Guidelines for prudent use of antibiotics and their implementation in real life

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Conflicts of interest

- None for this presentation

- Merck, unrestricted grant for University-accredited Expert degree course (paid to my University)
- Research funds, IMI (European Union and EFPIA)

Antimicrobial stewardship

- Objective: to improve the use of antibiotics
  - Improve the outcome of patients with infections and reduce adverse events
  - Contribute to control of resistance
  - Reduce healthcare costs

- Best way to achieve: AMS programmes
  - Comprehensive
  - Structured
  - Measurable results

The big gap is implementation

NEEDS for implementing AMS programmes

- Resources
- Expertise
- Organisation
- Institutional support

How to: the Spanish experience

- PRogramas de Optimización de uso de Antimicrobianos (PROA, Spanish for AMS programmes)
- PROA document (2012)
  - Supporting societies: ID and CM; Hospital pharmacy; Preventive Medicine. Now endorsed by the National Plan against AMR
  - PROA as quality programmes with levels of implementation
    - Basic
    - Advanced
    - Excellent
  - Guidance for implementation

How to: the Spanish experience

Enferm Infecc Microbiol Clin. 2012;30(1):22.e1–22.e23

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Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Documento de consenso

Programas de optimización de uso de antimicrobianos (PROA) en hospitales españoles: documento de consenso GEIH-SEIMC, SEFH y SEMPSPH☆,☆☆

Jesús Rodríguez-Baño[a,*], José Ramón Paño-Pardo[b,*], Luis Alvarez-Rocha[c], Ángel Asensio[d], Esther Calbo[e], Emilia Cercenado[f], José Miguel Cisneros[g], Javier Cobo[h], Olga Delgado[i], José Garnacho-Montero[j], Santiago Grau[k], Juan Pablo Horcajada[l], Ana Hornero[m], Javier Murillas-Angoiti[n], Antonio Oliver[o], Belén Padilla[f], Juan Pasquau[p], Miquel Pujol[m], Patricia Ruiz-Garbajosa[q], Rafael San Juan[r] y Rafael Sierra[s]

How to: the Spanish experience

- Organisational aspects
- Resources
- Indicators
- Activities, interventions
- Implementation

How to: the Spanish experience

- Organisational aspects
- Resources
- Indicators
- Activities, interventions
- Implementation

  - (Institutional support must be seeked)
  - Infections and antibiotics hospital committees
  - AMS team (operational)
    - Core: ID, CM, pharmacist
    - Also: epidemiologists, Intensive Care, Pediatrics, nurses, etc.

How to: the Spanish experience

- Organisational aspects
- Resources
  - Human (number; expertise)
  - Material (access to data; IT)
- Indicators
- Activities, interventions
- Implementation

How to: the Spanish experience

- Organisational aspects
- Resources
- Indicators
- Activities, interventions
- Implementation

– Process
  - Quality of prescription
  - Antibiotics consumption

– Outcomes
  - Clinical outcomes
  - Resistance rates

How to: the Spanish experience

- Organisational aspects
- Resources
- Indicators
- Activities, interventions
- Implementation

  - Education
  - Guidelines for antibiotic use
  - Non-compulsory interventions (audit and feed back, rounds, bacteraemia programmes, supporting tools, etc)
  - Restrictive interventions

How to: the Spanish experience

- Organisational aspects
- Resources
- Indicators
- Activities, interventions
- Implementation
  - Basic, advanced, excellent levels
  - Accreditation

Outcomes of the PIRASOA programme, an antimicrobial stewardship programme implemented in hospitals of the Public Health System of Andalusia, Spain: an ecologic study of time-trend analysis

J. Rodríguez-Baño [1], M.A. Pérez-Moreno [2], G. Peñalva [3], J. Garnacho-Montero [4], C. Pinto [5], I. Salcedo [6], R. Fernández-Urrusuno [7], O. Neth [8], M.V. Gil-Navarro [2], A. Pérez-Milena [9], R. Sierra [10], Á. Estella [11], C. Lupión [1], A. Irastorza [12], J.L. Márquez [12], Á. Pascual [1], M.D. Rojo-Martín [13], M.J. Pérez-Lozano [14], R. Valencia-Martín [2], J.M. Cisneros [3,*], on behalf of the PIRASOA Programme Group

