Aggiornamenti in tema di stewardship:
la nostra esperienza in due nosocomi milanesi

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BACKGROUND

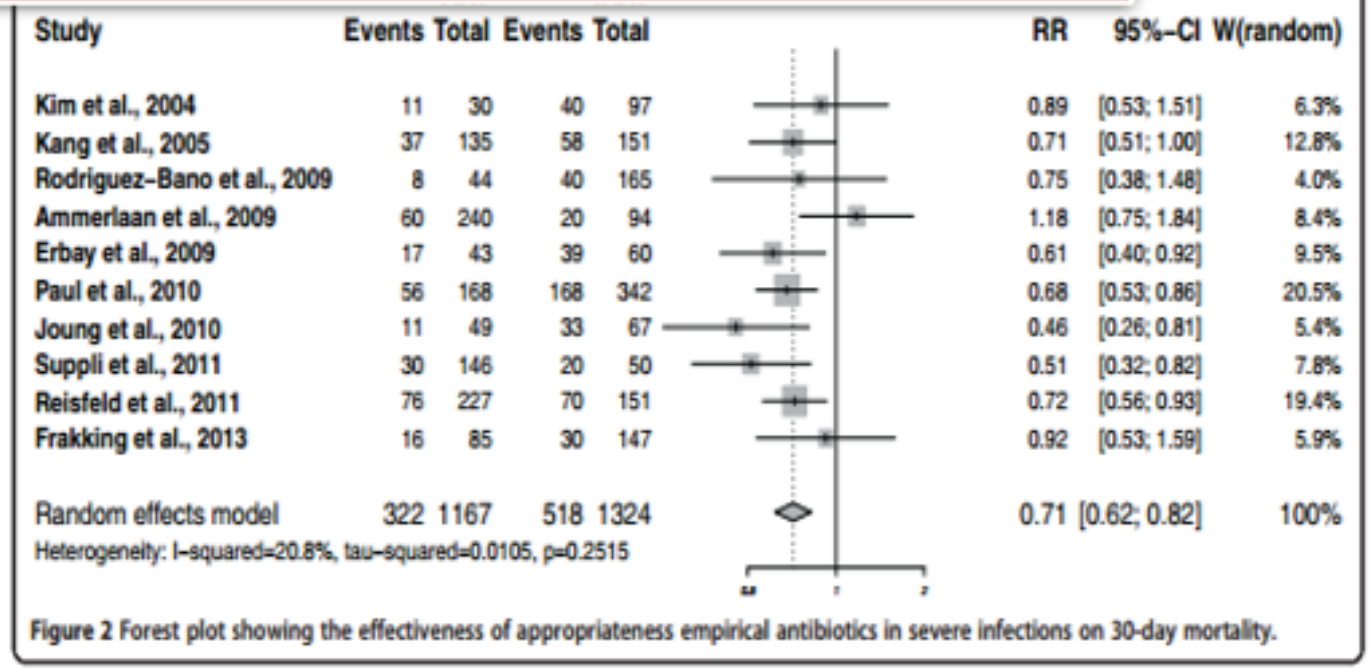
Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis

Kristel Marquet[1,2*], An Liesenborgs[2], Jochen Bergs[3], Arthur Vleugels[1,4] and Neree Claes[1,5]

- 27 studies included

- EFFECT OF APPROPRIATE THERAPY:

meta-analysis for 30-day mortality and in-hospital mortality showed RR of 0.71 (95% confidence interval 0.62 to 0.82) and 0.67 (95% confidence interval 0.56 to 0.80), respectively.



Study	Events	Total	Events	Total	RR	95%-CI	W(random)
Kim et al., 2004	11	30	40	97	0.89	[0.53; 1.51]	6.3%
Kang et al., 2005	37	135	58	151	0.71	[0.51; 1.00]	12.8%
Rodriguez-Bano et al., 2009	8	44	40	165	0.75	[0.38; 1.48]	4.0%
Ammerlaan et al., 2009	60	240	20	94	1.18	[0.75; 1.84]	8.4%
Erbay et al., 2009	17	43	39	60	0.61	[0.40; 0.92]	9.5%
Paul et al., 2010	56	168	168	342	0.68	[0.53; 0.86]	20.5%
Joung et al., 2010	11	49	33	67	0.46	[0.26; 0.81]	5.4%
Suppli et al., 2011	30	146	20	50	0.51	[0.32; 0.82]	7.8%
Reisfeld et al., 2011	76	227	70	151	0.72	[0.56; 0.93]	19.4%
Frakking et al., 2013	16	85	30	147	0.92	[0.53; 1.59]	5.9%
Random effects model	322	1167	518	1324	0.71	[0.62; 0.82]	100%

Heterogeneity: I-squared=20.8%, tau-squared=0.0105, p=0.2515

Figure 2 Forest plot showing the effectiveness of appropriateness empirical antibiotics in severe infections on 30-day mortality.

Marquet, Crit Care 2015

BACKGROUND

ANTIMICROBIAL CONSUMPTIONS:

- the pooled percentage change of **total antimicrobial consumption** after the implementation of ASPs was **-19.1%** (95% confidence interval [CI] -30.1 to -7.5)
- In **ICU** the decrease in antimicrobial consumption was **-39.5%** (95% CI -72.5 to -6.4)

MDR PATHOGENS:

the implementation of ASPs was associated with a decrease in infections due to:

- **MRSA** (risk difference [RD] = -0.017 [95%CI= -0.029 to -0.005])
- **ESBL *Klebsiella spp.*** ([RD] = -0.104 [95%CI= -0.153 to -0.055])

Cost and LoS:

the overall antimicrobial cost (-33.9% [95% CI= -42.0 to -25.9]), and the hospital length of stay (-8.9% [95% CI= -12.8 to -5]) decreased.

