Applying Implementation Science Concepts to Antibiotic Stewardship Practice

Nebraska Statewide Stewardship Summit

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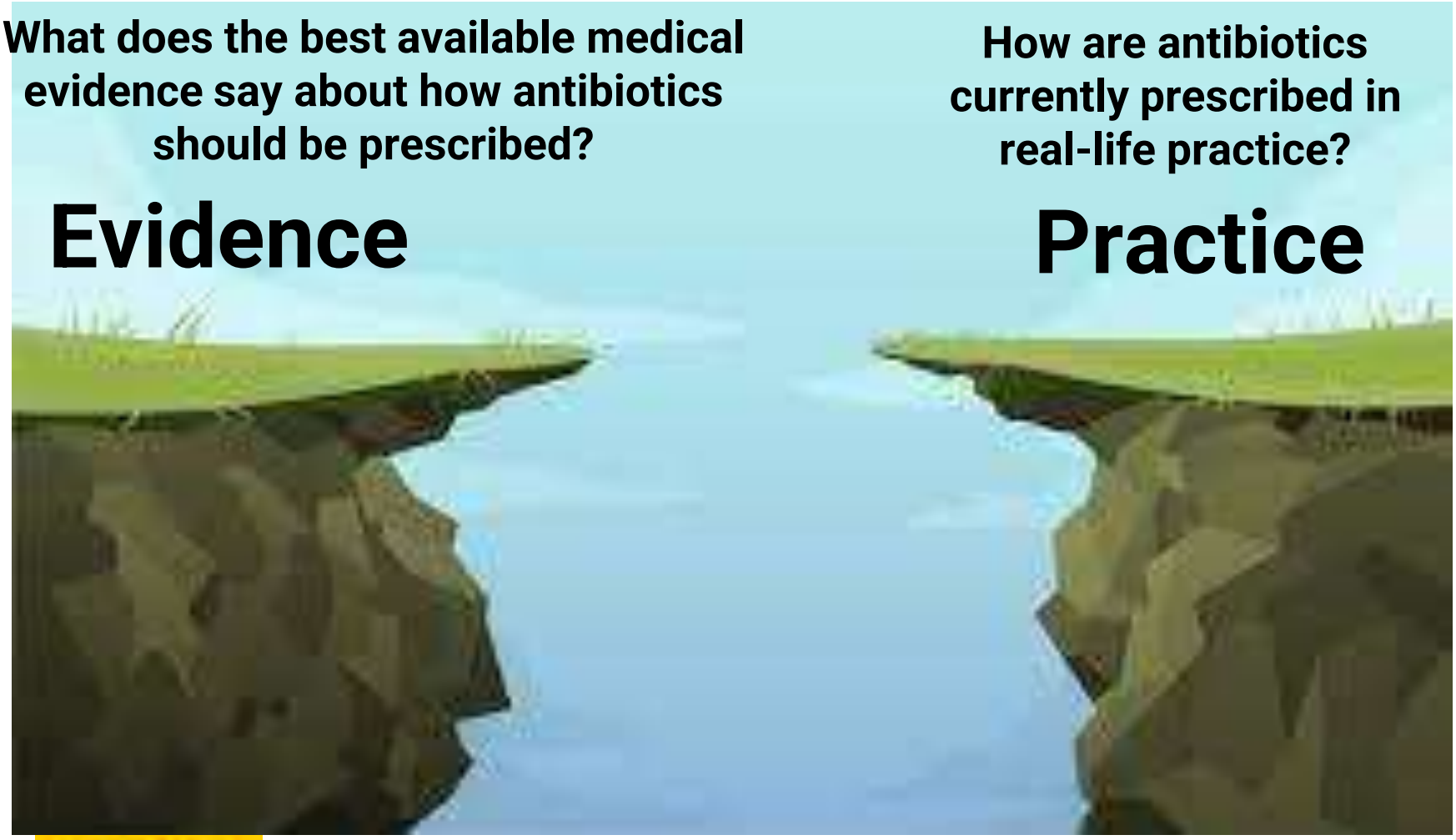
Disclosures

- I am disclosing the following:
  Independent Research Project: Merck & Co., Inc.

Evidence-practice gap



Examples of evidence-based antibiotic-prescribing practices

Short course antibiotic therapy for community-acquired pneumonia

Not giving antibiotics for asymptomatic bacteriuria

Stopping antibiotic prophylaxis at the time of surgical wound closure

Narrow-spectrum beta-lactam therapy for non-purulent cellulitis

Implementation science

Definition:

"The scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice"

In other words, implementation research asks:

- How can the evidence-practice gap be closed?
- How can it be closed quickly?

Eccles MP, Mittman BS. *Implement Sci* 2006; 1:1.

QI vs. implementation science

	Quality Improvement	Implementation Science
Starting point	A local problem	An evidence-based practice that is under-utilized in healthcare
Goal	To fix the specific problem within the single healthcare system	To generate generalizable knowledge on mechanisms of change
Approach	Design and trial strategies to improve the problem	
Evaluation	Mixed methods to measure processes, outcomes, and barriers/facilitators to change	
Models	Toyota Lean Six Sigma	RE-AIM CFIR

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doi:10.1017/ice.2021.480

SHEA

SHEA White Paper

Leveraging implementation science to advance antibiotic stewardship practice and research

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Antibiotics are among the most commonly prescribed medica-

from quali… …ough the 2 fields share much in …pply …udies …er on …lship …s can …n the …while …iples. …ctice …rock …w to

as prospective audit-and-feedback, prior authorization, education,

think about them in relation to antibiotic stewardship: frameworks

Key tasks:

- Identifying the evidence-practice gap
- Choosing an **implementation science framework**
- Engaging stakeholders and considering context
- Choosing a bundle of **implementation strategies**
- Evaluating the implementation process by measuring **implementation outcomes**

