Antimicrobial Stewardship Research Priorities: Where Do We Go From Here?
Dr. Caroline Nott and Dr. Kathryn Suh, The Ottawa Hospital
A Webber Training Teleclass

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ANTIMICROBIAL STEWARDSHIP RESEARCH PRIORITIES: WHERE DO WE GO FROM HERE?

CAROLINE NOTT, MBBS, FRCPC; AND KATHRYN SUH, MD, FRCPC, CIC®
ANTIMICROBIAL STEWARDSHIP PROGRAM
THE OTTAWA HOSPITAL, OTTAWA, ON CANADA

HOSTED BY PAUL WEBBER
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www.webbertraining.com November 21, 2019

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YOUR PRESENTERS

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OBJECTIVES

At the end of this session, participants will be able to:

1. Develop a plan for implementing an ASP (AMS program)
2. Describe methods for measuring success
3. Identify potential research questions to resolve current knowledge gaps related to ASP
4. Recognize determinants (barriers and facilitators) of appropriate antibiotic prescribing in hospitals

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OUTSIDE OF THE SCOPE OF THIS PRESENTATION

- Outpatient settings
- Long term care facilities
- Emergency departments

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OBJECTIVES

At the end of this session, participants will be able to:

1. Develop a plan for implementing an ASP (AMS program)

ANTIMICROBIAL STEWARDSHIP

- "coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting the selection of the optimal antibiotic drug regimen including dosing, duration of therapy, and route of administration"

  OR

- A systematic approach / set of actions to use antibiotics appropriately in order to 1) achieve optimal patient outcomes and 2) minimize unwanted effects…."to ensure sustainable access to effective therapy for all who need them"

IDSA; Dyar OJ et al, Clin Microbiol Infect 2017

REQUIREMENTS FOR AN ASP

- Recognition of the need and importance (executive leadership)
- Sustainable finances
- IT support
- Human resources
  - Physician leadership – credible, knowledgeable (Infectious Diseases or similar)
  - Pharmacists
  - Administrative support
  - Data analyst

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CORE ELEMENTS OF AN ASP

1. Hospital leadership
2. Accountability and defined responsibility
3. Available expertise in infection management
4. Education and training (for both staff as well as ASP team)
5. Other support and actions
6. Monitoring and surveillance
7. Reporting and feedback

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Pulcini C et al, Clin Microbiol Infect 2018

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CDC (US) CORE ELEMENTS OF ASP

1. Hospital leadership commitment
2. Accountability
3. Pharmacy expertise
4. Action
5. Tracking
6. Reporting
7. Education

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CDC 2019

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IMPLEMENTING AN ASP

- Assess the population, current practices, and resources
- Establish a multidisciplinary team
- Consider targets for interventions
- Measure and provide feedback

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STRATEGIES TO IMPROVE ANTIBIOTIC PRESCRIBING

- Persuasive vs. restrictive measures (more later)

- Laboratory:
  - Antibiogram, cascading results, rapid diagnostic testing
- Educational:
  - Diagnostic aides, prescribing pathways and guidelines

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STRATEGIES TO IMPROVE ANTIBIOTIC PRESCRIBING

- Pharmacy:
  - IV to oral conversion, dose optimization, drug monitoring, formulary restrictions
- Computer based:
  - Computer order entry with justification, pathway based prescribing
- Communication:
  - Audit and feedback (real time and aggregate), availability of ASP team

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OBJECTIVES

At the end of this session, participants will be able to:

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2. Describe methods for measuring success

MEASUREMENTS TO DEMONSTRATE SUCCESS

- Process measures
  - Compliance with prescribing guidelines, pathways
- Outcome measures
  - Antimicrobial use
  - Drug costs
  - Patient outcomes
  - Facility (or unit) outcomes

CHALLENGES WITH CURRENT MEASURES

- Evidence for optimal treatment may be lacking
- No clear “best” measure of antibiotic use
- Measures of antibiotic use do not assess appropriateness
- Cost savings / costs are subject to other biases
- Most appropriate clinical outcomes unclear
- Broader outcomes (e.g. CDI, resistance rates) are multifactorial - impact of ASP is difficult to evaluate

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MEASURES OF ANTIBIOTIC USE

- Defined daily doses, DDD
- Days of therapy, DOT
- Length of therapy, LOT
- Standardized antimicrobial administration ratio, SAAR
- Desirability of outcome ranking (DOOR) and response adjusted for duration of antibiotic risk (RADAR)

