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A MIXED METHODS APPROACH TO TAILORING EVIDENCE-BASED GUIDANCE FOR ANTIBIOTIC STEWARDSHIP TO ONE MEDICAL SYSTEM

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Abstract

Our objective is to operationalize a novel antibiotic advisor, called the personalized weighted incidence syndromic combination antibiogram (pWISCA), intended to help physicians with initial antibiotic choice in hospitals. Clinical decision support tools are a promising technology for providing evidence-based guidance that incorporates data about patients from electronic health records. Nevertheless, congruence with policies and procedures and local experts' opinions, as well as taking into account local resistance data for the medical center's patient population, is needed when selecting and ordering the antibiotic medication options provided by pWISCA. This paper presents findings from applying a mixed methods approach to identify and prioritize antibiotic medications and associated contextual data to display in a CDS tailored to the local hospital. We discuss implications of these findings.

BACKGROUND

The objective of the overall multi-year study, of which this paper describes one step in the effort, is to operationalize and test a novel antibiotic advisor, called the personalized weighted incidence syndromic combination antibiogram (pWISCA), intended to help providers with initial antibiotic choice. The emphasis is on the initial choice, where providers often must start an antibiotic regimen in patients with suspected infection before definitive culture results are available. To make this choice, the possible pathogenic

organisms, the available antibiotic medications in the formulary at the organization, the guidance on which antibiotic medication is recommended to be the ‘first line’ for preferred use for suspected pathogens, and the breadth of the coverage against other possible pathogenic organisms are important factors. The patient’s history is also relevant, particularly with respect to allergies to antibiotic medications, prior infections with resistant organisms, an increased likelihood of resistance to antibiotics secondary to healthcare exposure, and increased risks of adverse effects of antibiotics on organs such as the liver or heart.

Antimicrobial resistant bacteria cause over 2 million illnesses and 23,000 deaths annually in the United States. (CDC, 2013). Resistance to antibiotics is a key consideration in the empirical treatment of infections (i.e., before the organisms or related antibiotic susceptibility tests are known). In these situations, physicians may select antibiotics using antibiograms (summaries of local antibiotic susceptibility patterns), clinical practice guidelines, or clinical decision support (CDS) tools. Algorithms for supporting the selection of antibiotics with a CDS often use antibiotic susceptibility data and may also include experts’ opinions by integrating elements of clinical guidelines (Mullett & Thomas, 2003, Becher et al., 2012, Hoff et al., 2018). However, the use of guidelines has key limitations: 1) many clinical situations are not included in published guidelines, 2) published recommendations are often outdated following advances in medical knowledge (Tsopra, Venot, & Duclos, 2014), and 3) the guidelines often do not take into account local resistance patterns in a hospital’s population or local practice patterns.

Antimicrobial resistance is increasing worldwide. For example, the percentage of all Enterobacteriaceae that are carbapenem-resistant (CRE) increased from 1.2% to 4.6% from 2001 to 2012 (CDC, 2018) and are now present in all US states (CDC, 2017). Some CRE are resistant to all available antibiotic medications.

To address this gap, CDS tools for empirical antibiotic selection may incorporate local expert opinion in system development, allowing for more tailored ranking of recommended treatment regimens according to factors such as institutional priorities and risk of adverse events (Paul et al., 2006).

Interventions to improve antibiotic prescribing are a key component of the Centers for Disease Control and Prevention’s Core Elements of Hospital Antimicrobial Stewardship Programs (Pollack & Srinivasan, 2014). By evaluating factors important to clinical decision-making in the prioritization of antibiotics for the empirical treatment of a suspected Urinary Tract Infection (UTI), we aim to use this expert knowledge to optimize our antibiotic advisor tool and improve antibiotic prescribing. In this paper, we describe the findings from a mixed-methods study to determine the factors considered by voluntary members of an antibiotic stewardship committee at a large academic medical system. We explore two variations on a UTI patient scenario concerning overall patient condition and admission location in the hospital, three variations on additional specific health conditions, and two variations on the individual patient’s history.

