness trajectory*, some participants mentioned that a patient's response to current antimicrobial therapy helped to refine the microbiologic differential; others noted that they considered the degree of improvement on intravenous therapy before recommending stepdown therapy to an oral medication.

Provider and health care system factors

Participants mentioned several provider and health care system factors that influenced their antimicrobial reasoning. Some participants drew upon their *clinical experience* when choosing between antimicrobials. Others discussed how *team dynamics* – including understanding the physician thought processes underlying antimicrobial choice and recognizing the practices of different teams – and their desire to support these dynamics going forward were important aspects of their antimicrobial decision-making.

Treatment principles

Participants' antimicrobial reasoning was guided to varying degrees by different underlying prescribing principles, all of which related to treatment choice. Some participants mentioned specifically the need to choose antimicrobials directed toward the likely pathogens (*pathogen-based treatment*), while others stated that the antimicrobial regimen needs to involve as few agents as possible (*parsimony*). Participants also prioritized antimicrobial choices that were

supported by evidence, guidelines, or regulatory bodies (*evidence-based/guideline-supported decisions*).

Antimicrobial (therapy) script content

Participants described 14 different drug characteristics affecting antimicrobial choice, encompassing a therapy script that represented participants' prior knowledge of a particular medication (Table 2). Participants considered these static medication features both independently and in reference to the clinical factors present in the case. For instance, if participants raised concerns about a patient's ability to adhere to an antimicrobial regimen, they would discuss antimicrobial dosing.

Resources

Participants named a variety of resources they use to support antimicrobial reasoning decisions. In addition to the antibiogram mentioned previously, participants used both internal (e.g., local empiric infection treatment guides) and external resources (e.g., Sanford Guide, Lexicomp, national treatment guidelines). Some referred to primary literature and Clinical and Laboratory Standards Institute guidance.

Antimicrobial reasoning framework

Through our analysis we developed an antimicrobial reasoning framework consisting of three steps: *Naming the Syndrome*, *Delineating Pathogens*, and *Antimicrobial (Therapy Script) Selection*, though this process was not always linear (Figure 1). For example, after *Naming the Syndrome*, some participants 'revisited the syndrome' in light of new clinical data. *Pre-existing*

patient characteristics and *current case features* affected the delineation of pathogens and antimicrobial choice, while *provider and healthcare system factors* and *treatment principles* primarily influenced antimicrobial choice. Many participants described how these factors interplayed with specific aspects of the therapy script (drug characteristics) to inform antimicrobial choice.

Some participants were explicit in describing the connection between steps. The syndrome evokes a particular antimicrobial differential, which is broadened or narrowed in considering patient characteristics and case features. In turn, this list of potential pathogens dictates antimicrobial options, the individual features of which are considered alongside patient, case, institutional confines, and the participants' own practices. However, others merely referenced the steps without specifically delineating their connection.

Some participants mentioned one additional step, *Early Script Filtering,* that occurred prior to *Naming the Syndrome. Early Script Filtering* involved participants considering certain factors – such as microbiologic data or patient allergies – that constrained antimicrobial options from the very first stages of the reasoning process.

DISCUSSION

We identified a framework for pharmacists' antimicrobial therapeutic reasoning which encompassed three steps and was influenced by 23 factors. We also described 14 drug characteristics included in antimicrobial therapy scripts. Participants provided examples of both non-maleficent (e.g., avoiding adverse effects from specific antimicrobials) and beneficent (e.g., recommending medications with evidence of efficacy/guideline support) factors affecting their treatment choices, which further supports the pharmacists' role in these two domains.[13,14,28]

Participants in this study generally engaged in the same antimicrobial reasoning steps previously described by physicians.[24] One possible explanation for this finding is that both studies recruited participants from the same hospitals. Because participants in both studies mentioned health care system factors as guiding their reasoning processes, the practice environment may have resulted in similarities between the physician and pharmacist reasoning frameworks. Additionally, the vignettes in this study simulated therapeutic selection scenarios that pharmacists frequently encounter while working collaboratively with physicians, which may have also influenced the alignment of reasoning processes across these two participant groups.