Hospital ASPs result in significant decreases in antimicrobial consumption and cost, and the benefit is higher in the critical care setting

PROJECTS DESCRIPTION

To pursue these aims:

1. AMS programs
2. Infectious Diseases consultations

P1

"educational antimicrobial stewardship program implemented in an Internal Medicine Department"

P2

"Impact of daily versus weekly service of Infectious Diseases consultations on antimicrobial consumption"

AMS in Internal Medicine Department

Progetto PASCIA'

(Programma Antimicrobial Stewardship Controllo Infezioni Antibioticoresistenti)

Study design:

prospective-audit-and-feedback AMS program implemented in two **Internal Medicine wards** in two hospitals in Milan

Setting:

- San Paolo Hospital
- San Carlo Borromeo Hospital

Study period:

Five months (Feb-Jun 2017)

AMS team:

- **Infectious Diseases Unit**
- **Clinical Pharmacy Unit**
- **Microbiology Unit**

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- ***Prospective audit and feedback (PAF):***

  - AMS evaluations were performed **twice a week**: all the patients with an antimicrobial therapy at the time of the evaluation were reviewed and discussed with the bed-side physician

  - Re-evaluation of the patients based on the clinical course and on the results of the cultures

- ***Primary outcomes:***

  - **reduction of ABT consumption** expressed in defined-daily-dose/100patient-days (DDD/100pd) compared with the same period of the previous year

  - **increase of ABT prescription appropriateness** from the first to the last month of the project

- ***Secondary outcomes:***
  - no change in **in-hospital mortality and length of hospital stay**

Study design

AMS evaluations resulted in:

- confirmation of ABT
- modification of ABT → including dosage optimization, change of ABT, de-escalation, intensification and discontinuation of ABT

A therapy was considered APPROPRIATE in case of "confirmation of ABT"

"modification of ABT" was considered marker of INAPPROPRIATE therapy

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Results:

During the study period a total of 320 patients with an ongoing ABT were evaluated

Patients' characteristic	(Tot 320)
Mean Age	78 ± 10
Sex, F	41%
Chalson Index - age adj, mean	7 ± 2
Comorbidities:	
• Cardiovascular diseases	60.8%
• Ischemic Cardiomyopathy	41%
• COPD	30.4%
• Diabetes with or without organ damage	30%
• Dementia	19.2%
• Severe kidney disease	15.6%

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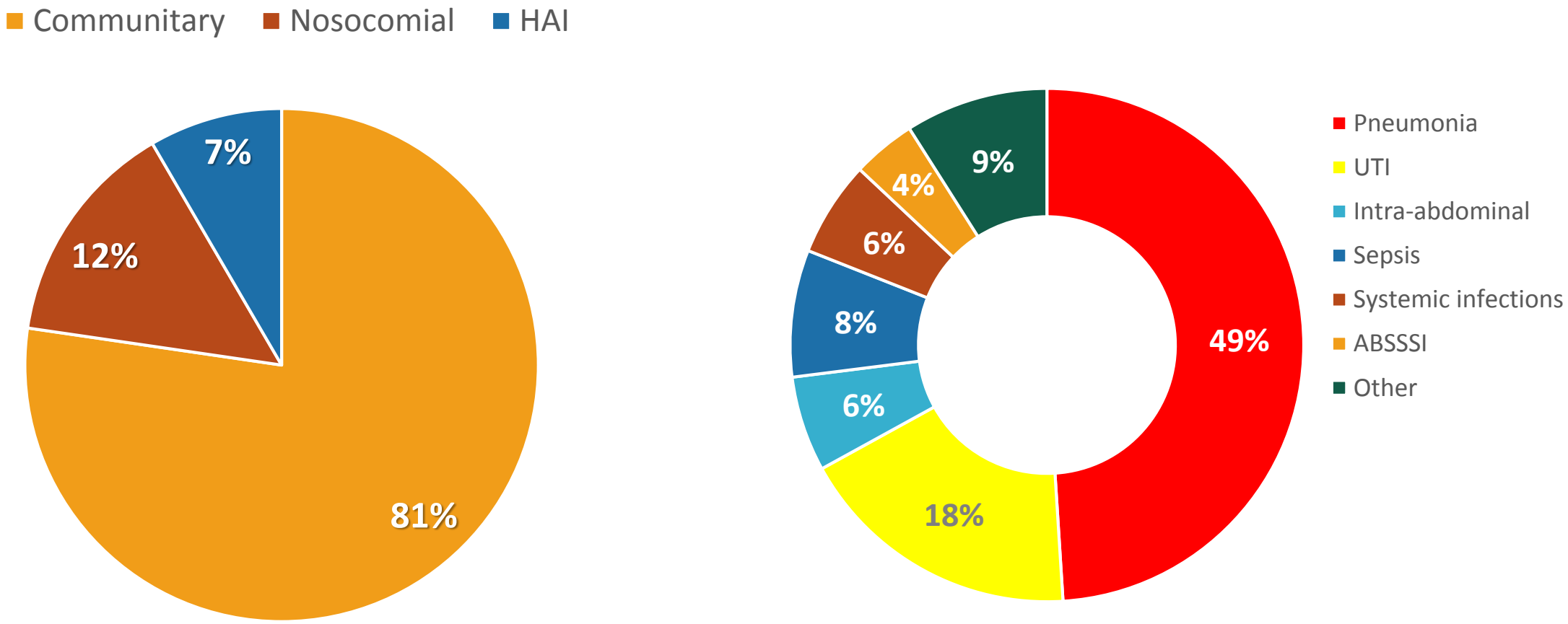
Epidemiology and type of Infections