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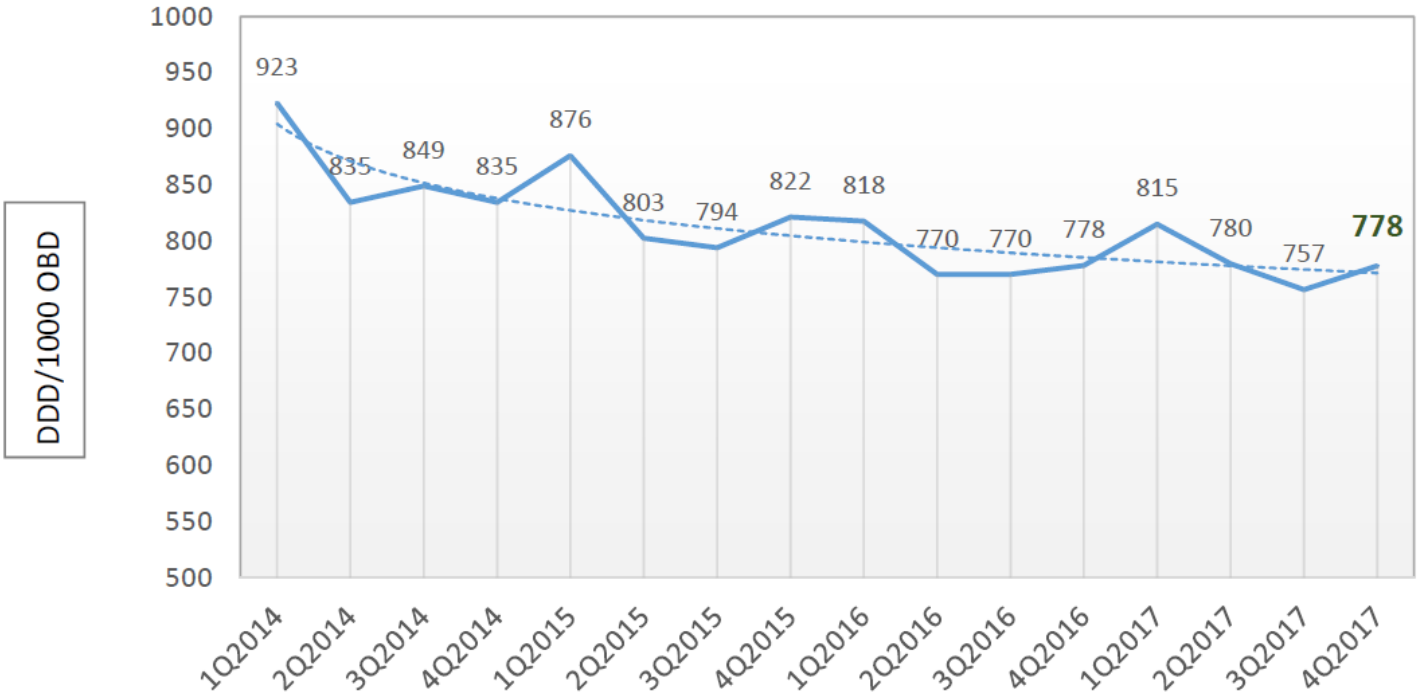


QPC = -0.9% (95% CI -1.2, -0.6; p < 0.001)

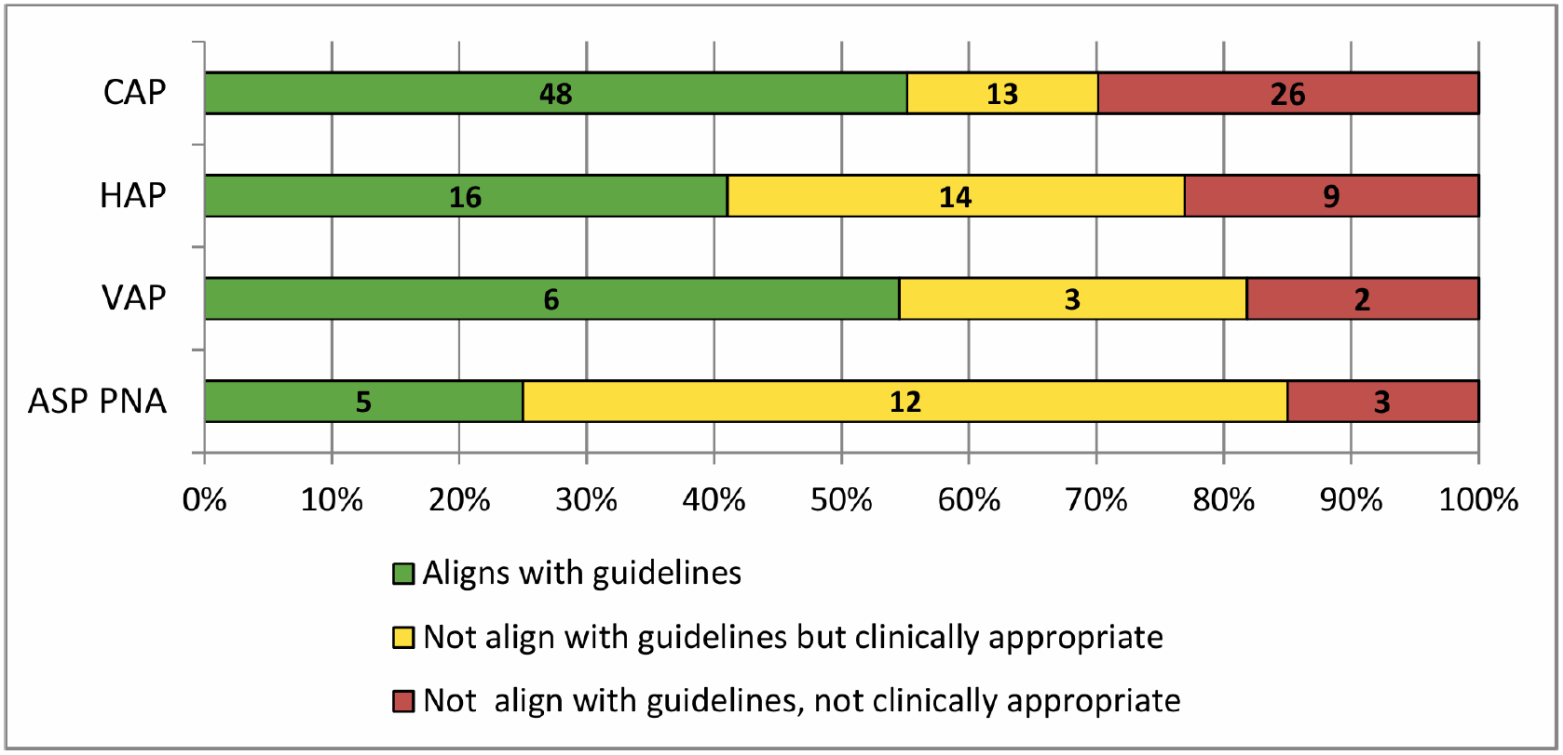
Evidence-based guidelines: challenges in antibiotics

