

# Antimicrobial Stewardship

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# Antimicrobial Stewardship

ICHE 2012; 33

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Coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration, and route of administration.



# Core Components of Antimicrobial Stewardship Program

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IDSA

- expertise necessary for program
  - multidisciplinary
- monitor antimicrobial use/resistance/infections
- promote prudent antimicrobial use



# Antimicrobial Stewardship Techniques

CID 2007; 44: 159

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- Front end: prescription authorization
- Back end: prescription review/feedback
- Clinical guidelines, treatment algorithms
  - computer-assisted decision support
  - streamlining/de-escalation
  - parenteral to oral conversion
- Education
- Pharmacodynamic dose optimization
  - pharmacy based dosing programs



# Antimicrobial Stewardship: Long Term Care Facilities

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- the problem
- the evidence for stewardship
- recommendations

# Antimicrobial Use in LTCF

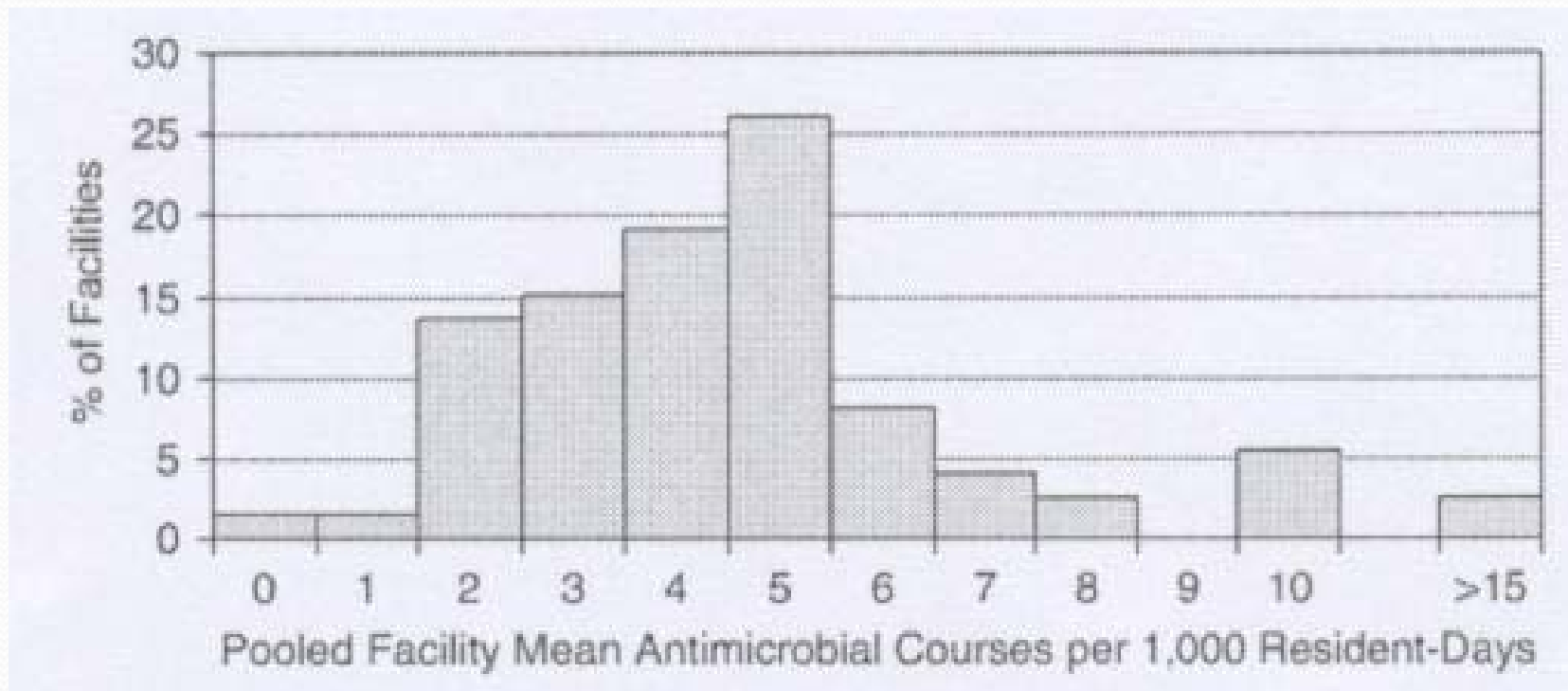
van Buul JAMDA, 2013

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Residents with systemic antibiotics/year	47 – 79 <sup>0</sup> %
Point prevalence	4.8 – 15.2 <sup>0</sup> %
Incidence	4.0 – 7.3/1,000 resident days

# Antimicrobial Use in US Nursing Homes

Benoit et al JAGS 2008; 56:2039



Mean: 4.8 courses/1,000 days; Range: (0.4 – 23.5)  
[Loeb, 2001; 2.9 – 13.9]

# Antimicrobial Use in LTCF

## Inappropriate Antimicrobial Use

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	<u>Inappropriate</u>
Zimmer et al, JAGS, 1986	40%
Warren et al, JAGS, 1991	~40%
Montgomery et al, J Ger Drug Ther, 1995	
systemic/topical	43%/60%
Loeb et al, J Gen Int Med 2001	35 – 72%
Boivin et al, MMI, 2013	82%
Peron et al, JAGS, 2013	> 43%



# Potential Inappropriate Treatment of UTI in Two Rhode Island NHs

Rotjanapan AIM 2011; 171:438

**N = 132 patients, 172 UA; 96 courses antibiotics**

## Appropriateness

Did not meet diagnostic guidelines,  
antibiotics given

70/146 (41%)

## Inappropriate use (IDSA criteria)

Antibiotic choice

56%

Antibiotic dosing

46%

Antibiotic duration

67%

*C. difficile* with inappropriate antibiotics: OR 8.5; 1.7 – 42.2

# Indications for antimicrobial prescribing in European nursing homes: results from a point prevalence survey

Latour, Pharmaco-epi & Drug Safety 2012; 21:937

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**323 NH; 21 countries**

Prevalence:	6.33%	(1.0 – 17.29)
Prophylaxis:	1.87%	(0 – 12.43)
UTI	1.67%	(0 – 12.0)

