Prevenzione delle resistenze negli ospedali

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- Note introduttive
- Caso clinico recente
- Depistaggio e prevenzione
- Studio COMPASS
- Conclusione

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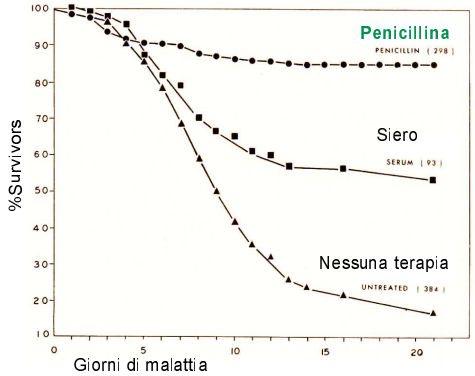
Chiaramente gli antibiotici fanno la differenza


Koch


Fleming

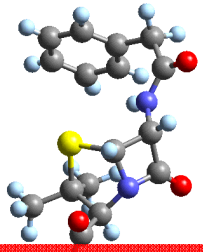

Ehrlich

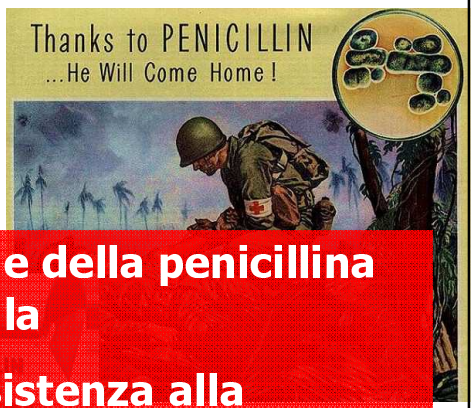
Effect of Therapy on % Survival in Pneumococcal Bacteremia



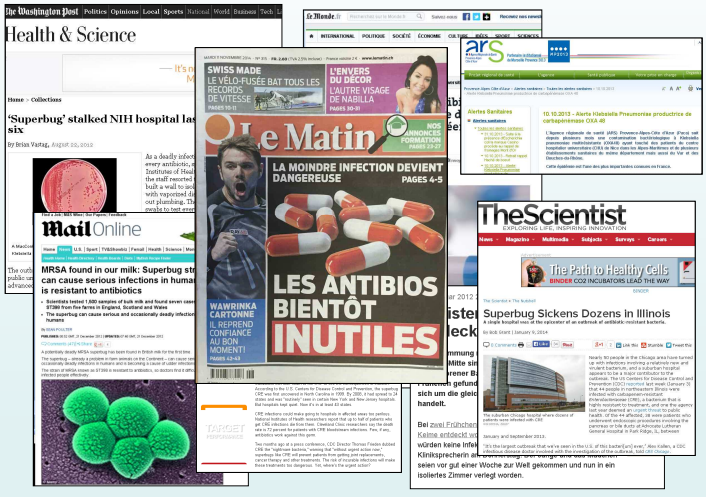
Austrian & Gold. Ann Int Med 60:759, 1964

Penicillina (Fleming, 1928)

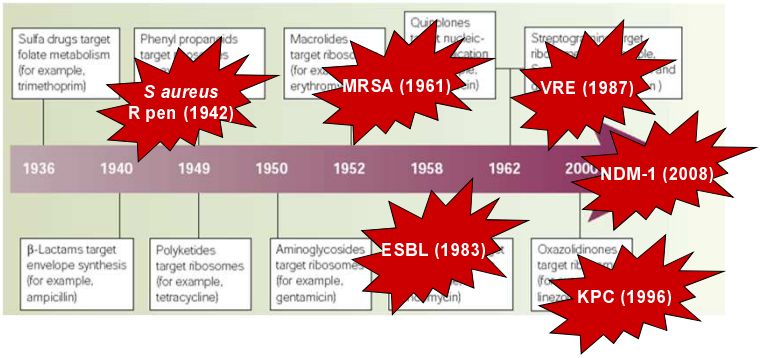




- 1945 distribuzione della penicillina su larga scala
- 1946 Tasso di resistenza alla penicillina, *S. aureus* = 6%