- Inherent problems of evidence evaluation
  - Pivotal, non-inferiority trials with low external validity (not real life)
  - Academic trials with low power and limitations
  - Observational studies
- Low level/no evidence for many specific clinical decisions
- Studies do not include stewardship outcomes
- Applicability
  - Heterogeneous epidemiology
  - Differences in drug availability

AMS in the ICU: empiric therapy and adherence to guidelines for pneumonia

Shelby Pflanzner,[1] Casey Phillips,[2] Jonathan Mailman,[1,3] Jason Robert Vanstone[4]

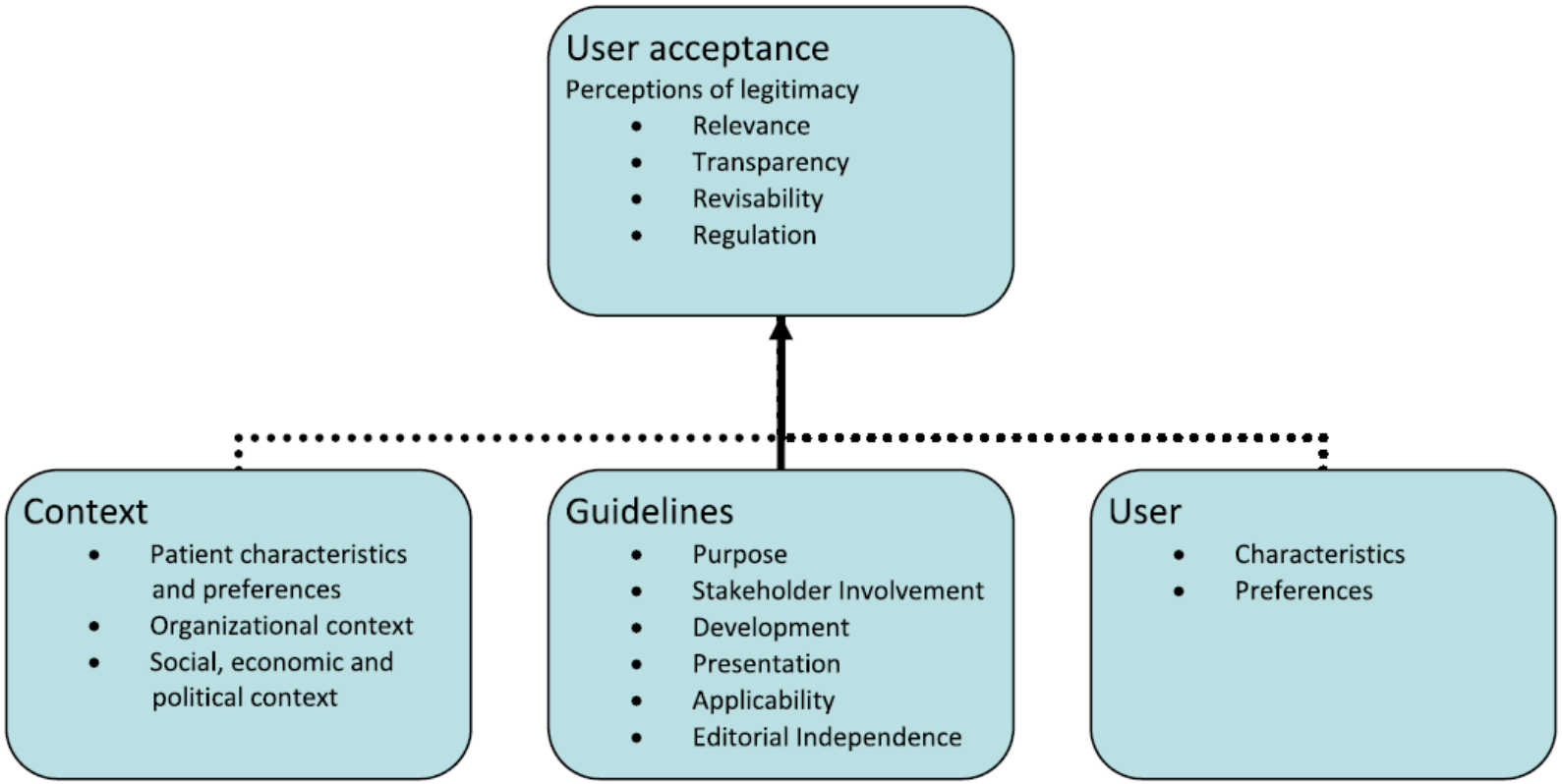
BMJ Open Quality 2019;**8**:e000554.



