Antimicrobial stewardship: istruzioni per l'uso

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Considerazioni preliminari

- **L'antibioticoterapia è diffusa e trasversale in ospedale per l'elevato indice terapeutico dei farmaci**
- **L'uso degli antibiotici ha spesso come finalità la cd "copertura": qualcosa di non ben definito tra profilassi e terapia empirica**
- **<u>Ampio margine di non appropriatezza ed impatto negativo sull'ecosistema: spreco di risorse ed incremento delle resistenze</u>**
- **Contributo diagnostico dei laboratori molto variabile: scarso ricorso alla documentazione microbiologica**
- **Quadro epidemiologico attuale preoccupante: rischio del ritorno all'era pre-antibiotica**

Antimicrobial Use Stewardship

“Programma o serie di interventi diretti al monitoraggio ed all’orientamento dell’utilizzo degli antimicrobici in ospedale, attraverso un approccio standardizzato che sia supportato dall’evidenza al fine di ottenere un uso giudizioso dei farmaci”

Tamma PD, Cosgrove SE. Infect Dis Clin N Amer 2011; 25: 245-60

Antifungal Stewardship Program

Antimicrobial stewardship programs focus on ensuring the proper use of antimicrobials to:

- **provide the best patient outcomes,**
- **lessen the risk of adverse effects,**
- **promote cost-effectiveness,**
- **reduce or stabilize levels of resistance.**

MacDougall C. and Polk RE Clinical Microbiology Rev., Oct. 2005, P. 638–656

List of interventions considered as part of antimicrobial stewardship

Table 1. List of interventions considered as part of antimicrobial stewardship[9,11,12]

Intervention*	Description/comment	Healthcare setting
Formulary restriction	Antibiotics may be prescribed only: • For certain approved clinical indications • By certain physicians (i.e., infectious diseases specialists)	Inpatient/outpatient
Drug preauthorization	Permission (from ASP team member or infectious diseases specialist) required for release of certain antibiotics. Often implemented together with formulary restriction.	Inpatient/outpatient
Prospective audit and feedback	Case review by trained ASP team member and feedback of recommendations if reviewed antibiotics are deemed to be inappropriately prescribed. Labor-intensive.	Inpatient
Prescriber education	More effective as a supplementary strategy to other interventions.	Inpatient/outpatient
Patient education	Usually focus groups or mass media campaigns.	Outpatient
Clinical guidelines	Treatment protocols for various infections – may be institution-specific	Inpatient/outpatient
Clinical decision support systems	Information technology systems for improving antibiotic prescription. Requires existing electronic records and electronic prescribing system to be effective.	Inpatient/outpatient
Point of care diagnostic tests	Mostly undergoing research evaluation. Diagnosis of non-bacterial etiologies may help reduce antibiotic prescription.	Inpatient/outpatient
Microbiology laboratory susceptibility reporting	Selective reporting of susceptibility profiles for positive cultures may dramatically alter prescribing patterns of physicians.	Inpatient/outpatient
Antimicrobial cycling	Substitution of selected antibiotics over pre-defined periods. Little clear evidence for efficacy.[12]	Inpatient

Clinical Appropriateness

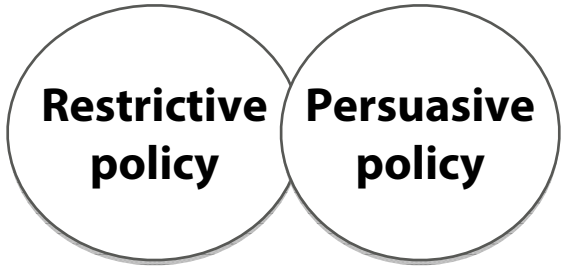
- **Focus on patient management**
- ***Capability to choose and realize the best diagnostic and therapeutic strategy in the single patient, translating knowledge driven from evidence based medicine***
- **Clinical appropriateness require a virtuous balance between clinical experience and evidence**

Assessing Appropriateness of Antimicrobial Therapy: In the Eye of the Interpreter

Daryl D. DePestel,[1] Edward H. Eiland III,[2,a] Katherine Lusardi,[3] Christopher J. Destache,[4] Renée-Claude Mercier,[5] Patrick M. McDaneld,[1,6,b] Kenneth C. Lamp,[1] Thomas J. Chung,[1] and Elizabeth D. Hermsen[1,7]

1. study site-specific definition
2. in vitro susceptibility data
3. national/local guidelines
4. physician opinion

Clinical Infectious Diseases 2014;59(S3):S154–61



Antimicrobial stewardship programs (ASPs)

The devil is in the details

"Antimicrobial stewardship is a developing field and every ASP must be tailored to its respective institution"

Spesa Farmaci AOUP 2009

Spesa complessiva: 55,848 milioni di euro

Spesa antinfettivi: 14,206 milioni (25,4%)