# Prevention of UTI in NHs: Lack of evidence-based prescription

Bergman BMC Ger 2011; 11:69

## Norway

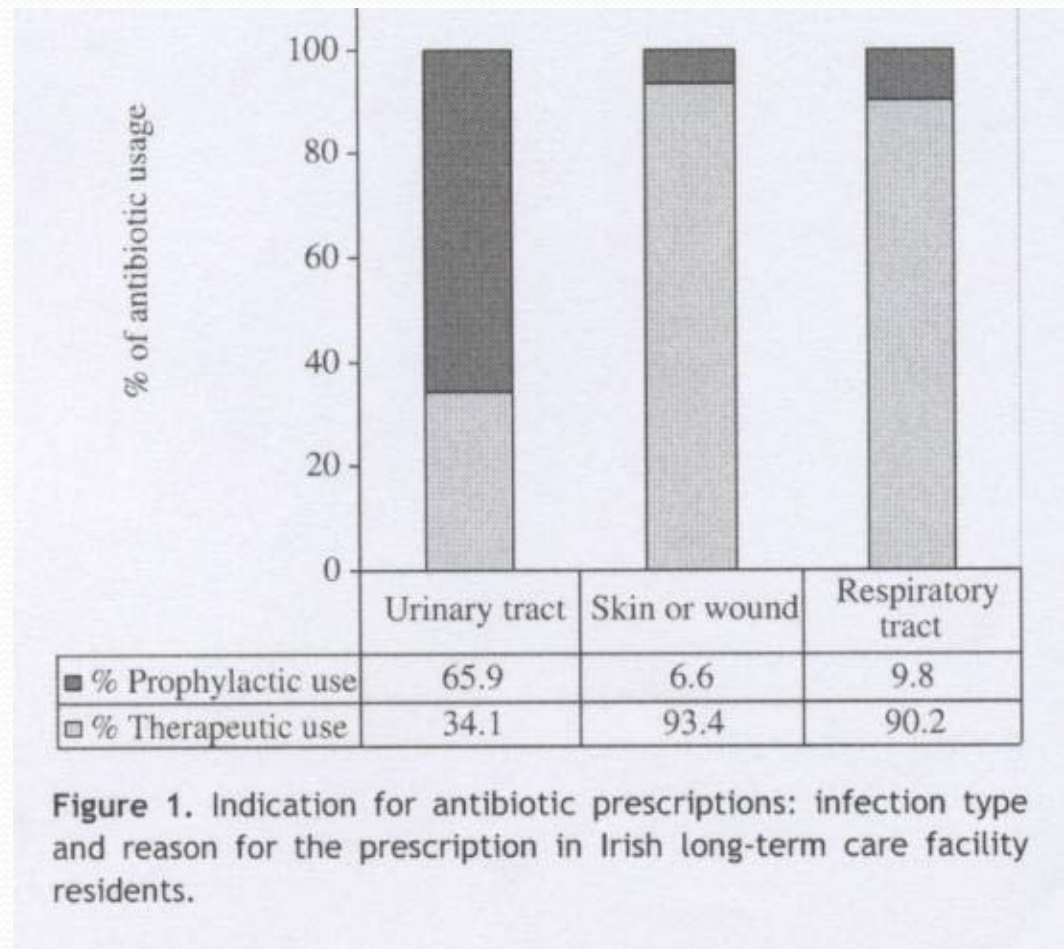
**Table 1 Prophylaxis regimes for urinary tract infections in 1473 nursing home residents, number and proportions (%) of all residents and of residents with prophylaxis.**

	Number	% of all residents	% of residents with prophylaxis
Residents given prophylaxis for UTIs	269	18%	
One agent	198	14%	74%
Two agents	63	4%	23%
Three or four agents	8	0.5%	3%
Agents used for prophylaxis			
Methenamine	130	8.8%	48%
Vitamin C	87	5.9%	32%
Estrogens	81	5.5%	30%
Cranberry	28	1.9%	10%
Trimethoprim	13	0.9%	5%
Nitrofurantoin	10	0.7%	4%

# Healthcare Infection in Irish LTCF: First National Prevalence Study

Cotter JHI 2012; 80:212

UTI prophylaxis: 35.8% total prescriptions  
Prophylaxis/catheter: 6.0%



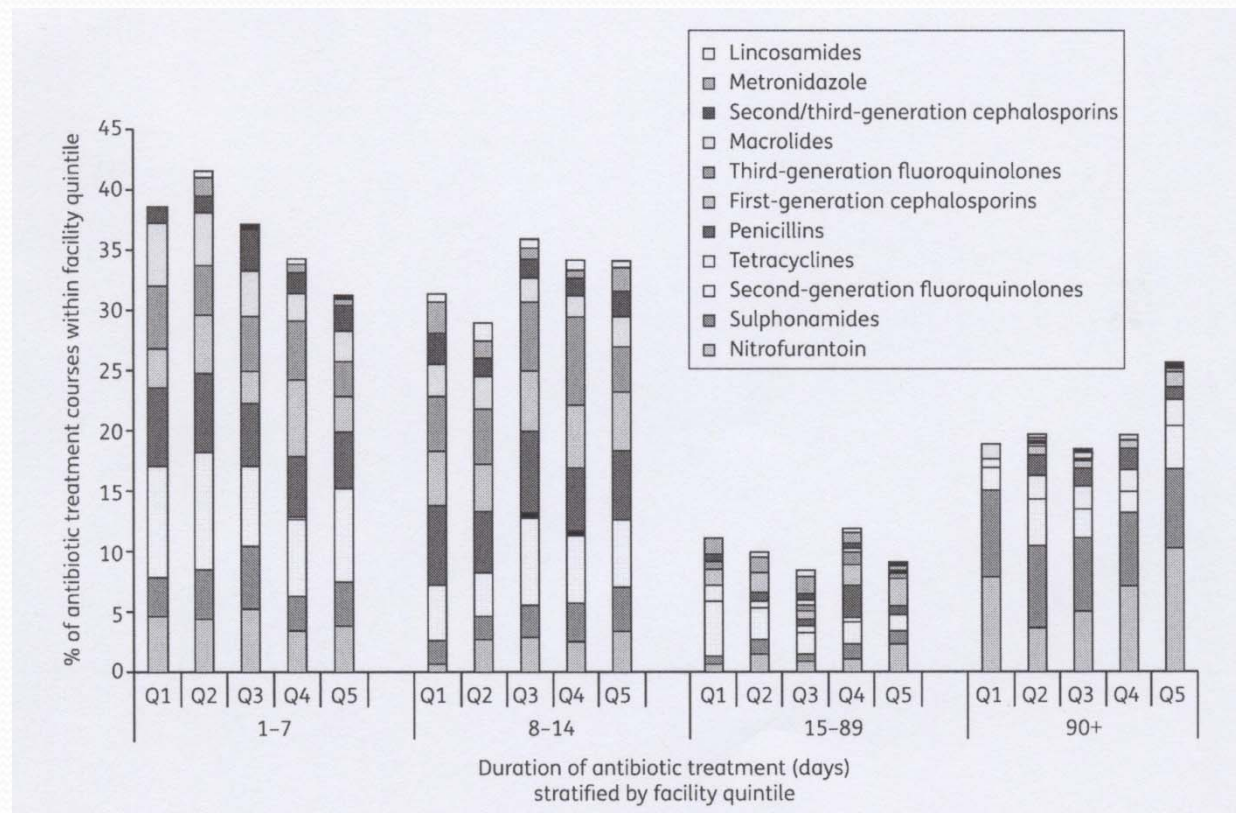
# Antibiotic Use in LTCF

Daneman, JAC 2011; 66:2856

Ontario LTCF; N = 363; point prevalence, residents 37,371

Treatment duration > 90 days: 21% of all receiving antibiotics

NF, TMP/SMX, ciprofloxacin, norfloxacin



## Asymptomatic bacteriuria, antibiotic use, and suspected urinary tract infections in four nursing homes

Charles D. Phillips, Omolola Adepoju, Nimalie Stone, Darcy K. McMaughan Moudouni, Obioma Nwaiwu, Hongwei Zhao, Elizabeth Frentzel, David Mehr, Steven Farfinkel, BMC Geriatrics, 2012

**Table 3 Antibiotic and laboratory use when antibiotics were prescribed for a suspected urinary tract infection (n= 204)\***

Characteristics	Asymptomatic prescription for UTI (N=95)	One or more symptoms of UTI (N=109)
Urine studies performed	89%**	89%
Lab results received prior to antibiotic prescription (Rx)	80%	69%
Antibiotics Used		
Fluoroquinolones	28%	36%
Nitrofurantoin	25%	19%
Sulphonamides	13%	10%
Penicillins	14%	10%
Cephalosporins	8%	10%
Others	12%	15%
Average days of antibiotic prescription (standard deviation)	7.6(2.20)	8.1(2.92)

\*Since this analysis is based on prescriptions, some residents appear in both categories. Our analyses of differences took this into account. None of the differences were statistically significant.