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WHO; van Santen et al, Clin Infect Dis 2018; Evans SR et al, Clin Infect Dis 2015

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MEASURES OF ANTIBIOTIC USE

Measure	Advantages	Disadvantages
DDD	• Standardized • "easy" to calculate	• Doses for DDDs are sometimes not commonly prescribed doses • Not accurate in some populations • Subject to change (WHO)
DOT	• Preferred metric (NHSN) • More intuitive, comparable	• Needs pharmacy data • Favours broad monotherapy > more appropriate combination therapy
LOT	• Allows assessment of treatment duration	
SAAR	• Allows comparison to benchmark	• Relies on submission of data to NHSN – generalizability?
DOOR/RADAR	• Research at present, not widely used	

WHO; van Santen et al, Clin Infect Dis 2018; Evans SR et al, Clin Infect Dis 2015

COST AS A MEASURE OF SUCCESS

- Antimicrobial costs
  - Based on use (actual dispensed drug)
  - Purchasing costs
- Initial large cost savings will decrease over time – cost containment vs cost savings
- Costs of related outcomes, e.g. *Clostridioides difficile* infection, resistance, difficult to determine

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QUALITY INDICATORS FOR ASP

	Morris, 2012	Moehring, 2017	Science, 2019
Antimicrobial Use	DOTS/patient days	DOTs/patient days DOTs/admissions	DOTS/patient days Total antimicr days
Clinical Outcomes	ARO mortality All cause mortality Conservable days 30d readmission	---	30d readmission
Adverse Outcomes	No. patients with AROs	CDI incidence (2 categories) Drug-resist infection	---
Process Measures	---	Redundant therapy	Adherence to ASP recommendations

Morris AM et al, Infect Control Hosp Epidemiol 2012; Moehring RW et al, Clin Infect Dis 2017; Science M et al, Pediatrics 2019

OBJECTIVES

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2. Describe methods for measuring success
3. Identify potential research questions to resolve current knowledge gaps related to ASP
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AREAS FOR FURTHER RESEARCH

1. Behavioural approaches to prescribing
2. Optimal prescribing practices
3. Strategies for implementing, sustaining AMS interventions
4. Optimal process and outcome measures
5. Research methods and reporting requirements to improve AMS studies
6. Evaluation of ASPs
7. Patient perspectives on AMS
8. Impact of government, policy

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Morris AM et al, Infect Control Hosp Epidemiol 2019; Rzewuska M et al, Clin Microbiol Infect 2019

WHY A BEHAVIOURAL APPROACH?

- Knowledge alone is insufficient to enable change ➔**knowledge translation** is key
- Need to first understand the determinants of physician antibiotic prescribing
  - Barriers
  - Facilitators
- Ultimately, develop and implement behaviour change techniques to influence prescribing behaviour

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BEHAVIOUR IS KEY

- Cochrane review (2017): enablement and restriction both independently associated with increased compliance with prescribing
  - Enablement ("increasing means/reducing barriers to increase capability or opportunity")
  - Restriction ("using rules to reduce the opportunity to engage in the target behaviour; or increasing the target behaviour by reducing the opportunity to engage in competing behaviours")
  - Enablement enhanced restrictions (high evidence)
  - Including feedback may be more effective (moderate evidence)

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Davey P et al, Cochrane Database of Systematic Reviews 2017

BEHAVIOUR CHANGE STRATEGIES

- Charani et al (2011): systematic review of prescribing behaviour in acute care settings, including both qualitative and quantitative studies
- Mixed results with respect to specified outcomes in 10 studies
- None of the included studies applied behavioural science approaches to influence desired (positive) behaviours
- Understanding barriers and facilitators of prescribing within the local context is requisite for effecting behaviour change
- Clear roles and accountability, and actions, also need to be defined

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Charani E et al, Clin Infect Dis 2011; Rzewuska M et al, Clin Microbiol Infect 2019

USING THEORY TO UNDERSTAND BEHAVIOURAL DETERMINANTS

- Provides factors to focus on
- Shared language for shared understanding
- More efficient, can use established framework
- Link to techniques and strategies best suited to address barriers