La «linea temporale» degli antibiotici



Walsh (2003). Nat Rev Microbiol 1:65-70

La vera «linea del tempo» degli antibiotici

Homo sapiens
0.2 milioni di anni

Daptomicina
30 milioni di anni

Vancomicina
240 milioni di anni

Streptomicina
610 milioni di anni

Eritromicina
880 milioni di anni

Beta-lattamasi
> 2 miliardi di anni

Wright (2007), Nat Rev Microbiol /Hall et Barlow (2004), Drug Resist Updat

The Shared Antibiotic Resistome of Soil Bacteria and Human Pathogens

Kevin J. Forsberg,[1*] Alejandro Reyes,[1*] Bin Wang,[1,2] Elizabeth M. Selleck,[3] Morten O. A. Sommer,[4,5†] Gautam Dantas[1,2†]

Soil microbiota represent one of the ancient evolutionary origins of antibiotic resistance and have been proposed as a reservoir of resistance genes available for exchange with clinical pathogens. Using a high-throughput functional metagenomic approach in conjunction with a pipeline for the de novo assembly of short-read sequence data from functional selections (termed PARFuMS), we provide evidence for recent exchange of antibiotic resistance genes between environmental bacteria and clinical pathogens. We describe multidrug-resistant soil bacteria containing resistance cassettes against five classes of antibiotics (β-lactams, aminoglycosides, amphenicols, sulfonamides, and tetracyclines) that have perfect nucleotide identity to genes from diverse human pathogens. This identity encompasses noncoding regions as well as multiple mobilization sequences, offering not only evidence of lateral exchange but also a mechanism by which antibiotic resistance disseminates.

Forsberg et al. Science. 2012 Aug 31;337(6098):1107-11

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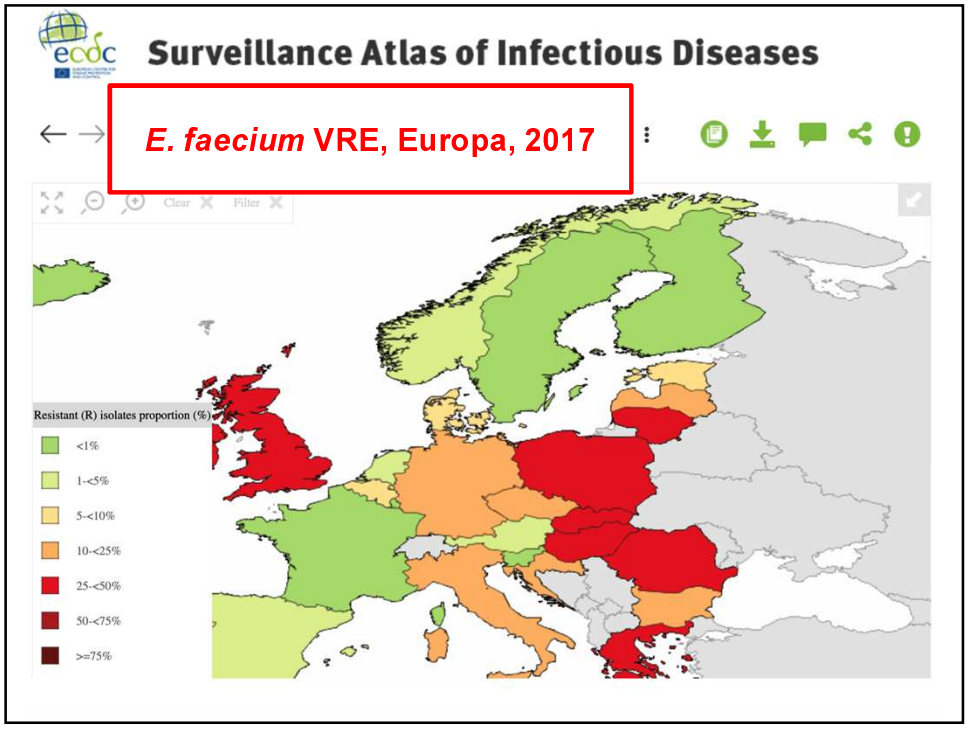
Alte Frau, 1925