\*\*Facility records identified all prescriptions as given for UTI treatment but chart review did not find documentation of laboratory results.

Positive urine cultures promote antimicrobial use



## Antibiotic use in LTCF

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- high prevalence/incidence
- wide variability across facilities
- substantial inappropriate use
  - prophylaxis
    - indications?
    - evidence of benefit?
    - extended duration

# Inappropriate Antimicrobial Use in LTC

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Potential negative outcomes:

- antimicrobial resistance
- C. difficile colitis
- adverse effects  
(Loeb, 2001; 6% resp or UTI, 4% skin)
- cost



**TABLE 4. Common causes of antibiotic misuse in long-term care facilities**

- Unnecessary antibiotic treatments for colonization (e.g. asymptomatic bacteriuria)
  - Unnecessary antibiotic treatments for urinary tract infection prophylaxis
  - Unnecessary antibiotic treatments for viral infections (e.g. influenza)
  - Unnecessary use of topical antibiotics
  - Absence of reassessment of antibiotic therapies at around day 3
  - Longer-than-necessary durations
-

# SHEA/APIC Guideline: Infection Prevention and Control in the LTCF

Smith et al, ICHE, 2008

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## IV. Antibiotic Stewardship

1. Infection control programs in LTCF should be encouraged to include a component of antibiotic stewardship (1B).
2. The ICP should monitor antibiotic susceptibility results from cultures to detect clinically significant ARO's. Changes in antibiotic-susceptibility trends should be communicated to appropriate individuals and committees (1B).

# Strategies and Challenges of Antimicrobial Stewardship in LTCFs

Dyar, Clin Microbiol Infect 2015; 21:10

**TABLE 1. Cross-sectional surveys of antimicrobial stewardship programmes in long-term care facilities**

	ESAC [21] Europe 2009 n = 260	HALT [24] Europe 2009 n = 117	Donlon et al. [20] Ireland 2013 n = 69	Van Schooneveld et al. [23] Nebraska (USA) 2011 n = 37
Antimicrobial stewardship committee	8%	16%	16%	36%
Therapeutic formulary	16%	57%	23%	19%
Antimicrobial guidelines	50%	45%	28%	27%
Data about antibiotic consumption	—	33%	16%	81%
Data about local antimicrobial resistance profiles	9%	17%	12%	76%
Regular training of prescribers on antibiotic use	16%	22%	7%	8%
Individual antimicrobial prescribing profiles	—	27%	10%	11%
Pharmacist advice on antibiotic use	—	19%	36%	—
Regular audits assessing antibiotic use	—	—	—	81%

—, not available.



# Is Antimicrobial Stewardship Effective in LTCFs?

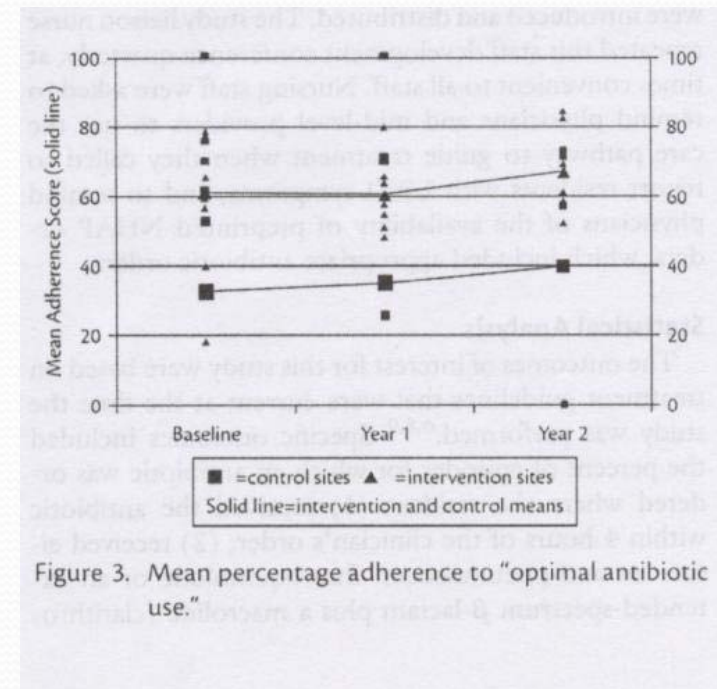
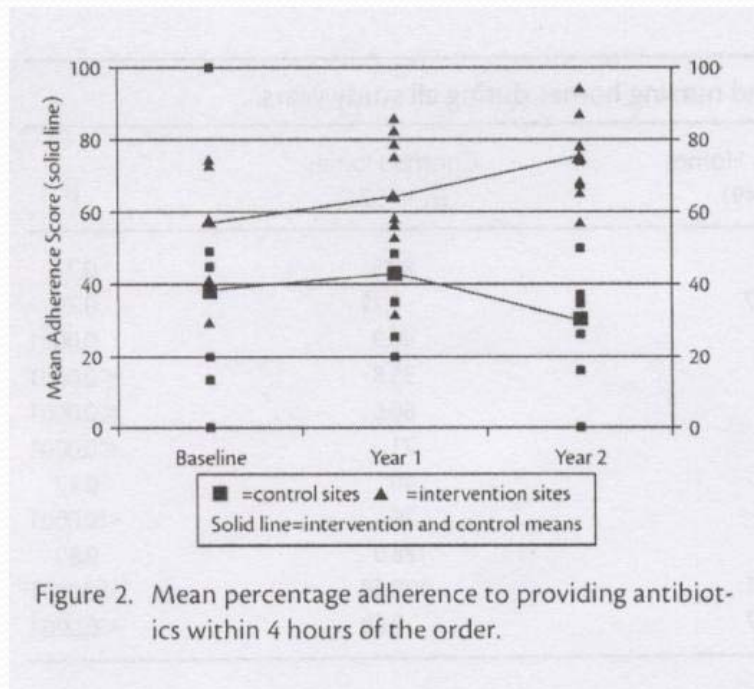
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What are the outcomes of interest?

- antimicrobial use
  - appropriateness
- other outcomes
  - ARO's
  - *C. difficile*
  - adverse effects
- costs

## Impact of multidisciplinary intervention on antibiotic use for NH Acquired Pneumonia

Linnebur, AJ Ger Pharm 2011; 9:442



Interventions: Facility improved immunization, diagnostic testing, treatment

- interactive staff educational skills to improve nursing assessment
- study liaison nurse to facilitate change
- academic detailing to physicians

## Sustained Reduction in Inappropriate Treatment of Asymptomatic Bacteriuria in a LTCF Though an Educational Intervention

Zabarsky, AJIC 2008; 36

**Table 4.** Effect of an educational intervention on inappropriate urine culture submission, treatment of asymptomatic bacteriuria, and total antimicrobial use in a long-term care facility

	3-Month preintervention	Initial 6 months postintervention	7 to 30 Months postintervention
Patient-days, n	13,151	27,846	124,849
Total urine cultures sent	49	43	164
Total urine cultures sent/1000 patient-days (95% CI)	3.7 (2.8-4.9)	1.5 (1.1-2.1)	1.3 (1.1-1.5)
Inappropriate cultures, n (%)	34 (69.4)	26 (60.5)	75 (45.7)
Inappropriate cultures/1000 patient-days (95% CI)	2.6 (1.8-3.6)	0.9 (0.6-1.4)	0.6 (0.5-0.8)
Total ASB identified	34	26	75
ASB treated, n. (%)	23 (67.6)	18 (69.2)	33 (44.0)
ASB treated/1000 patient-days (95% CI)	1.7 (1.1-2.6)	0.6 (0.4-1.0)	0.3 (0.2-0.4)
Antimicrobial days of therapy/1000 patient-days	167.7	117.4	109.0