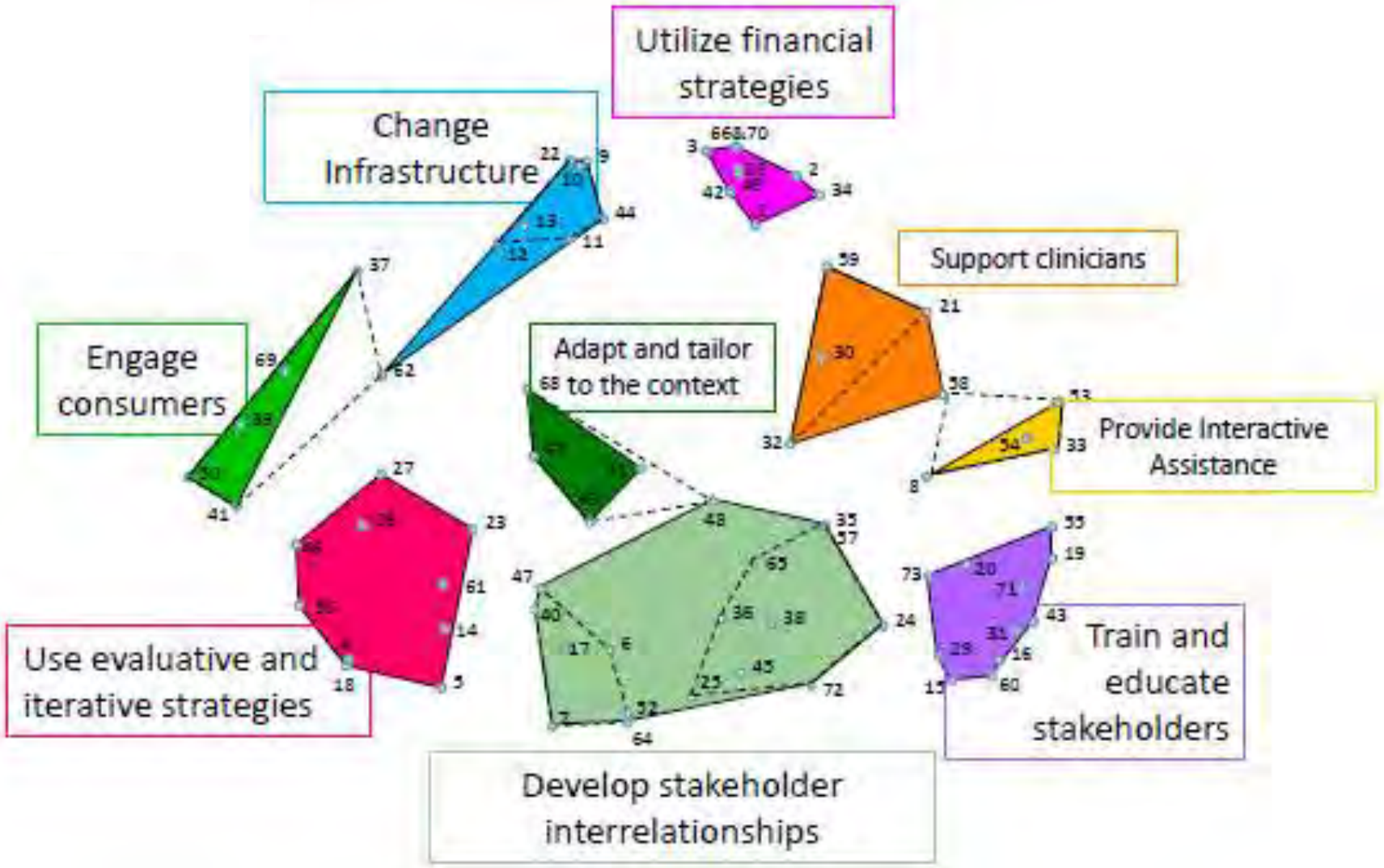
Implementation strategies

Definition

The methods and techniques you use to convince your target audience to adopt the evidence-based practice

- Strategies are informed by feedback from stakeholders and an understanding of your context.
- Strategies are meant to address barriers and leverage facilitators to people using the evidence-based practice.

Grouping of 73 implementation strategies



Waltz *et al.* Use of concept mapping to characterize relationships among implementation strategies and assess their feasibility and importance: results from the Expert Recommendations for Implementing Change (ERIC) study. Implement Sci. 2015;10:109.

Categories of implementation strategies

Evaluative and iterative strategies

Audit-and-provide feedback

Tools for quality monitoring, e.g., tracking NHSN data

Develop stakeholder relationships

Capture and share local data, e.g., antibiograms

Obtain formal commitments

Local consensus discussions, e.g., institutional guidelines

Train and educate stakeholders

Didactics

Academic detailing

Support clinicians

Use clinician prompts, e.g., order sets and antibiotic time outs

Relay clinical data to clinicians, e.g., real-time feedback on positive micro results

Waltz *et al.* Implement Sci. 2015;10:109.

Matching strategies to barriers (CFIR-ERIC)

https://cfirguide.org/choosing-strategies/

Disclaimer: This tool may help inform implementation planning efforts, but it is unclear how well it will apply to any given unique setting.

Waltz TJ, et al. Implement Sci 2019;14(1):42.

Using identified barriers to select implementation strategies

Barriers based on CFIR constructs

- Stakeholders see **no advantage** to implementing the innovation
- Stakeholders have a **negative perception** of the evidence behind the innovation
- Stakeholders see the **current situation as tolerable**
- Stakeholders **do not receive feedback** that is aligned with the goal

Recommended implementation strategies include the following:

- Identify and prepare champions
- Educate
- Audit and provide feedback

Real-life example #1

Using a bundle of implementation strategies for a local QI initiative: a real-world example

JAMA Network Open

Original Investigation | Pharmacy and Clinical Pharmacology

Pharmacist-Driven Transitions of Care Practice Model for Prescribing Oral Antimicrobials at Hospital Discharge

Nicholas J. Mercuro, PharmD; Corey J. Medler, PharmD; Rachel M. Kenney, PharmD; Nancy C. MacDonald, PharmD; Melinda M. Neuhauser, PharmD, MPH; Lauri A. Hicks, DO; Arjun Srinivasan, MD; George Divine, PhD; Amy Beaulac, PharmD; Erin Eriksson, PharmD; Ronald Kendall, PharmD; Marilen Martinez, PharmD; Allison Weinmann, MD; Marcus Zervos, MD; Susan L. Davis, PharmD

Mecuro NJ, et al. JAMA Netw Open 2022;5(5):e2211331.

Pharmacist-driven transition of care model

- **Evidence-based practice:** optimal antibiotic-prescribing at hospital discharge
  - Defined by selection, dose, and duration
  - Specific uncomplicated infections, e.g. pneumonia, UTI, skin/soft tissue
- **Goal:** To increase the use of optimal antibiotic-prescribing
- **Design:** nonrandomized stepped-wedge
- **Dates:** September 2018-August 2019
- **Setting:** 5 hospitals (17 service teams) within the Henry Ford Health system
  - Each hospital had at least partial FTEs for a stewardship PharmD and doctor
  - Each hospital had clinical pharmacists integrated with medical teams

Mecuro NJ, et al. JAMA Netw Open 2022;5(5):e2211331.

Bundle of implementation strategies

- **Engaged stakeholders**
- **Physician champion**
- **Educational tools**:
  - Institutional protocol for optimizing discharge prescriptions
  - Workflow guide for pharmacists.
- **Quality management**
  - Clinical/stewardship pharmacists audited and provided feedback
  - Monitoring of adherence to audit-and-feedback
- **Support clinicians**:
  - Clinical/stewardship pharmacist nudged the prescriber by entering discharge antibiotic order for co-signature

Mecuro NJ, et al. JAMA Netw Open 2022;5(5):e2211331.