We noted one additional antimicrobial reasoning step described by our participants that differed from those previously described by physicians.[24] Some pharmacists used patient or case features to narrow treatment options before naming the syndrome (*Early Script Filtering*). This behavior aligns with the pharmacists' role in evaluating medication appropriateness[29], where certain factors (e.g., pre-existing medications, allergies, organ function) render a medication inappropriate or unfavorable for a given patient. As an inherent aspect of pharmacy practice, participants may have chosen to incorporate these factors earlier in their reasoning process to rule out inappropriate therapies. Our results indicated that both ID and non-ID pharmacists engaged in this early script filtering process, supporting the notion that a pharmacist's role in evaluating medication appropriateness transcends all specialty practice areas. Some pharmacists discussed confirming the physician's diagnosis as part of *Naming the Syndrome*, reflecting pharmacists' antimicrobial stewardship role in auditing medication orders for appropriateness.[22]

Pharmacists in our study identified one factor, *team dynamics*, in their antimicrobial reasoning that did not appear in physicians' antimicrobial reasoning.[24] *Team dynamics* illustrates the collaborative role of pharmacists in antimicrobial decision-making[22], where participants

mentioned working with prescribers to understand case features that affect antimicrobial selection. Our participants also expanded on two factors previously mentioned by physicians[24]: *evidence-based/guideline-supported decisions* and *ability to adhere*. Under *evidence-based/guideline-support*, pharmacists added that treatments should be supported by regulatory bodies and/or payers, reflecting pharmacists' attention to evidence-based and less costly medications, respectively. Under *ability to adhere*, pharmacists added that a patient's predetermined disposition can influence the type of chosen regimen, which highlights the pharmacist's role in planning for transitions of care beyond the hospital setting.[30]

There were also several factors (*likelihood of follow-up*, *patient preferences*, and *supporting trainee choices*) and one therapy script characteristic (*safety in pregnancy*) that physicians previously mentioned[24] but our participants did not. Participants in this study described several social factors that impacted their reasoning (e.g., financial factors and social support), but these factors did not clearly involve the patient's preference nor likelihood of follow-up. It is possible these two factors did not arise in our participant's reasoning processes due to practicing in a hospital setting where pharmacists may have limited direct patient contact. Participants also did not mention supporting trainee choices, but the *team dynamics* factor seemed related insofar as pharmacists sought to support the choices of physicians whenever safe and possible. *Safety in pregnancy* was not part of our participants' therapy script, although it is worth noting that the vignettes did not include any individuals of childbearing age.

Our antimicrobial reasoning framework aligns with two proposed models of therapeutic reasoning.[13,28] Wright and colleagues previously describe three steps: reasoning through medication options based on relevant factors, judging the risks and benefits of these options, and deciding which medication to prescribe.[28] Participants in our study completed these three steps

when mentioning key factors, weighing medication risks and benefits in their therapy script, and selecting an antimicrobial. Participants also described the importance of team dynamics and collaborative decision-making while reasoning through cases. Croft and colleagues highlight the role of 'collaborative planning' in community pharmacists' reasoning, though participants in their study described collaborating with patients rather than other health care providers.[13] Wright and colleagues also offered a collaborative therapeutic reasoning model where pharmacists and other health care professionals conduct independent clinical reasoning and judgments, followed by a joint therapeutic decision.[28]

One key component missing from our reasoning model, but mentioned in other models[13,31], is a reflective or metacognitive process. Marcum describes a clinical reasoning model where providers reflect upon their intuition/experience and logic/critical thinking both before and after making a clinical decision.[31] It is possible participants in our study did not describe this process due to their familiarity with the management of these common infections, or because the act of explaining their reasoning process fulfilled the same metacognitive purpose.[32] Nonetheless, given the role of metacognition in developing clinical expertise[33], a therapeutic reasoning model aimed at instructing trainees or early practitioners would likely benefit from the inclusion of an explicit metacognitive step in the reasoning process.

This framework has potential applications to aid in teaching pharmacy students how to reason through therapy choices. Given the similarities we found between pharmacist and physician antimicrobial reasoning processes, there are also potential applications for interprofessional education and practice. With a shared model across professions, this framework could be used to facilitate communication around antimicrobial selection between disciplines and augment stewardship efforts around antimicrobial prescribing.