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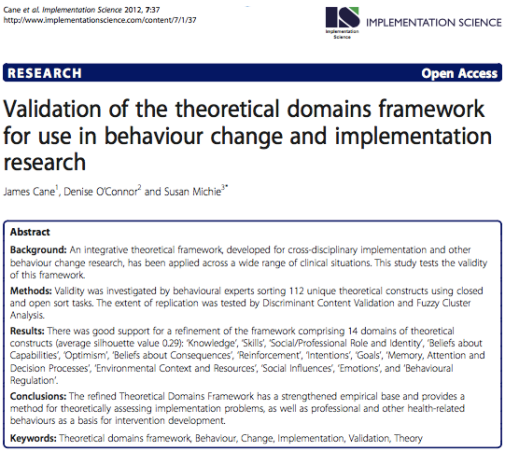
USING THEORY TO UNDERSTAND BEHAVIOURAL DETERMINANTS



Cane et al. Implementation Science 2012, 7:37
http://www.implementationscience.com/content/7/1/37

IMPLEMENTATION SCIENCE

RESEARCH Open Access

Validation of the theoretical domains framework for use in behaviour change and implementation research

James Cane[1], Denise O'Connor[2] and Susan Michie[3*]

Abstract

Background: An integrative theoretical framework, developed for cross-disciplinary implementation and other behaviour change research, has been applied across a wide range of clinical situations. This study tests the validity of this framework.

Methods: Validity was investigated by behavioural experts sorting 112 unique theoretical constructs using closed and open sort tasks. The extent of replication was tested by Discriminant Content Validation and Fuzzy Cluster Analysis.

Results: There was good support for a refinement of the framework comprising 14 domains of theoretical constructs (average silhouette value 0.29): 'Knowledge', 'Skills', 'Social/Professional Role and Identity', 'Beliefs about Capabilities', 'Optimism', 'Beliefs about Consequences', 'Reinforcement', 'Intentions', 'Goals', 'Memory, Attention and Decision Processes', 'Environmental Context and Resources', 'Social Influences', 'Emotions', and 'Behavioural Regulation'.

Conclusions: The refined Theoretical Domains Framework has a strengthened empirical base and provides a method for theoretically assessing implementation problems, as well as professional and other health-related behaviours as a basis for intervention development.

Keywords: Theoretical domains framework, Behaviour, Change, Implementation, Validation, Theory

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Cane et al. Implementation Science 2012;7:37.

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USING THEORY TO UNDERSTAND BEHAVIOURAL DETERMINANTS

- **Theoretical Domains Framework (TDF)**
- Modifiable factors that determine behaviour across a range of settings
- Applicable to any target, action, context, time and actor (TACT-A)
- Many theories and many more constructs distilled into 13 domains that may explain health-related behaviour
- Makes the application of health psychology theory more available to those without a background in psychology

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Cane et al. Implementation Science 2012;7:37.

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THEORETICAL DOMAINS FRAMEWORK (TDF)

Domain	Description
Knowledge	Existing procedural knowledge, knowledge about guidelines, knowledge about evidence and how that influences what the participants do
Skills	Competence and ability about the procedural techniques required to perform the behaviour
Social / professional role and identity	Boundaries between professional groups (i.e., is the behaviour something the participant is supposed to do or someone else's role?)
Beliefs about capabilities	Perceptions about competence and confidence in doing the behaviour
Optimism	Whether the participant's optimism or pessimism about the behaviour influences what they do
Beliefs about consequences	Perceptions about outcomes, advantages, and disadvantages of performing the behaviour and how that influences whether they perform the behaviour
Reinforcement	Previous experiences that have influenced whether or not the behaviour is performed

Cane et al. Implementation Science 2012;7:37.

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THEORETICAL DOMAINS FRAMEWORK (TDF)

Domain	Description
Intention	A conscious decision to perform a behaviour or a resolve to act in a certain way
Goals	Priorities, importance, commitment to a certain course of actions or behaviours
Memory, attention, and decision processes	Attention control, decision-making, memory (i.e., is the target behaviour problematic because people simply forget?)
Environmental context and resources	How factors related to the setting in which the behaviour is performed (e.g., people, organisational, cultural, political, physical, and financial factors) influence the behaviour
Social influences	External influence from people or groups to perform or not perform the behaviour How the views of colleagues, other professions, patients and families, and doing what you are told, influence the behaviour
Emotion	How feelings or affect (positive or negative) may influence the behaviour
Behavioural regulation	Ways of doing things that relate to pursuing and achieving desired goals, standards, or targets Strategies the participants have in place to help them perform the behaviour Strategies the participants would like to have in place to help them

Cane et al. Implementation Science 2012;7:37.