Macro cognition is defined as cognitive adaptation to complexity (Klein, Klein, & Klein, 2000). In macro cognition, we have previously proposed that there are five primary functions (Patterson & Hoffman, 2012): detecting problems, sensemaking, re-planning, deciding, and coordinating. In this effort, we focus on two macro cognition functions:

1. *sensemaking*, which is defined as collecting, corroborating, and integrating information [typically from the patient regarding history, from the electronic health record, and from laboratory results] and assessing how the information maps onto potential explanations [likely pathogenic organisms], and
2. *re-planning*, which is defined as adaptively responding [by ordering an antibiotic medication and possibly monitoring for side effects of the medication] to changes in objectives, from any of a variety of sources including supervisors and peers, obstacles, opportunities, events, or changes in predicted future trajectories (Patterson & Hoffman, 2012).

For both of these functions, although there are ready-to-hand default plans formalized as evidence-based recommendations instantiated in policies, there is still a need to adapt these plans into actions (Klein, Woods, Klein, & Perry, 2016). These adaptations occur within a window of opportunity as defined by 1) how long the patient is expected to stay in the hospital, while taking into account local contextual factors, including patient factors, 2) the effectiveness of antibiotic medications in the hospital's patient population including the resistance profile of the population, and 3) organizational constraints, including the comparative cost of the medication options, the opinions of local experts, and priorities of hospital administration personnel.

METHODS

A mixed methods approach was used, with study participants filling out an electronic survey before a one-hour focus group. We recruited participants from a standing committee on antimicrobial stewardship for a large, academic medical center. Members of the committee include pharmacists, infectious disease physicians, and microbiologists. Members include senior personnel, such as attending physicians as well as trainees, including fellow physicians.

For data collection, an anonymous survey requested respondents to identify which antibiotics they would include in a CDS tool for empiric antibiotic selection for the treatment of UTIs and to obtain quantitative measures of antibiotic breadth. Within a series of questions about antibiotics, participants were asked to, "Please select the antimicrobials that you would like to see listed in an empirical antibiotic clinical decision support tool for a patient being admitted to the hospital with a UTI (i.e., all those that you would possibly consider as part of empirical regimens for a patient)." We presented participants with a list of 20 antibiotics typically used to treat UTIs. This list was generated through a review of institutional and international clinical practice guidelines (Gupta et al., 2011). Before distribution of the survey, multiple clinicians on the study team independently reviewed the questions for face validity and the antibiotic choices to validate that the list was comprehensive and appropriate.

For data collection, participants in the focus group were recruited from the same committee. The focus group was scheduled for 60 minutes during a standard meeting time and the objectives of the session were explained at the prior meeting and reiterated at the beginning of the focus group. It was explained that the participants were expected to come to consensus on the prioritization of initial choices of antibiotics for variations on a UTI patient scenario. During the meeting, they were asked to serve as an expert representing their specialized expertise while establishing consensus where none currently exists nationally about how to trade off the benefits of broader coverage for antibiotics with adverse events and cost in the empirical treatment of a suspected UTI. We presented the focus group with the same antibiotic choices from the survey on post-it notes displayed on a whiteboard, as well as blank post-it notes for options that should be added. We asked participants to establish consensus on the ranking of empirical UTI treatment regimens for seven patient conditions: two general patient conditions: stable (admitted from the emergency department) and septic (going to the intensive care unit); three conditions in a stable patient: prolonged QT interval, abnormal renal function, and elevated liver enzymes; and two prior conditions in a stable patient: history of seizure(s) and history of *Clostridium difficile* (C. diff) infection. Antibiotic selection was not limited to the initial choices presented.

The initial codebook was adapted from a prior study on the prioritization options for ordering imaging tests (CT scan, MRI, ultrasound) for patients by hospitalization physicians (Rayo et al., 2018).

The relationship of the codes in the codebook to each other is portrayed in Figure 1. In selecting antibiotics for the empirical treatment of suspected infections, we hypothesized that clinicians would make decisions based on the properties of three key elements: the patient, the antibiotic medication, and the likely infecting bacterial organism. When prioritizing efficacy of treatment, then the COVER code is defined as the expectation that a particular antibiotic will treat the likely pathogenic organism(s) that a patient has. This code contrasts with the BROAD code in that a selection is made that will cover a large proportion of pathogenic organism(s) that a patient may have, thus indicating a greater uncertainty about the organism. In the event that a patient is suspected to be infected with a resistant bacteria, and thus the preferred choice for a likely pathogenic organism is less likely to be effective, then another choice could be made of an alternative antibiotic (RESIST). Contextual factors specific to the individual patient include historical data (HIST) and immediate patient safety risks (PSS), such as potential allergies and addressing the possibility of a patient having sepsis, which would require immediate intervention to avoid mortality. Other factors anticipated to impact the decision include less immediate patient safety factors, such as minimizing damage to the liver which may not occur for many days after starting an antibiotic (PSL), cost as an organizational constraint (COST), and evidence-based guidance. Evidence-based guidance includes published studies (EBM), local data (DATA), local experts (LEAD), and policies and procedures (GUIDELINES).