Antivirali: 7,304 milioni

Antibiotici: 4, 542 milioni

Antifungini: 2,360 milioni

Pisa University Hospital, Antibiotic Stewardship Program
ID approval required

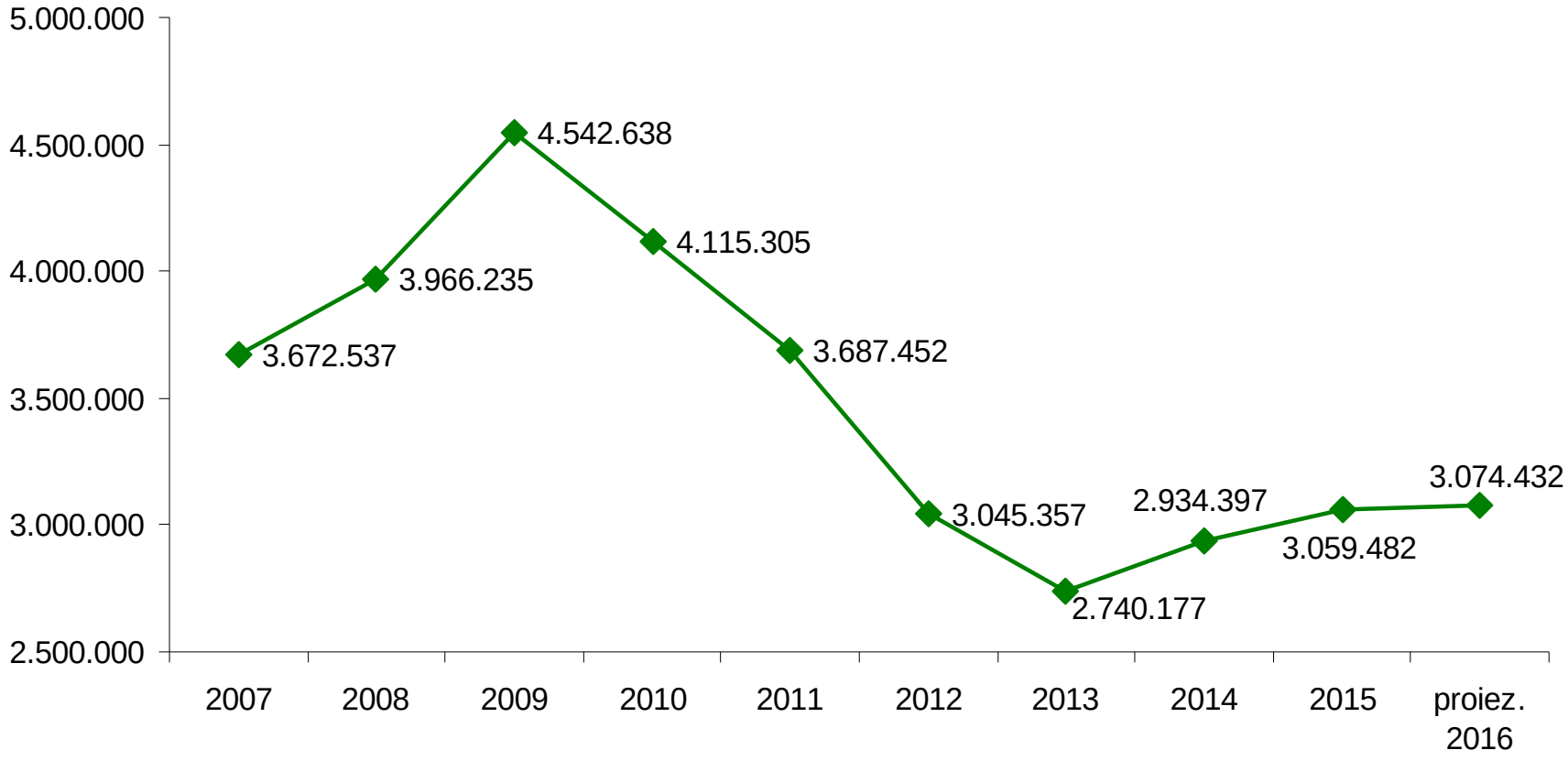
Antibacterials (14)

Free use only for ICU & hematologist.

- Levofloxacina ev
- Colistina
- Linezolid
- Teicoplanina
- Daptomicina
- Meropenem
- Imipenem
- Ertapenem
- Tigeciclina
- Ceftarolina
- Ceftobiprolo
- Dalbavancina *
- Ceftolozane/tazobactam *
- Fidaxomicina *