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TDF IN ACTION: SYSTEMATIC REVIEW

- Application of TDF to results of qualitative studies of behavioural determinants of physician antibiotic prescribing
- Systematic review of qualitative studies (n=14), limited to high-income settings, hospitalized inpatient, physician prescribers
- Results synthesized according to the TDF
- Significant behavioural determinants of appropriate antibiotic prescribing were identified as potential targets for interventions to improve physician antibiotic prescribing

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TDF IN ACTION: SYSTEMATIC REVIEW

- Prominent domains
  - Environmental Context and Resources
  - Social Influence
  - Social and Professional Role and Identity
  - Beliefs about Capabilities
  - Knowledge
  - Beliefs about Consequences
  - Skills

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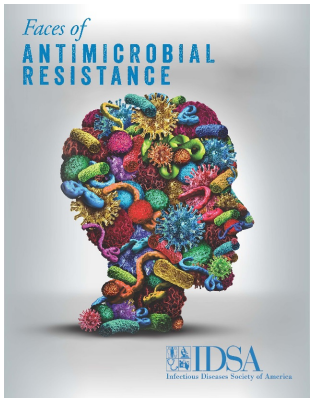
TDF IN ACTION: SYSTEMATIC REVIEW

- Cross-cutting themes
  - Differences in junior vs. senior physician determinants of antibiotic prescribing
  - Relatively low perceived threat of antimicrobial resistance



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TDF IN ACTION: NON-ID PHYSICIAN BARRIERS AND FACILITATORS

- What are the barriers to/facilitators of appropriate antibiotic prescribing by non-ID physicians?
- Qualitative, semi-structured, in-depth interviews conducted with 16 physicians
- Interviews were recorded, transcribed, quotes were coded into TDF domains
- Themes developed from individual quotes
- Determinants of appropriate antibiotic prescribing described

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TDF IN ACTION: NON-ID PHYSICIAN BARRIERS

Selected TDF Domains	Dominant Examples (order does not reflect frequency or relevance)
Intention	• I intend to prescribe appropriately • I intend to follow guidelines as much as possible
Memory, attention and decision	• I follow guidelines to help make decisions • The sicker the patient, the more anxious I am, the more broadly I prescribe • For various steps of antibiotic prescribing my decisions are automatic
Skills	• Experience and knowledge of guidelines improve confidence in antibiotic prescribing • I have/ have not received training in antibiotic prescribing
Environment, context and resources	• I have / do not have access to adequate resources to appropriately prescribe antibiotic • Prescribing is influenced by the culture where I work • My knowledge about prescribing comes from speaking with colleagues
Goals	• Appropriate antibiotic prescribing is / is not a priority to me • The "5-steps" of prescribing are important to me (i.e. Does this patient require antibiotic? What empiric antibiotic? Dose? Duration? Switch IV to oral?) • Compliance with guidelines
Beliefs about consequences	• Fear of under-treatment • Antibiotic prescribing has consequences (including side effects)

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USING THEORY TO ENACT CHANGE

- **Behaviour Change Techniques (BCTs)**
- Which strategies can be effectively used to target those factors?
- Which BCTs are best suited to specifically target the identified barriers and enablers?

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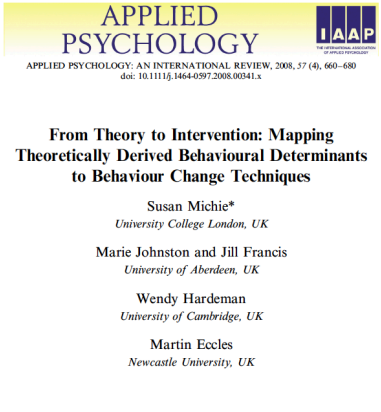
BEHAVIOUR CHANGE TECHNIQUES