During analysis of the survey data, responses recorded before the focus group session were aggregated to report the selection frequency of each antibiotic across all respondents.

During the preliminary analysis of the focus group data, two investigators first wrote memos next to a parsed verbatim transcript of the focus group about patterns in how decisions were made for prioritizing choices for antibiotic prescribing. Based upon this activity, we modified definitions of the majority of the initial codes, removed several codes, and added several new codes. The resulting codebook from Table 1 was then used by the same two investigators to generate codes independently for a parsed transcript from the focus group meeting. We used multiple codes as needed for each parsed transcript segment, with no restriction on the number of codes applied. A consensus meeting was held with the two investigators in conjunction with a third investigator to come to a consensus on code discrepancies.

The consensus was reached on all final codes via discussion between coders and subsequently also via discussion with a physician subject matter expert to gain additional insights when the decision factors were not clear from the focus group data.

The analysis of the focus groups concerning the prioritization of choices of antibiotics was conducted by assigning sequential prioritization numbers to the post-it notes placed on the wall during the focus group session from top to bottom. These data were aggregated and compared with the results of the survey.

RESULTS

Nine physicians and pharmacists from the hospital's antimicrobial stewardship committee started the survey with complete responses recorded for six of these participants. Out of the 20 antibiotics presented, at least one respondent selected 15 (Table 2). However, only one antibiotic, ceftriaxone, was selected by all six respondents. Five of the six respondents selected piperacillin-tazobactam (also known as pip-tazo), and four selected cefepime. Cefazolin, ciprofloxacin and ertapenem were each selected by half of respondents. The remaining nine antibiotics selected were chosen by fewer than half of respondents.

Five members of the antimicrobial stewardship committee participated in the focus group session. We display the results in Tables 3–5. In Table 3, the most notable difference in antibiotic selection was for the patient with a history of sepsis, where broader-spectrum and combination regimens were included.

Using the stable patient case as the reference point, selection and rank order of antibiotics differed for all three variations on the patient condition presented, where findings indicated the potential for patient safety considerations (Table 4).

In Table 5, we modified the patient history for the same stable patient with a suspected UTI. For patients with a history of a *C. diff* infection, the participants achieved consensus to consider additional antibiotic options for that patient. The list reflects the intent to include additional antibiotics that do not get systemically absorbed or have less anaerobic coverage.

There were 24 code discrepancies out of 77 after the initial coding by the two independent investigators. The majority of the discrepancies related to whether a single code or multiple codes were appropriate, such as whether COVER was sufficient, or whether both COVER

and BROAD was needed. Three code discrepancies suggested a bias toward efficacy (COVER) with one coder and a bias toward patient safety and patient-specific factors with the other. We resolved these discrepancies through a better understanding of the specific antibiotic medications. Six codes were deferred until an infectious diseases physician was included to achieve consensus with all four investigators, at which time we achieved full consensus on all codes with the exception of four codes, where we agreed that there was insufficient data to identify the reason for the decision to prioritize a particular antibiotic in a certain order.

In Table 6, we present the final counts of the codes by the patient scenario variations. Overall, the efficacy of the antibiotic medications was the most prominent factor, and primarily the coverage and breadth of the antibiotic medication. Short-term patient safety consideration was a prominent factor. Patient-specific historical factors were also taken into consideration. The most common code for evidence-based medicine was the internal data regarding resistance in the local medical center's population.

DISCUSSION

Overall, the efficacy of the antibiotic medications was the most prominent factor, similar to the findings from Rayo et al. (2018) regarding imaging choices by hospitalist physicians. Both the coverage of the antibiotic for the suspected pathogenic agent as well as the breadth of the coverage in the event that an unexpected pathogenic organism is responsible for the patient condition were the most frequent options. This pattern is similar to findings from intelligence analysis where analysts prepared plans that simultaneously addressed both the Most Likely Course of Action (MLCOA) of the enemy fighters as well as the Most Dangerous Course of Action (MDCOA) (Trent, Patterson, & Woods, 2007).