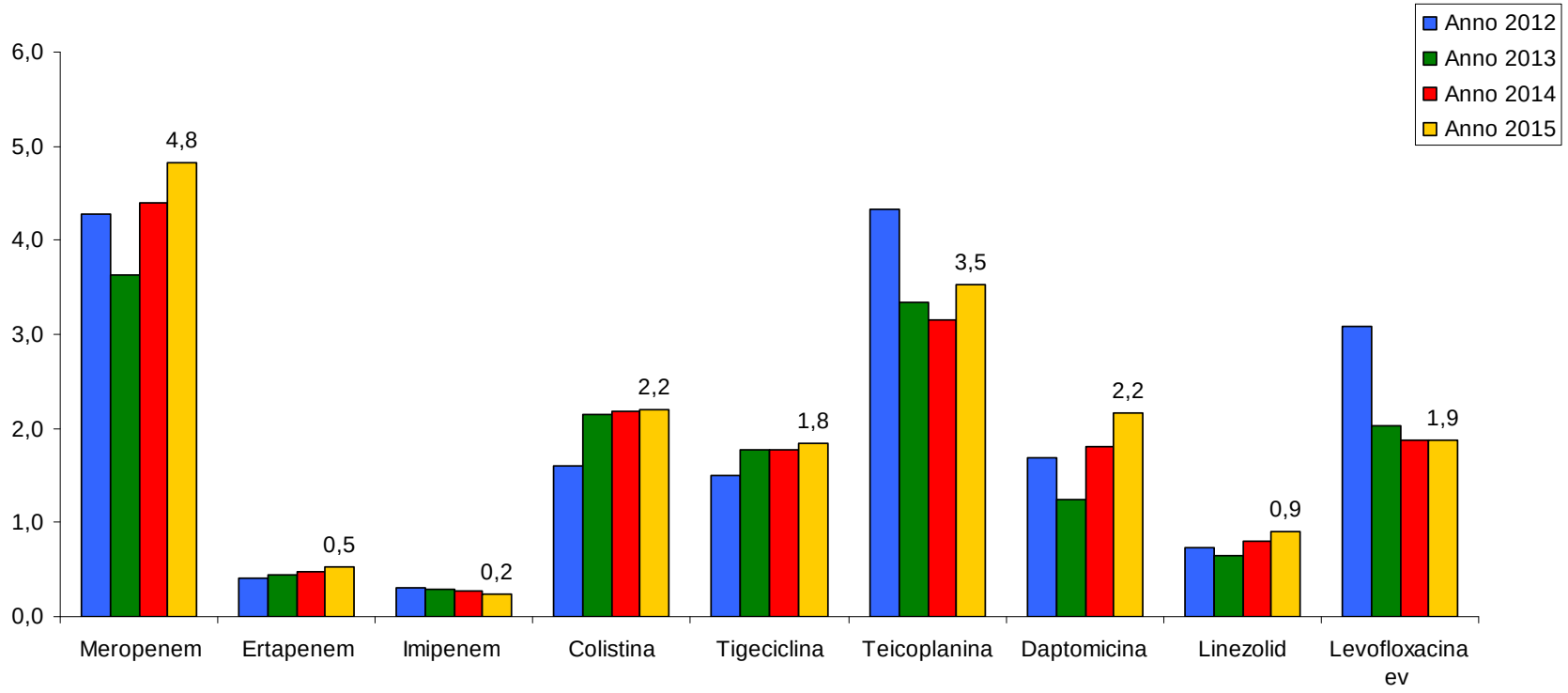
* SCHEDA AIFA

SPESA ANTIBATTERICI AOUP

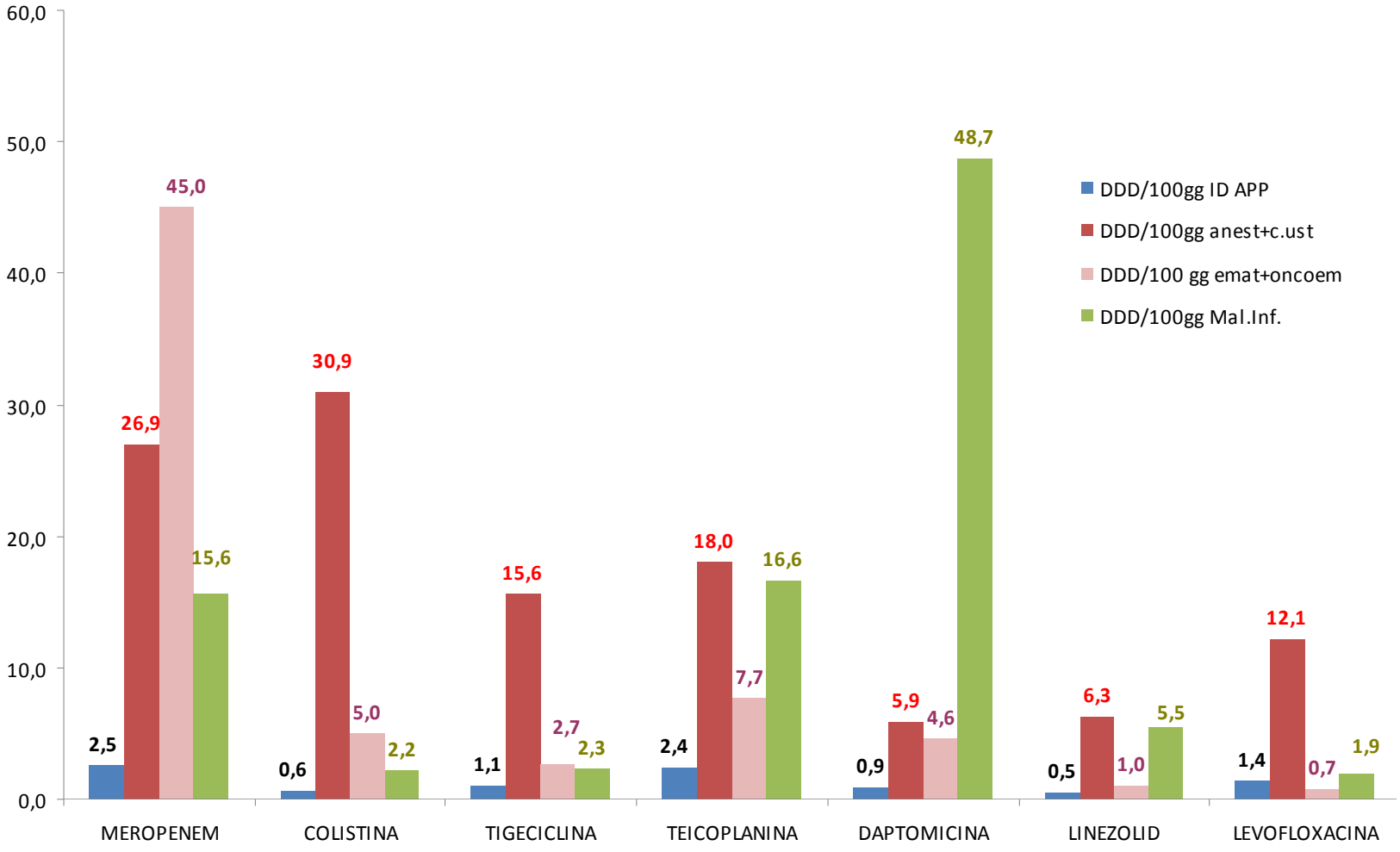


ANTIBATTERICI	Gen-Ago 2016 Quantita	Gen-Ago 2015 Quantita	Gen-Ago 2016 Valore	Gen-Ago 2015 Valore	Diff. QTA	Diff. Valore	Perc
FIDAXOMICINA CPR RIV 200MG	720	780	€ 44.284	€ 48.974	-60	-€ 4.690	-10%
TEICOPLANINA*IM IV 1F 200MG+F 3ML	3.554	5.494	€ 73.924	€ 113.743	-1.940	-€ 39.820	-35%
TEICOPLANINA*IV 1F 400MG/3ML+F 3ML	5.341	5.520	€ 222.176	€ 227.641	-179	-€ 5.465	-2%
DALBAVANCINA*EV 1FL 500MG	69		€ 29.354		69	€ 29.354	100%
DAPTOMICINA*EV 1FL 10ML POLV 350MG	1.422	1.499	€ 117.821	€ 124.624	-77	-€ 6.803	-5%
DAPTOMICINA*EV 1FL 10ML POLV 500MG	1.558	1.381	€ 175.738	€ 155.831	177	€ 19.908	13%
LINEZOLID*10CPR RIV 600MG BLIST	1.200	1.540	€ 73.121	€ 93.837	-340	-€ 20.716	-22%
LINEZOLID*10SAC INF 2MG/ML 300ML	2.990	2.805	€ 182.194	€ 170.886	185	€ 11.307	7%
COLISTINA*IM FL 1000000U 4ML+F	13.406	15.192	€ 46.921	€ 53.172	-1.786	-€ 6.251	-12%
TIGECICLINA*INFUS 10FL 5ML 50MG	9.288	8.943	€ 510.129	€ 483.374	495	€ 26.755	6%
FOSFOMICINA 1 G EV FL	700	1.911	€ 6.695	€ 16.773	-1.211	-€ 10.078	-60%
FOSFOMICINA 2 G EV FL	500		€ 9.532		500	€ 9.532	
FOSFOMICINA 4 G EV FL	180		€ 5.487		180	€ 5.487	100%
IMIPENEM CILAST 500+500MG FL EV	7.264	1.615	€ 22.516	€ 5.226	5.649	€ 17.290	331%
ERTAPENEM 1 G EV FL	1.067	1.134	€ 42.371	€ 45.031	-67	-€ 2.661	-6%
MEROPENEM 1 G EV FL	12.031	21.496	€ 43.499	€ 77.721	-9.465	-€ 34.222	-44%
MEROPENEM 500 MG EV FL	326	2.359	€ 735	€ 9.149	-2.033	-€ 8.415	-92%
LEVOFLOXACINA 500 MG EV FL	3.355	4.876	€ 2.400	€ 3.523	-1.521	-€ 1.123	-32%
CEFTAROLINA 600 MG EV FL	100	150	€ 5.152	€ 7.728	-50	-€ 2.576	-33%
CEFTOBIPROLO 500 MG EV FL	621	50	€ 68.104	€ 26.606	571	€ 41.498	156%
CEFTOLOZANO/TAZOBACTAM 1 G + 0,5 G FL EV	140		€ 14.586		140	€ 14.586	
ANTIBATTERICI ID APPROVAL			**€ 1.696.738**	**€ 1.663.840**		**€ 32.898**	**2%**
ANTIBATTERICI LIBERA PRESCRIZIONE			**€ 352.884**	**€ 369.342**		**-€ 16.458**	**-4%**
TOTALE ANTIBATTERICI			**€ 2.049.621**	**€ 2.033.181**		**€ 16.440**	**1%**