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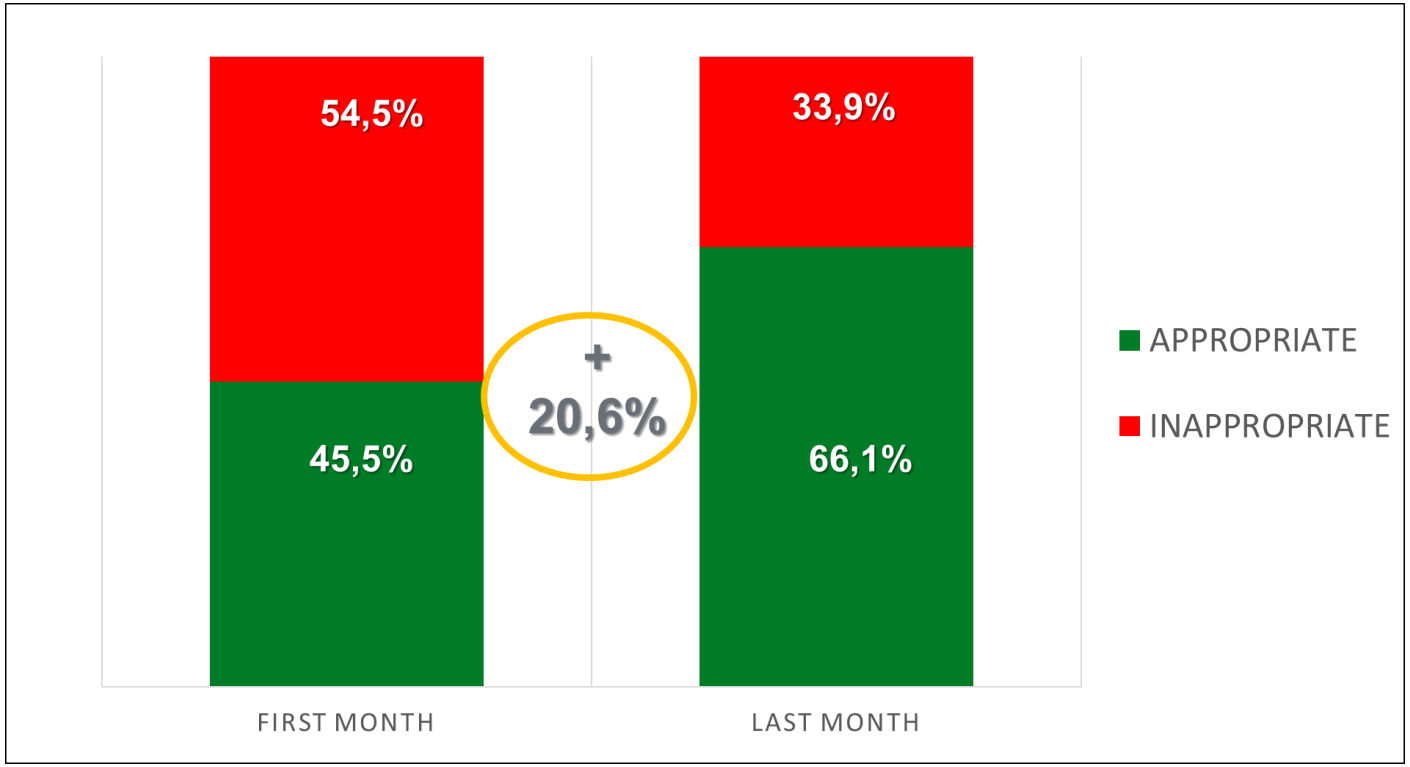
Appropriateness of ABT:

Out of 320 ABT therapies,
158 (49.4%) were considered appropriate and
162 (50.6%) inappropriate

Reasons for inappropriateness were:
- excessive duration of therapy (59%)
- lack of "de-escalation" (16%)
- incorrect dosage (11%)
- wrong choice of ABT" (10%)
- lack of "intensification" (4%)

Appropriateness of ABT rose from 45.5% to 66.0% in Feb-Jun (p=0.01)



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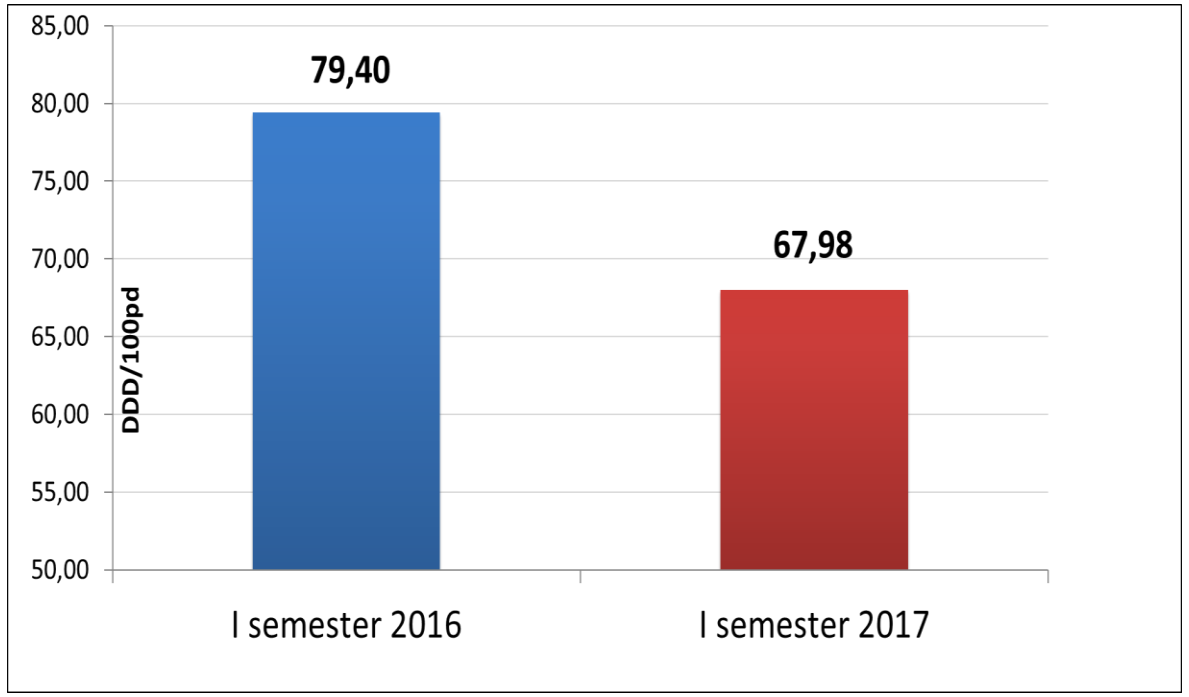
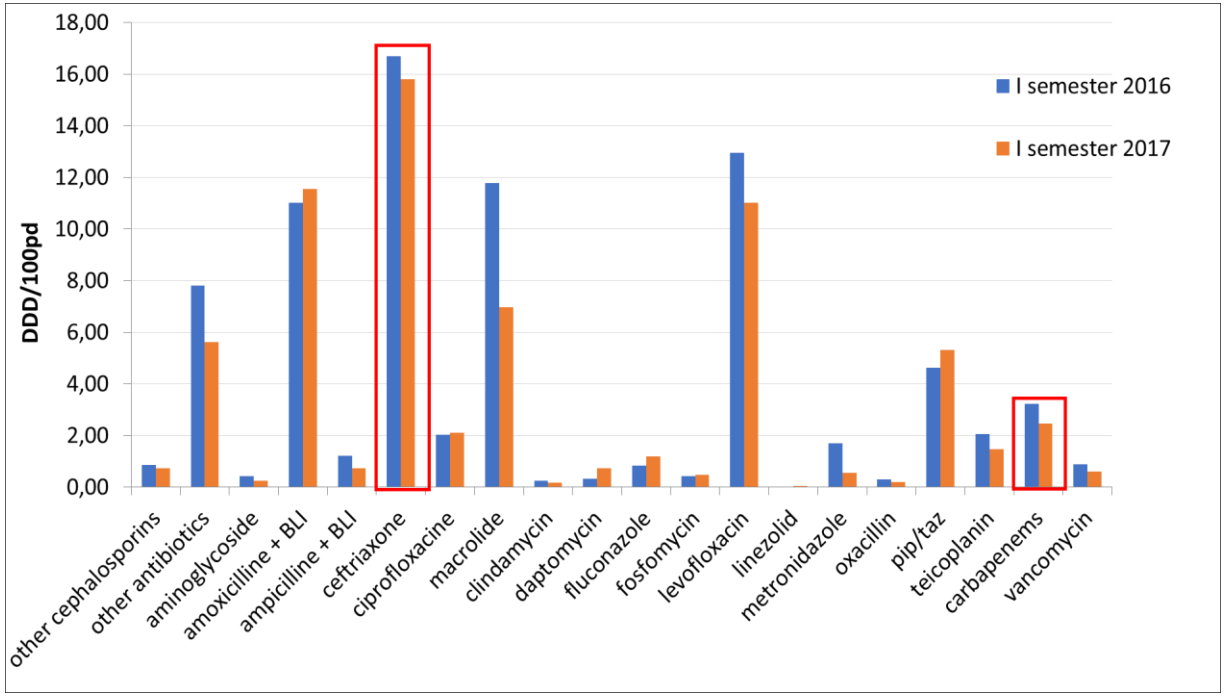
Antimicrobial Consumption:





ABT consumption decreased from 79.4 DDD/100pd to 67,9 DDD/100pd, with a reduction of 11.4%

Ceftriaxone usage decreased from 16.7 to 15.5 DDD/100pd (p=0.8) while carbapenems decreased from 3.23 to 2.45 DDD/100pd (p=0.2)

Progetto PASCIA'
(Programma Antimicrobial Stewardship Controllo Infezioni Antibioticoresistenti)

In-hospital mortality and Length of hospital stay:

No difference in in-hospital overall mortality rate and in the length of hospital stay (LOS) were observed during the AMS phase as compared to the previous year:

- **overall in-hospital mortality** → 113/785 (**14.4%**) vs 124/773 (**16%**) first semester 2016 vs first semester 2017, p=0.60

- **LOS** → **10.8** (CI95% 10-11.5) vs **11.2** (CI95% 10.5-11.6; p=0.40) first semester 2016 vs first semester 2017

Progetto PASCIA'
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Conclusions:

Our program led to:

I. an **increase of appropriateness of antimicrobial therapy of 20.5%**
II. a **reduction of 11% of global antimicrobial consumption**
III. a **reduction of 24% and 5% in carbapenems and ceftriaxone use**

- One of the main limitation to appropriateness of prescriptions was the lack of microbiological findings due to the small number of microbiological exams requested by the bed-side physicians

- Our intervention failed to increase significantly the number of blood cultures requested (10.7 BC/100pd in 2016 vs 11.2 BC/100pd in 2017)

AMS in Internal Medicine Unit – Follow up

Project title:

Long-term positive effect of an educational antimicrobial stewardship program implemented in an Internal Medicine Department: a prospective analysis and a point prevalence survey on long-term effect

Authors:

Andrea Cona, Nathalie Iannotti, Lidia Gazzola, Chiara Aldieri, Ottavia Viganò, Teresa Bini, Giulia Marchetti, Antonella d'Arminio Monforte

AMS in Internal Medicine Unit – Follow up

Aim of the study:

to evaluate **antimicrobial consumption and appropriateness** of antimicrobial prescriptions during and **one year after** the implementation of an Antimicrobial Stewardship (AMS) program in an **Internal Medicine Department**

Design:

2 years-prospective analysis of an AMS program, structured in two phases:

- the "**AMS phase**", five months (Feb-Jun 2017) AMS program based on an audit-and-feedback model
- **the "follow-up phase", 5 months point prevalence survey (one day per month) conducted one year later (Feb-Jun 2018)**

Main outcomes:

- antimicrobial consumption
- appropriateness of antimicrobial therapy

AMS in Internal Medicine Unit – Follow up

Results:

During the "follow-up pahse", a total of 83 patients on ongoing ABT therapy were evaluated

Patients' characteristic	AMS Phase (tot 320)	Follow-up Phase (tot 83)
Mean Age	78 ± 10	79 ± 10
Sex, F	41%	46.9%
Charlson Index - age adj, mean	7 ± 2	7 ± 2
Comorbidities:		
• Cardiovascular diseases	60.8%	66.2%
• Ischemic Cardiomyopathy	41%	14.5%
• COPD	30.4%	28.9%
• Diabetes with or without organ damage	30%	25.3%
• Dementia	19.2%	25.3%
• Severe kidney disease	15.6%	14.5%

71 (**82.5%**) of the infections were community-acquired

42 (**50.6%**) were pneumonias, 10 (**12%**) urinary tract infections and **12%** gastroenteritis/intrabdominal infections

Sepsis occurred in 4 cases (**4.8%**)