Antimicrobial stewardship: a qualitative study of the development of national guidelines for antibiotic use in hospitals

Eli Feiring[1*] and Anne Berit Walter[2]

BMC Health Services Research (2017) 17:747



(Local) guidelines?

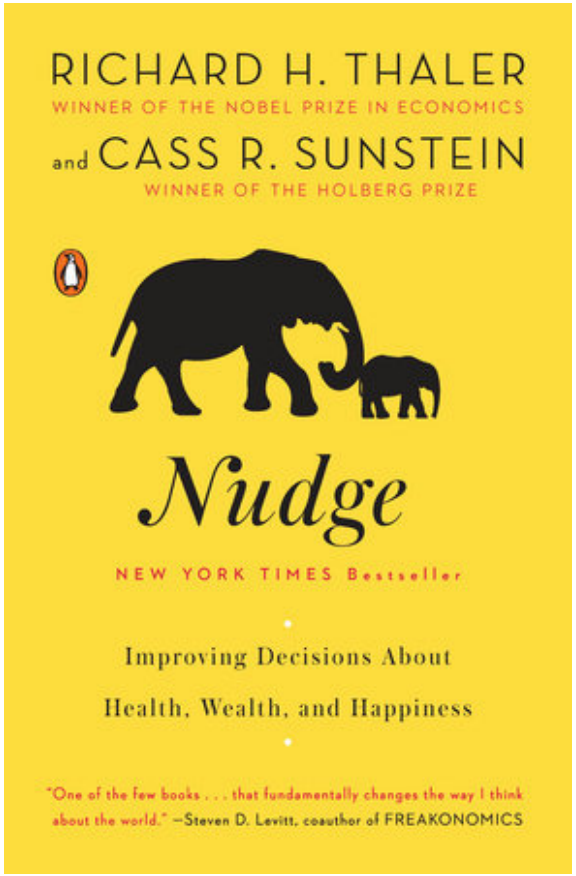
- Why
  - Critical (but insufficient) tool for prescribers
  - Reference for evaluation, audits, etc.

- Some tips for succesful local guidelines
  - Locally adapted
    - Local epidemiology, available drugs, etc.
  - Based on evidence but also on consensus
  - Accesibility, usability
  - Understandable and acceptable

The wrong way

AMS experts

Prescriber



Nudge is a concept in behavioral science, political theory and behavioral economics which proposes positive reinforcement and indirect suggestions as ways to influence the behavior and decision making of groups or individuals. Nudging contrasts with other ways to achieve compliance, such as education, legislation or enforcement.

What's in a local guideline

- Prophylaxis
- Empirical treatment for syndromes, according to
  - Acquisition, severity, individual risk factors
  - First choice and alternatives
- Definitive treatment of the most frequent infections and pathogens
  - Drug(s) of choice
  - Duration of therapy, follow-up
- Information about antibiotics
  - Dosing, adverse events, cost
- Allergies management

UTI	Drug
Community-acquired pyelonephritis	Ceftriaxone 1 g/24h IV

UTI	First choice	Alternative	Comments
Community-acquired pyelonephritis			
Not severe, no risk factors	Admission: Ceftriaxone 1 g/24h IV. Discharge: Cefuroxime 500 mg/12h	Allergy	Blood and urine cultures Ultrasound indications Criteria for admission and referral to outpatient clinic
Sepsis or risk factors for ESBL	Ertapenem 1 g/24h or ceftriaxone 1 g 24/h + amikacin 15 mg/kg /24h (low risk or AKI)	Allergy	See above Risk of AKI If amikacin, follow renal function and review culture results in 24h

Some tips

The local guideline is just (and nothing more than) a tool

It must be useful and accepted

“An imperfect but useful and followed local guideline is preferable to another perfect one which nobody look at”