Antibatterici ID approval
AOUP
n.DDD/100 giornate di degenza



Antibatterici ID approval
AOUP
Dettaglio Reparti Anno 2015



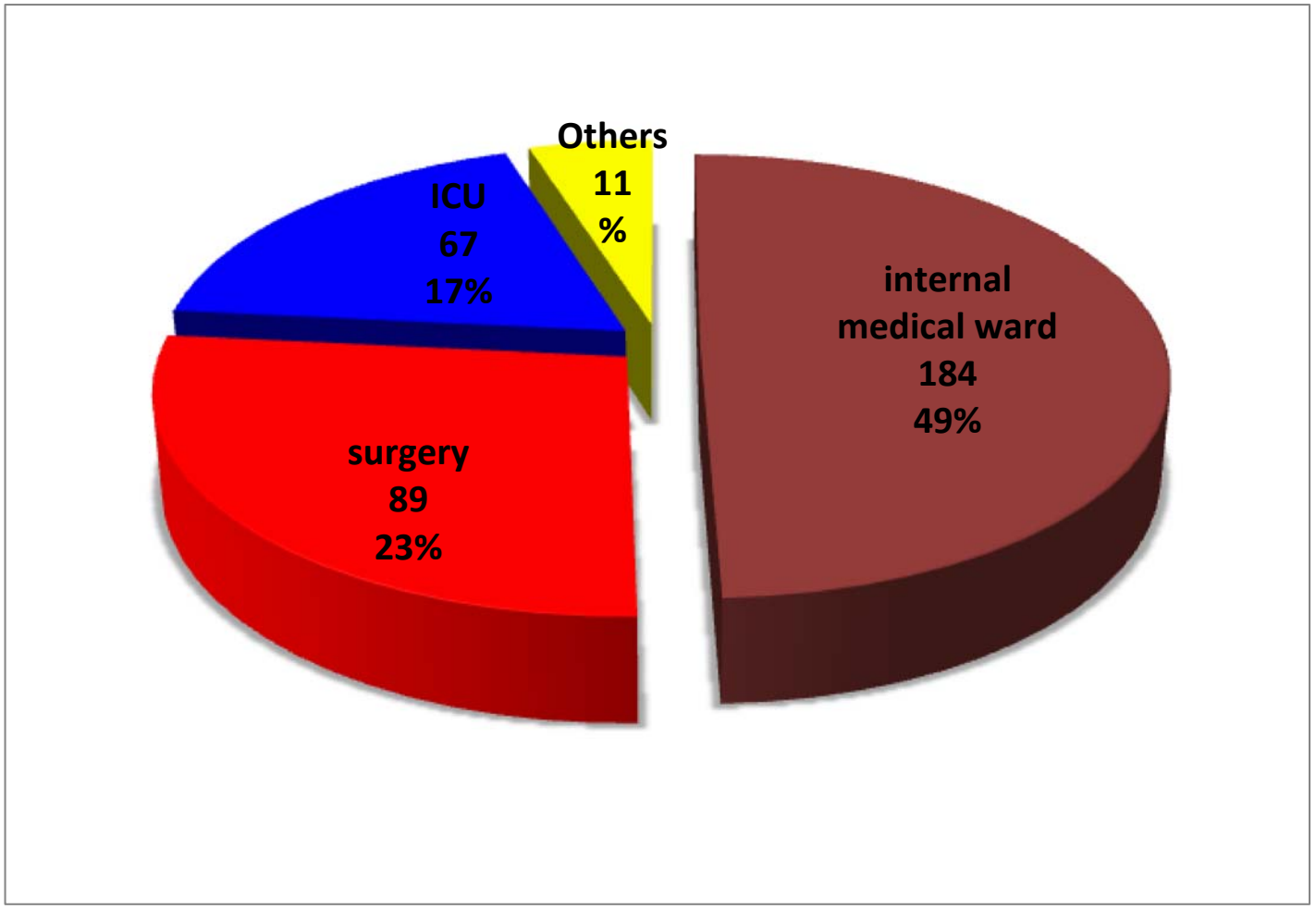
ID consultation ?

Infectious Diseases Specialty Intervention Is Associated With Decreased Mortality and Lower Healthcare Costs

Steven Schmitt,[1] Daniel P. McQuillen,[2] Ronald Nahass,[3] Lawrence Martinelli,[4] Michael Rubin,[5] Kay Schwebke,[6] Russell Petrak,[7] J. Trees Ritter,[8] David Chansolme,[9] Thomas Slama,[10] Edward M. Drozd,[11] Shamonda F. Braithwaite,[11] Michael Johnsrud,[12] and Eric Hammelman[11]

[1]Department of Infectious Diseases, Medicine Institute, Cleveland Clinic, Ohio; [2]Center for Infectious Diseases and Prevention, Lahey Hospital & Medical Center, Tufts University School of Medicine, Burlington, Massachusetts; [3]ID Care, Hillsborough, New Jersey; [4]Covenant Health, Lubbock, Texas; [5]Divisions of Clinical Epidemiology and Infectious Diseases, University of Utah School of Medicine, Salt Lake City; [6]OptumInsight, Eden Prairie, Minnesota; [7]Metro ID Consultants, LLC, Burr Ridge, Illinois; [8]French Hospital Medical Center, San Luis Obispo, California; [9]Infectious Disease Consultants of Oklahoma City, Oklahoma; [10]Indiana University School of Medicine, Indianapolis, Indiana; [11]Data Analytics, and [12]Health Economics and Outcomes Research, Avalere Health, Washington, D.C.

