

Evidence-based Synthesis Program (ESP)

Antimicrobial Stewardship Programs in Outpatient Settings

A Systematic Review of the Evidence

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VA Evidence-based Synthesis (ESP) Program Overview

- Sponsored by VA Office of R&D and Quality Enhancement Research Initiative (QUERI).
- Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers and policy-makers, as they work to improve the health and healthcare of Veterans.
- Builds on staff and expertise already in place at the Evidence-based Practice Centers (EPC) designated by AHRQ. Four of these EPCs are also ESP Centers:
 - Durham VA Medical Center; VA Greater Los Angeles Health Care System; Portland VA Medical Center; and Minneapolis VA Medical Center.

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- Provides evidence syntheses on important clinical practice topics relevant to Veterans, and these reports help:
 - develop clinical policies informed by evidence,
 - the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
 - guide the direction for future research to address gaps in clinical knowledge.
- Broad topic nomination process – e.g. VACO, VISNs, field – facilitated by ESP Coordinating Center (Portland) through online process:

<http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm>

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- Steering Committee representing research and operations (PCS, OQP, ONS, and VISN) provides oversight and guides program direction.
- Technical Expert Panel (TEP)
 - Recruited for each topic to provide content expertise.
 - Guides topic development; refines the key questions.
 - Reviews data/draft report.
- External Peer Reviewers & Policy Partners
 - Reviews and comments on draft report
- Final reports posted on VA HSR&D website and disseminated widely through the VA.

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

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Current Report

Antimicrobial Stewardship Programs in Outpatient Settings

A Systematic Review of the Evidence (September, 2013)

Full-length report available on ESP website (VA INTRANET only):

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

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Background

- >3 million kilograms of antimicrobials administered to human patients in the United States in 2009 (Spellberg 2013)
- Antimicrobial use influences the patient being treated AND the surrounding ecosystem (Fleming 1945, Avorn 2000, CDC 2010)

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Background

- Inappropriate/excessive antimicrobial use associated with:
 - **Increasing microbial resistance**
 - **Higher incidence of antimicrobial associated *Clostridium difficile* infection (CDI)**
 - **Other drug related toxicities and increased healthcare costs (Jacob 2010)**
- Inadequate antimicrobial use associated with increased mortality (Kollef 1999, Ibrahim 2000, Micek 2010)

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Background

- Antimicrobial Stewardship Programs
 - Effort to *optimize* antimicrobial use
 - Administer an antimicrobial?
 - Which one?
 - What dose?
 - What route?
 - What duration?
 - Goals include:
 - Improve patient outcomes
 - Limit antimicrobial resistance
 - Reduce adverse antimicrobial effects
 - Deliver cost-effective therapy

(Avorn 2000, Fishman 2006, Dellit 2007, Jacob 2010, Ohi 2011)

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Background

- Antimicrobial Stewardship Programs may involve:
 - **Multidisciplinary teams (infectious disease physicians, clinical pharmacists, clinical microbiologists, infection control specialists, epidemiologists)**
 - **Support and collaboration of hospital (clinic) leadership and administration**
 - **Computer systems for decision making and tracking antimicrobial use, infections, resistance trends, adverse drug events**

(Avorn 2000, Fishman 2006, Dellit 2007, Jacob 2010, Ohi 2011)

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Background

- Intervention types include:
 - **Prospective audit with feedback (inpatient only?)**
 - **Formulary restriction and preauthorization**
 - Education
 - **Guidelines and clinical pathways**
 - Antimicrobial cycling
 - **Order forms**
 - Streamlining or de-escalation of therapy
 - Dose optimization

(Dellit 2007)

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Purpose of Review

Synthesize evidence about effectiveness & harms of antimicrobial stewardship programs implemented in outpatient settings

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Key Questions

- Key Question #1

What is the effectiveness of antimicrobial stewardship programs in outpatient settings on the following:

- a) Primary Outcome: Antimicrobial prescribing (decision to prescribe, selection of antimicrobial, duration of treatment, guideline concordant use)
- b) Secondary Outcomes:
 - 1) Patient centered outcomes (return clinic visits, hospital admission, adverse events, late antimicrobial prescription, patient satisfaction with care)
 - 2) Microbial outcomes (resistance in study population)
 - 3) Costs (program costs, drug costs)

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Key Questions

- Key Question #2

What are the key intervention components associated with effective outpatient antimicrobial stewardship?