The finding that short-term patient safety considerations impacted the choice of antibiotic medication prominently differed from Rayo et al. (2018), where patient safety was typically only considered for patient cohorts such as pregnant patients. On the other hand, long-term patient safety considerations impacted the desire to monitor the impacts of the medication, but did not affect the selection of the medication. Therefore, the long-term patient safety considerations were treated similarly as the imaging decisions. It is likely that the imminent need to avoid the risk of mortality due to sepsis by quickly ordering a medication drove the consideration of short-term patient safety concerns.

The finding that published evidence-based guidance was not the most prominent form of decision-making, but instead, internal data regarding resistance in the local medical center's population is notable. It is possible that this finding is due to the specific methodology employed, in that the focus group session was not sufficiently long to look up published evidence during the discussion. Similarly, the participants were well-informed of local data regarding resistance due to their role on the antibiotic stewardship committee, and therefore that could have biased the findings. Future research can help to clarify the type of evidence that would be useful to provide links for in a usable fashion under time pressure. We anticipate that a 'details upon demand' navigation paradigm will be found useful and usable

by physicians during the antibiotic ordering process in the CDS in the next stages of this research.

There were differences in the findings regarding the selection and ranking of antibiotic medications between the survey and focus group, even though the study participants were recruited from the same committee. Of the 15 antibiotics selected by respondents in the survey, only nine (60%) were also selected by the focus group. This is likely due in part to the ease of selecting antibiotics in a single survey as opposed to being required to come to consensus on the ordering of antibiotics as a group. It is also likely, based upon reviewing the transcript, that possible antibiotics were removed upon further consideration based upon the discussions, but that typically additional options were not added based upon the discussion. For specific patients, there are likely more possibilities to consider, but for the initial choice before much is known about the pathogenic organisms, there appears to be more clear preferences based upon the evidence of efficacy combined with data about local resistance to antibiotics in the medical center.

In the survey, only one participant selected Trimethoprim-Sulfamethoxazole (TMP/SMX), also known as Bactrim. In the focus group setting, there were three instances where TMP/SMX was discussed. Disagreement centered on whether this medication should be prescribed for patients admitted to the hospital for UTI. For the stable patient case, TMP/SMX was selected but given low priority. In discussing this case, focus group participants noted that use would depend on patient condition (i.e., how “sick” the patient is). TMP/SMX was also selected (with low priority) for the cases of a stable patient with prolonged QT interval syndrome or a history of *C. diff* infection. In the discussion of a stable patient with prior *C. diff* infection, it was noted that TMP/SMX would be used conditional on a known history of the patient having a UTI susceptible to TMP/SMX. In the survey, only one of six respondents selected TMP/SMX as a medication to include in an empirical antibiotic clinical decision support tool.

International clinical practice guidelines recommend the use of TMP/SMX for acute uncomplicated UTI, but caution against use if local resistance exceeds 20% (Gupta 2011). A review of local guidelines based on hospital antibiogram data revealed that TMP/SMX is ranked fifth of six antibiotics recommended for the empirical treatment of a UTI. Based on the low selection frequency of TMP/SMX in the survey and the conditional appropriateness in the case scenarios during the focus group, it appears that this medication is not a preferred choice for the empirical treatment of a suspected UTI in the inpatient setting, though use may be considered for a very specific subset of patients when more detailed information on the patient or previous microbiology results are available.

The findings from this study have potential implications for the design of the CDS tool. Specifically, these findings suggest what information would be useful to providers to display along with the rankings for the antibiotic medications. As one example, all of the patient-specific information assessed during the focus group affected the selection of antibiotic medications, and so that information should be displayed, including a history of *C. diff* infections, a history of seizures, QT prolongation, abnormal renal function, and elevated liver enzymes. Currently, the preliminary mock-up of the CDS displays an indication of

whether a patient is sick or less sick, which appears to match the factor regarding the possibility of having sepsis impacting decision making. On the other hand, the focus group participants appeared to be inferring a substantial amount about the patient on the basis of anticipated disposition from the emergency department to the hospital as compared to the intensive care unit or home. Therefore, it might be helpful to display an anticipated disposition for the patient. Alternatively, if this information is uncertain or could be inaccurate, that might have unintended consequences on the decision process. Finally, no organizational constraints, including cost, were considered during the focus group. Therefore, it is possible that displaying that information on a CDS could result in consideration of a factor that would not otherwise be considered without a memory prompt. It is anticipated that comparative cost between alternatives will be more important than the individual cost of ordering a particular antibiotic.