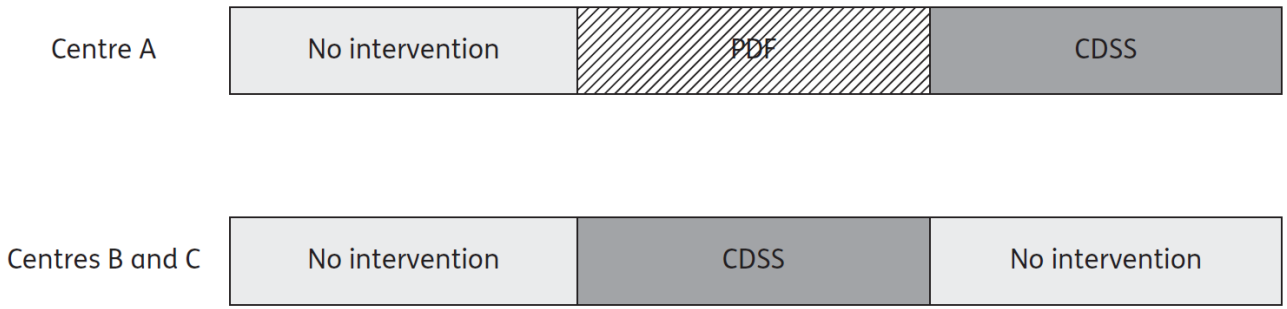
IT integration

- Not integrated
- Integrated in prescription application (compulsory or not)
  - Support system
  - Machine learning

Impact of a computerized decision support system on compliance with guidelines on antibiotics prescribed for urinary tract infections in emergency departments: a multicentre prospective before-and-after controlled interventional study

Elisa Demonchy[1,2], Jean-Charles Dufour[3,4], Jean Gaudart[3,4], Emmanuel Cervetti[5], Pierre Michelet[6], Nicolas Poussard[7], Jacques Levraut[1,8] and Céline Pulcini[1,2,4*]

J Antimicrob Chemother 2014; **69**: 2857–2863



The CDSS was used in 59% (182/307) of cases

Factor	Appropriate antibiotic and duration		Appropriate antibiotic		Appropriate duration	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
No intervention	1	—	1	—	1	—
CDSS intervention	1.07 (0.69–1.66)	0.77	0.91 (0.58–1.41)	0.67	1.36 (0.90–2.06)	0.14
PDF intervention	1.58 (0.98–2.54)	0.06	1.30 (0.81–2.08)	0.27	1.57 (0.99–2.47)	0.05
No CDSS use	1	—	1	—	1	—
CDSS used by clinicians	1.50 (0.90–2.49)	0.12	1.94 (1.13–3.32)	0.016*	1.01 (0.62–1.64)	0.98
Junior doctor	1	—	1	—	1	—
Senior doctor	0.65 (0.47–0.89)	0.009*	0.77 (0.55–1.07)	0.11	0.61 (0.45–0.83)	0.002*
Weekdays	1	—	1	—	1	—
Nights and weekends	0.98 (0.71–1.34)	0.89	0.84 (0.61–1.18)	0.32	1.08 (0.79–1.46)	0.63
Diagnosis						
cystitis	1	—	1	—	1	—
pyelonephritis	1.04 (0.76–1.42)	0.82	5.68 (4.13–7.82)	<0.001*	0.47 (0.35–0.63)	<0.001*
prostatitis	3.56 (2.25–5.63)	<0.001*	7.11 (4.11–12.29)	<0.001*	1.85 (1.16–2.94)	0.012*

Conclusions: The CDSS only partially improved compliance with guidelines on antibiotic prescriptions in UTIs.

J Antimicrob Chemother 2014; **69**: 2857–2863

Machine learning for clinical decision support in infectious diseases: a narrative review of current applications

N. Peiffer-Smadja [1,2,*], T.M. Rawson [1], R. Ahmad [1], A. Buchard [3], G. Pantelis [4], F.-X. Lescure [2,5], G. Birgand [1], A.H. Holmes [1]

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Artificial intelligence (AI) for clinical infectious diseases

- Corresponds to a system that emulates the decision-making ability of a human expert on a specific task, e.g. a physician prescribing antibiotics
- Sometimes called "narrow" or "weak" AI as compared to "general" or "strong" AI which describes a way to simulate whole human minds

Expert systems

- Represent most current Clinical Decision Support Systems (CDSS) or computer-assisted/aided tools
- Stereotyped architecture
  - Knowledge base: data from experts
  - Inference engine: logical rules manually programmed
- Knowledge-intensive or knowledge-based systems
  - The most important element is the quality of the experts' knowledge
- "Old" AI
  - No more included in "AI" by most AI scientists

Machine learning

- Systems with the ability to automatically learn and improve from experience without being explicitly programmed
- Sometimes called machine learning clinical decision support systems (ML-CDSS)
- Various algorithms
  - Deep learning / Artificial Neural Networks
  - Support Vector Machines
  - Etc.
- Data-intensive systems
  - The most important element is the quality of the patients' data
- "Modern" AI