Oral Antibiotic Discharge: Selection and Duration Guideline

See full guideline for additional details; See Renal dose guidelines for dose adjustments

Respiratory Tract Infections	Community-acquired pneumonia, with or without risk factors (without microbiologic data)	• Amox/clav 1000/62.5 mg 2 tabs BID (non-formulary)
		  • + azithromycin 500 mg daily or doxycycline 100 mg BID
		• Amoxicillin 1000 mg TID + macrolide or doxycycline (above)
		• Cefuroxime 500 mg BID OR cefpodoxime 400 mg BID
		  • + azithromycin 500 mg daily or doxycycline 100 mg BID
		• Doxycycline 100 mg BID
		• Moxifloxacin 400 mg OR levofloxacin 750 mg daily (non-form)
			5 days in patients with prompt clinical response
			7-10 days in patients with structural lung disease or delayed response

	Acute exacerbation of COPD (AECOPD)	• Doxycycline 100 mg BID (preferred) • Azithromycin 500 mg x1 then 250 mg daily	5-7 days
	Hospital acquired pneumonia (without microbiologic data)	• Moxifloxacin 400 mg OR levofloxacin 750 mg daily (non-form)	7 days w/prompt clinical response: tailor therapy to microbiologic data
	Influenza	• Oseltamivir 75 mg BID	5 days
Urinary Tract Infections	Uncomplicated UTI/cystitis: Align with organism susceptibility	• Nitrofurantoin (NFT) 100 mg BID • Sulfamethoxazole/trimethoprim (SMT) 1 DS tab BID • Beta-lactam (targeted to organism) • Fosfomycin 3 gm oral sachet (ESBL history only)	• NFT: 5 days • SMT: 3 days • Beta-lactams: 3-7 days • Fosfomycin: 2-3 doses
	Complicated UTI/ pyelonephritis Align with organism susceptibility	• Sulfamethoxazole/trimethoprim (SMT) 1-2 DS tab BID • Ciprofloxacin 500 mg BID • Beta-lactams (targeted to organism)	• SMT: 10-14 days* • Fluoroquinolones: 7 days • Beta-lactams: 10-14 days* *updated for new guidelines 2/19
	Asymptomatic bacteriuria	• Do not treat if not pregnant, or perioperative prophylaxis	0 days
Skin Structure Infection	Non-purulent cellulitis	• Cephalexin 500 mg QID, Cefuroxime 500 mg BID • Dicloxacillin 500 mg QID • Clindamycin 300-450 mg TID (severe beta lactam allergy)	5 days with prompt clinical response
	Purulent cellulitis/cutaneous abscess (suspected MRSA)	• Doxycycline 100 mg BID • Sulfamethoxazole/trimethoprim 1-2 DS BID	5 days with prompt clinical response
Intra-abdominal infection	Spontaneous bacterial peritonitis	• Moxifloxacin 400 mg or levoflox 750 mg daily (non-form)	5 days
	Complicated, community acquired intra-abdominal infection **with source control** eg appendicitis, cholangitis, diverticulitis s/p removal of foci	• Moxifloxacin 400 mg daily • Ciprofloxacin 500 mg BID + metronid 500 mg BID/TID • Cefuroxime 500 mg BID + metronidazole 500 mg BID/TID • Amox/clav 875/125 mg BID	4-7 days after source control* *7 days targeted therapy in transient bacteremia after foci removed

Oral Antibiotic Discharge: Pharmacist Workflow

Patient Identification and Included Infections

Assess patient list for active antibiotic (IV or PO)

Uncomplicated SSTI	Respiratory	Urinary tract	Intra-abdominal
Cellulitis Cutaneous abscess Wound	CAP HAP AECOPD Influenza	Cystitis cUTI CAUTI APN, uncomp	SBP Complicated achieved source control

Excluded Infections

- Endocarditis
- Meningitis/CNS
- Lack of source control
- Bacteremia due to fungi, *S. aureus, Enterococci*
- Fungal pneumonia
- Solid organ transplant
- Febrile neutropenia
- Prostatitis

Assess for Discharge

Review anticipated DC dates and readiness with Epic column and progress notes

Attend progressive rounds when possible. Assess discharge readiness: Clinically stable for discharge?

No

Yes

Collaborate w/ physician for optimal guideline-driven selection/duration

Anticipate definitive antibiotic therapy

- Encourage transition to targeted oral therapy when clinically stable with the optimal agent per HFHS guidelines
- Adjust stop dates/orders of inpatient antibiotics to help facilitate transition

Documenting and Prescribing

Enter Plan of Care Note in Epic for AMS Transitions of Care

Anticipated discharge in next 24 hours?

No: Handoff with TOC i-Vent include discharge information. Enter order for oral stepdown with stop date in Epic

Yes: Enter or edit the active and discharge medication in Epic to include stop date. Account for active inpatient antibiotic days

Discharge Order Tips

- Account for active inpatient antibiotic days for total duration
- Consider costs and tests scripts if financial barriers are anticipated
- Contact Antimicrobial Stewardship pharmacist if further guidance needed

Prospective monitoring of process measures

Protocol adherence:
What percentage of eligible patients received the intervention?

	Nov		Dec		Jan		Feb		Mar		Apr		May		Jun		Jul		Aug	
Phase A	54	57	80	60	85	83	46	75	70	83	87	70	31	83	83	77	55	79	75	71
Phase B	Pre-intervention period								83	46	78	71	55	57	63	79	36	29	75	53
Phase C	Pre-intervention period														36	45	29	45	45	64

Transition of care practice model

- Optimal antibiotic-prescribing at discharge increased:
  - 36% in the pre-intervention period, to
  - 82% in the post-intervention period.
- No differences in 30-day re-admissions or mortality.
- Fewer severe antibiotic-related adverse effects were identified in the postintervention groups: 9% vs. 3%.

Mecuro NJ, et al. JAMA Netw Open 2022;5(5):e2211331.

Implementation science concepts in Henry Ford TOC project

Evidence-based practice	Optimal antibiotic-prescribing at discharge for common conditions
Engaged stakeholders	Yes
Tools for assessing context	Interviews
Duration of pre-implementation phase	6 months
Implementation strategies, number	≥ 6

Mecuro NJ, et al. JAMA Netw Open 2022;5(5):e2211331.