Candidemie 2012-2014
Pisa Hospital: 373 episodes



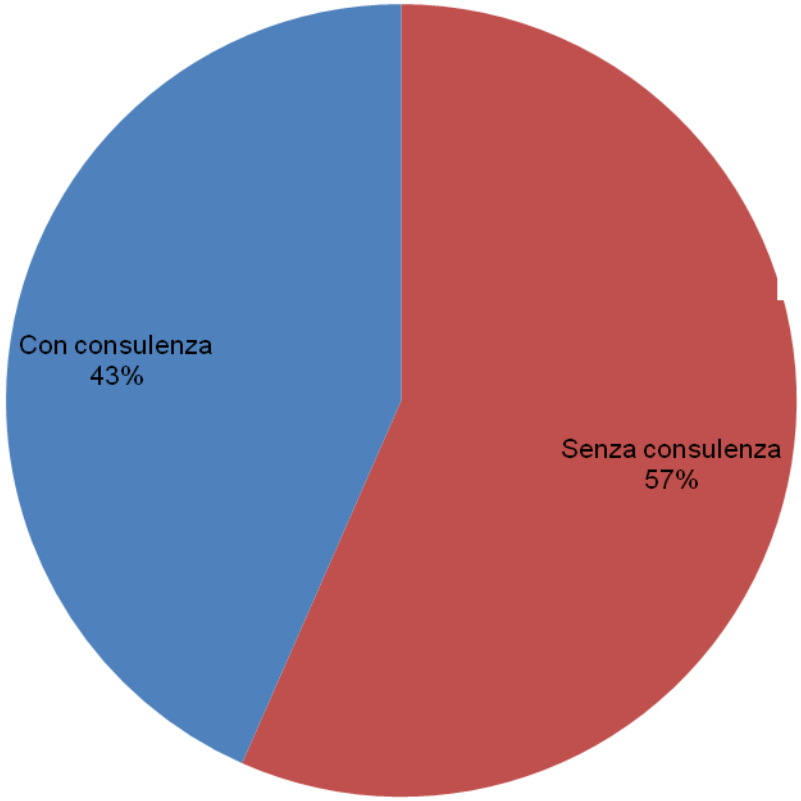
Candidemie 2012-2014
Pisa Hospital: 373 episodes

Isolates	**373**	
Patients	**351**	
C. albicans	**188**	**(50%)**
C. parapsilosis	**98**	**(26%)**
C. glabrata	**38**	**(10%)**
C. tropicalis	**23**	**(6%)**
C. krusei	**8**	
others	**22**	

REPORT ON ID CONSULTATIONS: CANDIDEMIA, PISA HOSPITAL, 2014

129 CANDIDEMIA

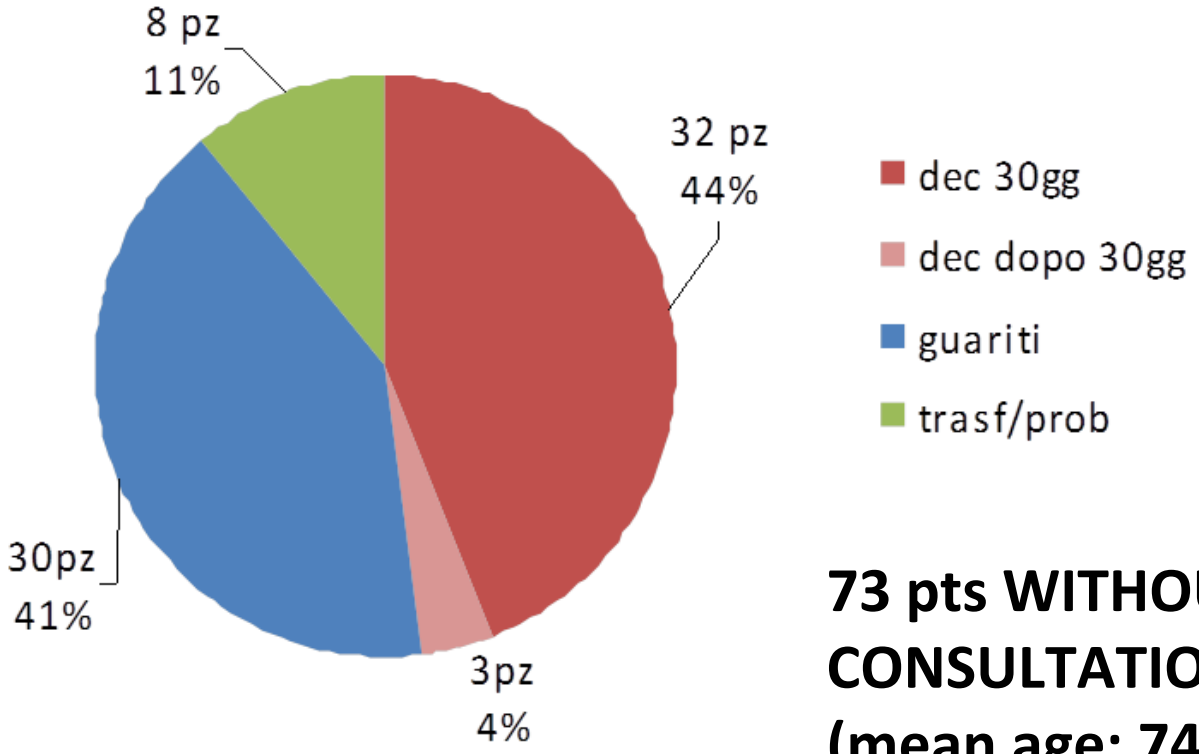
56 pts
WITH ID consultation
(mean age: 68 y)



73 pts
WITHOUT
ID consultation
(mean age: 74 y)