AMS in Internal Medicine Unit – Follow up

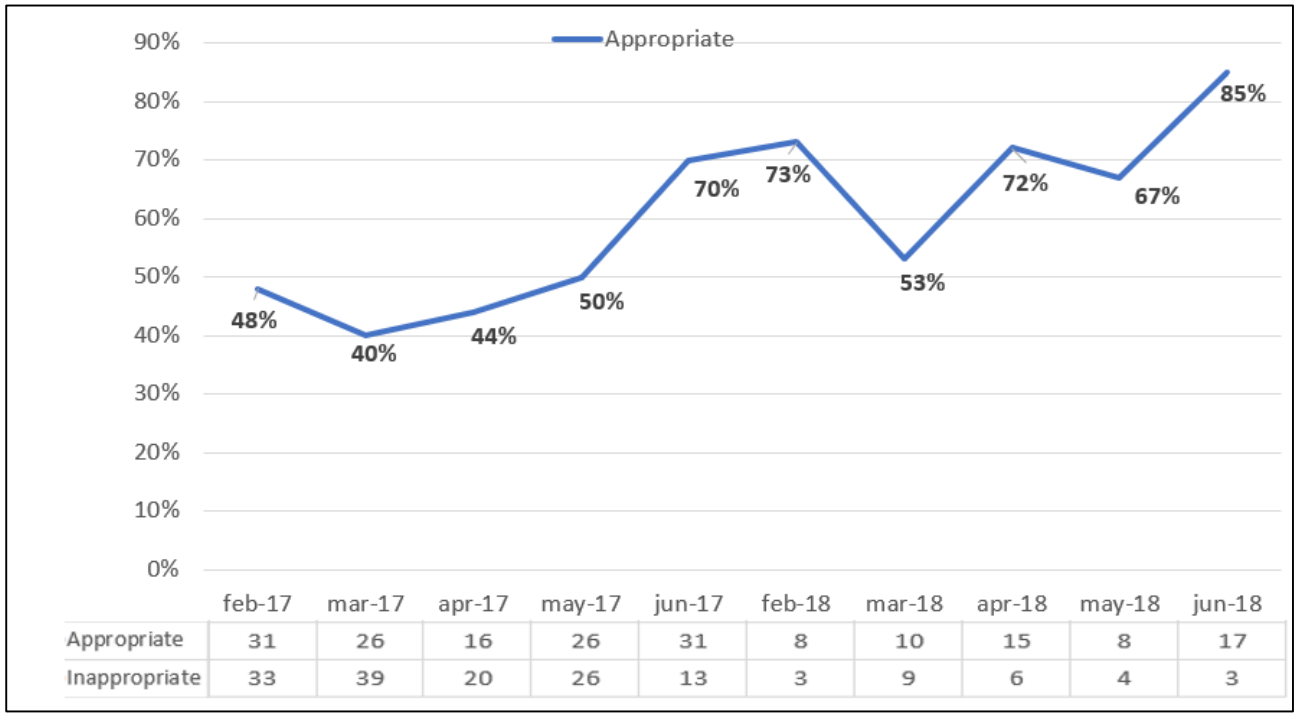
Appropriateness of ABT:

The increment of appropriateness observed during the AMS phase (from 48% to 70%) was confirmed at the point prevalence survey conducted during the "follow-up phase" (from 73% to 85%; p=0.14) resulting in a **significant increase of the appropriateness over the two years (from 48% to 85%, p<0.01)**

During the "follow-up phase", 58 (69.9%) of the therapies were considered appropriate

Reasons for inappropriateness were:

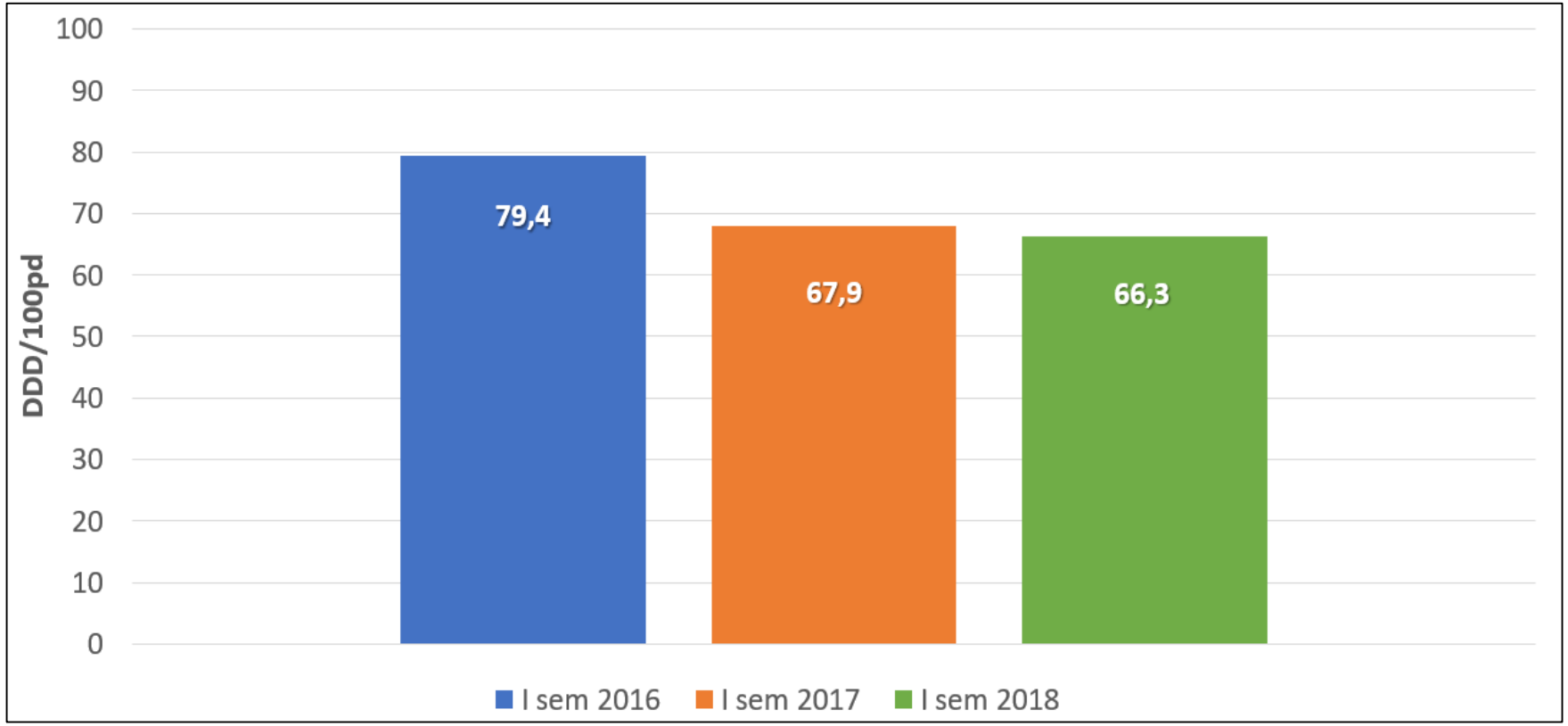
- excessive duration of therapy (52%)
- lack of "de-escalation" (28%)
- lack of "intensification" (8%)
- incorrect dosage (8%)
- wrong choice of ABT" (4%)