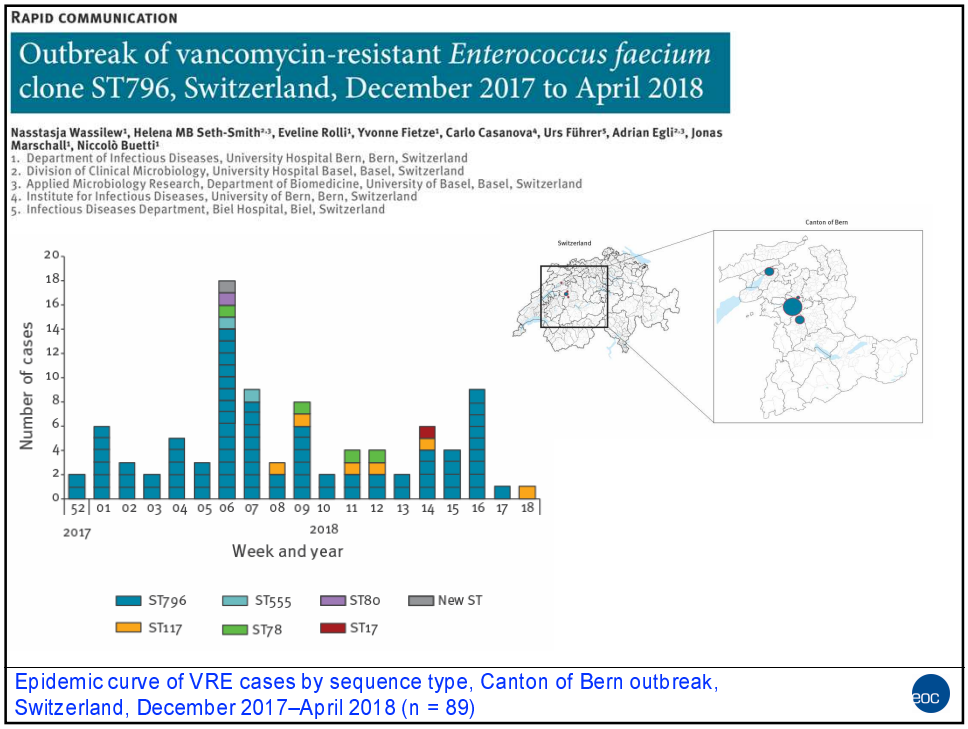
- Residente a Stoccarda in vacanza a Morcote
- Pronto Soccorso: stato febbrile, sospetta infezione delle vie urinarie
- 3 settimane prima ricovero in un ospedale di Stoccarda
  - Escissione di 2 carcinomi squamocellulari alle gambe
  - A destra infezione cutanea, prescrizione di ciprofloxacina e co-amoxicillina

Siete preoccupati per un eventuale rischio epidemiologico?

La «sorpresa» nello striscio ferita

- Screening VRE: POSITIVO (*E. faecium* Van B)
- Screening ESBL: POSITIVO (*E. coli* ESBL)
- Screening CRE: NEGATIVO, ma P. aeruginosa multiresistente (S solo amicacina e colistina)





Epidemic curve of VRE cases by sequence type, Canton of Bern outbreak, Switzerland, December 2017–April 2018 (n = 89)

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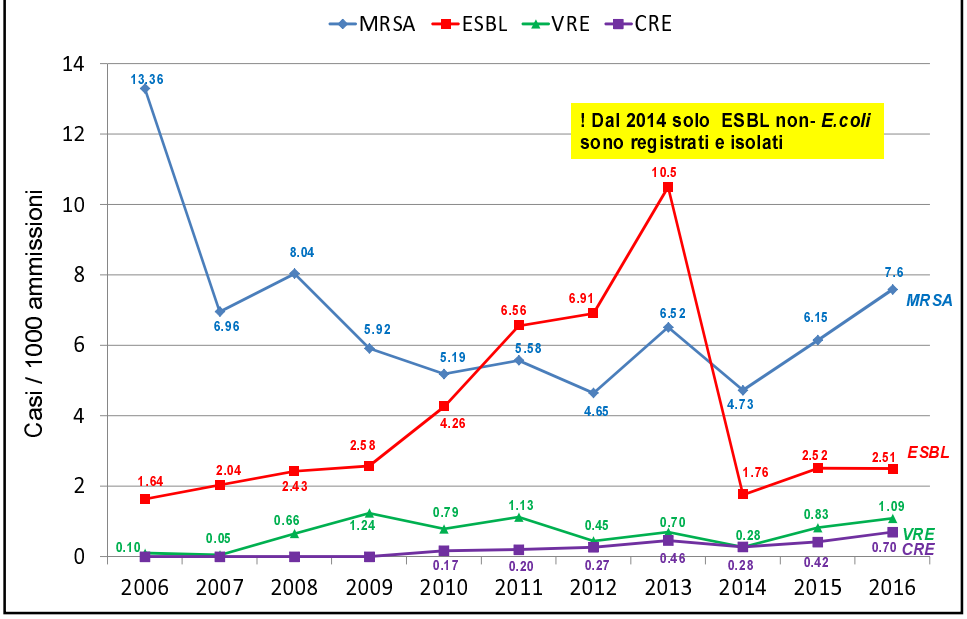
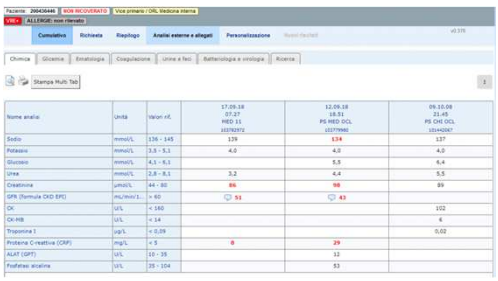
Incidenza germi multiresistenti (EOC)