Implementation outcomes

2

- Indicate whether implementation strategies were successful
- Measured from the perspective of clinicians or patients
- Measured before, during and/or after the strategies are deployed
- Qualitative or quantitative assessments

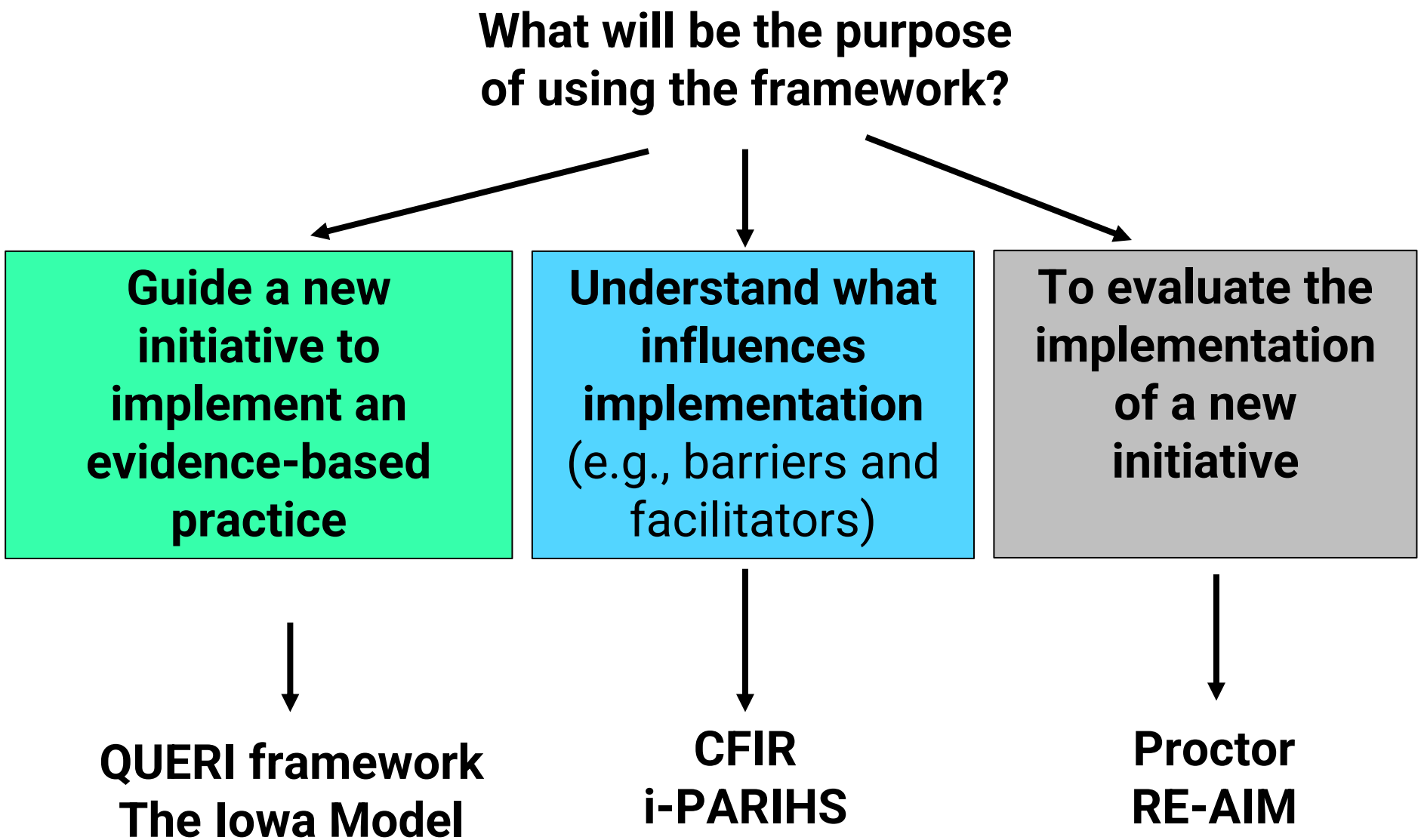
Examples of implementation outcomes

Outcome	Description
Acceptability	Perception that an evidence-based practice or implementation strategy is agreeable or satisfactory
Cost	Financial resources and time required to implement an evidence-based practice
Feasibility	Extent to which an evidence-based practice or implementation strategy can be used in a given setting
Fidelity	Adherence to the original protocol of how to use the implementation strategies

Implementation science frameworks

3

- Systematic approach to developing, managing and evaluating the implementation process
- Standardizes concepts and terminology
- (Too) many frameworks to choose from
  - Consult with an implementation scientist!


What will be the purpose of using the framework?
Guide a new initiative to implement an evidence-based practice
Understand what influences implementation (e.g., barriers and facilitators)
To evaluate the implementation of a new initiative
QUERI framework
The Iowa Model
CFIR
i-PARIHS
Proctor
RE-AIM

Domains and constructs of the Consolidated Framework for Implementation Research (CFIR)

Intervention characteristics	**Outer setting**	**Inner setting**	**Characteristics of individuals**	**Process**
Evidence strength and quality	Patient needs and resources	Culture	Knowledge and beliefs	Planning
Relative advantage	Peer pressure	Leadership engagement	Self-efficacy	Engaging
Adaptability	External policies and incentives	Compatibility	Individual identification with organization	Opinion leaders
Cost	Networking with other organizations	Relative priority	Other personal attributes	Executing
Complexity		Available resources		Reflecting and evaluating
		Readiness for change		

Damschroder LJ, et al. *Implementation Science* 2009;4:50.

QUERI Implementation Roadmap

PRE-IMPLEMENTATION

1. Identify a high-priority evidence-practice gap
2. Cultivate stakeholder support
3. Assess barriers to delivering the evidence-based practice and potential solutions
4. Match implementation strategies to barriers
5. Develop measures and data

IMPLEMENTATION

1. Deploy implementation strategies tailored to the local setting
2. Report progress to stakeholders
3. Adjust plan based on feedback