- 6 full time primary care providers
- discourage urine cultures
- case based feedback/nursing



# Reduction in inappropriate prevention of UTI in LTCF

Rummakainen et al Am J Infect Control 2012; 40:711-714

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- Finland
- visit of team to facility with
  - structured interview individual patients
  - review systemic antimicrobials
  - diagnostic practices for UTI
- regional guidelines developed, published
- annual questionnaire to reinforce guideline consistent use of antibiotics

# Reduction in inappropriate prevention of UTI in LTCF

Rummukainen, AJIC 2012; 40:711

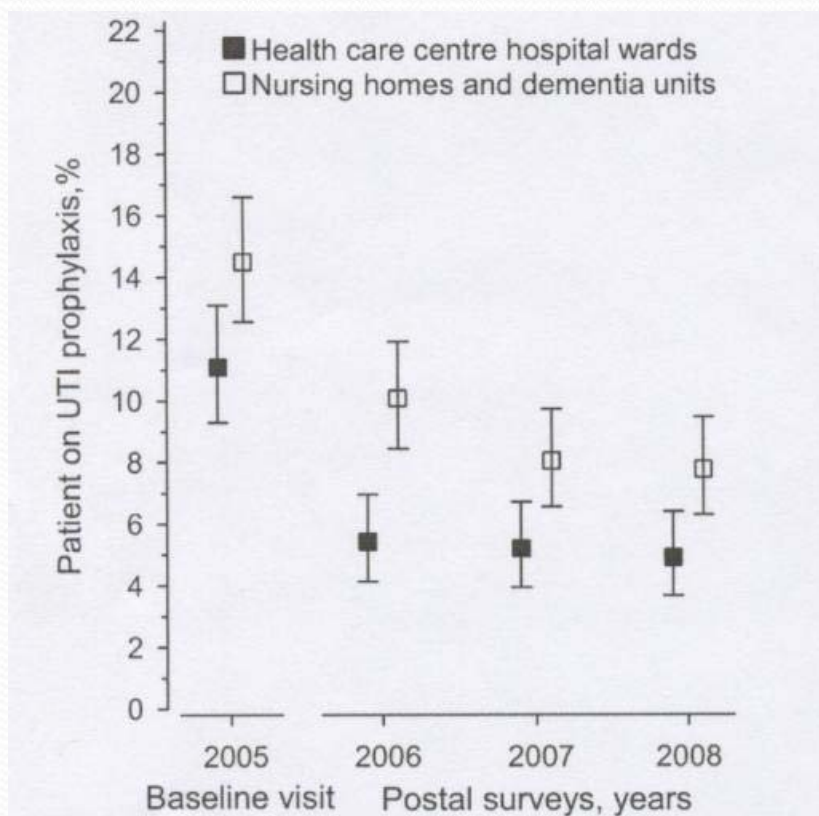


Fig 1. Patients on antimicrobials used in the prevention of UTIs (percentages with 95% confidence intervals).

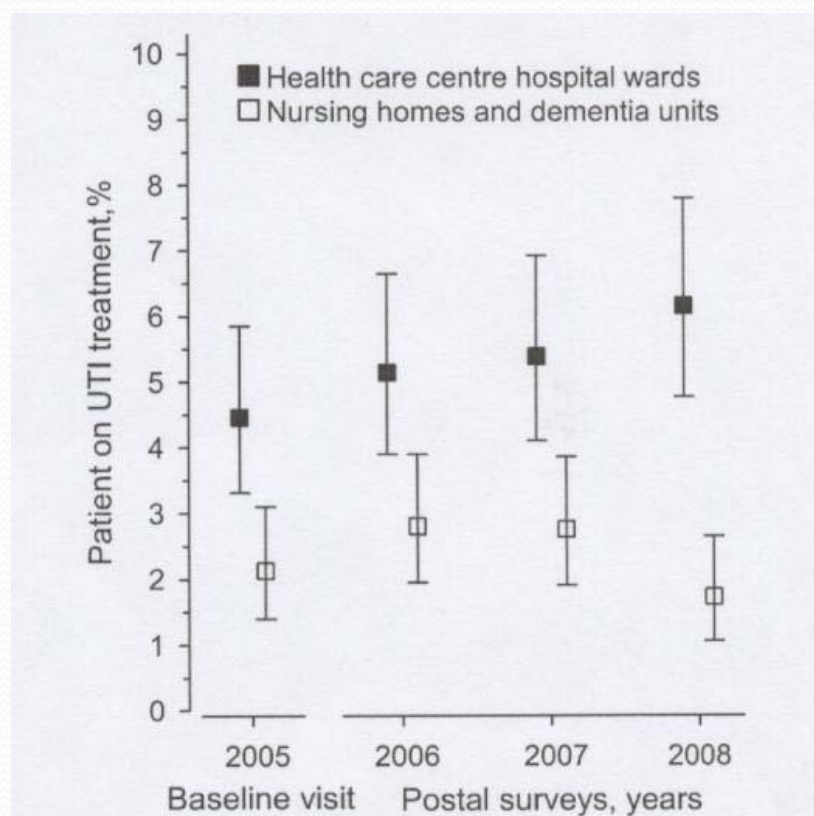


Fig 2. Patients on antimicrobials used in the treatment of acute UTIs (percentages with 95% confidence intervals).





# Effect of a multifaceted intervention on number of antimicrobial prescriptions for UTI in residents of nursing homes: cluster randomized controlled trial

Loeb M et al BMJ 2005; 331:669

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- Minimal criteria for antibiotic initiation
- Small group interactive sessions for nursing
- Videotapes, written material, continuing outreach visits

