Perspectiva nacional y europea en el manejo de la infección por piel y partes blandas complicadas por SARM

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Infección piel y partes blandas – *Etiología Europa (1998-04)*

1. *S. aureus*	1732 (37.5)
2. *P. aeruginosa*	555 (12.0)
3. *E. coli*	501 (10.8)
4. *Enterococcus* spp.	281 (6.1)
SARM	**22,8%**
6. CoNS	235 (5.1)
7. β-Streptococcus	215 (4.7)
8. *Klebsiella* spp.	205 (4.4)
9. *P. mirabilis*	145 (3.1)
10. *Acinetobacter* spp.	87 (1.5)
Total isolates tested (% of top 10)	4622 (90.8)

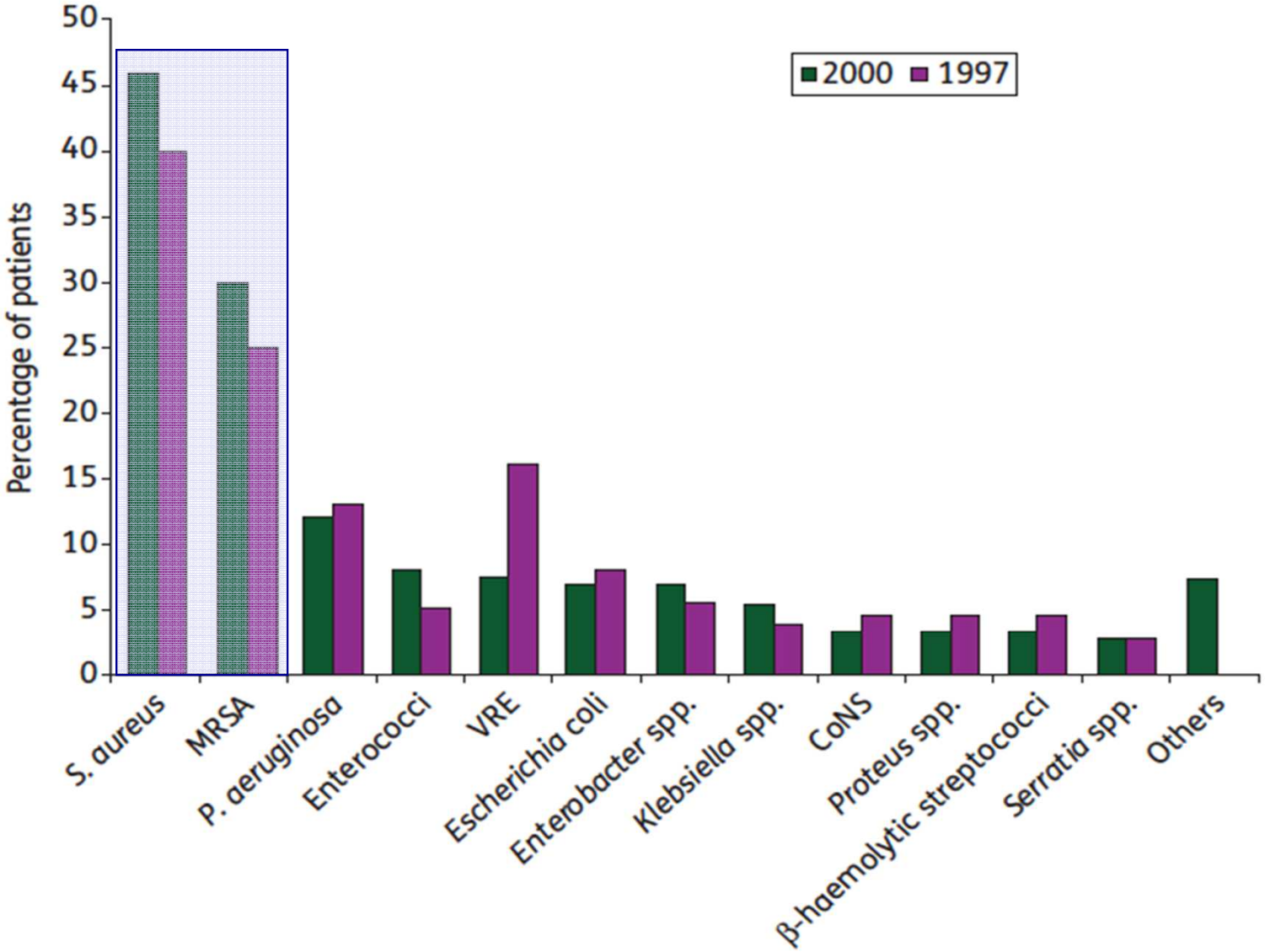
Moet GJ et al. Diagn Microbiol Infect Dis 2007

Infección piel y partes blandas – *Etiología Europa (1998-04)*

1. *S. aureus*	1732 (37.5)
2. *P. aeruginosa*	555 (12.0)
3. *E. coli*	501 (10.8)
4. *Enterococcus* spp.	281 (6.1)
SARM	**22,8%**
***E. coli* BLEE**	**12.4%**
***Klebsiella* spp. BLEE**	**24.9%**
***P. aeruginosa* MR**	**10.8%**
8. *Klebsiella* spp.	205 (4.4)
9. *P. mirabilis*	145 (3.1)
10. *Acinetobacter* spp.	87 (1.5)
Total isolates tested (% of top 10)	4622 (90.8)