Limitations

We used the vignettes in this study because they illustrated common antimicrobial reasoning scenarios and common infectious syndromes. However, it is unlikely this study identified all possible factors impacting pharmacists' antimicrobial reasoning process, in part due to the failure of the vignettes to trigger consideration of certain factors (e.g., pregnancy). Additionally, these cases focused on antimicrobial selection rather than evaluation of pre-existing antimicrobial prescriptions. Thus, this framework may not adequately represent pharmacists' reasoning process for antimicrobial medication review and may limit application to settings where this is the pharmacists' primary role/focus. Future studies may consider providing a larger variety of cases with a broader range of patient characteristics, case features, and pharmacist roles (medication selection vs review). This study also took place at two local institutions, which may limit applicability to other locales. Additionally, while individuals engaging in antimicrobial stewardship were included, this study was not designed to identify how engagement in antimicrobial stewardship specifically may impact antimicrobial reasoning processes.

CONCLUSION

We identified a framework for pharmacists' antimicrobial therapeutic reasoning that is similar to physicians' reasoning processes. Differences we identified in physician and pharmacist reasoning may be due to pharmacist's unique role in several areas, such as evaluating medication appropriateness and antimicrobial stewardship. This framework could be applied to didactic and clinical instruction of antimicrobial therapeutic reasoning and interprofessional practice.

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Table 1. Factors Influencing Antimicrobial Reasoning

Factor ***Sub-factor***	**Examples from Interviews [Participant Code]**
Preexisting patient characteristics	
Age	For an 85 year-old woman, I like to avoid the fluoroquinolones…because they can cause tendon rupture and elderly patients are at increased risk for tendon rupture. [GP-105]
Allergies	… go to beta-lactam therapy by itself, assuming he is not allergic...[GP-110]
Exposures	I don't believe that she's had any hospital admissions or exposure to the health care setting…so I would consider it to be a community-acquired pneumonia. [GP-106]
Medical history	
Ability to take oral drugs	Are they able to take PO meds…do I need to think about IV antibiotics, enteral absorption of PO antibiotics? [GP-103]
Comorbidities	She has some comorbidities that put her at risk for some toxicities…associated with trimethoprim-sulfa, like her type 2 diabetes and her recent kidney injury... [IDP-107]
Past infections	Has he had previous infections…that might be contributing to this infection? [GP-110]
Medications	
Prior exposure to antimicrobials	…strong predictors of multidrug resistance are…antibiotic exposures [IDP-111]
Current medications	…I'm going to stay away from things that prolong the QT interval, because she's on methadone... [GP-110]
Existing pill burden	Cephalexin, I think it's 3 times a day...Septra's twice a day so it's easier to remember with her morning and evening meds. [GP-105]
Social factors	
Ability to adhere	…I'm also considering their ability to be compliant with the medication regimen. [GP-103]
Financial factors	Based on his insurance, the next step to think about is what's available to him from a cost standpoint. [GP-106]
Current Case Features	
Differentiating case features	…purulent cellulitis versus nonpurulent cellulitis, the pathogens can be slightly different, and then your coverage can also certainly be different. [GP-106]
Microbiologic data	I would review any culture data…to better target antibiotic therapy to whatever the patient's organism is. [IDP-109]
Severity of illness	The severity of illness can kind of dictate how aggressive you want to be with therapy…suggests the types of pathogens that you might be more concerned about based on severity. [GP-106]
Trajectory of illness	The way I would assess or select which antibiotics to send this patient home on are to assess how he's clinically improved on his current regimen. [IDP-109]
Provider & Health Care System Factors	
Antibiogram	…our in-house antibiogram has very good susceptibility, and that's why we picked it [ceftriaxone] as our core agent. [IDP-102]
Clinical experience	I definitely wouldn't feel comfortable with Keflex. I know some people would but, personally not for bacteremia associated with urosepsis. [IDP-101]
Institution-specific practices	…typical regimen for community-acquired pneumonia…would be ceftriaxone and azithromycin…at our hospital we use doxycycline for atypical coverage.[IDP-107]
Team dynamics	…talk it over with the team…and then say here is what I would suggest...[IDP-101]
Treatment Principles	
Pathogen-based treatment	…doxycycline or azithromycin to cover the atypical bugs…ceftriaxone to cover strep pneumo, and other Gram-negatives... [GP-104]
Evidenced-based/guideline-supported decisions	…azithromycin has to be tied back to what's stated in some of the guidelines and also reimbursement... to bill for a community acquired pneumonia in the ICU, you should be on azithromycin rather than doxycycline. [GP-104]
Narrow coverage	…select an antibiotic…as narrow as possible [IDP-111]
Parsimony	…I feel fine with levofloxacin…instead of doing…cefpodoxime plus doxy...[GP-203]