SUSTAINMENT

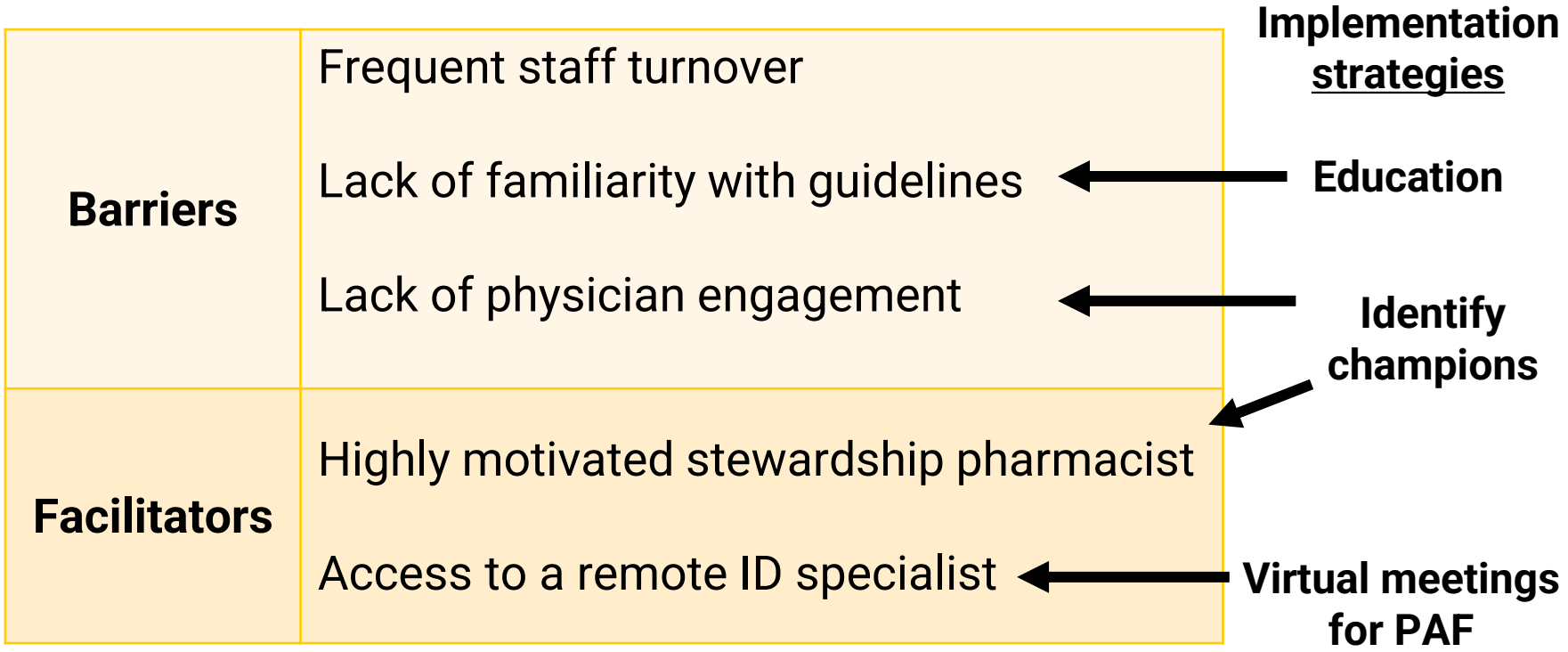
1. Weigh the costs of maintenance
2. Transition ownership to stakeholders
3. Ongoing evaluation and reflection

https://www.queri.research.va.gov/tools/roadmap.cfm

Real-life example #2

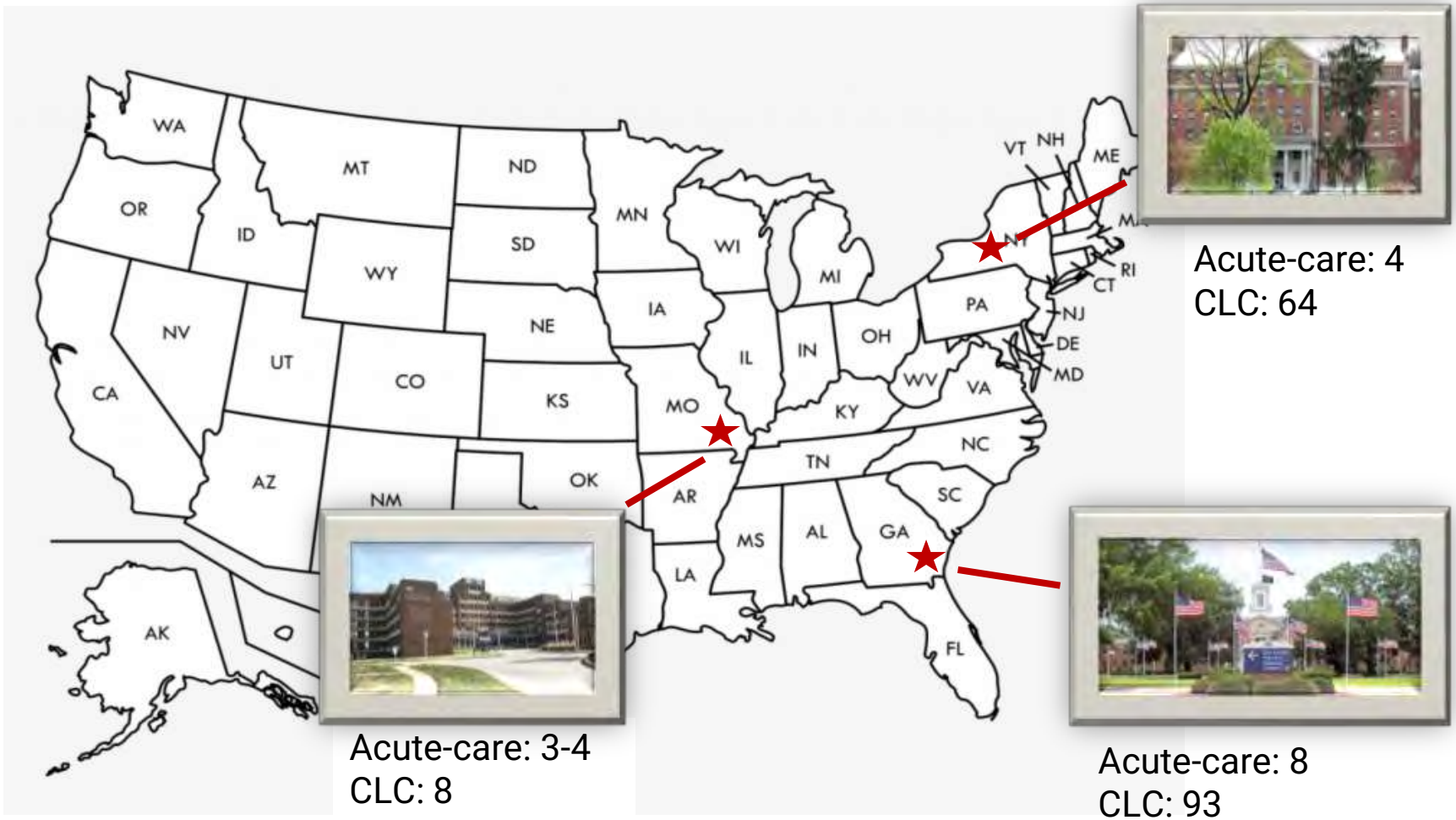
Barriers and facilitators to stewardship at 7 VA hospitals without on-site ID specialists

Based on in-person and virtual site visits during 2019-2020



Livorsi DJ, et al. Infect Control Hosp Epidemiol 2022; 43: 576-581.