APPLIED PSYCHOLOGY

APPLIED PSYCHOLOGY: AN INTERNATIONAL REVIEW, 2008, 57 (4), 660–680
doi: 10.1111/j.1464-0597.2008.00341.x

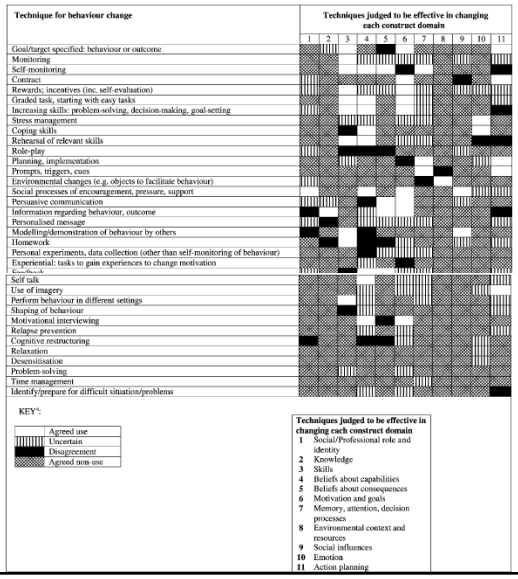
From Theory to Intervention: Mapping Theoretically Derived Behavioural Determinants to Behaviour Change Techniques

Susan Michie*
University College London, UK

Marie Johnston and Jill Francis
University of Aberdeen, UK

Wendy Hardeman
University of Cambridge, UK

Martin Eccles
Newcastle University, UK



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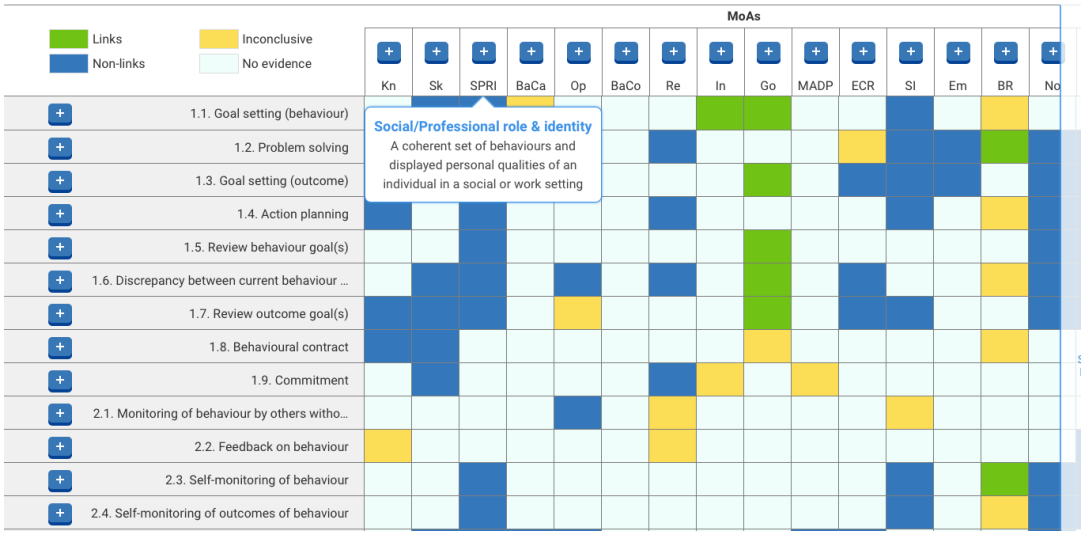
USING THEORY TO ENACT CHANGE



https://theoryandtechniquetool.humanbehaviourchange.org/tool

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TDF IN ACTION: ID PHYSICIAN BEHAVIOUR CHANGE TECHNIQUES (BCTS)

- What BCTs are ID physicians currently using to influence their non-ID colleagues' antibiotic prescribing behaviours?
- Qualitative, semi-structured, in-depth interviews with 12 ID physicians
- Interviews were recorded, transcribed, quotes were coded into TDF domains
- Themes developed from individual quotes
- Explored whether ID physicians see themselves as agents of change for their non-ID peers and described BCTs currently in use

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TDF IN ACTION: ID PHYSICIAN BEHAVIOUR CHANGE TECHNIQUES (BCTS)

Most Frequently Used Strategies by ID Physicians	Examples
Give instructions on how to perform the behaviour	• Write the recommendation in the chart • Refer recommendation to the specific patient, but generalize when possible • Discuss in person
Provide social support	• Agree on next steps together • "Permission" for non-ID approach first, if appropriate, then ID approach • Promote autonomy of non ID physicians
Inform about consequences	• Explain rationale for prescribing antibiotics • Reinforce key messages in consult
Be a credible source	• Provide evidence (e.g. guidelines, published evidence, local data)
Focus on past successes	• Remind non-ID physicians of their past successes