- Key Question #3

Does effectiveness vary by:

- a) clinic type or setting?**
- b) suspected patient condition?**

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Key Questions

- Key Question #4

What are the harms of antimicrobial stewardship programs in outpatient settings?

- Key Question #5

Within the included studies, what are the barriers to implementation, sustainability, and scalability of outpatient antimicrobial stewardship programs?

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Methods

- Agency for Healthcare Research and Quality review (Ranji, 2006) with search to 2004 partially addressed key questions
- MEDLINE search 2000 to November 2013, based on Cochrane search strategy, limited to English language
- Additional studies from systematic reviews, reference lists of retrieved articles, and suggestions from technical expert panel and peer reviewers

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Methods

- Excluded
 - **Setting not relevant to medicine in the US (e.g., antimicrobials available without prescription) or involving a population or infectious disease not relevant to US population**
 - **Studies without an intervention/intervention of interest (i.e., education only)**
 - **Antimicrobials for medical or surgical prophylaxis**
 - **Viral or fungal infections, tuberculosis**
 - **Provider education only or community/public health campaigns**
 - **Descriptions of interventions with no outcome assessment**
 - **Design other than randomized controlled trial, cluster randomized controlled trial, controlled clinical trial, controlled before and after study, or interrupted time series**
 - **Studies not reporting outcomes of interest**

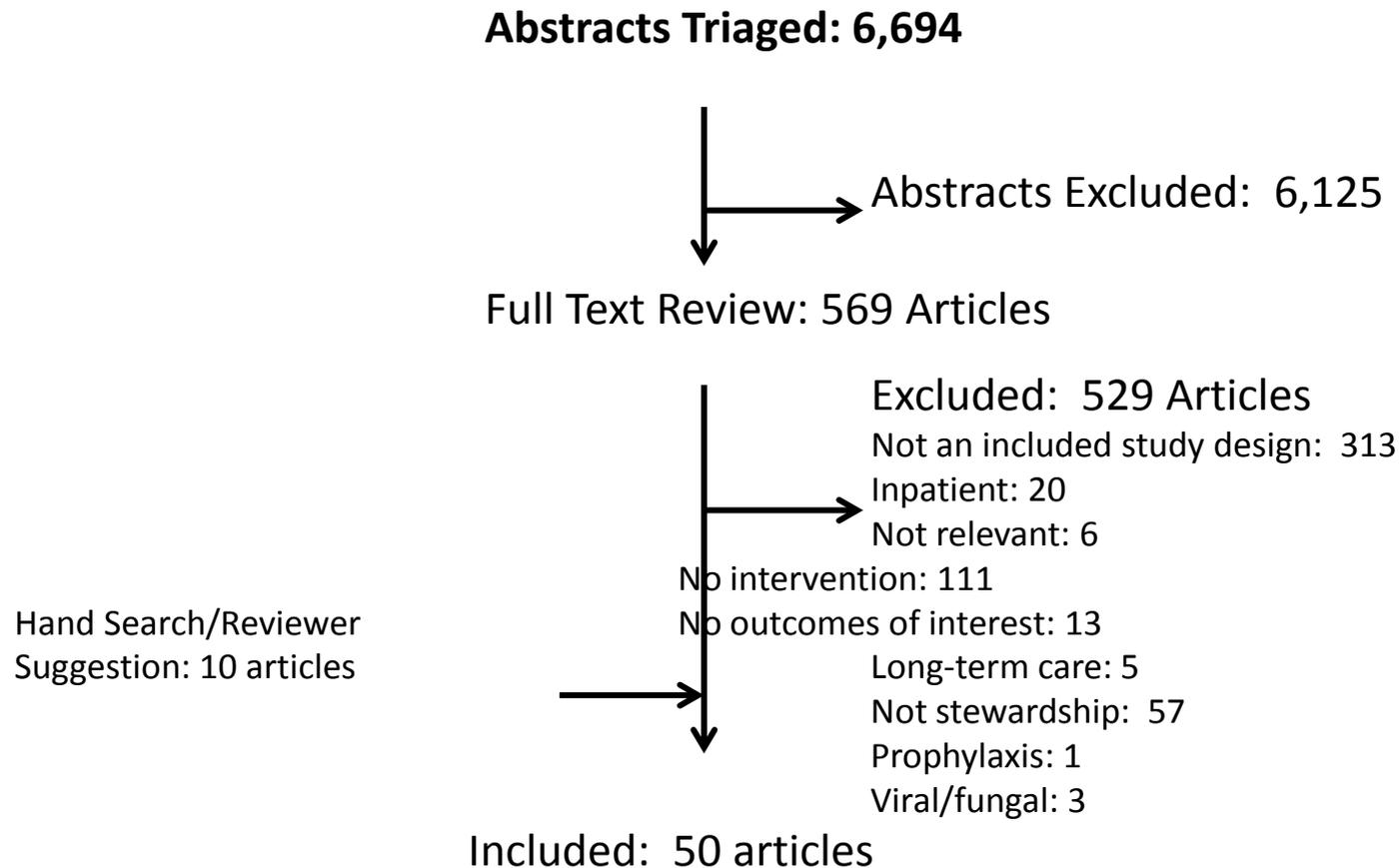
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Methods