Participating VA medical centers



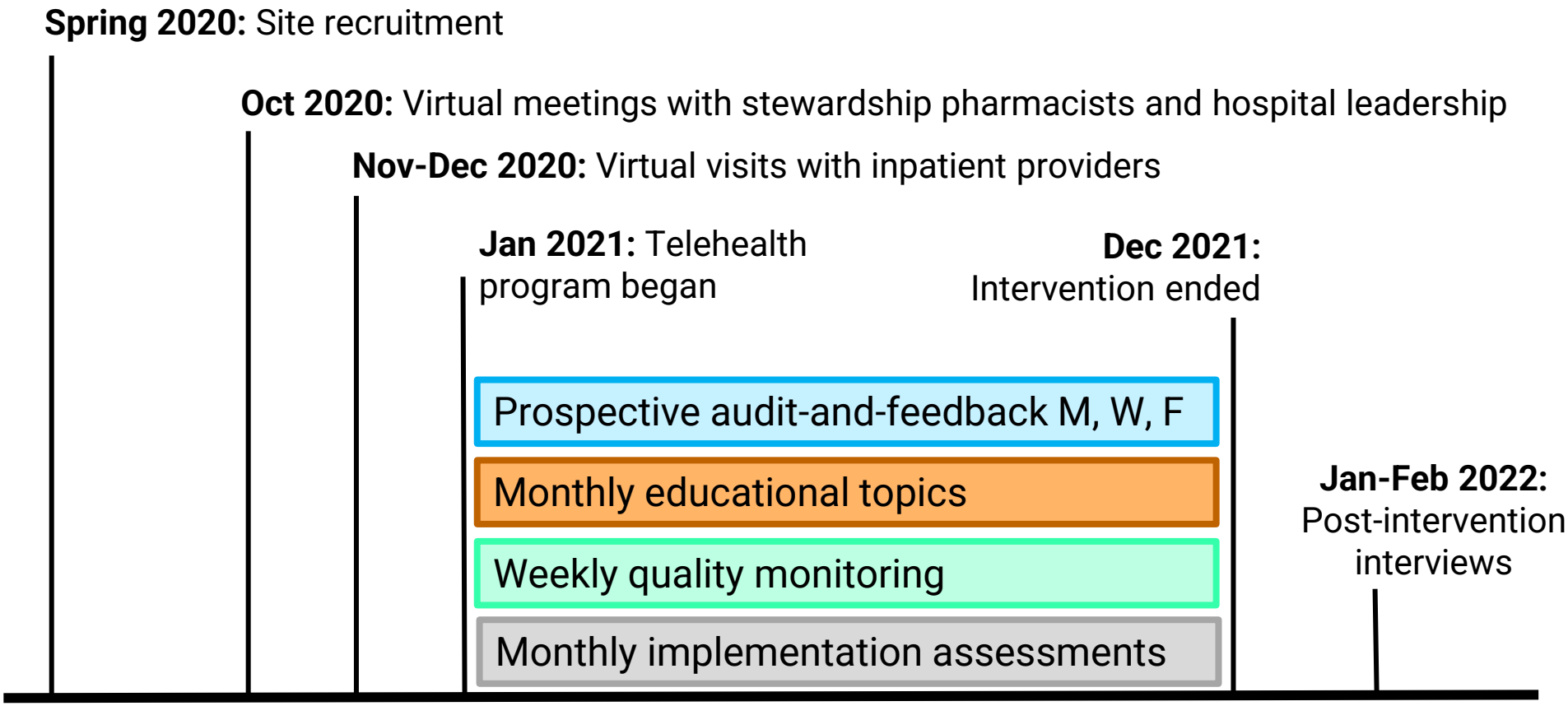
Acute-care: 4
CLC: 64

Acute-care: 3-4
CLC: 8

Acute-care: 8
CLC: 93

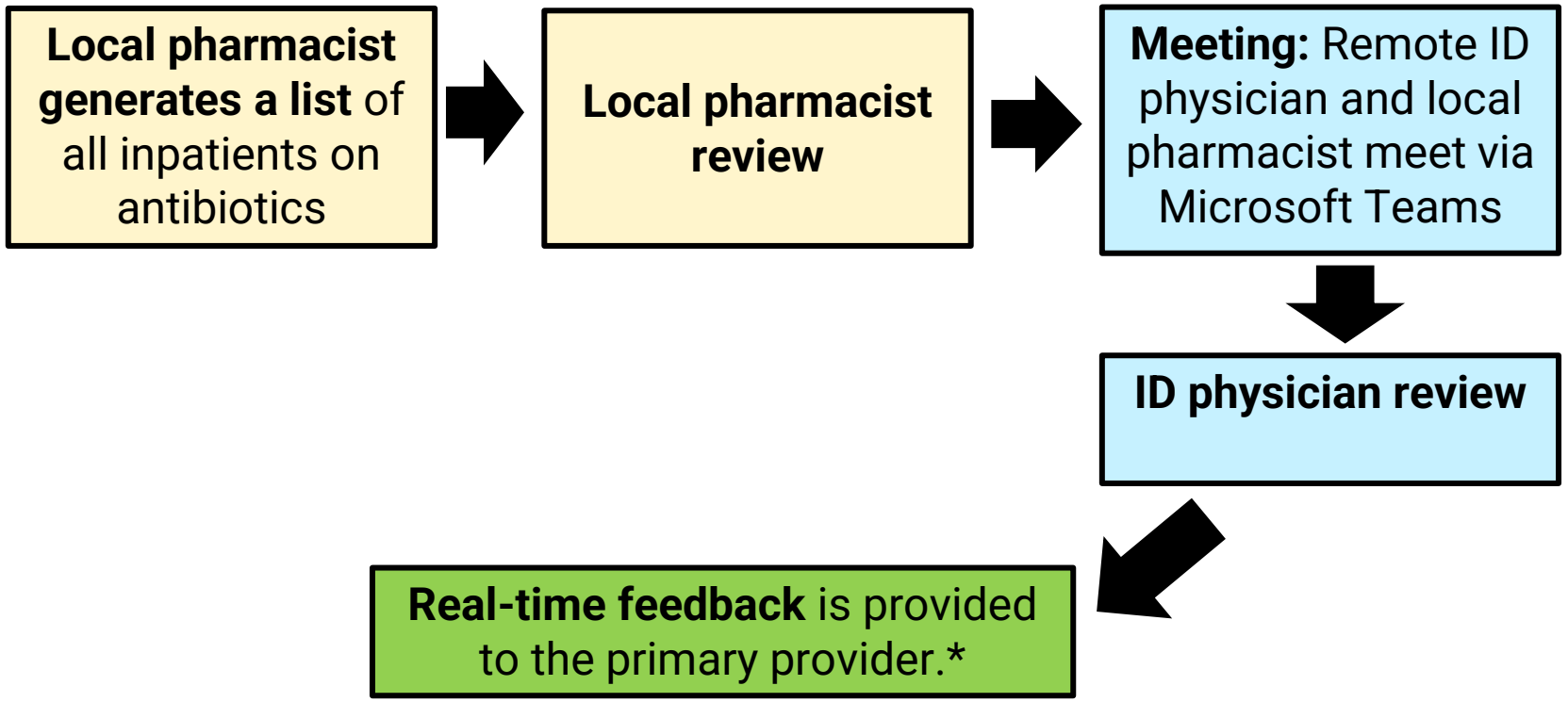
CLC = Community Living Center, which is similar to both a SNF and a nursing home.