	feb-17	mar-17	apr-17	may-17	jun-17	feb-18	mar-18	apr-18	may-18	jun-18
Appropriate	31	26	16	26	31	8	10	15	8	17
Inappropriate	33	39	20	26	13	3	9	6	4	3

AMS in Internal Medicine Unit – Follow up

Antimicrobial Consumption:



ABT consumption one year later, during follow-up phase, remained stable

In fact, in the first semester of 2018 a total of 66.3 DDD/100bd were consumed (vs 67.9 DDD/100bd in 2017, p=0.9)

ID-consultant

Project title:

Impact of daily versus weekly service of Infectious Diseases consultations on antimicrobial consumption

Authors:

Andrea Cona, Lidia Gazzola, Ottavia Viganò, Salvatore Nurra, Domenica Di Benedetto, Chiara Aldieri, Teresa Bini, Giulia Marchetti, Antonella d'Arminio Monforte

Presented as oral presentation at the 29th European Conference of Clinical Microbiology and Infectious Diseases (ECCMID, Amsterdam 13-16 April 2019)

ID-consultant

Aim of the study:

To verify whether intensifying to **daily Infectious Diseases consultations**, as compared to weekly ID-cons, is effective in **reducing antimicrobial consumption** without affecting clinical outcome

Design:

Two-years observational analysis of the ID-cons provided at San Carlo Hospital in Milan

Study period:

2017 (weekly ID-cons) vs 2018 (daily ID-cons)

Main outcomes:

- ATB consumption in the whole hospital
- Overall and sepsis-related in-hospital mortality

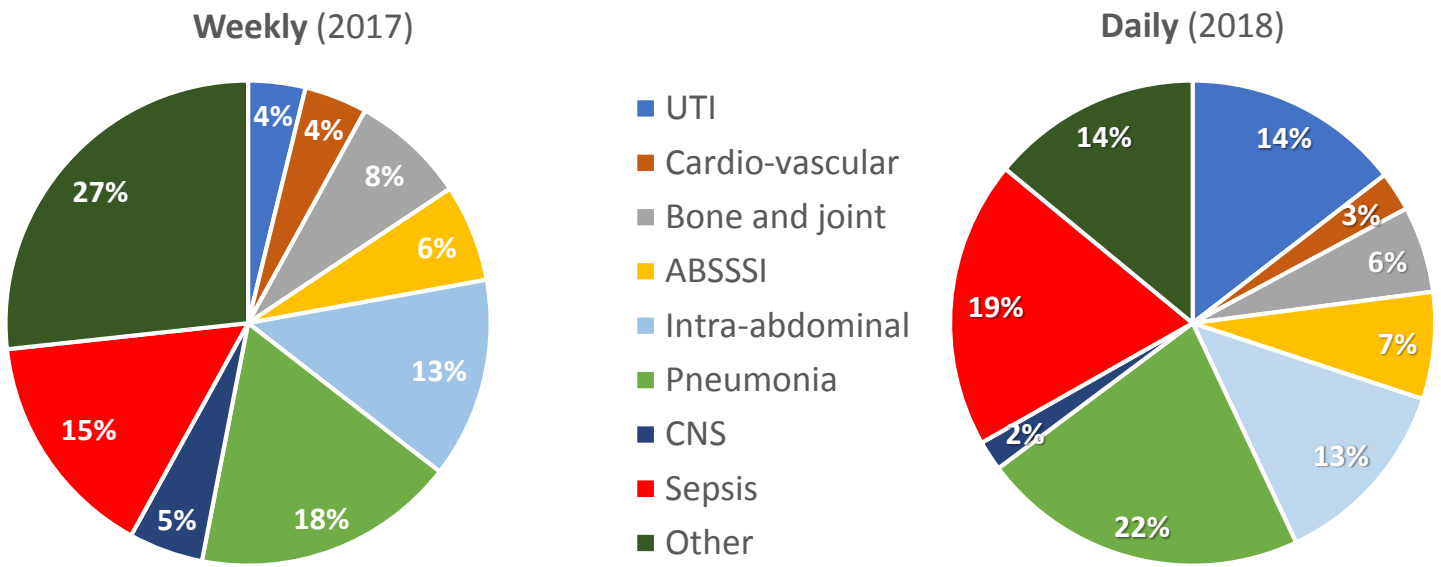
Statistical analysis:

- ATB consumption was expressed as DDD/100bd
- Chi-square and Wilcoxon test as appropriate
- Sensitivity analysis including units with high number of ID-cons/100bd (≥ 25th percentile of the ID-cons distribution)

