How to decrease quinolone consumption

Emilio Bouza
H. Gregorio Marañón.
Madrid, Spain
Disclosures

Participation in meetings and advisory boards with:
- Pfizer
- Novartis
- Janssen
- Baxter
- McDonalds
- Astellas
- Wyeth Lederle
- Optimer
- Several Scientific Societies and non-profit foundations (Fundación de Ciencias de la Salud)

Research funds received from private and public origins:
- Pfizer
- Astra-Zeneca
- Novartis
- Schering-Plough
- and other pharmaceutical companies
- Covidien
- FIS
- CIBER Enf Respiratorias
- REIPI
- Mutua Madrileña
- European Community funds
- Fundación del Pino

Payment for conferences:
- Pfizer
- Novartis
- Astellas
- Wyeth Lederle
- and other private and public sources

Nothing to disclose for this talk
Index

Trends in quinolone use

Risks associated with high quinolone use

Types of quinolone stewardship programs

Outcome of these programs
Trends in quinolone use
Dramatic increase of third-generation cephalosporin-resistant *E. coli* in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001 to 2008

53 German ICU
2001-2008, Mean AB use
Quinolone use: 151 → 163
DDD/pt-d <0.001)
Risks associated with high quinolone consumption
Unwanted consequences of AB therapy

1. Adverse reactions
2. Increased morbidity
3. Increased length of stay
4. Increased cost of hospitalization
5. Predisposition to secondary infections
6. Emergence of drug-R microorganisms

Polk RE, Fishman NO. Mandell's 2010
Increase consumption → Increase in $R$: 

1. Quinolone-R *Streptococcus pneumoniae*
2. Quinolone-R *Streptococcus pyogenes*
3. Quinolone-R *Enterobacteriaceae*
4. Quinolone-R *Pseudomonas aeruginosa*
5. ESBL-producing *Enterobacteriaceae*
6. MRSA
7. Multi-R *Acinetobacter* spp.
8. *Clostridium difficile*
Antibiotic Resistance Among Gram-Negative Bacilli in US Intensive Care Units
Implications for Fluoroquinolone Use

35,790 Gram-negative aerobic isolates

From ICU pts (district of Columbia, USA)

1994-2000

Cipro-R: 14%→24%

In Pseudomonas: 11%→32%
Figure 1

Annual number of hospital discharges with enterocolitis caused by *Clostridium difficile* (ICD10 diagnosis code DA04.7) and annual consumption of fluoroquinolones and cephalosporins for human use, Denmark, 1997-2007
Types of quinolone stewardship
# Antimicrobial stewardship strategies

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<td>Direct interaction</td>
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<td>Therapeutic substitution</td>
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Outcomes of quinolone stewardship
Antimicrobial practice

The successful introduction of a programme to reduce the use of iv ciprofloxacin in hospital

T. M. A. Weller*

Department of Microbiology, City Hospital NHS Trust, Dudley Road, Birmingham B18 7QH, UK

753-bed hospital with 8 ICU beds
Quinolone consumption during 1998-2000
Jan 99: letter concerning quinolone use
Jun 99: full restriction for iv ciprofloxacin (pre-approval) + factsheet
Outcome:
Reduction of consumption by 34%
Savings of £36,000 for 2 consecutive years
Control of Fluoroquinolone Resistance through Successful Regulation, Australia

Allen C. Cheng, John Turnidge, Peter Collignon, David Looke, Mary Barton, and Thomas Gottlieb

<0.60 DDD / 1,000 inhabitants-days.
Quinolones prohibited in food-producing animals

Restriction in humans:

✈ NOT for UTI. Only pyelonephritis, if R (second choice) or Pseudomonas
✈ Diabetic foot infections: only in Pen-allergy
   Only in water-related SSTI caused by Aeromonas
✈ Moxifloxacin NOT recommended in LRTI except for Pen-allergy
✈ Cipro for Legionella, or directed therapy for infections with a susceptible pathogen

5.2% resistance in community-acquired infections (2010 data)
Optimizing use of ciprofloxacin: a prospective intervention study

Babette C. van Hees¹*, Erica de Ruiter¹,², Ed H. Wiltink², Bartelt M. de Jongh¹
and Matthijs Tersmette¹

584-bed tertiary hospital. 22,000 annual admissions
5.72 DDD / 100 bed-days
Intervention: personal discussion Microbiologist-Clinician; educational presentations to clinicians
Reduction in prescriptions:

Pre-intervention 81 /1000 admissions
Intervention 32 / 1000 admissions
Follow-up 23 / 1000 admissions
Fluoroquinolones use at the Saint-Louis hospital: Investigations before and after diffusion of recommendations and interventions of the anti-infectious referent

B. Politis\textsuperscript{a,*}, V. Pagnon\textsuperscript{a}, C. Lescot\textsuperscript{a}, P. Faure\textsuperscript{a}, S. Touratier\textsuperscript{a}, M. Lafaurie\textsuperscript{b}

646-bed acute-care hospital.