Finally, these methods might be useful for others designing algorithm-based CDS tools which pull data from the electronic health record. A known challenge is generating computable knowledge for use with individual patients based on guidance designed around patient populations, and this paper presents an example of using a feasible methodology for achieving this goal. Also, this methodology is potentially unique in leveraging the human factors research base on the use of policies and procedures in organizations to control end-user behavior, as well as the limitations of relying on evidence-based medicine, to capture more timely and institution-specific recommendations compared to published guidelines. It is possible that hospitals will be interested in using this methodology to tailor antibiotic stewardship recommendations to the local context, as documented in policies and procedures or designed into CDS alerts.

This study has several limitations. This sample is a small sample from one organization, which limits generalizability of our findings; however, we believe that the methods used can be generalized to other sites. As such, another focus group is planned at another medical center. It is possible that study participants did not include all perspectives on the choices for selecting antibiotics. Similarly, trainee physicians with less experience may be less knowledgeable about the reasons for selecting particular antibiotics than our study population, and so might need additional links for further information or more explanation of the reasons for selecting antibiotics. Therefore, we will target their participation in future usability studies with the CDS interface. This focus group was limited to sixty minutes, and some factors might have changed with more discussion. However, the findings from the survey and focus group differed, possibly indicating that discussion and reflection may impact the selection of medications for the CDS tool.

Finally, the primary significance of this work lies in how to effectively design and implement clinical decision support technologies in electronic health records in areas where expertise is specialized and complex. Although the Delphi technique (Hasson, Keeney, & McKenna, 2000) addresses situations where experts disagree in complex, emerging areas, there are not many techniques that address expertise that needs to be integrated across fields and how to transform those insights into a computable format.

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Figure 1.
Conceptual relationship of main codes used for decision factors in initial choice for antibiotic prescribing

Table 1.

Codebook of factors and codes with examples (adapted from Rayo, in press 2018)

Factor: Subgroup (Code)	Definition	Representative Example
Efficacy: Coverage (COVER)	Expectation that an ordered antibiotic will treat the likely pathogenic organism(s) infecting a patient	If you[re] really not sure that that's a UTI, I will maybe do vanc[omycin] because they[re] septic
Efficacy: Breadth (BROAD)	Assessment that a specific antibiotic would cover a large proportion of pathogenic organisms	Prefer Cefepime, anything without anaerobic coverage, before ertapenem or [piperacillin/tazobactam]
Efficacy: Resistance (RESIST)	Assessment that patient(s) will likely have resistance to a medication that would typically be used first	Mero[penem] would be used only if you suspect a patient will have additional resistance
Patient Safety: Immediate (PSS)	Involves weighing the potential short-term side effects of an action with the benefits provided	If you are really not sure that that's an UTI, I will maybe do vanc[omycin] because they might be septic
Patient Safety: Not immediate (PSL)	Involves weighing the potential long-term unintended side effects of an action with the benefits provided for the patient or for a population	Beta lactams can increase liver enzymes, but the liver enzyme increases because of other things...usually we would just monitor...and then if it increases, switch to a different beta lactam
Patient Safety: Patient History (HIST)	Selection of antibiotics depends on patient history	This may be depending on the history...I wouldn't start vanco[mycin] with this patient
Organizational Constraint: Cost (COST)	Monetary cost of treating with an ordered antibiotic	Not observed
Evidence-Based Guidance: Evidence-based (EBM)	Selecting a medication or ordering the preference of medications based on published studies	You see Cefepime from that review article
Evidence-Based Guidance: Local data (DATA)	Selecting a medication or ordering the preference of medications based on data from the hospital	Technically isn't our [TMP-SMX] susceptibilities for E.coli better than fluoroquinolones?
Evidence-Based Guidance: Local expert (LEAD)	Selecting a medication or ordering the preference of medications based on the leadership of an acknowledged expert	The [person in the leadership position] agreed
Evidence-Based Guidance: Evidence-based guidelines (GUIDELINES)	Selecting a medication or ordering the preference of medication based on guidelines	Not observed

Table 2.