Moet GJ et al. Diagn Microbiol Infect Dis 2007

Infección piel y partes blandas - *Etiología*



Dryden MS IJAA 2009

IPPB por *S. aureus* - *Tratamiento*

Gravedad	SASM	SARM
Leve	Amoxicilina/clavulánico Cefalexina Clindamicina Minociclina Doxiciclina	Cotrimoxazol Clindamicina Linezolid Minociclina Doxiciclina
Moderada o alta	Cloxacilina[1] Linezolid Daptomicina	Linezolid Daptomicina Vancomicina

[1] ± clindamicina o linezolid

Mensa J et al.. Rev Esp Quimioter 2013; 26 (Suppl. 1):1-84

IPPBc – *Fracaso terapéutico inicial*

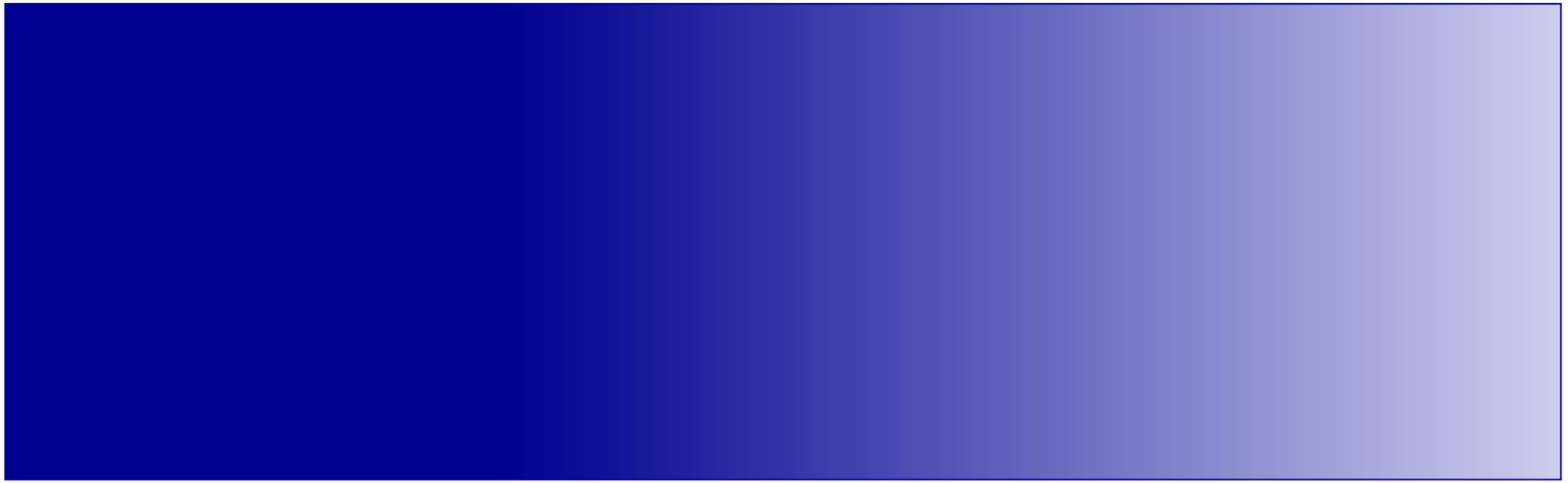
Variable	Resultado	p
Mortalidad hospitalaria	1,7% vs 0,5% (x4)	< 0,01
Días antibiótico iv adicional	10,3 vs 4,6 días (5,7*)	< 0,01
Coste económico	9353 *vs* 4068 $ (5285*)	< 0,01

*Incremento medio

Edelsberg J et al. ICHE 2008

Tratamiento IPPB – *Oral vs. Parenteral*

Parenteral ——— *Switch therapy* ——— *Oral* →



Hospital ——— *Infusion centre* ——— *Home* →

Esposito S. IJAA 2009; 34 S1:S30-S35

IPPB – *Carga clínica y económica*

Outcome	Model type	Effect of SSSI	*P*	95% CI
LOS	Fixed effect	3.81 days[a]	<0.0001	3.68–3.93 days
Log LOS	Fixed effect	51% longer[b]	<0.0001	49–52%
Total charges	Fixed effect	$14 794[a]	<0.0001	$13 799–$15 789
Log total charges	Fixed effect	35% more[b]	<0.0001	34–38%
Mortality	Conditional logistic	1.32[c]	<0.0001	1.22–1.42

SSSI in hospitalized patients using a matched cohort study design.