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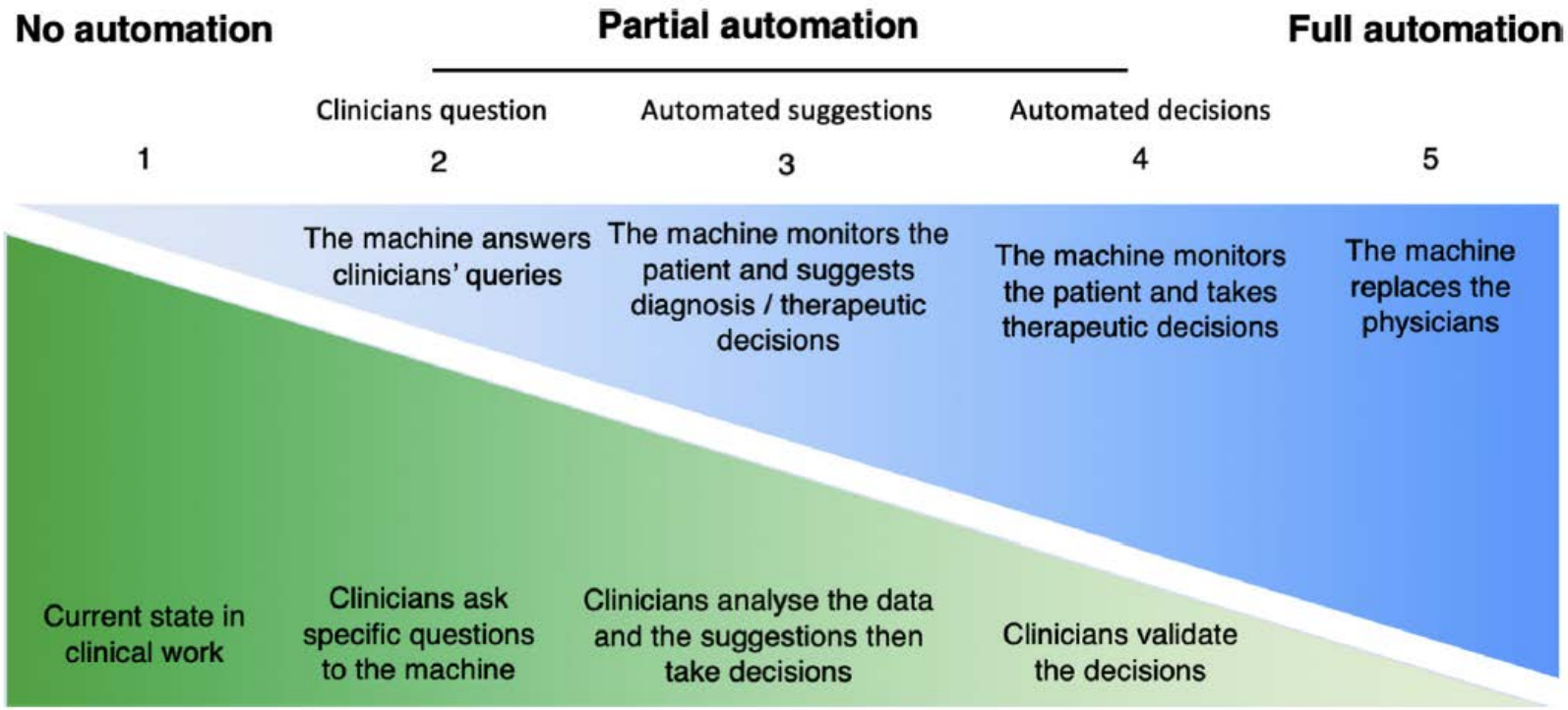

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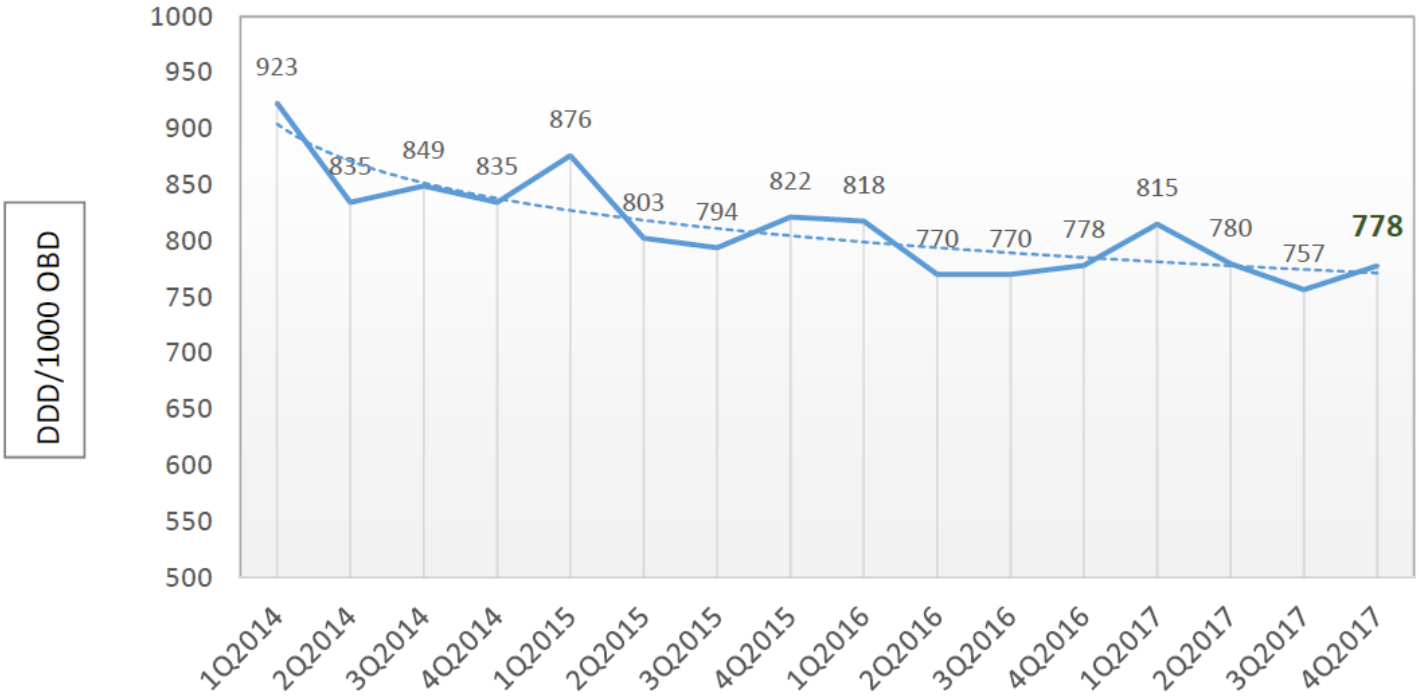