Background:
145 DDD/1000 H-D in 2005.

One-day point prevalence study in Feb 2005 and Jan 2007

Intervention: \textbf{Education}

AB counselling by ID specialist
9.7\%→6.2\% patients on quinolones
74\%→50\% empirical treatment
45\%→27\% IV administration

FQ consumption: 30\% decrease
Outcomes of quinolone stewardship in MRSA
Effect of reduction in ciprofloxacin use on prevalence of meticillin-resistant *Staphylococcus aureus* rates within individual units of a tertiary care hospital

P.P. Cook a,*, P. Catrou b, M. Gooch c, D. Holbert d

Pitt County Memorial Hospital, East Carolina Univ., USA
731 tertiary care, teaching
From March 2005, **EDUCATION program**
Monitoring Cipro use, recommendations to change or discontinue

Cipro use decreased by 31.2% \((p<0.0001)\)

MRSA decreased from 59.6% to 54.2% \((n.s.\)\)
Modification in prescribing practices for third-generation cephalosporins and ciprofloxacin is associated with a reduction in meticillin-resistant *Staphylococcus aureus* bacteraemia rate

L.D. Liebowitz*, M.C. Blunt

Queen Elizabeth Hospital, Norfolk, UK (general 480-bed)
Preintervention: 18 months before
Intervention: Jul-Aug 2005
Post-intervention: 16 months after

**EDUCATION**: New AB guidelines, lectures (annual update; for new staff), senior microbiologist in hematology and ICU rounds, hospital-wide AB-prescribing advice by senior microbiologist)

**Outcome**:
MRSA BSI reduction by 63% (down to <0.1 isolates/1000 bed-days)
Cipro dispensing reduced by 80%
Hospital-wide modification of fluoroquinolone policy and meticillin-resistant *Staphylococcus aureus* rates: a 10-year interrupted time-series analysis

J.-J. Parienti a,b,*, V. Cattoir c, P. Thibon d, G. Lebouvier e, R. Verdon b, C. Daubin f, D. du Cheyron f, R. Leclercq b, P. Charbonneau f

1558-bed tertiary university hospital at Caen, France

- **Period 1.** One-year period of FQ restriction (prohibited): Jan 01-Jan 02
- **Period 2.** Increase in FQ use to previous levels
- **Period 3.** ABHR (alcohol-based hand rub) from Jan 05-June 09. Hand hygiene surveillance

**Monthly % of MRSA:**
- **Period 1.** 31.5%
- **Period 2.** 33.0%
- **Period 3.** 26.3%
Monthly MRSA rate (%)

% of FQ use

% of optimal ABHR

Parienti. J Hosp Infect. 2011
Outcomes of quinolone stewardship in Enterobacteriaceae
Outpt Israeli population (167,000 inhabitants)
Nov 2001-May 2002
Intervention: **RESTRICTION** of cipro & preapproval
Outcome: reduction -1827,3 DDD/month (50% reduction in consumption)
Decreased cipro-R in *E.coli* isolates from urine by 36%
(12% → 9%)
Post-intervention: back to previous situation
1370-bed teaching hospital. 41,712 admissions in 2006

**Multifaceted intervention:**
- Switch from IV to oral
- New AB guideline
- Restriction note on Microbiology reports; letter to physicians on increasing R to cipro
- Active monitoring of prescriptions and feed-back

**Cipro use:** decline from 2.7 DDD/100 pt-days to 1.7

**Reduction of 107 PDD/month**

**Resistance in *E. coli* leveled off**

**Savings in 2 years:** € 114,000
**Annual cost:** € 32,000
Outcomes of quinolone stewardship in CDI
450-bed district hospital in UK

1. **Restriction**: banning routine use of ceftriaxone and cipro (starting Aug 2008)

2. **Plus Educational campaign**

Outcomes:

1. **Cipro monthly consumption**: 72.5% reduction
   
   109.8 → 30.2 DDD/1000 pt-occupied bed-days

2. **C. difficile** reduction of 77% (2.4 → 0.5 cases/1000 pt-bds)

3. **MRSA reduction** of 25% (1.2 → 0.9 cases/1000 pt-bds)
Outcomes of quinolone stewardship in *Pseudomonas aeruginosa*
An Antimicrobial Stewardship Program with a Focus on Reducing Fluoroquinolone Overuse

Annie Wong-Beringer, Pharm.D., Lee H. Nguyen, Pharm.D., Michelle Lee, Pharm.D., Kimberly A. Shriner, M.D., and Jean Pallares, Pharm.D.