MORTALITY, 30 days

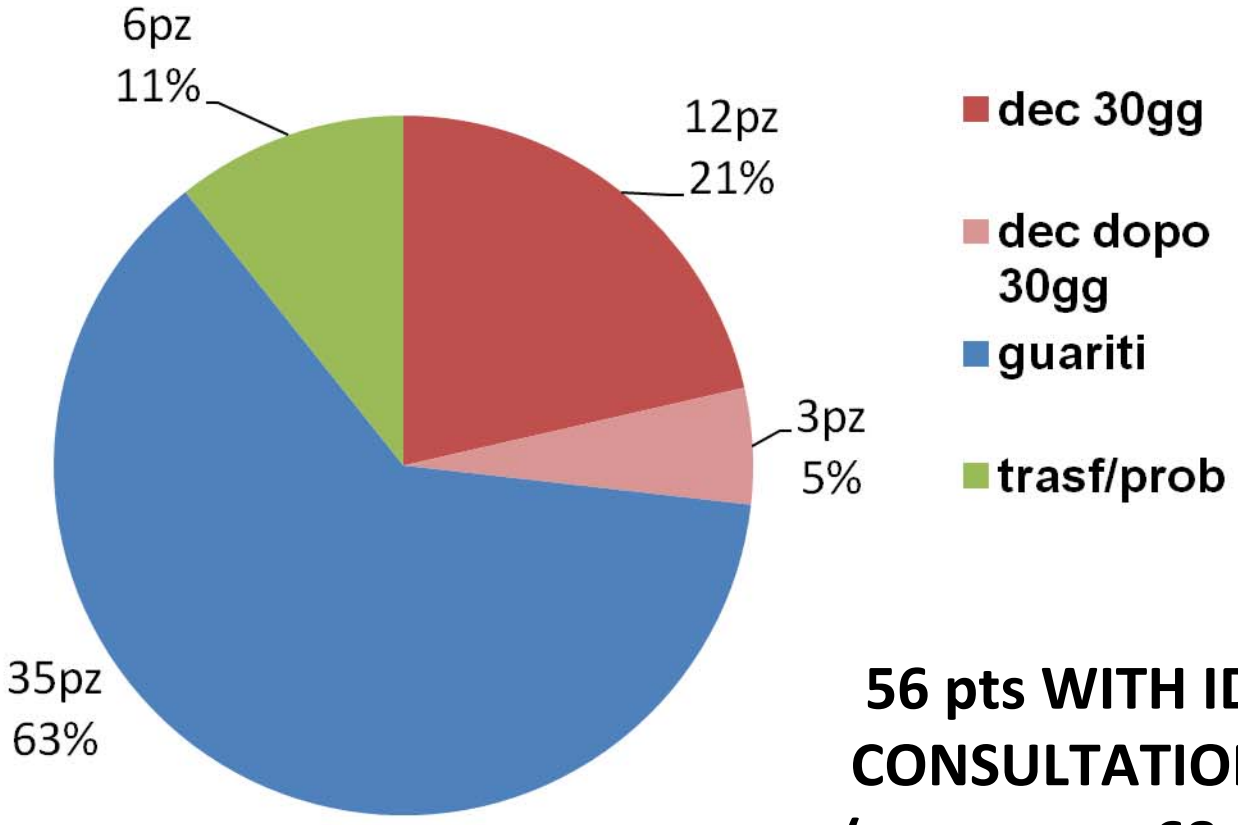
44 %



73 pts WITHOUT ID CONSULTATION (mean age: 74 y)

MORTALITY 30 days

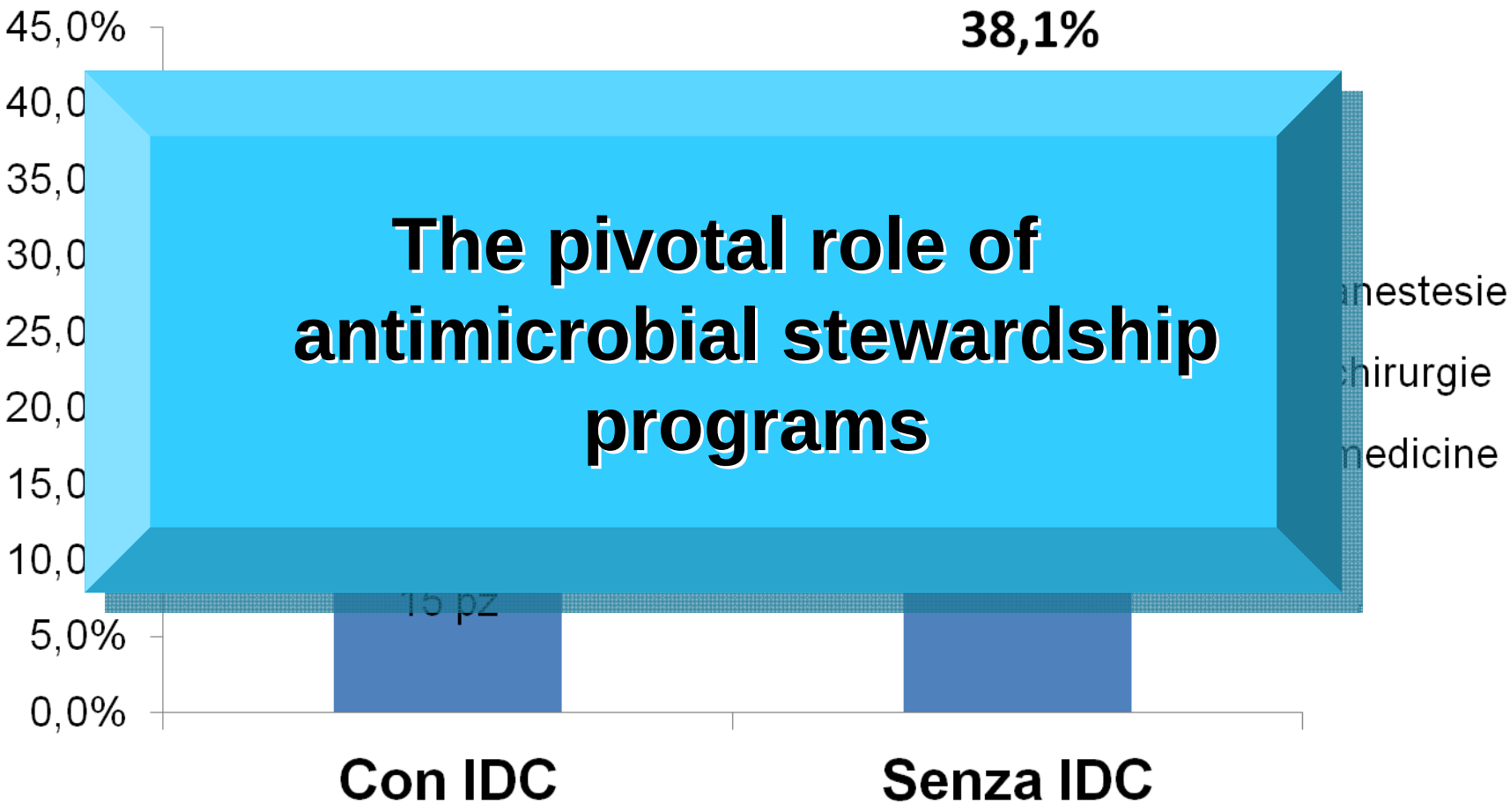
21 %



56 pts WITH ID CONSULTATION (mean age: 68 y)