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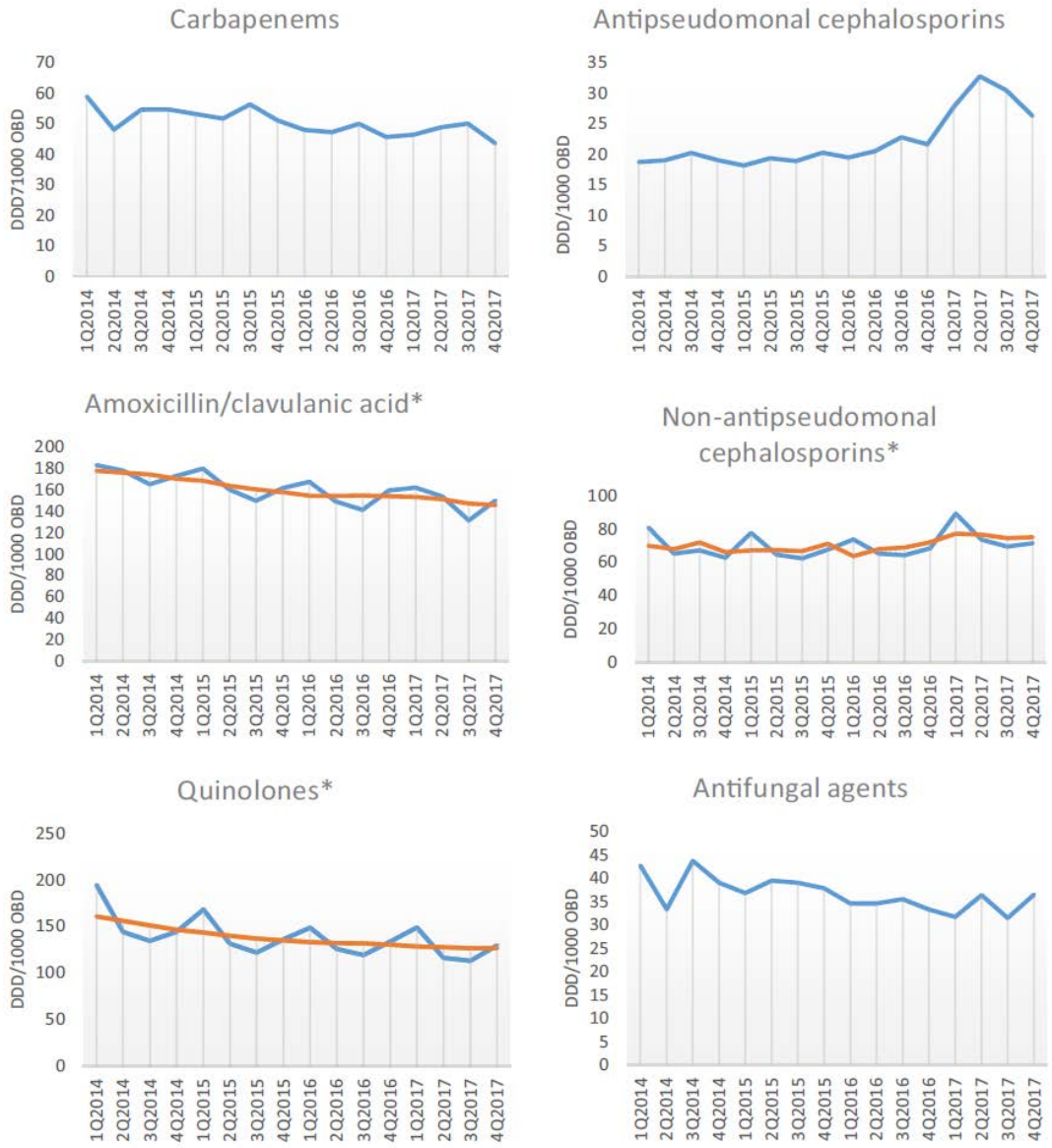