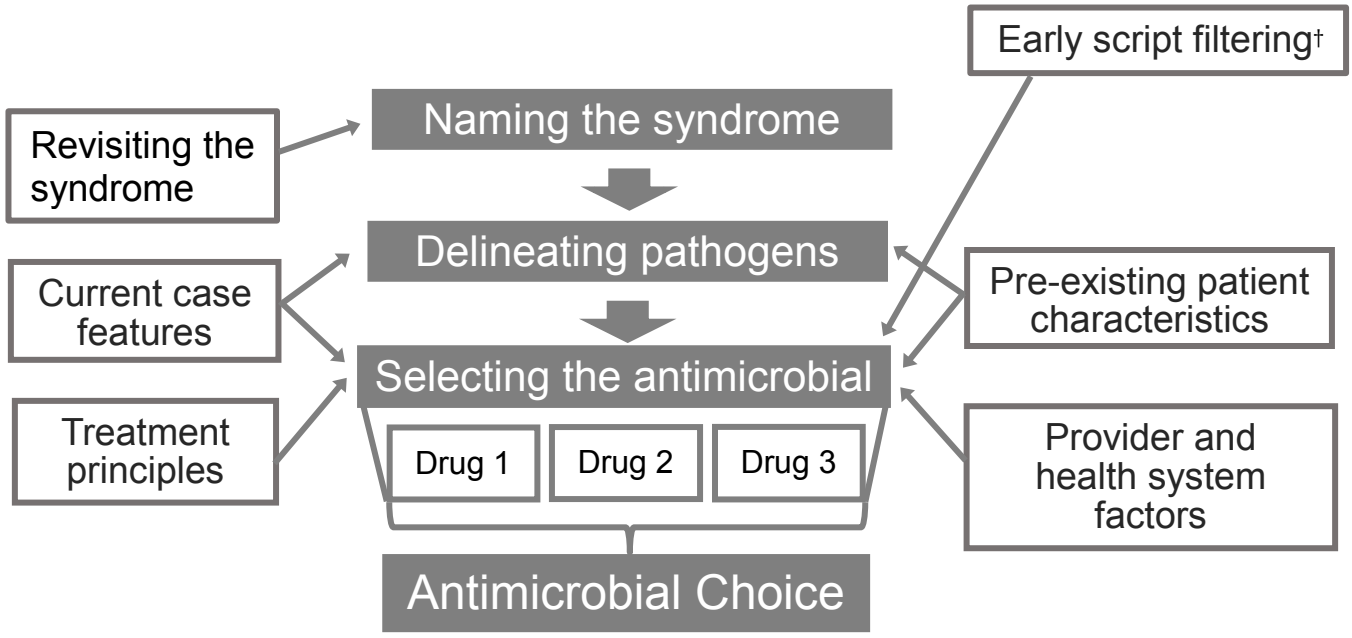
ICU = intensive care unit; IDP = Infectious diseases pharmacist; IV = intravenous; GP = General practitioner; PO = oral.