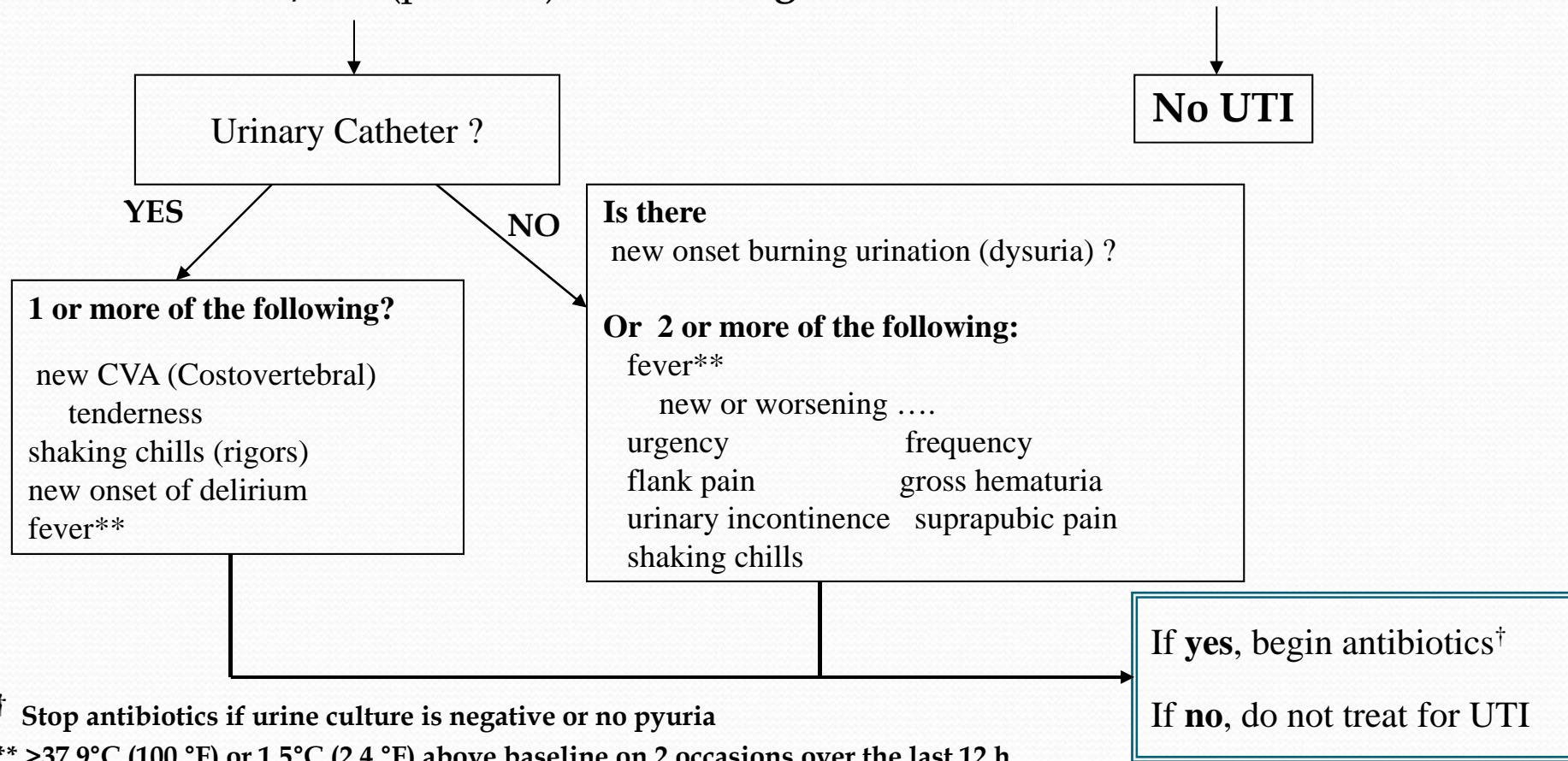
# Treatment Pathway

*Does the resident in my care need antibiotic treatment for a symptomatic UTI?*

Results of the urine culture ?

> 10<sup>5</sup> CFU/mL (positive) OR **Pending**

Negative (no growth or mixed)



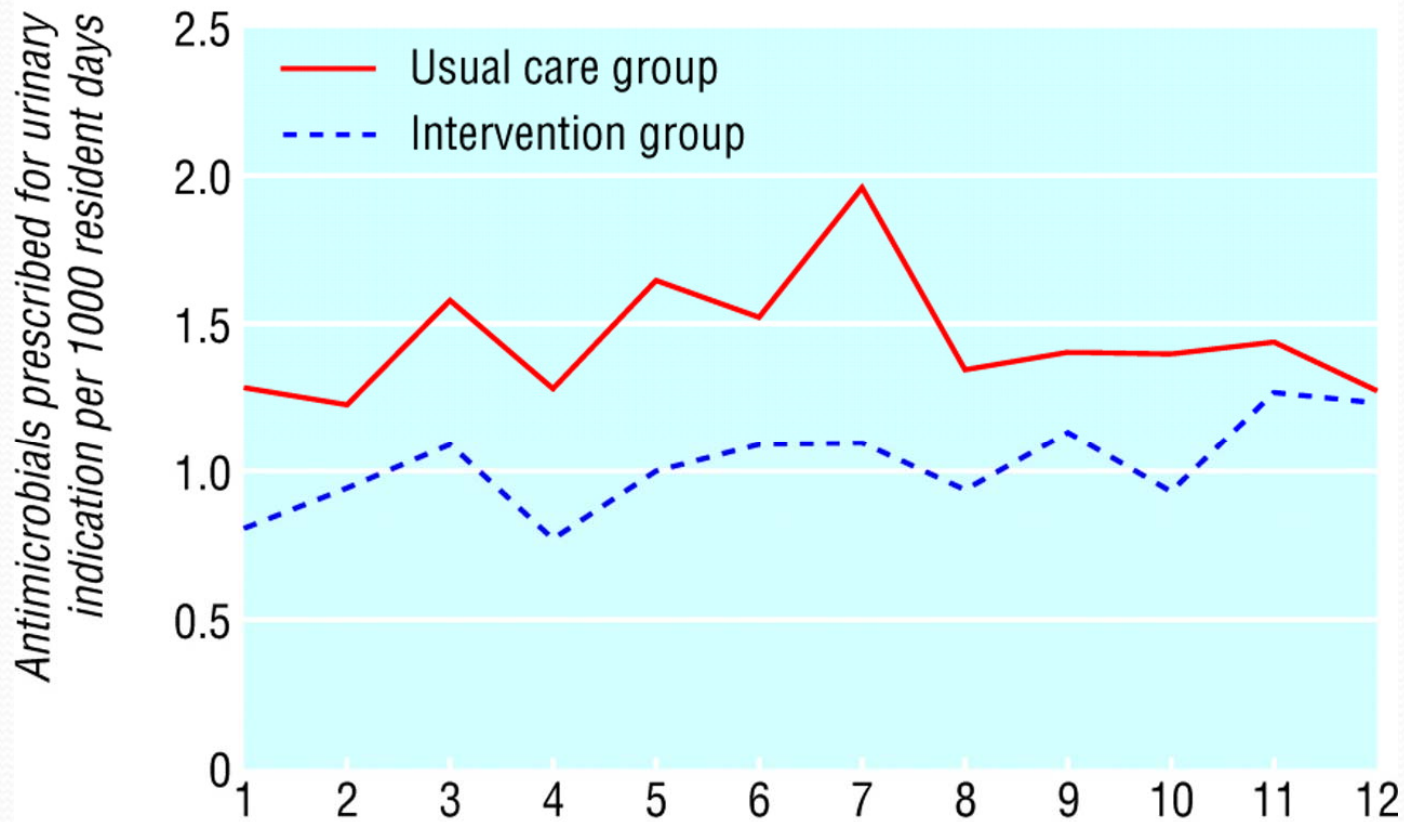
† Stop antibiotics if urine culture is negative or no pyuria

\*\* >37.9°C (100 °F) or 1.5°C (2.4 °F) above baseline on 2 occasions over the last 12 h

Note: the recommended treatment duration for uncomplicated cystitis in women is 7 days and 7-14 in males. For an uncomplicated pyelonephritis, treatment duration is 10-14 days. For a complicated cystitis, treatment duration is 10 days. For a complicated pyelonephritis, treatment duration is from 14 to 21 days.