Project timeline



Livorsi DJ, et al. Infect Control Hosp Epidemiol 2023 Dec; 44: 2028-2035.

Prospective audit-and-feedback workflow



*Stewardship notes in the EMR were entered at 2 of the 3 sites.

RE-AIM Framework guided our evaluation

- **Reach:** Who participates or is exposed to the program?
- **Effectiveness:**
  - Does the program achieve the desired benefit? Are there negative effects?
- **Adoption**:
  - Which settings are willing to initiate the program? And why?
- **Implementation:**
  - How consistently was the program delivered (i.e., fidelity)?
  - Was it acceptable?
  - How much did it cost (or how much time did it take)?
- **Maintenance:** To what extent does the program become a routine practice?

Glasgow RE, et al. *Am J Public Health*. Sep 1999.

ADOPTION

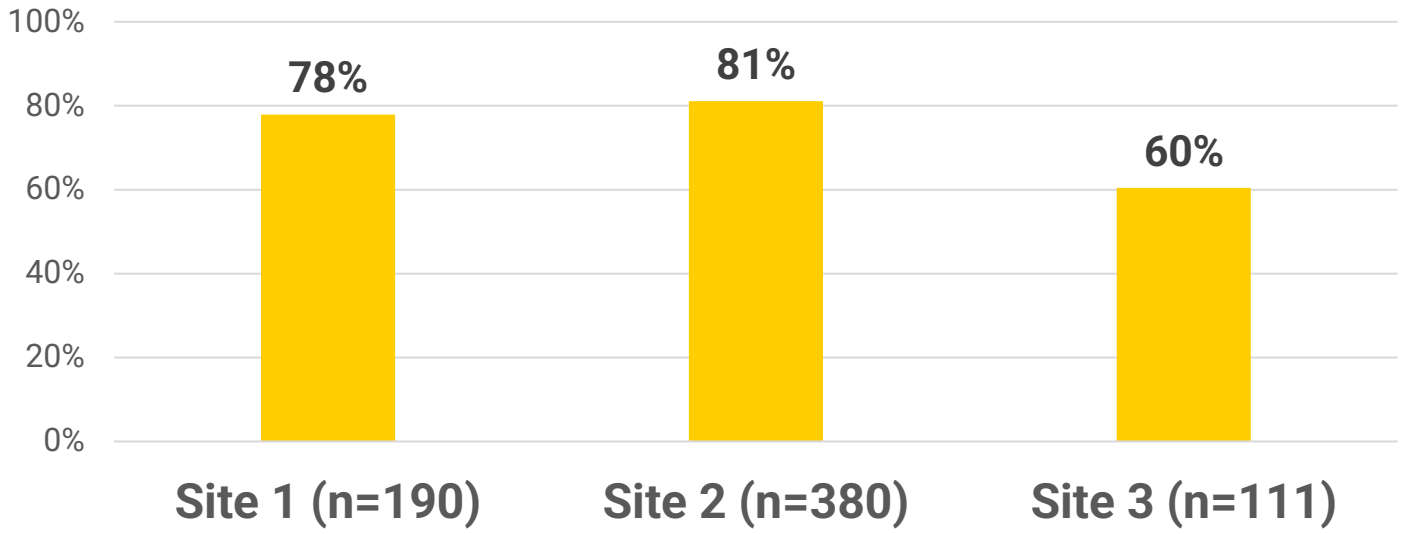
- All 3 invited sites agreed to enroll.
- The primary motivation was the lack of ID support.

Chief of Medicine (site 3): *“We're looking at this as an opportunity to get better personally, as well as benefit the Veterans by preventing unnecessary use of antibiotics for prolonged durations.”*

Livorsi DJ, et al. Infect Control Hosp Epidemiol 2023 Dec; 44: 2028-2035.

REACH

- Feedback was provided to 24 providers across the 3 sites.
- Off-hour providers were not reached.
- **Frequency of accepting recs stratified by site**



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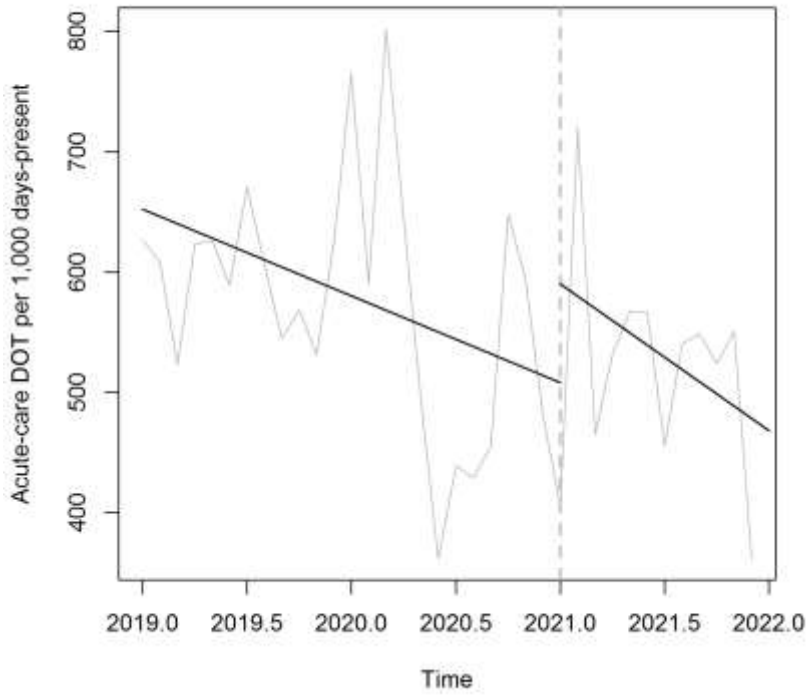
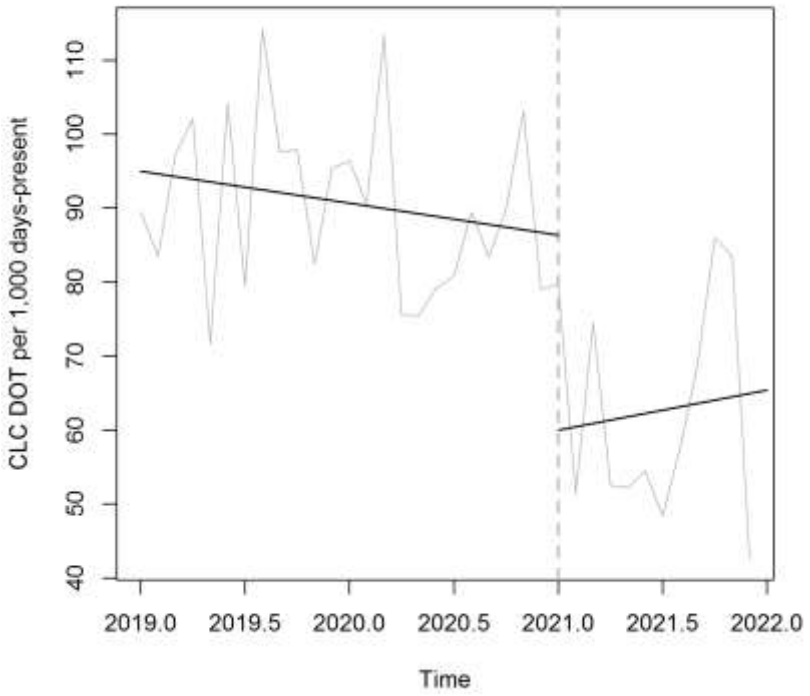
EFFECTIVENESS