- Standard methods for data extraction
- Assessed risk of bias of individual studies (**Cochrane Effective Practice and Organization of Care method**) and **strength of evidence for patient-centered outcomes**
- Categorized studies by intervention type
 - **Difficult for some studies - multiple interventions, hybrid interventions**
- Unable to pool data due to heterogeneity of interventions, study designs, patient populations, and outcomes reporting

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Literature Flow



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Results

- Existing AHRQ Review (Ranji, 2006)
- Focused on:
 - 1) Reducing unnecessary prescribing**
 - 2) Improving antimicrobial selection**

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Results (Ranji 2006)

- Reducing unnecessary prescribing
 - **30 trials included in pooled analysis**
 - **Interventions reduced median absolute proportion of visits at which an antimicrobial was prescribed by -9.7% (IQR -6.6 to -13.7%)**
 - **6 months median follow-up.**
 - **Additional 18 trials where effect size unknown; relative reductions described in most (Median, 12%)**
 - **Few studies reported patient centered outcomes, resistance, or cost**

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Results (Ranji 2006)

- Improving antimicrobial selection
 - **22 trials included in pooled analysis**
 - **Interventions increased recommended antimicrobial prescribing by 10.6% (IQR 2.4 to 18.2%)**
 - **Additional 11 trials where effect size unknown; improvement in recommended antimicrobials, decrease in non-recommended**
 - **No studies reported patient centered outcomes or resistance; 3 reported cost decreases**

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Results

- VA-ESP Evidence
 - 17 RCTs, 18 CRCTs, 3 CCTs, 6 CBAs, 6 ITS studies
 - Categorized studies by intervention type:
 - 16 provider or patient education
 - 5 provider feedback
 - 6 guidelines
 - 4 delayed prescribing
 - 6 communication skills training
 - 2 restriction policies
 - 6 computerized clinical decision support
 - 1 financial incentive
 - 9 laboratory guidance (procalcitonin, PCR, CRP, etc)

***Number of studies is greater than 50; studies with multiple interventions are included under each intervention**

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- Studied conditions:
 - Respiratory tract infections (n = 29)
 - Multiple or not specified (n = 17)
 - UTI (n = 2)
 - Dental pain (n = 1)
 - Sexually transmitted infections (n = 1)

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KQ1a – Program Effectiveness: Prescribing Outcomes (1/2)

| ASP Intervention (# studies) | Prescribing Rate/Use | Selection | Duration | Guideline Concordant Use |
|--|---|--|-----------|--------------------------------|
| Provider and/or Patient Education (5 RCT, 6 CRCT, 1 CCT, 4 CBA) | Improved: + 9 studies ≈ 6 studies | + 3 studies ≈ 5 studies | ≈ 1 study | NR |
| Provider Feedback (1 RCT, 2 CRCT, 1 CCT, 1 CBA) | Improved: + 3 studies ≈ 2 studies | + 2 studies ≈ 1 study | NR | ≈ 1 study |
| Guidelines (1 CRCT, 1 CCT, 4 ITS) | Improved: + 3 studies ≈ 1 study | + 3 studies ≈ 1 study | ≈ 1 study | NR |
| Delayed Prescribing (4 RCT) | Improved: + 3 studies ≈ 1 study | + indicates sig difference favoring intervention ≈ indicates no sig difference - Indicates sig difference favoring control +/- Indicates mixed results across drugs | | |
| Communication Skills Training (6 CRCT) | Improved: + 5 studies ≈ 1 study | | | |