Misure di depistaggio e controllo dei germi multiresistenti (MR)

- **Screening pazienti a rischio** (diapositiva screening)
- **Pazienti portatori di MDR:**
  (ad es. MRSA, VRE, ESBL-non *E.coli*, CRE):
  - **Precauzioni contatto/ ev. goccioline**
- **Sistema di allerta informatico per pazienti MR**



Cortesia C. Balmelli

Misure di depistaggio e controllo dei germi multiresistenti (MR) - 2

- **Investigazione dei contatti (stessa camera)**
  - Se ≥ 3 casi: annuncio UMC
  - Se > 5 casi info a Swissnoso
- **Set di screening di controllo per dichiarare il paziente negativo** (2-5)
- **Segnalazione germi MR** (lettera di dimissione)

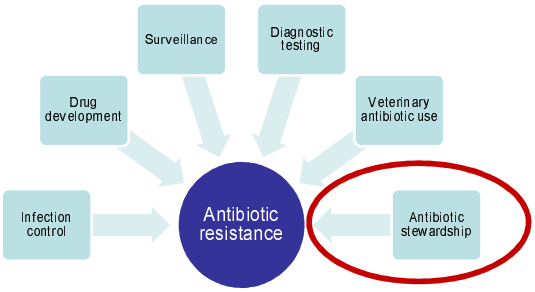
Cortesia C. Balmelli

Screening pazienti a rischio MR
(MRSA, VRE, ESBL-non *E. coli, CRE*)

- Se possibile isolamento preventivo in attesa dei risultati
- Pazienti trasferiti da un ospedale estero
- Pazienti ricoverati in un ospedale estero negli ultimi 6-12 mesi (implementazione difficile)
- Pazienti noti in passato per uno dei germi MR
- Pazienti che sono oggetto di un indagine di contatto (in camera con paziente risultato MR+)

Cortesia C. Balmelli

Lotta alle resistenze microbiche



Laxminarayan et al. Lancet Infect Dis. 2013 Dec;13(12):1057-98

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The goals of antibiotic stewardship

Antibiotic stewardship seeks to achieve optimal clinical outcomes… and limit the selection of antimicrobial resistance"

http://www.idsociety.org/stewardship_policy

Policy statement on antimicrobial stewardship (SHEA, IDSA, PIDS), 2012

Antimicrobial stewardship refers to coordinated interventions designed to improve and **measure the appropriate use of antimicrobials**….

… by promoting the selection of **the optimal antimicrobial drug regimen, dose, duration of therapy,** and route of administration.

http://www.idsociety.org/stewardship_policy

72 NRP Antimicrobial Resistance
National Research Programme
A one-health approach

GE COMPASS TI

COMPuterized Antibiotic Stewardship Study

Background

72 NRP Antimicrobial Resistance
National Research Programme
A one-health approach

Call for proposals

Module 1: Potential reservoirs and mechanisms of transmission .....
Module 2: Rapid diagnostic techniques, novel antimicrobial molecules.....
Module 3: Implementation measures and public health recommendations..

Stratégie Antibiorésistance StAR

Utilisation optimisée des antibiotiques

Utilisés à mauvais escient ou de manière excessive, les antibiotiques favorisent le développement de résistances. De nouveaux processus et aides à la décision doivent permettre aux médecins, vétérinaires et agriculteurs d'en faire un usage plus ciblé.