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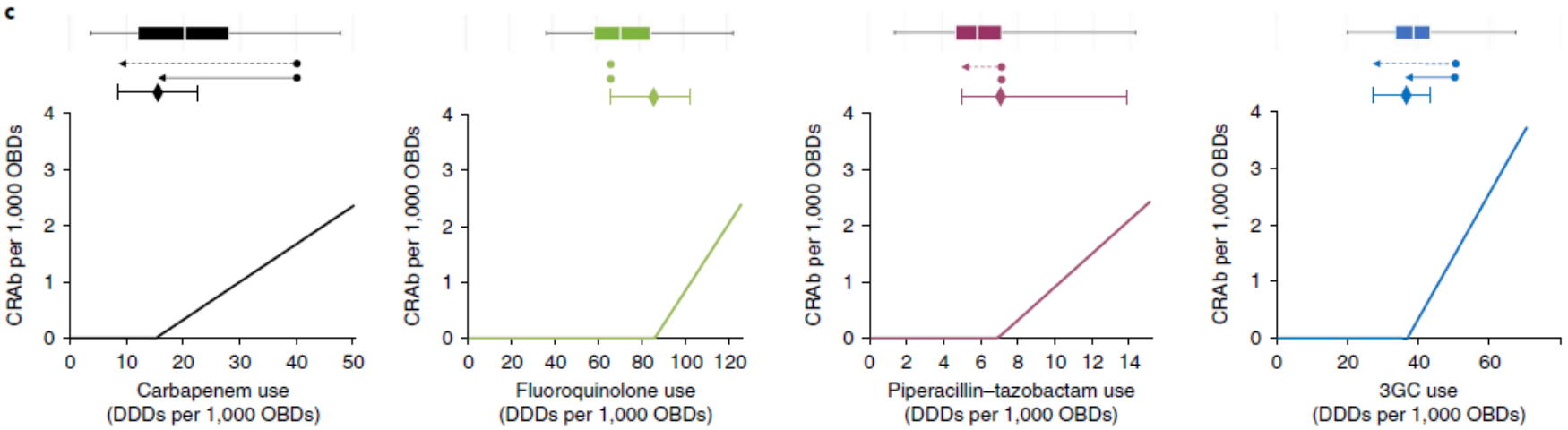
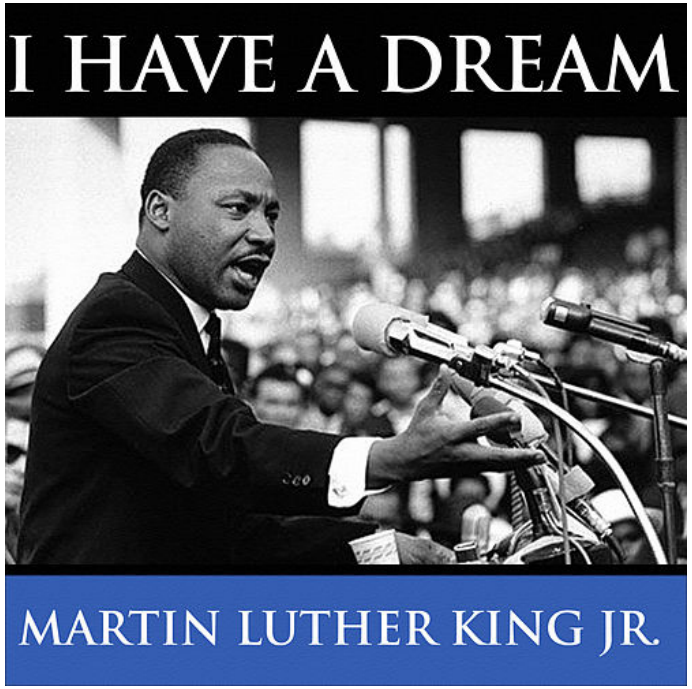
ARTICLES
https://doi.org/10.1038/s41564-019-0410-0
nature microbiology

A nonlinear time-series analysis approach to identify thresholds in associations between population antibiotic use and rates of resistance

José-María López-Lozano[1], Timothy Lawes[2*], César Nebot[3], Arielle Beyaert[4], Xavier Bertrand[5,6], Didier Hocquet[5,6], Mamoon Aldeyab[7], Michael Scott[8], Geraldine Conlon-Bingham[8], David Farren[9], Gábor Kardos[10], Adina Fésüs[11], Jesús Rodríguez-Baño[12,13], Pilar Retamar[12,13], Nieves Gonzalo-Jiménez[14], Ian M. Gould[15] and THRESHOLDS study group[16]





The THRESHOLDS Study Group

Knowing in real time how many prescriptions of each antibiotics we must avoid in order to reduce resistance, or how many can still make without increasing resistance…

Conclusions

- Local guidelines are needed but insufficient tools
- Avoid oversimplification
- Consensus and usability are critical for their success
- New technology is here or coming

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  - **Infectious Diseases:** P Retamar
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  - **Pediatrics:** P Terol
  - **Nurses:** T Quesada
  - **Quality service:** A Vilaplana
  - **ER champion:** F. Oltra
- **ESGAP**

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