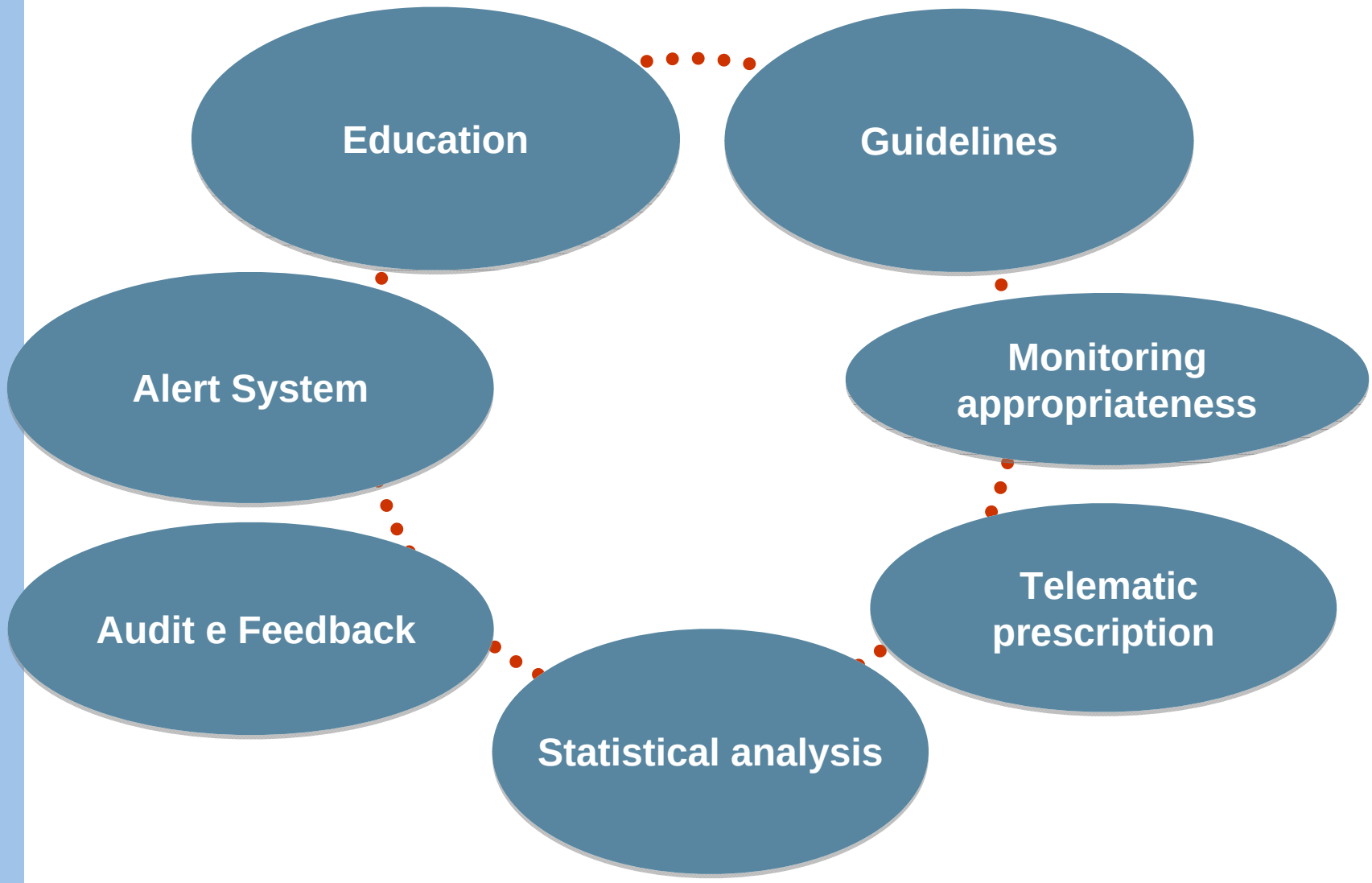
Pisa Hospital 2012-2014

341 CANDIDEMIA **MORTALITY 30 DAYS**

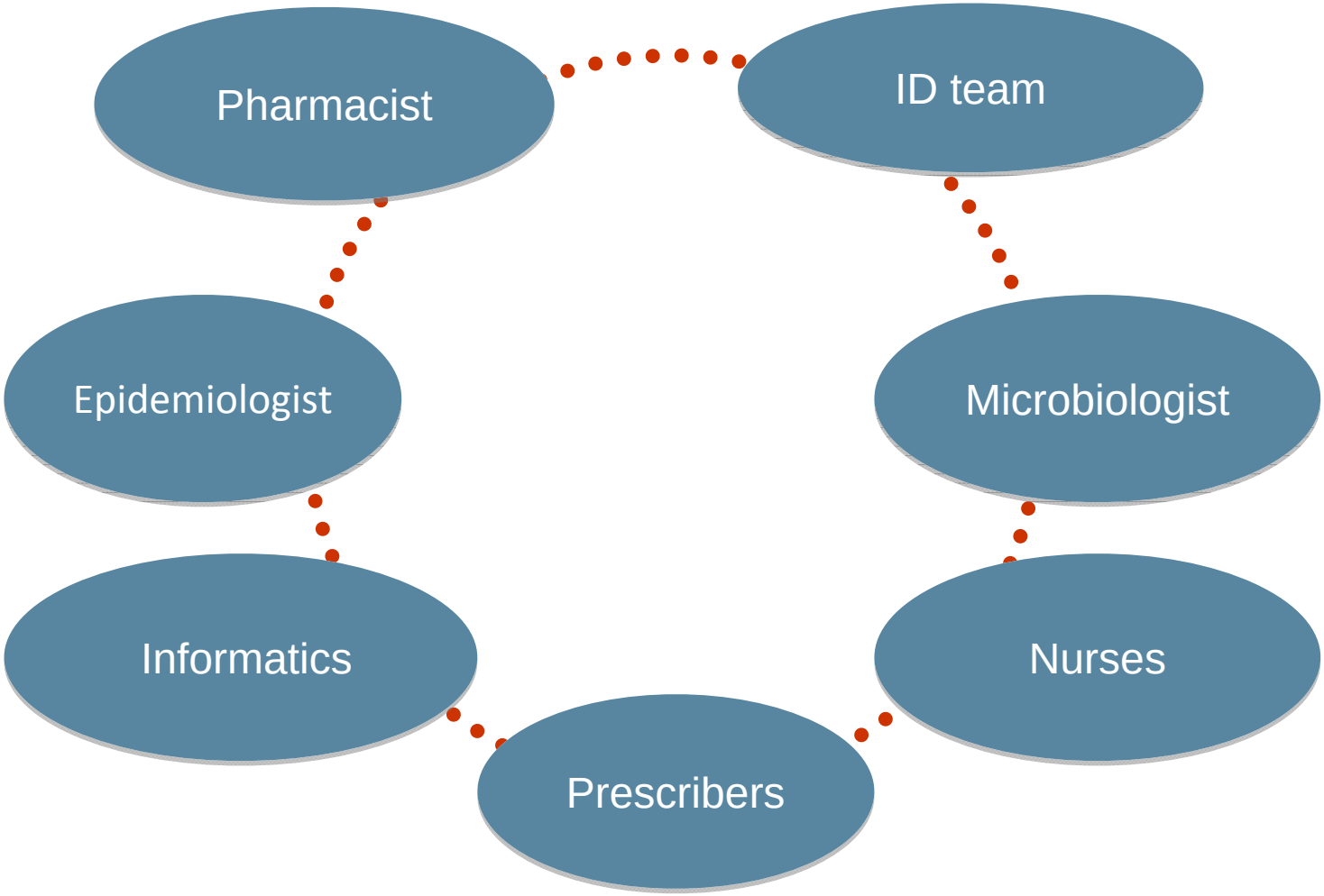


The pivotal role of antimicrobial stewardship programs

ASP: how to improve the program



ASP: how to increase the network



G.I.S.A.

GRUPPO ITALIANO PER LA STEWARDSHIP ANTIMICROBICA

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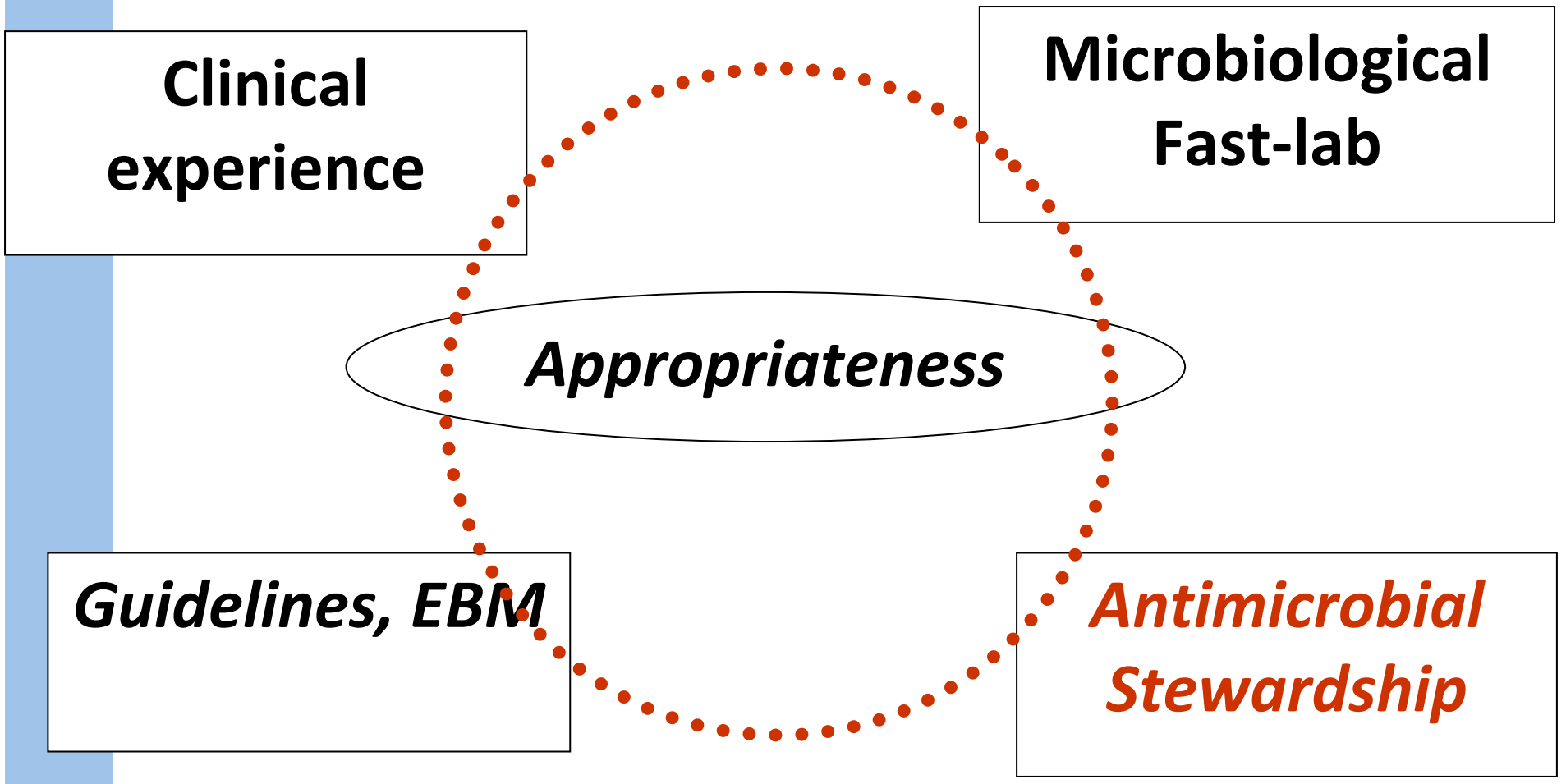
The virtuous circle of appropriateness



Le direttrici principali della resistenza antimicrobica (AMR)

Determinanti/criticità *	Obiettivo	Strumenti
Pressione selettiva antibiotici	Contenimento uso improprio	Antimicrobial Stewardship
Diffusione crociata microrganismi resistenti	Contenimento fenomeno	Infection Control
Carenza nuovi farmaci *	Rilancio ricerca IF	Nuove regole, fast-track, incentivi
Carenza strategie terapeutiche validate*	Acquisire evidenze scientifiche	Fondi per la ricerca indipendente

Conclusions

- **Well designed and conducted stewardship program may generate appropriateness and virtuous cost-saving**
- **To fight the spiral of empirism you need more diagnostic accuracy**
- **Clinical judgement and prudence are always required**
- ***Guidelines are not the Bible: we need to translate the recommendations to the single patient requirement in daily clinical practice***