Projets approuvé

Procalcitonin and lung ultrasonography point-of-care testing to decide on antibiotic prescription in patients with lower respiratory tract infection at primary care level: cluster randomised trial
Dr. Noémie Boillat Blanco, Université de Lausanne

Routine antibiotic prescription and resistance monitoring in primary care physicians: A nationwide pragmatic randomized controlled trial
Prof. Heiner C. Bucher, Universität Basel

Improvement of antibiotic use in hospitals through pragmatic, multifaceted, computerized interventions: a multicentre, cluster-randomized trial
Dr. Benedikt Huttner, Université de Genève

Potentials of incentive-based instruments to an animal-friendly reduction of antibiotics usage
Dr. Stefan Mann, Forschungsanstalten Agroscope

A novel concept for veal calf production: "the outdoor veal calf"
Prof. Mireille Meylan, Universität Bern

AntibioticScout: Online tool for antimicrobial stewardship in veterinary medicine
Prof. Hanspeter Naegeli, Universität Zürich

Impact of routine audit and feedback on the use of protected antibiotics: a multicenter, randomized trial
Dr. Laurence Senn, Université de Lausanne CHUV

Problems with existing antibiotic stewardship interventions

- Resource intensive
- Cover often only a minority of antibiotic prescriptions
- Often limited to regular work hours
- Are often "back-end" interventions
  - i.e. occurring after the prescription (and the potential damage) has been made

Problems with existing antibiotic stewardship interventions

Informatics-based interventions: a potential solution ?

- Resource intensive
  - **in the long run probably cheaper than "manual" interventions => sustainability**
- Cover often only a minority of antibiotic prescriptions
  - **Can cover a large proportion of prescriptions**
- Often limited to regular work hours
  - **Available 7/7 - 24/24**
- Are often "back-end" interventions
  - **Can be "front-end"**

Generalizability?

Unintended consequences ?

Acceptability by prescribers (physician autonomy) ?

Few high-quality studies

Open-label, parallel-group, cluster randomized superiority trial

Study question: "Can overall antibiotic exposure in hospitalized patients be reduced through a multimodal computerized antibiotic stewardship intervention?"

Population	**Adult patients** hospitalized in acute-care wards of three secondary and tertiary care centers **Physicians** prescribing antimicrobials for these patients
Intervention	Multimodal, **computerized antibiotic stewardship intervention** • implemented on the ward level
Control	**"Standard-of-care"** antibiotic stewardship
Outcome	Overall **antibiotic exposure** • measured in days of therapy per admission
Time	12 months

Benedikt HUTTNER (antibiotic stewardship)

Enos BERNASCONI (ID & internal medicine)

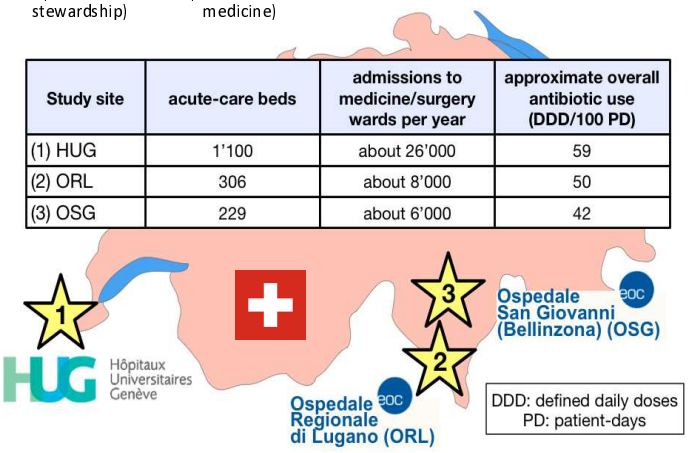
GE COMPASS TI

Stephan HARBARTH (antibiotic stewardship)

Rodolphe MEYSER (Informatics)

Laurent KAISER (infectious diseases)

Study site	acute-care beds	admissions to medicine/surgery wards per year	approximate overall antibiotic use (DDD/100 PD)
(1) HUG	1'100	about 26'000	59
(2) ORL	306	about 8'000	50
(3) OSG	229	about 6'000	42