Table 2. Antimicrobial (Therapy) Script Content

Drug Characteristic ***Sub-characteristic***	**Example Excerpts From Interviews (Participant Code)**
Adverse effects	Quinolones in an elderly person is not the best either because of the potential for CNS toxicity... [IDP-101]
Cost and pharmacy considerations	…super long-acting Vanco-like agents [are]…non-formulary. We probably don't want to go the non-formulary approval route. [GP-104]
Dosing	Cipro is twice daily, levo is once daily... [GP-108]
Duration of therapy	I'd probably do…trimethoprim-sulfa because…[the patient] wouldn't probably experience a lot of toxicity in a shorter amount of time. [IDP-107]
Drug-drug interactions	Fluoroquinolones…[have] QTC prolongation in combination with Methadone so that would be something that I would consider... [GP-106]
Evidence of efficacy/ guideline support	…could consider cefpodoxime, the only thing is I'm not sure if it has a urine indication. [IDP-101]
Monitor adverse effects	…he will need more monitoring if we…send him out on IV Vancomycin [GP-104]
Pharmacodynamics	…doxy having good MRSA coverage [IDP-102]
Pharmacokinetics	Nitrofurantoin is an antibiotic that can be used for UTI, but we wouldn't want to use it for a systemic infection like a bacteremia, or even for a pyelonephritis just because of its pharmacokinetics. [IDP-109]
Bioavailability	Cefpodoxime actually has much better bioavailability than cefdinir. [IDP-101]
Drug distribution	Am I treating a CNS infection? That is going to affect whether I use things to penetrate the CNS or not. [GP-110]
Clearance/metabolism	…does he have like a reasonable [creatinine] clearance? And if that were true, I'd probably do something like trimethoprim-sulfa because…he wouldn't probably experience a lot of toxicity... [IDP-107]
Route of delivery	…she would be a candidate for transition to PO antibiotic. [IDP-109]
Spectrum	…we're trying to choose the narrowest spectrum antibiotic PO option... [GP-102]

CNS = central nervous system; GP= General practitioner; IDP= Infectious diseases pharmacist; IV = intravenous; MRSA = methicillin-resistant *Staphylococcus aureus*; PO = oral; UTI = urinary tract infection.

Figure 1. Antimicrobial reasoning framework. Though this process generally was found to be linear, some participants reported these steps in a different order. We chose to represent the most common configuration of the steps for the purpose of the figure. †Some participants mentioned *Early Script Filtering,* which affected their antimicrobial choice, prior to *Naming the Syndrome*. This was a new antimicrobial reasoning step that differed from those previously described by physicians[24]



Appendix: Interview Guide

1. Which of the following best describes roughly how many years of clinical practice experience you have (not including training)? 0-4, 5-10, 11-15, >15?

2. What percentage of your work time is dedicated to patient care?

> **POTENTIAL PROBE:**
> **How much time is spent working with physician teams and patients?**
> **Is any portion of your time dedicated to antibiotic stewardship? If so, how much?**

3. Do you work in the inpatient setting, the outpatient setting, or both?

VIGNETTES
Now I would like to share three vignettes structured like board-style questions that will help explore your antibiotic reasoning process. I will read them aloud, but please take all the time you need to read them independently and feel free to mark on them if it would prove useful for you.

VIGNETTE #1 [*will be provided to the interviewee to follow along as the interviewer reads*]
A 60 year-old woman with a past medical history of type 2 diabetes mellitus and atrial fibrillation presents with fevers and progressively worsening shortness of breath for the past 3 days. On review of systems, she also endorses fatigue, malaise, and productive cough. She takes metformin, glyburide, metoprolol XL, and warfarin. She has no known drug allergies. She works as a nurse and lives with her spouse in an apartment. She has a 5 pack-year smoking history but quit 37 years ago. She denies alcohol or drug use.

On exam, her vitals are: T 39.3, HR 89, BP 146/89, RR 32, O_2 Sat 88% on room air that corrects to 100% on 3 liters of oxygen via nasal cannula. She appears unwell but is not in acute distress, and there are crackles in her left lower lobe. Laboratory studies reveal:

WBC 16.3	Creatinine 1.4 (baseline is 0.7)
HGB 15	
HCT 47	
Platelets 227	
+Immature granulocytes, Left Shift	

Chest x-ray shows a consolidation in the left lower lobe. She is admitted to the hospital.

4. How would you choose what antibiotics to use in this case? Please explain the steps in your reasoning process as you would to a pharmacy student on clinical rotation who has not had to manage this type of patient before.

VIGNETTE #2 [*will be provided to the interviewee to follow along as the interviewer reads*]
A 73 year-old man with a past medical history of type 2 diabetes mellitus, chronic kidney disease stage 2, and hypertension on metformin, lisinopril, and several over-the-counter vitamins and supplements presented two days ago with a right lower extremity redness and pain concerning for severe cellulitis. He denied any fevers. He has improved on vancomycin since admission. He has no known drug allergies. He lives in an assisted living facility and is a retired schoolteacher. He is a lifetime nonsmoker and denies drug use but has approximately 4 alcoholic beverages weekly.