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TDF AND BCTS IN ACTION

- Themes were mapped to identify the highest impact BCTs that ID physicians might apply in clinical interactions, for inclusion in a BCT toolkit and workshop
- Workshop designed to train ID physicians to
  - ➔ "Diagnose" the barrier
  - ➔ Choose from a toolkit of potential BCTs to address the barrier
- Behaviour change skills represent a potential new area of competency for ID physicians and ASPs

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TDF AND BCTS IN ACTION

Four Areas for ID Physicians to Address

"What to do" (knowledge)	
Outside of scope of BCTs →	Redirect to available resources
"Worried about this patient" (motivation and insight)	
Social reward →	Offer verbal "reward" for prescribing most appropriate treatment and duration
Positive reinforcement →	Remind of previous positive experiences / good outcomes
Goal setting →	Share treatment goal for a particular case
Pros and cons →	Support recommendation with information about health consequences

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TDF AND BCTS IN ACTION

Four Areas for ID Physicians to Address

"Someone else prescribed" (social influence)	
Pros and cons →	Explain pros and cons of changing what others have ordered
"This is how I do things" (automatic actions)	
Instructions on how to perform the behaviour →	Check people out of routine
Action planning →	Create a new routine to change old habits
Mental rehearsal →	Give an example and make them think prospectively about a similar situation

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BEHAVIOURAL RESEARCH GAPS

- Feasibility of introducing BCTs to change antibiotic decision-making
- Effectiveness of using BCTs to improve antibiotic prescribing
- Most effective method of providing antimicrobial prescribing feedback to individual physicians

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ASP RESEARCH GAPS

Infection Control & Hospital Epidemiology (2019), 1–10
doi:10.1017/ice.2019.276

SHEA

SHEA White Paper

Research needs in antibiotic stewardship

Andrew M. Morris MD, MS[1,2], Michael S. Calderwood MD, MPH[3], Scott K. Fridkin MD[4], Daniel J. Livorsi MD, MSc[5,6], Jessina C. McGregor PhD[7], Lona Mody MD, MSc[8], Rebekah W. Moehring MD, MPH[9,10], Amy L. Pakyz PharmD, MS, PhD[11], Edward Stenehjem MD, MSc[12], Julia E. Szymczak PhD[13] and Pranita D. Tamma MD, MHS[14]

[1]Sinai Health, University Health Network, and University of Toronto, Toronto, Ontario, Canada, [2]Division of Infectious Diseases, Department of Medicine, University of Toronto, Ontario, Canada, [3]Section of Infectious Disease and International Health, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, [4]Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia, [5]Iowa City Veterans Affairs Health Care System, Iowa City, Iowa, [6]Division of Infectious Diseases, University of Iowa Carver College of Medicine, Iowa City, Iowa, [7]Department of Pharmacy Practice, Oregon Health & Science University College of Pharmacy, Oregon State University, Portland, Oregon, [8]University of Michigan and VA Ann Arbor Healthcare System, Ann Arbor, Michigan, [9]Duke Center for Antimicrobial Stewardship and Infection Prevention, Durham, North Carolina, [10]Duke University School of Medicine, Durham, North Carolina, [11]Virginia Commonwealth University School of Pharmacy, Richmond, Virginia, [12]Office of Patient Experience, Intermountain Healthcare, Salt Lake City, Utah, [13]Division of Infectious Diseases, Department of Biostatistics, Epidemiology, and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania and [14]The Johns Hopkins University School of Medicine, Baltimore, Maryland

Morris AM et al, Infect Control Hosp Epidemiol 2019

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ASP RESEARCH GAPS

1. Optimal prescribing practices
2. Strategies for implementing, sustaining AMS interventions
3. Optimal process and outcome measures
4. Research methods and reporting requirements to improve AMS studies

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Morris AM et al, Infect Control Hosp Epidemiol 2019

OPTIMAL ANTIBIOTIC PRESCRIBING

- New data
  - Duration of therapy
    - Bacteremia (BALANCE, ongoing)
    - Intra-abdominal infections (STOP-IT, 2015)
  - PO vs. IV therapy
    - Endocarditis (POET, 2019)
    - Bone and joint infections (OVIVA, 2019)

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OPTIMAL ANTIBIOTIC PRESCRIBING