**Fig 4 Monthly rates of antimicrobial prescriptions for urinary indications in intervention and usual care nursing homes**

Loeb, M. et al. BMJ 2005;331:669



Antibiotics/UTI: 1.17 vs 1.59/1,000 (-0.49; -0.93, -0.06)

Month

Total antibiotic use: Usual care: 3.93, Intervention: 3.52 (-.37; -1.17, .44)

BMJ



## Educational Intervention to Improve Antimicrobial Use in a Hospital-Based LTCF

Schwartz, JAGS 2007; 55:1236

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- LTC wards of acute hospital; ID consultation
- 20 salaried physicians providing care
- Guidelines, hospital resistance data, physician feedback (4 sessions/18 mo)
- Booklets

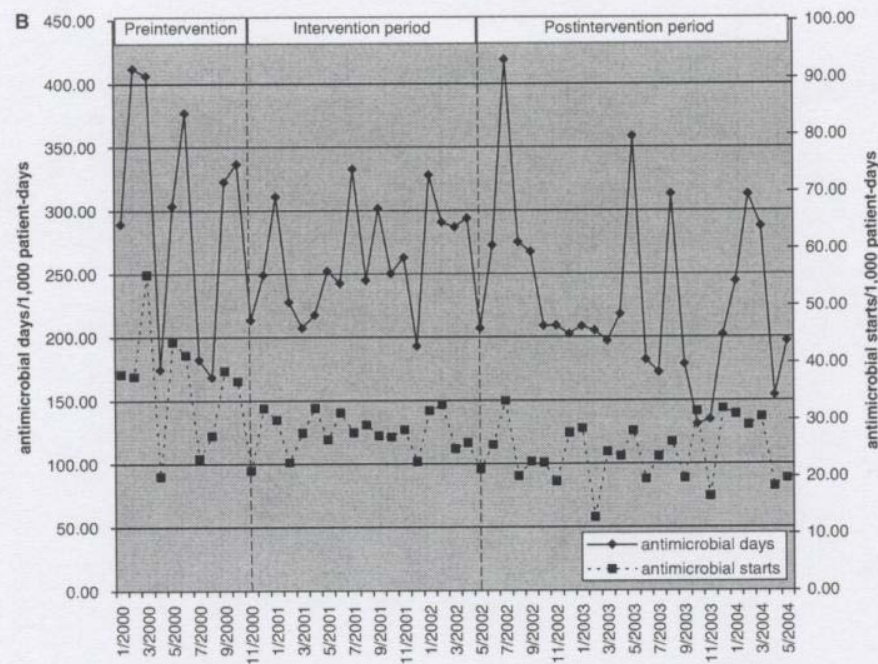
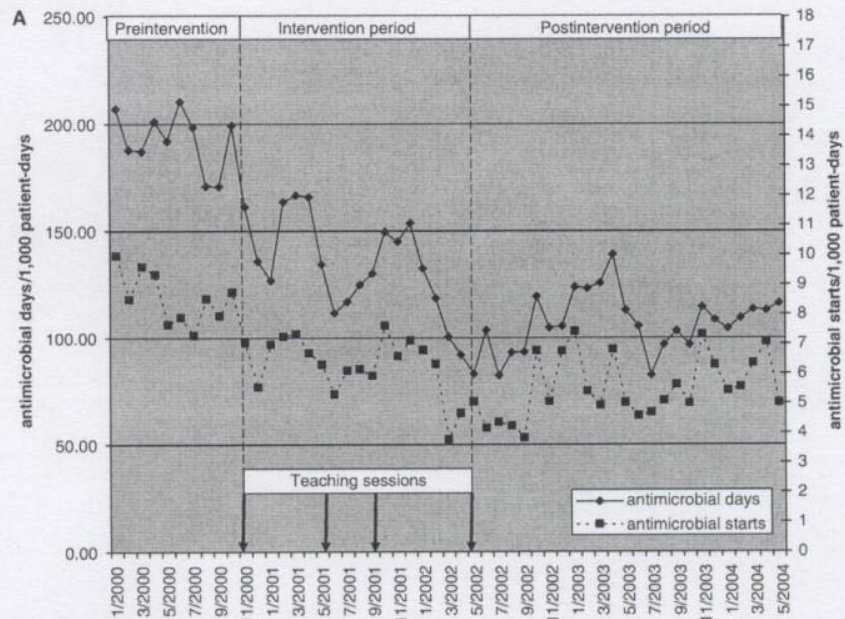


Figure 1. Antimicrobial days and starts per 1,000 patient-days in LTC (A) and rehabilitation (B). The x-axis represents the calendar months January 2000 to May 2004.

## Educational Intervention to Improve Antimicrobial Use in a Hospital-Based LTCF

Schwartz, JAGS 2007; 55:1236

- met diagnostic criteria 32% vs 62%;  $p = 0.06$
- initial antibiotics met guidelines 11% vs 9.6%,  $p < 0.001$
- improvements sustained 2 yrs

# Effect of an Educational Intervention on Optimizing Antibiotic Prescribing in LTCF

Monette JAGS 2007; 55:1231

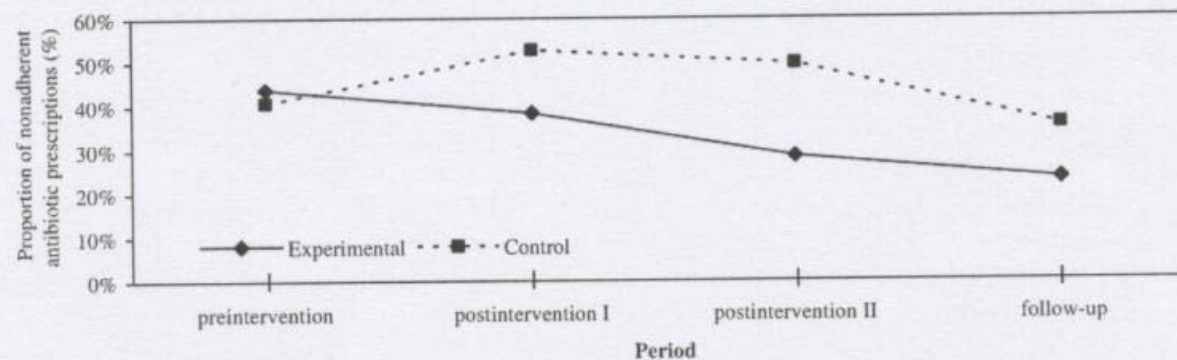


Figure 1. Proportion of nonadherent antibiotic prescriptions over study period. Preintervention = December 2001 to February 2002, postintervention I = May to July 2002, postintervention II = September to November 2002, follow-up = December 2002 to February 2003.

- Quebec
- mailed guidelines & individual feedback



# Can a multifaceted educational intervention targeting both nurses and physicians change the prescribing of antibiotics to nursing home residents? A cluster randomized controlled trial

Pettersson E, Vernby A, Molstad S, Lundborg CS. J Antimicrob Chemother 2011; 66:2659-2666

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- Cluster randomized, controlled
- 46 NH; 1537 residents
- Interventions
  - guidelines: local consensus
  - teaching sessions
  - educational materials
  - feedback



# Multi-faceted Educational Intervention

Pettersson et al JAC 2011; 66:2659

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## Primary Outcome

- proportion of UTI in women treated with fluoroquinolones

## Secondary Outcomes

- number of UTI's/resident
- proportion all infections treated antibiotics
- proportion all infections “wait and see”
- proportion nitrofurantoin for lower UTI woman



# Multifaceted Educational Intervention for Antibiotics in Nursing Homes

Pettersson et al 2011; 66:2659-2666

Difference 2003 (pre) and 2005 (post)			
	Intervention	Control	Difference (95% CI)
Lower UTI FQ	-0.196	-0.224	0.028 (-0.19, 0.25)
Lower UTI NF	-0.014	0.063	-0.077 (-0.24, 0.09)
UTI's/resident	-0.031	-0.070	0.038 (-0.013, 0.09)
All infections:			
antibiotics	-0.072	0.048	-0.124 (-0.228, -0.019)
"wait and see"	0.093	0.039	0.143 (0.047, 0.24)



# Multifaceted Educational Intervention for Antibiotics in Nursing Homes

Pettersson et al 2011; 66:2659-2666

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Conclusions: Educational intervention had no effect on the primary outcome, but decreased overall prescribing of antibiotics.