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KQ1a – Program Effectiveness: Prescribing Outcomes (2/2)

| ASP Intervention (# studies) | Prescribing Rate/Use | Selection | Duration | Guideline Concordant Use |
|--|--|---------------|----------|--------------------------------|
| Communication Skills Training (6 CRCT) | Improved: + 5 studies ≈ 1 study | NR | NR | NR |
| Restriction (2 ITS) | Improved: +/- 2 studies | +/- 2 studies | NR | + 1 study |
| Decision Support (2 RCT, 3 CRCT, 1 CBA) | Improved: + 4 studies* ≈ 2 studies | + 2 studies | NR | + 1 study |
| Financial Incentive (1 CBA) | Improved: + 1 study | NR | NR | NR |
| Procalcitonin, Rapid Antigen Detection Tests, PCR Assay, CRP (6 RCT, 2 CRCT, 1 CBA) | Improved: + 8 studies ≈ 1 studies | + 1 study | NR | NR |

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KQ1b – Program Effectiveness: patient centered outcomes (1/2)

| ASP Intervention (# studies) | Return Clinic Visits | Hospitalizations | Adverse Events | Late Antimicrobial Prescribing | Patient Satisfaction with Care |
|--|--------------------------------|----------------------------|-------------------|--------------------------------------|--------------------------------------|
| Provider and/or Patient Education (5 RCT, 6 CRCT, 1 CCT, 4 CBA) | ≈ 2 studies - 1 study | ≈ 2 studies | ≈ 1 study | NR | ≈ 1 study |
| Provider Feedback (1 RCT, 2 CRCT, 1 CCT, 1 CBA) | NR | NR | NR | NR | NR |
| Guidelines (1 CRCT, 1 CCT, 4 ITS) | NR | NR | NR | NR | ≈ 1 study |
| Delayed Prescribing (4 RCT) | + 1 study ≈ 1 study | NR | ≈ 1 study | NR | NR |
| Communication Skills Training (6 CRCT) | ≈ 3 studies | ≈ 1 study p=NR, 1 study | ≈ 4 studies | + 1 study | ≈ 3 studies + 1 study |

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KQ1b – Program Effectiveness: patient centered outcomes (2/2)

| ASP Intervention (# studies) | Return Clinic Visits | Hospitalizations | Adverse Events | Late Antimicrobial Prescribing | Patient Satisfaction with Care |
|---|----------------------------|------------------|-------------------|--------------------------------------|--------------------------------------|
| Restriction (2 ITS) | - 1 study | - 1 study | ≈ 1 study | NR | NR |
| Decision Support (2 RCT, 3 CRCT, 1 CBA) | ≈ 4 studies | ≈ 2 studies | p=NR, 1 study | ≈ 2 studies | NR |
| Financial Incentive (1 CBA) | NR | NR | NR | NR | NR |
| Procalcitonin, Rapid Antigen Detection Tests, Polymerase Chain Reaction Assay, and C-Reactive Protein (6 RCT, 2 CRCT, 1 CBA) | ≈ 4 studies | ≈ 4 studies | ≈ 6 studies | + 2 studies ≈ 1 study | + 1 study ≈ 2 studies |

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KQ1b – Program Effectiveness: microbial and cost outcomes

- Microbial outcomes: no studies reported
- Costs:
 - **7 studies reported dispensing costs (6 with significant decreases, one mixed)**
 - **3 reported program costs (ranged from \$6/patient for CRP testing, to \$4,800 annually for provider education intervention)**

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KQ2 Results – Key Implementation Components

- Limited evidence available
 - **Speculation by authors and focus group interviews**
 - **Suggested key components:**
 - **Supportive leadership**
 - **Team approach**
 - **Patient education materials**
 - **Provider reminders**
 - **User-friendly interfaces**
 - **Evidenced-based materials**

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KQ3 Results – Effectiveness in Different Settings or Different Suspected Conditions

- Vast majority in primary care clinics (exceptions: dental clinic, STI clinic, urgent care, outpatient infectious disease clinic)
- Respiratory (29) and multiple/unspecified infections (17) predominated
- For both setting/conditions: too little data to determine whether effectiveness varies by either

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KQ4 Results – Harms of Programs

- No studies reported possible harms
- Limited reporting of return clinic visits, hospitalizations, adverse events
 - Those that did: no significant differences between groups

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KQ5 Results – Barriers to Implementation, Sustainability, Scalability

- Implementation
 - Limited data to draw on. Convenience of interventions, access to training materials, efforts to include patients raised as potential facilitators
- Sustainability
 - 7 studies provided follow-up; 1-4 years, mixed results
 - Several showed initial improvement, but equal at one year
 - But: others showed:
 - Sustained benefit (3 years) despite decreasing intensity of intervention (education)
 - Sustained benefit (4 years) after computer-decision support