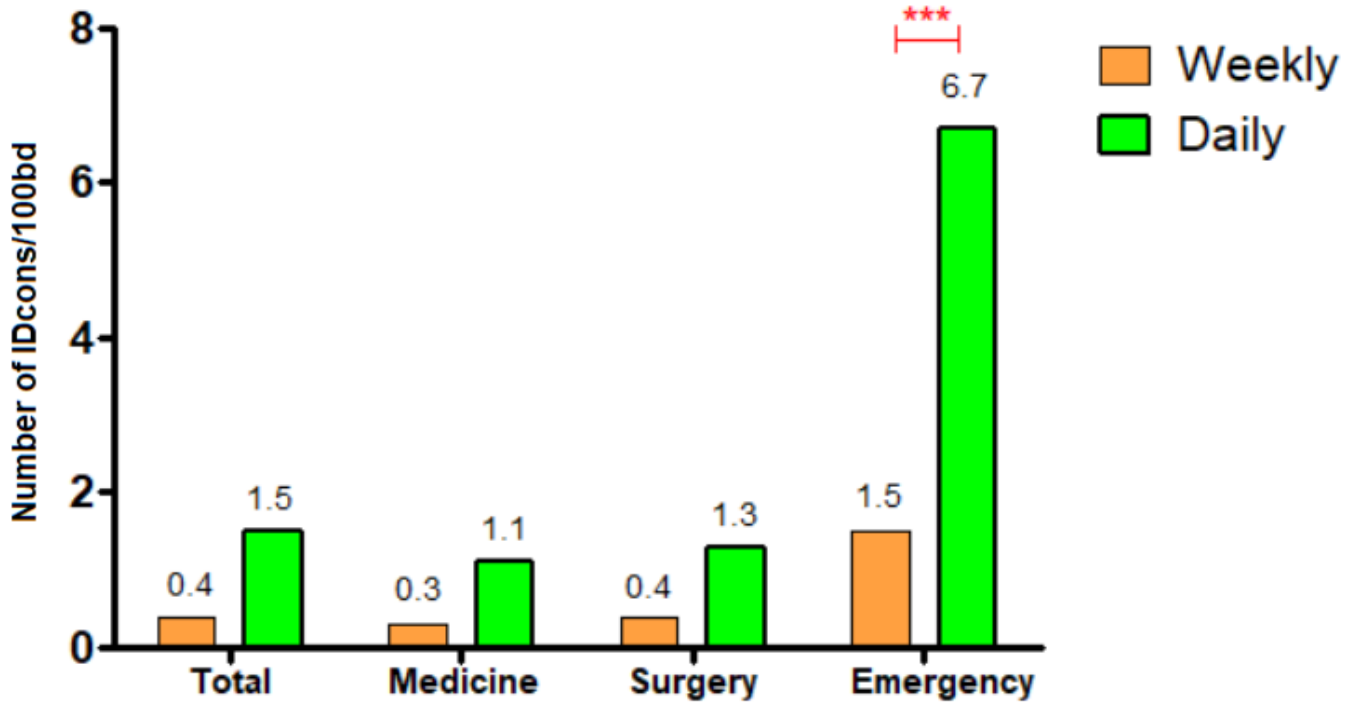
ID-consultant

2552 ID-cons
in 1111 pts

Pts. 1111	Weekly (pts. 273)	Daily (pts. 838)	P value
Female	115 (42%)	345 (41%)	0.7
Age	72 (61-81)	75 (61-82)	0.1
Charlson Index Age ad.	6 (4-8)	6 (4-8)	0.2
Cons per patient	1.74	2.47	<0.0001
HAI	118 (43.2%)	457 (54.5%)	0.0012