# Antimicrobial Stewardship in LTCF

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## Effective Antimicrobial Stewardship in a Long-Term Care Facility through an Infectious Disease Consultation Service: Keeping a LID on Antibiotic Use

Robin L. P. Jump, MD, PhD;<sup>1,2,3</sup> Danielle M. Olds, RN, PhD;<sup>4</sup> Nasim Seifi, MS;<sup>1</sup> Georgios Kypriotakis, MS;<sup>1,3</sup>  
Lucy A. Jury, RN, CNP;<sup>1</sup> Emily P. Peron, PharmD;<sup>5</sup> Amy A. Hirsch, PharmD;<sup>3,6</sup> Paul E. Drawz, MD;<sup>2,3</sup>  
Brook Watts, MD;<sup>2,3</sup> Robert A. Bonomo, MD;<sup>1,2,3,7,8</sup> Curtis J. Donskey, MD<sup>1,2,3,7</sup>

# Antimicrobial Stewardship in LTCF ID consultation

ICHE 2012; 33:1185

TABLE 1. Comparison of the Long-Term Care Facility (LTCF) and the Hospital before and after the Intervention

Variable, location	Preintervention <sup>a</sup>	Postintervention <sup>b</sup>	Reduction, %	<i>P</i> value
Antibiotics, mean DOT/1,000 DOC ± SD				
Total in LTCF	175.1 ± 28.0	122.3 ± 26.9	30.1	<.001
Total in hospital	631.8 ± 44.9	649.0 ± 38.4	-2.7	.15
Oral in LTCF	136.1 ± 25.6	93.1 ± 22.0	31.6	<.001
Oral in hospital	185.3 ± 18.8	182.3 ± 19.4	-4.5	.59
Intravenous in LTCF	39.0 ± 14.5	29.3 ± 10.6	25.0	.01
Intravenous in hospital	446.7 ± 39.0	466.7 ± 42.5	1.6	.10
Admissions, per month				
LTCF	58.6 ± 11.3	48.1 ± 7.7	18.0	<.001
Hospital	671.6 ± 36.1	720.4 ± 39.9	-7.3	<.001
Transfers to hospital, per month				
LTCF	19.0 ± 4.6	17.6 ± 4.5	7.6	.27
Hospital	Not applicable	Not applicable		

NOTE. DOT/1,000 DOC, days of therapy per 1,000 days of care; SD, standard deviation.

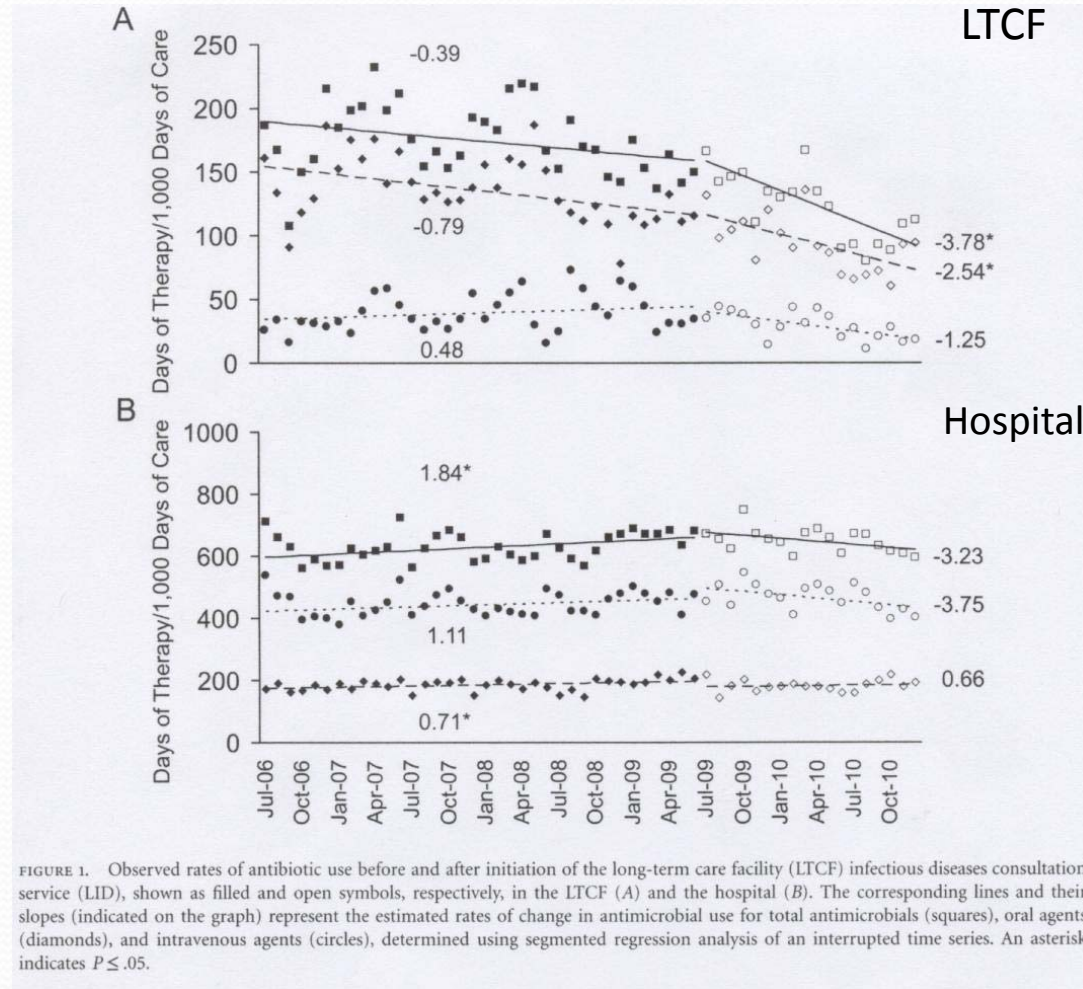
<sup>a</sup> July 2006–June 2009 (36 months).

<sup>b</sup> July 2009–December 2010 (18 months).

# Antimicrobial Stewardship in LTCF

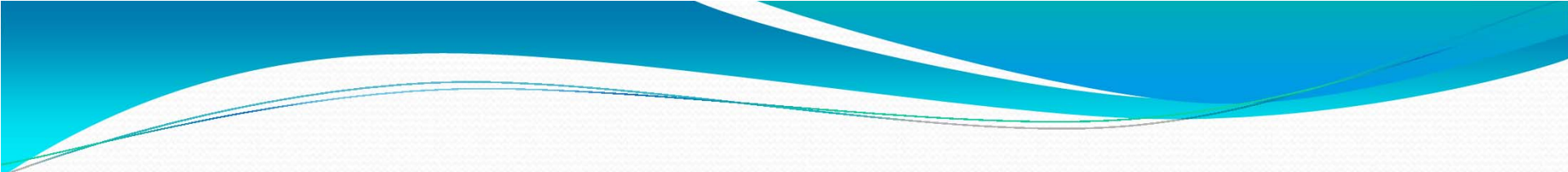
## ID consultation

ICHE 2012; 33: 185



Total  
Oral  
Intravenous

Positive *C. difficile*/1,000 patient days, decline  $p = 0.04$



# Impact of implementation of a novel antimicrobial stewardship tool on antibiotic use in nursing homes: a prospective cluster randomized control pilot study

Fleet, JAC 2014; 69:2265

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## Resident Antimicrobial Management Plan (RAMP)

- Pilot cluster RCT
- 30 NH London

RAMP preprinted form:

A. Initiation of treatment

B. Review 48 – 72 hrs.

# Resident Antimicrobial Management Plan (RAMP)

Fleet, JAC 2014; 69:2265

**Table 3.** Summary of compliance with individual 'good practice points' in RAMP

RAMP: Part A—Initiation of Treatment (n= 372)		Yes (%)
A1	clinical signs and symptoms present or 'none at present' recorded	85
A2	whether resident examined by doctor, where and when documented	97
A3	initial diagnosis/suspected site of infection documented	93
A4	details of clinical specimens/swabs/urine dipstick or 'none taken' recorded	84
A5	check made that antibiotic supplied appropriate for	
	(a) clinical indication (type of infection suspected)	(a) 67
	(b) individual resident in terms of allergy status and medical history	(b) 97
A6	prompt initiation: time and date of administration of first dose recorded	97
RAMP: Part B—Review of Treatment (n= 337)		Yes (%)
B1	review of clinical progress after 48–72 h treatment documented	78
B2	stop date for antibiotic or planned review date documented	77
B3	whether resident re-examined by doctor, where and when documented	64
B4	results of specimens/swabs or 'not available yet' or 'none taken' recorded	42
B5	outcome of antibiotic treatment documented	59

**Total antibiotic consumption**

**Intervention group: -4.9% (95% CI 1.0-8.65; p=0.02)**

# Successfully Reducing Antibiotic Prescribing in Nursing Homes

Zimmerman, JAGS 2014; 62:907

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- 9 mo, 12 NA (6 control, 6 intervention), 336, 522 resident days
- Intervention
  - health care providers/nurses training re prescribing guidelines
    - situations where antibiotics not indicated
  - residents/families sensitized
  - feedback on prescribing



# Successfully Reducing Antibiotic Prescribing in Nursing Homes

Zimmerman, JAGS 2014; 62:907

## Rates of antibiotic prescribing/1,000 res days

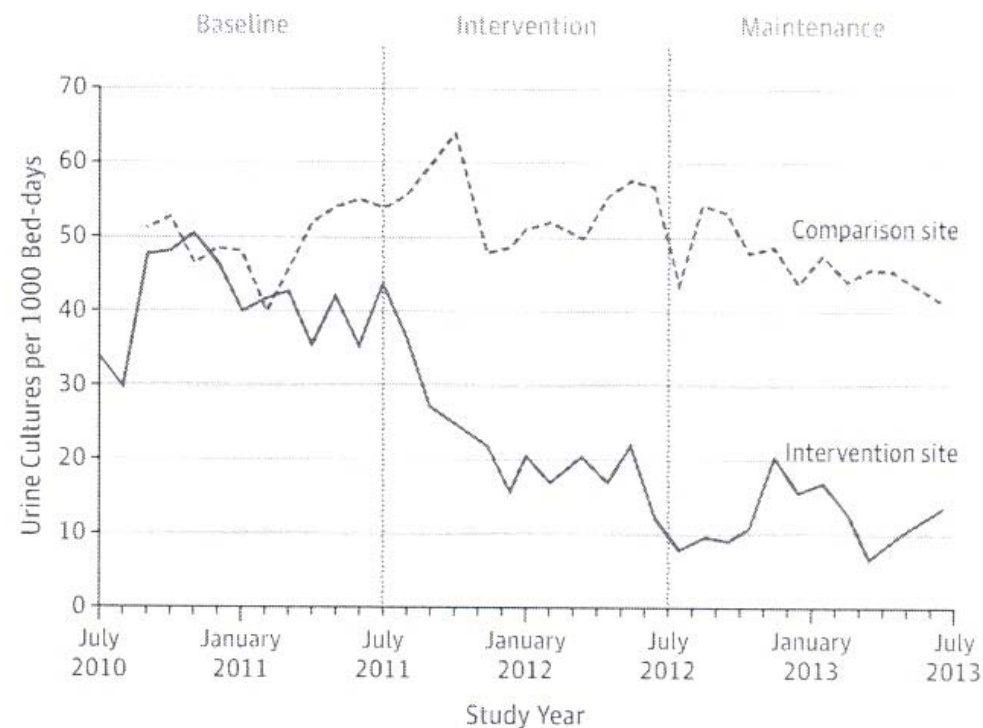
	Intervention sites	Comparator sites
Pre	13.6	12.7
During	9.51	11.8
Adjusted RR	0.86 (0.79 – 0.95), p=0.002	

# Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria

Barbara W. Trautner, MD, PhD; Larissa Grigoryan, MD, PhD; Nancy J. Petersen, PhD; Sylvia Hysong, PhD; Jose Cadena, MD; Jan E. Patterson, MD, MS; Aanand D. Naik, MD

Figure. Monthly Rates of Urine Culture Orders per 1000 Bed-days

JAMA IM 2015; 175: 1120



Shown are the intervention vs comparison sites across the 3 study periods ( $P < .001$ ).

# Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria

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JAMA IM 2015; 175: 1120

## Intervention site

## Comparison site

Long-term Care Patients Only	Intervention site			Comparison site			
	Baseline (n = 208)	Intervention (n = 36)	Maintenance (n = 14)	Baseline (n = 58)	Intervention (n = 30)	Maintenance (n = 44)	
Cases of ASB	135 (64.9)	25 (69.4)	10 (71.4)	31 (53.4)	10 (33.3)	26 (59.1)	NA
Cases of CAUTI	73 (35.1)	11 (30.6)	4 (28.6)	27 (46.6)	20 (66.7)	18 (40.9)	NA
Overtreatment of ASB	70/135 (51.9)	5/25 (20.0)	1/10 (10.0)	2/31 (6.5)	4/10 (40.0)	5/26 (19.2)	.001 <sup>d</sup>
Undertreatment of CAUTI	9/73 (12.3)	2/11 (18.2)	0/4	2/27 (7.4)	5/20 (25.0)	3/18 (16.7)	.74



## Evidence to support Antimicrobial Stewardship in LTCF's

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- most studies report some positive effect
- no standardization of interventions or evaluation
- ? relevant outcomes (ARO, *C. difficile*)
- ? sustainability
- ? cost-effectiveness

# CDC: Core Elements of Antibiotic Stewardship in Nursing Homes.

Sept 2015

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## Leadership Commitment

- Demonstrate support and commitment to safe and appropriate antibiotic use in your facility.

## Accountability

- Physician, nurse, pharmacy leads responsible for promoting and overseeing antibiotic stewardship activities in your facility

## Drug Expertise

- Access to consultant pharmacists or other individuals with experience or training in antibiotic stewardship for your facility

## Action

- Implement at least one policy or practice to improve antibiotic use



# CDC: Core Elements of Antibiotic Stewardship in Nursing Homes.

Sept 2015

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## Teaching

- Monitor at least one process measure of antibiotic use and at least one outcome from antibiotic use in your facility

## Reporting

- Provide regular feedback on antibiotic use and resistance to prescribing clinicians, nursing staff, and other relevant staff

## Education

- Provide resources to clinicians, nursing staff, residents and families about antibiotic resistance and opportunities for improving antibiotic use.

# Antimicrobial Stewardship for LTCF

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## Challenges

- resources
  - cost effectiveness
- standardization/programs & components
- diagnostic criteria
  - laboratory access/interpretation
- relevant outcomes
  - clinical
  - antimicrobial resistance

# Antimicrobial Stewardship

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## Low Hanging Fruit: “winnable battles”

- Monitor antimicrobial use/feedback
- Optimize laboratory use
  - Urine culture criteria
  - Respiratory viruses
- Prophylaxis
  - UTI
- Duration of therapy
- ? Topical



# Antimicrobial Stewardship

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## Policies/practices: More Complex to Implement

- restrictive diagnoses for clinical illness
  - guidelines
  - algorithms
- monitoring for appropriateness
  - feedback to prescribers
- culture change:
  - default to “not treat”