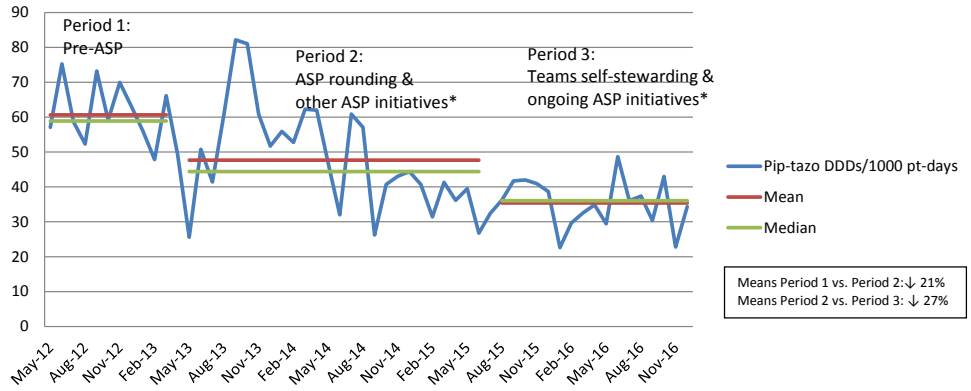
- Completion of therapy with PO beta-lactams
- Relationship between treatment of asymptomatic bacteriuria and resolution of delirium
- Role for prophylactic PO vancomycin for *C. difficile* prevention

... and many more!!

EFFECTIVENESS, SPREAD, AND SUSTAINABILITY OF ASP INTERVENTIONS

- Combinations of strategies
- Transitions of care (ex. ED to LTC/home, ICU to ward)
- Spread through the hospital; interventions to address specific services' needs
- Sustainability over time ("self-stewardship"); less reliance on resource-intensive interventions
- Behavioural, social and systems considerations

Monthly Piperacillin-Tazobactam DDDs/1000 Patient-Days
General Medicine, Civic Campus
May 2012 to December 2016



*ASP initiatives: Development, update and promotion of antibiotic tools (e.g., clinical pathways), educational presentations

TOH Antimicrobial Stewardship Program 2017

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OPTIMAL AND STANDARDIZED OUTCOME AND PROCESS MEASURES

- Asses appropriateness of antibiotics
- Benchmark antibiotic use between similar prescribers, similar services, similar institutions
- Determine best antibiotic use measure (DOT vs DDD vs other)
- Decide on a globally accepted metric for measuring ASP success
- Incorporate patient outcomes and facility/healthcare systems outcomes

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ADVANCED STUDY DESIGNS

- Standardize process metrics
- Report patient-focused outcomes
- Identify methods to avoid major sources of bias
- Evaluate new initiatives in the context of established ASP activities
- Incorporate economic analysis of interventions

SUMMARY

We have discussed how to:

1. Develop a plan for implementing an ASP (AMS program)
2. Describe methods for measuring success
3. Identify potential research questions to resolve current knowledge gaps related to ASP
4. Recognize determinants (barriers and facilitators) of appropriate antibiotic prescribing in hospitals

ADDITIONAL RESOURCES

- ESCMID generic competencies: Clin Microbiol Infect 2019;13-9. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(18)30662-1/fulltext
- Infectious Diseases Society of America Guidelines
  - Developing an ASP: Clin Infect Dis 2007;44:159-77
  - Implementing an ASP: Clin Infect Dis 2016;62:e51-77. https://www.idsociety.org/practice-guideline/implementing-an-ASP/
- CDC. Core elements of hospital antibiotic stewardship programs. 2019. www.cdc.gov/antibiotic-use/core-elements/hospital.html
- British Society for Antimicrobial Chemotherapy 2013. http://bsac.org.uk/wp-content/uploads/2013/07/Stewardship-Booklet-Practical-Guide-to-Antimicrobial-Stewardship-in-Hospitals.pdf

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www.webbertraining.com/schedulep1.php

November 21, 2019	PRIORITIZING RESEARCH AREAS FOR ANTIBIOTIC STEWARDSHIP PROGRAMS Speaker: **Dr. Caroline Nott** and **Dr. Kathryn Suh**, The Ottawa Hospital
December 5, 2019	HOW TO COMMUNICATE ABOUT HEALTHCARE-ASSOCIATED INFECTION WITH X, Y AND Z GENERATIONS Speaker: **Dr Anne-Gaëlle Venier**, Hôpital Pellegrin - CHU de Bordeaux, France
December 18, 2019	*(FREE Teleclass)* CLEANING IN HEALTHCARE Speaker: **Prof. Andreas Voss**, Radboud University, The Netherlands

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