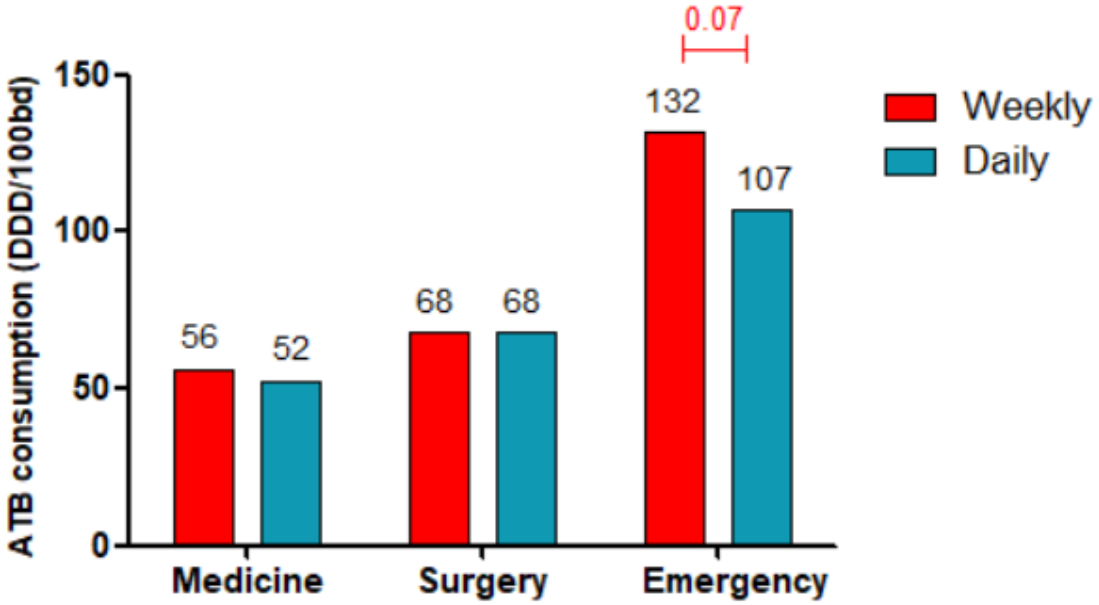
ID-consultant



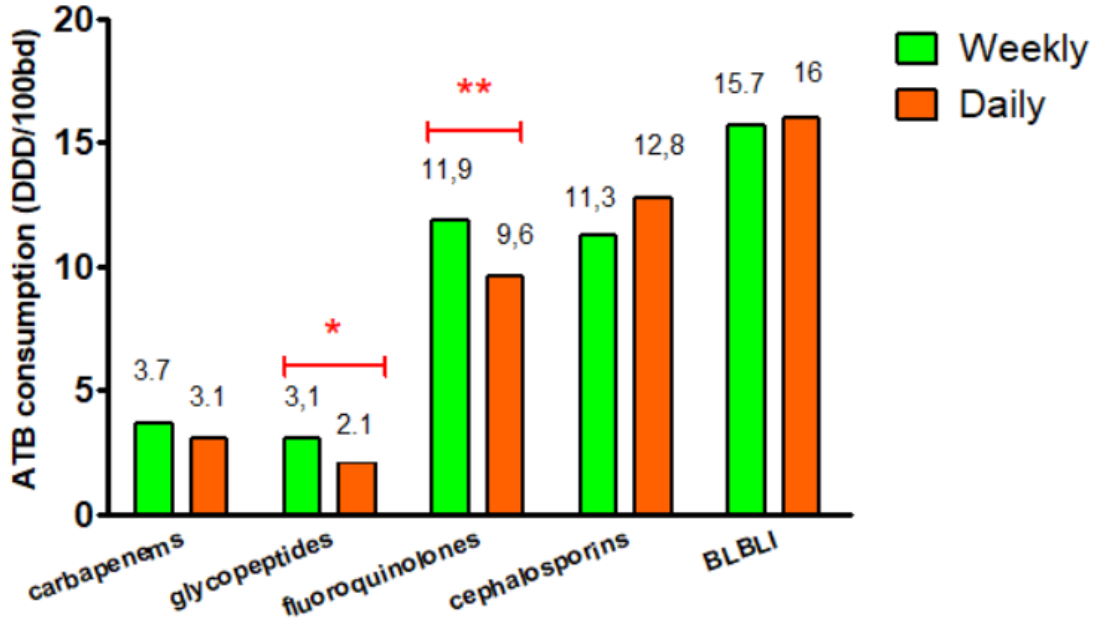
	Weekly	Daily	P value
days-from-admission-to-first-ID-cons	10 (6-19)	6 (2-13)	**<0.0001**
Start-of-ATB by ID-consultant	38/475 (8%)	242/2077 (11.6%)	**0.02**

ID-consultant

	Weekly	Daily	P value (Wicoxon test for paired data)
Hospital ATB consumption	64 DDD/100bd	60 DDD/100bd	0.07
Sensitivity analysis on selected units	67 DDD/100bd	64 DDD/100bd	**0.01**

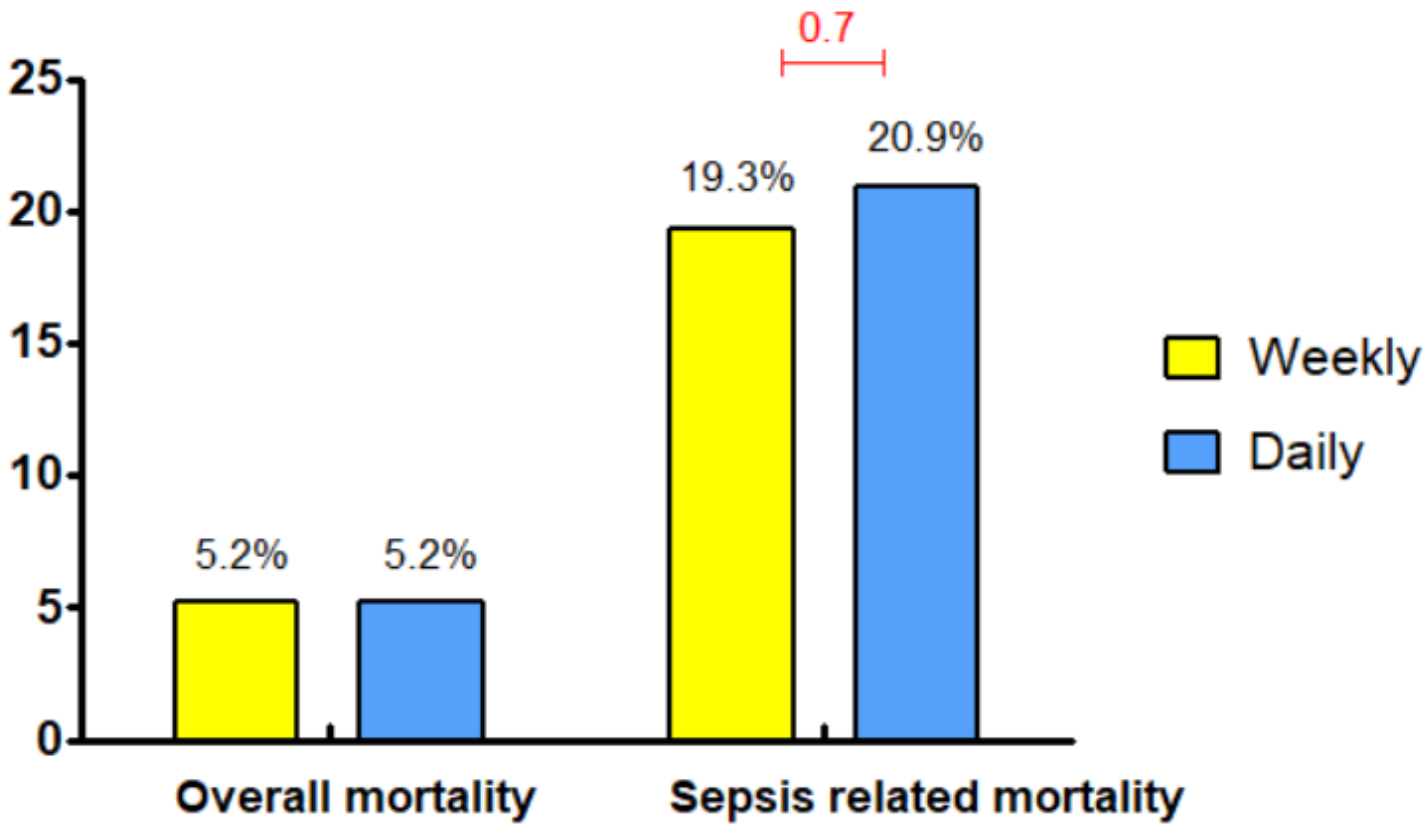


The greatest reduction in the emergency department



Glycopeptides and fluoroquinolones' use significantly decreased

ID-consultant



ID-consultant

- In spite of a similar burden of infections, daily ID-cons was associated with a lower ATB consumption in the whole hospital
- Glycopeptides and quinolones were reduced without a significant increase of other ATB classes

Our findings confirm the importance of the ID-consultant as component of a successful large scale stewardship program


Thanks for your
attention !