565-bed acute care, community teaching hospital

**Multifaceted intervention** starting in 2004:
- Reporting & regular monitoring of institutional antibiograms
- Drug audits with intervention and feedback
- Parenteral-to-oral conversion
- Guidelines for empirical AB therapy
- Education prescribers

**Outcomes**
- Empiric quinolone-prescription reduced by 30%
- Improved susceptibility of *P. aeruginosa* (10% increase)
- 2-fold decrease in mortality of *P. aeruginosa* infections
Decreased Resistance of *Pseudomonas aeruginosa* with Restriction of Ciprofloxacin in a Large Teaching Hospital’s Intensive Care and Intermediate Care Units

G. Jonathan Lewis, DO;¹ Xiangming Fang, PhD;² Michael Gooch, RPh;² Paul P. Cook, MD¹

Pitt County Memorial Hospital, East Carolina Univ., USA
861 tertiary care, teaching
11 ICU and intermediate care units with 295 beds
All adult nosocomial clinical specimens from Jan 2004-Dec 2010
July 2007: *Cipro restriction* + preapproval by on-call ID

Outcomes:

- **Cipro use:** 87 → 8 DDD/1000 pt-d
- Group 2 carbapenem use: 12 → 28.2 DDD/1000 pt-d
- 13.2% decrease in carbapenem-R *Pseudomonas*
- 13.7% decrease in cipro-R *Pseudomonas*
- No changes in susceptibilities of *Enterobacteriaceae* or *A. baumannii*
Cost reduction
<table>
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<tr>
<th>Setting</th>
<th>Key team members</th>
<th>Intervention ABs assessed</th>
<th>Effect on AB-rel costs</th>
<th>Reference</th>
</tr>
</thead>
</table>
| 200-bed community teaching Carney Hospital, Boston | ID physician (25% time)  
ID pharmacist (fulltime) | Review and feedback | US$243,000-293,000 reduction in AB costs per year  
Cost: US$43,000 | 3GC, aztreonam, FQ, imipenem Carling P. ICHE 2003 |
| 600-bed Louis Stokes Veterans hospital, Cleveland | ID physician  
ID pharmacist | Education. Guideline development. Review and feedback | US$48,000 reduction in AB costs in 3 years  
Cost: not provided (NP) | FQ, vancomycin Feuht CI. Ann Pharmacother 2003 |
| 11-bed ICU  
860-bed h Toulon, France | ICU physicians | Guideline development  
Education | 35% relative reduction in AB costs over 4 years  
Cost: NP | FQ, aminoglycoside Geissler A. Intensive Care Med 2003 |
# Cost outcomes (II)

<table>
<thead>
<tr>
<th>Setting</th>
<th>Key team members</th>
<th>Intervention ABs assessed</th>
<th>Effect on AB-rel costs</th>
<th>ABs assessed</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two hosps 150-bed teaching \nCambridge 180-bed non-teaching \nSomerville</td>
<td>Infection Control Committee \nPharmacy &amp; Therapeutics Committee</td>
<td>Antimicrobial cycling</td>
<td>31% increase per 1000 patient days during a 2-yr cycling period Cost: not provided</td>
<td>FQ, \n\n$\beta$lactams</td>
<td>Bruno-Murtha LA. ICHE 2005</td>
</tr>
<tr>
<td>279-bed teching \nDetroit Receiving Hospital</td>
<td>ID pharmacist</td>
<td>Education Review and feedback</td>
<td>US$110 reduction in AB acquisition costs per patient Cost: NP</td>
<td>FQ</td>
<td>Cook P. JAC 2004</td>
</tr>
<tr>
<td>410-bed government \nHadera hospital, Israel</td>
<td>Infection control physician. Pharmacy services head</td>
<td>Automatic iv-to-oral. Feedback. Restriction &amp; pre-approval</td>
<td>66,190 (18%) reduction in AB acquisition costs in 3 years. Cost: NP</td>
<td>FQ</td>
<td>Schwartzberg E. J Clin Pharm Ther 2006</td>
</tr>
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# AB resistance and superinfection (I)