GE COMPASS Framework

Three component informatics-based intervention

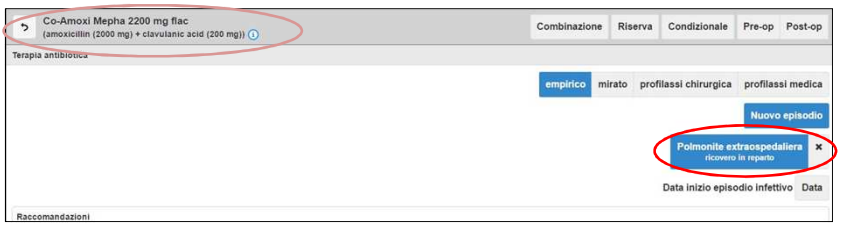
- Decision support for empiric treatment
- Self-evaluation of treatment
- Audit and feedback

(1) Decision support for empiric treatment

A- Selezione del tipo di trattamento

(1) Decision support for empiric treatment

B- Inserimento dell'indicazione della terapia antibiotica



(1) Decision support for empiric treatment

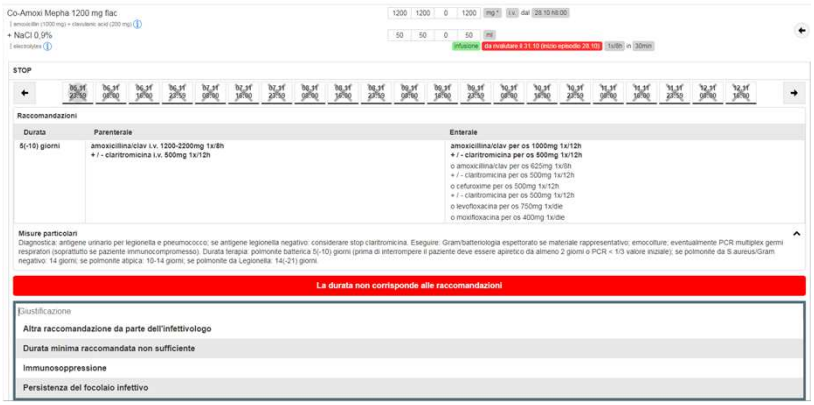
C- Supporto decisionale per la terapia antibiotica

(2) Accountable justification

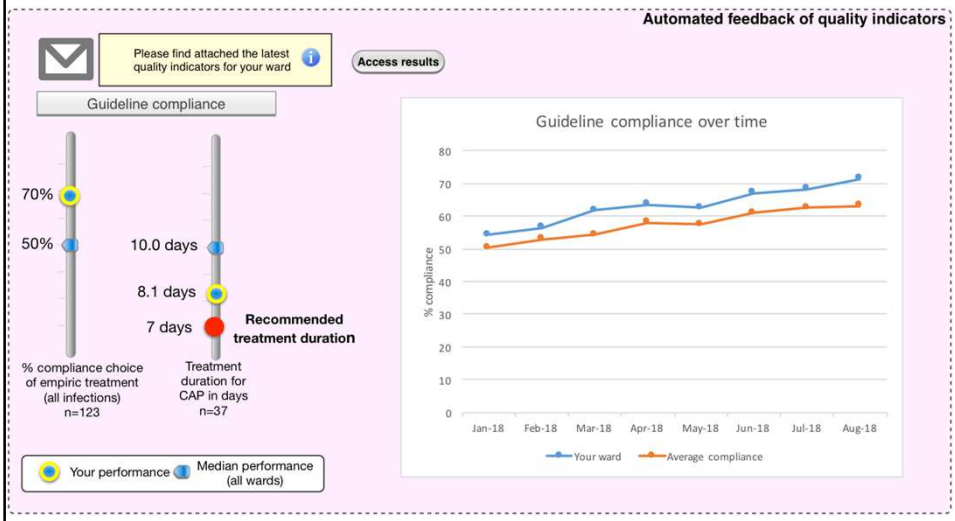
Fornire una giustificazione in caso di deviazione dalle raccomandazioni

(2) Self-evaluation of treatment (72h)