Now on hospital day 2, his vitals are: T 37, HR 72, BP 135/84, RR 16, O_2Sat 99% on RA. On exam, he appears well. His right lower extremity remains mildly erythematous, but the redness has receded several inches from the line of previous demarcation, and no other skin abnormalities are apparent besides a small healing abrasion on his right lower shin where he scraped his leg a week ago; the erythema extends from this abrasion. There is trace right lower extremity edema, and the erythematous area remains slightly warm to the touch. You think he is ready for discharge from the hospital.

5. How would you choose what antibiotics to use in this case? Please explain the steps in your reasoning process as you would to a pharmacy student on clinical rotation who has not had to manage this type of patient before.

VIGNETTE #3 [*will be provided to the interviewee to follow along as the interviewer reads*]
An 85 year-old woman with a past medical history of hypertension, type 2 diabetes mellitus, and chronic pain presented with fevers and confusion two days ago. She was unable to participate in review of systems at the time of admission. She is on lisinopril, metformin, and methadone. She has no known drug allergies. She lives with her sister and is a retired office manager. She is a lifetime nonsmoker and does not use alcohol or drugs. On initial exam on the day of admission, her vitals were: T 39.3, HR 105, BP 146/89, RR 20, O_2Sat 98% on RA. She appeared unwell but was not in acute distress. She was confused but had a nonfocal limited neurologic exam. Her abdomen was non-distended and soft, but she groaned and grimaced with palpation of her suprapubic area. There was no CVAT. Laboratory studies revealed:

WBC 15.7
HGB 14.6
HCT 37
Platelets 335
+Immature granulocytes, Left Shift

Creatinine 1.4 (baseline is 0.5)

Urinalysis: 0 RBCs/hpf, >50 WBCs/hpf, +leukocyte esterase, +nitrite, no squamous cells

She was started on ceftriaxone and admitted to the hospital. Now on hospital day 3, she is back to her neurologic baseline, has normal vital signs, and her creatinine has improved to 0.9. You think she is ready for discharge. However, the following microbiology results from the day of admission return:

Blood Culture: *Escherichia coli* in both bottles
Urine Culture: *Escherichia coli*

The *Escherichia coli* in both cultures has the following susceptibility pattern:

ANTIBIOTIC	**MIC** (mcg/mL)	**INTERPRETATION**
Ampicillin/Sulbactam	16	Resistant
Aztreonam	≤ 1	Sensitive
Cefazolin	2	Sensitive
Ceftriaxone	≤ 0.5	Sensitive
Ciprofloxacin	≤ 0.5	Sensitive
Gentamicin	≤ 2	Sensitive
Levofloxacin	≤ 1	Sensitive
Nitrofurantoin	≤ 32	Sensitive
Piperacillin/Tazobactam	≤ 8	Sensitive
Tobramycin	≤ 2	Sensitive
Trimethoprim/Sulfamethoxazole	≤ 2	Sensitive

6. How would you choose what antibiotics to use in this case? Please explain the steps in your reasoning process as you would to a pharmacy student on clinical rotation who has not had to manage this type of patient before.

GENERAL QUESTIONS
Now I would like to ask you some general questions about your infectious diseases reasoning.

7. Reflecting on the last few questions, please write out the steps in your general antibiotic reasoning process on these 3x5 notecards and arrange them in the order they occur. If two steps occur at the same time, place them side-by-side.

POSSIBLE PROBES
Why did you put those [INDICATE CARDS] side-by-side?
What do you mean by [WHATEVER IS WRITTEN ON CARD]?
Are there any other steps you can think of?

8. What clinical resources do you use when managing infectious diseases or antibiotics?

POSSIBLE PROBES
Have you used: the local antibiogram, IDMP, UpToDate, IDSA Guidelines, Abx dosing cards, Micromedex/pharm resource, Mandell's, Hopkins Guide, Sanford Guide?

9. When do you use these resources? (In what clinical situations do you use…)

POSSIBLE PROBES
How do you use these resources?

10. How often do you use these resources?

POSSIBLE PROBES
Do you use them every day? Every case?

11. Is there anything else that I didn't ask that you want to convey?