Selection frequency (descending order) of antibiotics that clinicians or pharmacists would include in an empirical antibiotic CDS tool for the treatment of a suspected UTI based upon survey results (n=6)

Antimicrobial	Count
Ceftriaxone	6
Piperacillin-tazobactam	5
Cefepime	4
Cefazolin	3
Ciprofloxacin	3
Ertapenem	3
Vancomycin	2
Ampicillin-Sulbactam	1
Aztreonam	1
Daptomycin	1
Levofloxacin	1
Linezolid	1
Meropenem	1
Piperacillin/tazobactam + Vancomycin	1
Trimethoprim-sulfamethoxazole (TMP-SMX)	1
Fosfomycin trometamol	0
Meropenem+Linezolid	0
Meropenem+Vancomycin	0
Nitrofurantoin monohydrate/macrocrystals	0
Piperacillin/tazobactam + Linezolid	0

Table 3.

Focus group rankings of antibiotic regimens by the general patient condition for a suspected UTI Of the 15 antibiotics selected by survey respondents in (Table 2), focus group participants selected nine (9/15; 60%) (Table 3). These antibiotics are: ceftriaxone, cefepime, piperacillin/tazobactam, ciprofloxacin, levofloxacin, ertapenem, vancomycin, piperacillin/tazobactam + vancomycin, and trimethoprim-sulfamethoxazole (TMP/SMX).

	Stable		Septic
1	Ceftriaxone	1	Piperacillin/tazobactam
2	Ciprofloxacin	2	Cefepime
2	Levofloxacin	3	Meropenem
3	Ertapenem	4	Aztreonam
4	Cefepime	5	Piperacillin/tazobactam + Vancomycin
4	Piperacillin/tazobactam	6	Meropenem + Vancomycin
5	Trimethoprim-sulfamethoxazole (TMP-SMX)	7	Cefepime + Vancomycin

Table 4.

Focus group rankings of antibiotic regimens for three patient scenario variations with patient safety considerations

	Prolonged QT Interval Syndrome		Abnormal renal function		Elevated liver enzymes
1	Ceftriaxone	1	Ceftriaxone	1	Ceftriaxone
2	Ertapenem	2	Ciprofloxacin	2	Ciprofloxacin
3	Cefepime	2	Levofloxacin	2	Levofloxacin
3	Piperacillin/tazobactam	3	Ertapenem	3	Ertapenem
4	Trimethoprim-sulfamethoxazole (TMP-SMX)	4	Cefepime	4	Cefepime
		4	Piperacillin/tazobactam	4	Piperacillin/tazobactam

Table 5.

Focus group rankings of antibiotic regimens for two patient scenario variations with patient history

	History of Seizure(s)		History of <i>C. diff</i> infection
1	Ceftriaxone	1	Ceftriaxone
2	Ciprofloxacin	2	Ciprofloxacin
2	Levofloxacin	2	Levofloxacin
3	Ertapenem	3	Cefepime
4	Piperacillin/tazobactam	4	Ertapenem
5	Cefepime	5	Piperacillin/tazobactam
		6	Trimethoprim-sulfamethoxazole (TMP-SMX)
		6	Nitrofurantoin
		6	Fosfomycin

Table 6.

Counts of decision factor codes by scenarios

Code	Stable	Septic: ICU	Stable: prolonged QT	Stable: abnormal renal function	Stable: elevated liver enzymes	Stable: seizure history	Stable: C.diff history	Total n(%)
Cover	3	15	0	0	1	0	2	21(27.3)
Broad	5	7	0	0	1	0	2	15(19.5)
Resist	1	1	0	0	0	0	0	2(2.6)
PSS	2	11	1	1	0	0	1	16(20.8)
PSL	0	0	0	1	4	1	1	7(9.1)
Hist	3	2	0	0	1	0	1	7(9.1)
Cost	0	0	0	0	0	0	0	0(0.0)
EBM	0	0	0	0	0	0	0	0(0.0)
Data	3	0	0	0	0	0	1	4(5.2)
Lead	0	1	0	0	0	0	0	1(1.3)
Guidelines	0	0	0	0	0	0	0	0(0.0)
Unknown	0	2	0	0	1	1	0	4(5.2)
Total n (%)	17 (22.1)	39 (50.6)	1 (1.3)	2 (2.6)	8 (10.4)	2 (2.6)	8 (10.4)	77 (100)

EBM = Evidence-based medicine, Hist = Patient history, Lead = Local expert, PSL = Patient safety not immediate, PSS = Patient safety short-term