Acute-care days of therapy per 1,000 days present



CLC days of therapy per 1,000 days present



Acute-care DOT/1,000 days-present	**Estimate**	**p-value**
Baseline slope	-6.0	0.03
Intercept change	82.3	0.22
Intervention slope change	-4.2	0.62
CLC DOT/1,000 days-present	**Estimate**	**p-value**
Baseline slope	-0.36	0.24
Intercept change	-26.40	**<0.01**
Intervention slope change	0.81	0.41

IMPLEMENTATION, part 1

Fidelity: Audits were consistently performed MWF except during off-days

Acceptability:

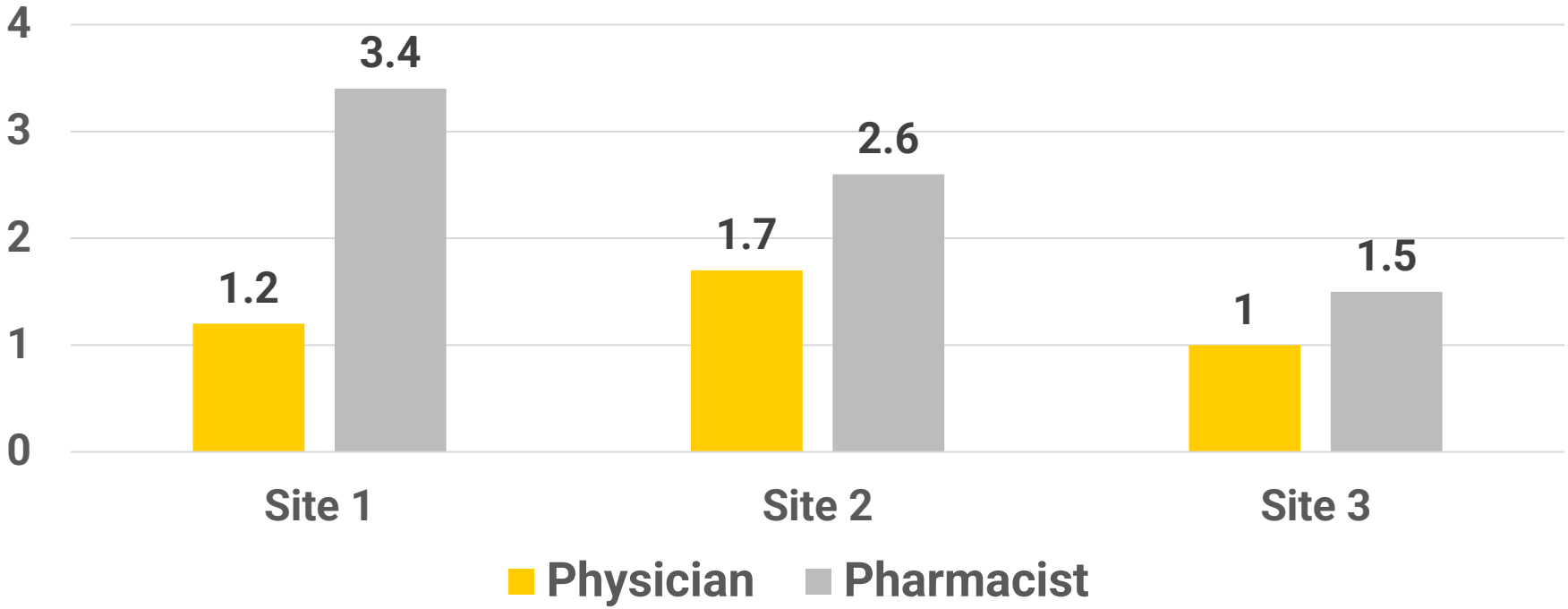
- Most providers appreciated feedback and some actively sought it out.
  - **Chief of Medicine (site 2):** *"I actually really loved that he [the ID physician] is doing this because being a rural facility, we sometimes don't always have the most up-to-date providers."*

- Facilitator: the stewardship team's communication style
- Barriers:
  - Some physicians did not want to receive input from the pharmacist and/or were concerned by lack of bedside assessments.

Livorsi DJ, et al. Infect Control Hosp Epidemiol 2023 Dec; 44: 2028-2035.

IMPLEMENTATION, part 2

Weekly commitment to project activities (mean hours)



Livorsi DJ, et al. Infect Control Hosp Epidemiol 2023 Dec; 44: 2028-2035.

MAINTENANCE

- Potential sustained benefits even once the program ended:
  - Increased self-efficacy: *"I'm probably a little bit more confident just because of the experience and the frequency that we had contact and were able to talk about cases."* (Pharmacist, site 1).
  - Greater awareness of stewardship targets: "I think they've taught us a lot. We are definitely over-prescribing some antibiotics." (Hospitalist, site 3)
- Two sites sufficiently valued the program that they wanted to continue.
    - Adaptations were made to promote sustainability.

Non-scientific language to explain implementation science

- The practice or innovation is **THE THING**
- Efficacy and effectiveness studies assess whether **THE THING** works
- Implementation research looks at how best to help people and places **DO THE THING**
- Implementation strategies are the stuff we do to try to help people and places **DO THE THING**
- Implementation outcomes are **HOW MUCH** and **HOW WELL** they **DO THE THING**

Curran, GM. Implementation Science Communications 2020; 1: 27.

Conclusions

Frameworks can help organize your thinking about implementation and guide your planning.

Prior to implementation, identify barriers to using the evidence-based practice. Choose implementation strategies to address these barriers.

Measuring implementation outcomes can help explain why an initiative succeeds or fails.

Questions?

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