<table>
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<th>Setting</th>
<th>Key team members</th>
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<th>AB resistance. Superinfections</th>
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<tr>
<td>200-bed community teaching Carney Hospital, Boston</td>
<td>ID physician (25% time) ID pharmacist (fulltime)</td>
<td>Review and feedback</td>
<td>CAZ-R: Coliforms: 60% reduction in 7 yrs C. difficile: 36% reduction in 7 yrs</td>
<td>3GC, aztreonam, FQ, imipenem Carling P. ICHE 2003</td>
</tr>
<tr>
<td>600-bed Louis Stokes Veterans hospital, Cleveland</td>
<td>ID physician ID pharmacist</td>
<td>Education. Guideline development Review and feedback</td>
<td>Ciprofloxacin resistance: <em>P. aeruginosa</em>. Non-significant (NS) in 3 yrs</td>
<td>FQ, vancomycin Feuht CI. Ann Pharmacother 2003</td>
</tr>
<tr>
<td>Setting</td>
<td>Key team members</td>
<td>Intervention ABs assessed</td>
<td>AB resistance. Superinfections</td>
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<tr>
<td>Two hosps 150-bed teaching Cambridge</td>
<td>Infection Control Committee</td>
<td>Antimicrobial cycling</td>
<td>In 2 years Cambridge hosp • CAR-R: $\nabla 63%$ • CTX-R: $\nabla 44%$ • Levo, PIP-TZP, TIC-CLAV: NS • Va-R <em>Enterococcus:</em> $\nabla 80%$ • MRSA: non-significant <em>(NS)</em> • <em>C. difficile:</em> NS</td>
<td>FQ, βlactams Bruno-Murtha LA. ICHE 2005</td>
</tr>
<tr>
<td>180-bed non-teaching Somerville</td>
<td>Pharmacy &amp; Therapeutics Committee</td>
<td></td>
<td>Sommerville hosp NS for all organisms &amp; all AB</td>
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## AB resistance and superinfection (III)

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<th>Intervention ABs assessed</th>
<th>AB resistance. Superinfections</th>
<th>ABs assessed Reference</th>
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<tr>
<td>470-bed university hospital</td>
<td>ID physician and AB committee-formulary decisions (members from surgery, pediatrics, internal medicine, transplant units, critical care, ID, pharmacy and nursing)</td>
<td>Formulary change</td>
<td>In 4 years</td>
<td>CAZ, CTX removed from formulary. Cefepime added. Ceftriaxone, carbapenems restricted &amp; pre-approval. Vanco stop order. Cipro substituted by Levo. Martin C. Am J Health Syst Pharm 2005</td>
</tr>
<tr>
<td>Chandler Medical Center, Kentucky University</td>
<td></td>
<td>Restriction &amp; pre-approval</td>
<td>PIP-TZP-R: Paer (\nabla17%) CAZ-R: Paer (\nabla5%); Kpneu (\nabla91%) Carbapenem-R: Paer (\nabla36%) FQ-R: Paer 13% MRSA: (\nabla23%)</td>
<td></td>
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<td></td>
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<td>Automatic stop order</td>
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# Adverse event outcomes

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<td>FQ, β-lactams Bruno-Murtha LA. ICHE 2005</td>
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<td>Pharmacy &amp; Therapeutics Committee</td>
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Conclusions
1. - Trends in FQs use are still increasing in some European countries

2. - Potential risks of FQs overuse include the increase in FQ Resistant microorganisms

3. - Quinolone overuse increase also Resistance to other agents (ESBL's)

4. - FQs consumption ruse have been linked to *C. difficile* infections

5. - Programs to reduce overuse are profitable
6. Most control programs are short-term.

7. The role of quinolone reduction is not well separated from other parallel activities.

8. The risk of reducing sequential (IV oral therapy are not considered).

9. The risks and cost of substituting drugs are not generally taken into account.

10. Reduction programs should consider the community and not only the hospitals.
Bundle proposal

1. - Regular reporting and surveillance of FQ’s use and misuse

2. - Clarify the empirical indications of FQs in treatment and practice guidelines

3. - Implement Microbiology advice in the Laboratory reports

4. - Pharmacy-advice on prescription requests
Bundle proposal

5. - Pharmacy control on duration of FQ’s prescription (stop-orders)

6. - Local Guidelines easily available

7. - Educational interactive programs

8. - Interventions in the community

9. - Assessment of the use of alternative drugs

10. - Assessment of the Long-term impact
Thank you