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KQ5 Results – Barriers to Implementation, Sustainability, Scalability

- Scalability
 - 3 studies reported information related to implementing programs on larger scale
 - In one, favorable effect of a pilot study (100 providers) not seen when increased to group of 300 providers
 - Speculation of less rigorous intervention
 - In 2nd: authors speculated that need to train multiple “academic detailers” resulted in differences in effectiveness
 - In 3rd: concern that adopting web-based training would not translate across borders/cultures (European study)

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Discussion

- Outpatient Antimicrobial stewardship can decrease antimicrobial prescribing in the outpatient setting
 - Strength of evidence greatest (medium strength) for:
 - Communication skills training
 - Laboratory testing
 - Strength of evidence low for other interventions
- Patient outcomes, when reported, not adversely affected
- Little data on cost
- No data on resistance
- Little data outside of primary care clinics
- Limited data on sustainability, scalability

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Discussion

- The results of our review largely agree with prior AHRQ report (Ranji 2006)
- New to this review is information regarding laboratory testing
 - Procalcitonin, CRP, rapid antigen detection tests, and rapid PCR diagnostics are promising tools that appear to significantly decrease antimicrobial use
 - Objective results provided may provide welcome aid to clinicians, vs. largely subjective data available in past
- Public awareness of antimicrobial resistance (CDC Threat Report, “Get Smart” campaign, etc) may enhance stewardship efforts in future

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Overall Conclusions

- Outpatient Antimicrobial Stewardship effective in reducing antimicrobial prescribing
- Optimal interventions unknown
- No adverse effects on patient outcomes
- Sustainability and scalability barriers are poorly defined

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Future research needs

- Large scale studies to evaluate patient outcomes would be welcome
- Challenging to conduct; as large systems introduce stewardship efforts, tracking such outcomes may be way to gather such data
- Comparative effectiveness studies to define effective strategies (vs. bundle approach)

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Questions?

If you have further questions,
feel free to contact:

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The full report and cyberseminar presentation is available on the ESP website (Intranet Only):

<http://www.hsrd.research.va.gov/publications/esp/>

Antimicrobial Stewardship Programs in Outpatient Settings

View from the VA Antimicrobial Stewardship Taskforce
(ASTF)

Matthew B. Goetz, M.D.

Chair, VA ASTF Implementation Subcommittee

VA Greater Los Angeles HCS



VA Antimicrobial Stewardship Taskforce

- Charge: To optimize care by developing, deploying, and monitoring a national-level strategic plan for improvement in antimicrobial therapy management
- Objectives
 - Summarize current performance and improvement priorities for antimicrobial stewardship
 - Catalog where possible ongoing current antimicrobial therapy improvement activities across VHA
 - Develop a plan to leverage clinical information tools
 - Define key leadership actions in response to specific needs

Key Messages for ASTF from ESP Review

- Modest benefits demonstrated
 - Improved prescribing rates, selection of therapy
 - Few data on patient centered outcomes
 - No microbial outcomes data
 - Decreased dispensing costs
- No evidence of harm
- While more research is needed, the evidence is more than sufficient to continue to promote prudent prescribing practices

Key Messages for ASTF from ESP Review

- Many approaches, few comparative data
 - PCT, rapid antigen detection, CRP: 8/9 studies +*
 - Communication skills training 5/6 studies +
 - Decision support: 4/6 studies +
 - Provider and patient education: 9/15 studies +
 - Provider feedback: 3/5 studies +
 - Guidelines: 3/4 studies +
 - Delayed prescribing: 3/4 studies +
- No single approach is likely to be sufficient

* Effect on prescribing rate/use

Key Messages for ASTF from ESP Review

- Implementation: little specific guidance
 - Benefit of convenient interventions, training materials
 - Leadership support, team approach (champions)
 - Include stakeholders (patients)
 - Large scale interventions are challenging
 - Laboratory results provide objective data
- Scalability:
 - Need to assure consistency of approach
 - Simplicity is likely a virtue
- Sustainability is achievable
 - Benefits of computer-decision support

Future research needs

- Large scale studies to evaluate patient outcomes would be welcome
- Comparative effectiveness studies to define effective strategies (vs. bundle approach)
 - Antibiotic specific interventions: e.g., quinolones
 - Disease specific interventions: UTI, ARI
- VA is well positioned
 - Large, integrated healthcare system
 - Electronic medical records
 - Corporate data warehouse