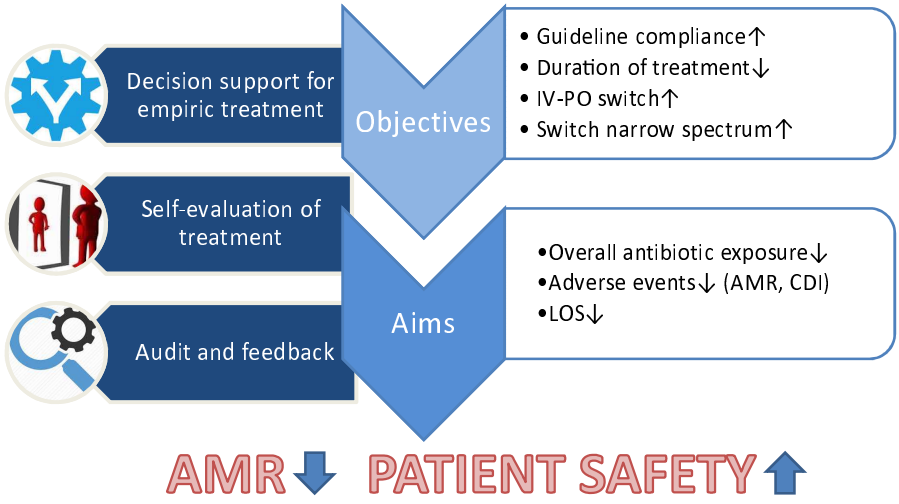
Rivalutazione (microbiologia?) e durata del trattamento



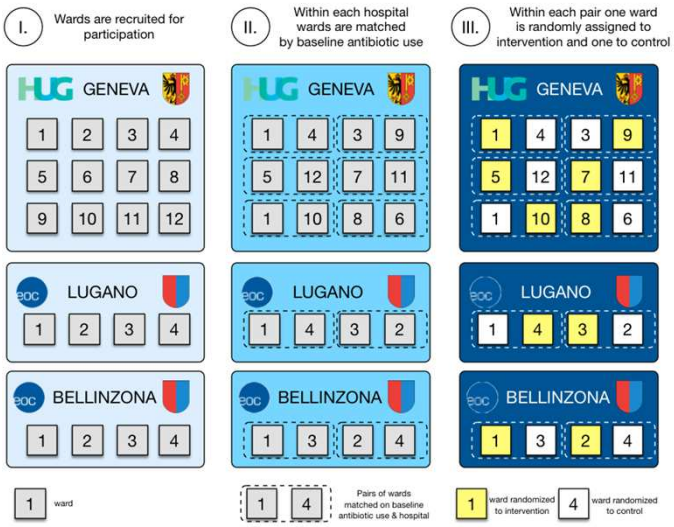
(3) Audit and feedback



COMPASS Framework



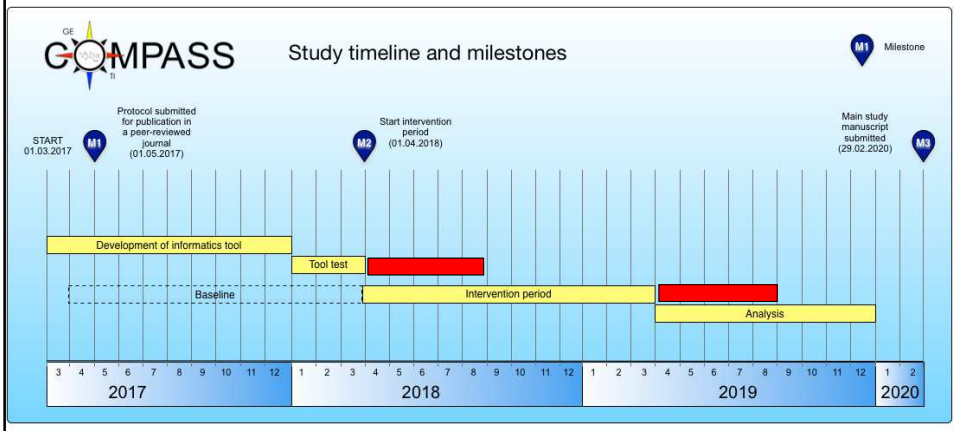
Randomization scheme



PRIMARY OUTCOME

- Systemic antibiotic treatment in days of therapy by admission
  - Objective
  - Reliably and objectively assessable in both intervention and control group
  - Ability to detect a meaningful difference given the achievable sample size

Timeline



BMJ Journals

Open access Protocol

BMJ Open **Study protocol for a multicentre, cluster randomised, superiority trial evaluating the impact of computerised decision support, audit and feedback on antibiotic use: the COMPuterized Antibiotic Stewardship Study (COMPASS)**

Gaud Catho,[1] Marlieke De Kraker,[2] Brigitte Waldispühl Suter,[3] Roberta Valotti,[4] Stephan Harbarth,[1,2] Laurent Kaiser,[1] Luigia Elzi,[5] Rodolphe Meyer,[6] Enos Bernasconi,[4] Benedikt D Huttner[1,2]

BMJ Open, 27 June 2018

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