Hatoum HT et al DMID 2009

Pan-European early switch/early discharge opportunities exist for hospitalized patients with methicillin-resistant Staphylococcus aureus complicated skin and soft tissue infections.
Nathwani D et al. Clin Microbiol Infect 2014

Influence of real-world characteristics on outcomes for patients with methicillin-resistant Staphylococcal skin and soft tissue infections: a multi-country medical chart review in Europe.
Nathwani D et al. BMC Infect Dis 2014; 14:476

Antibiotic treatment patterns across Europe in patients with complicated skin and soft-tissue infections due to meticillin-resistant Staphylococcus aureus: A plea for implementation of early switch and early discharge criteria.
Eckmann C et al. Intern J Antimicrob Chemother 2014; 44:56-64

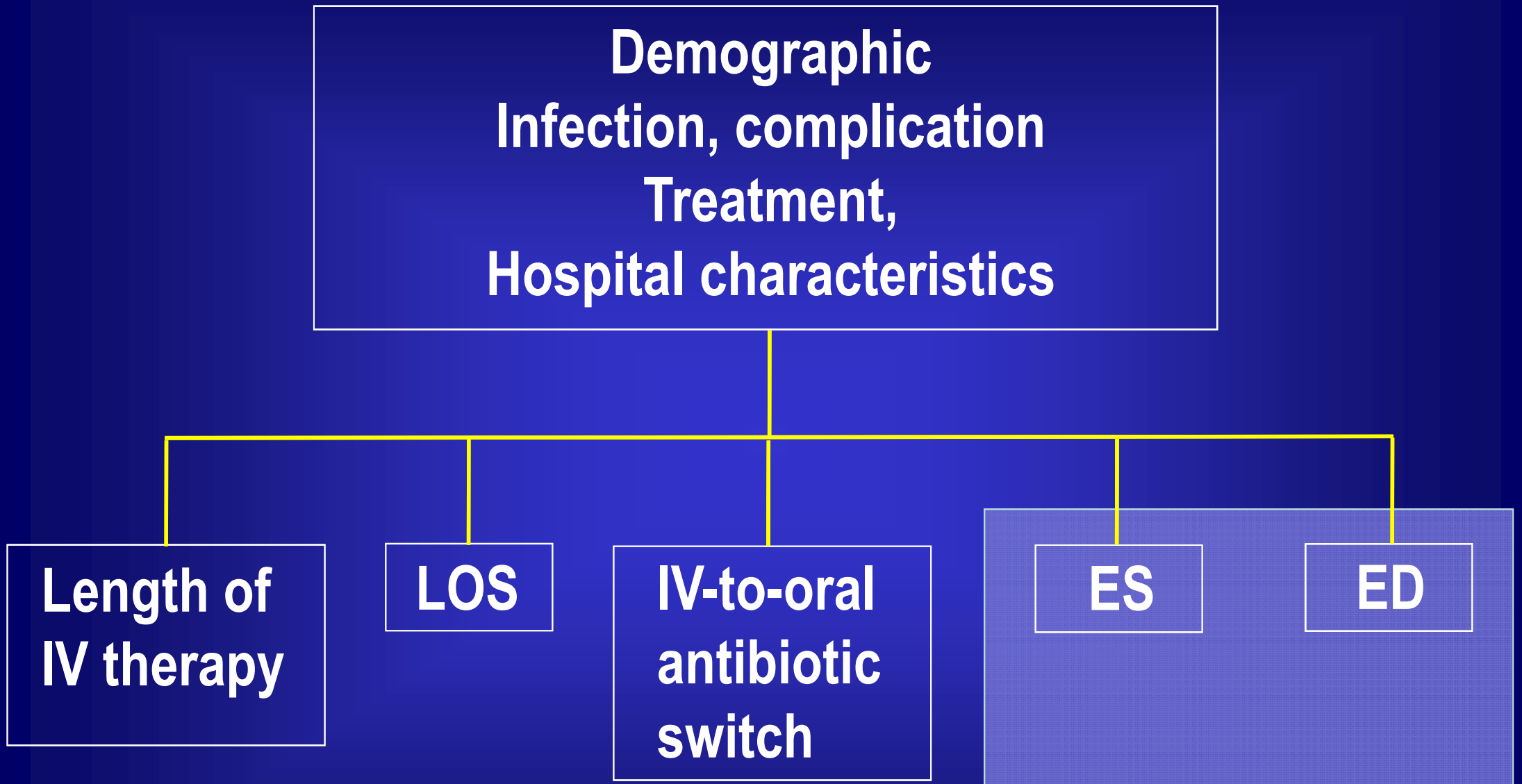
Pan-European early switch/early discharge opportunities exist for hospitalized patients with methicillin-resistant *Staphylococcus aureus* complicated skin and soft tissue infections

Clin Microbiol Infect 2014

D. Nathwani[1], C. Eckmann[2], W. Lawson[3], J. M. Stephens[4], C. Macahilig[5], C. T. Solem[4], D. Simoneau[6], R. Chambers[7], J. Z. Li[8] and S. Haider[9]

Methods

- Pan-European (12 countries) retrospective observational medical chart study
- Hospitalized patients ≥ 18 years with microbiologically MRSA cSSTIs
- To document real-world treatment patterns and healthcare resource and estimate opportunities for ES and ED
- Hospitalization July 1, 2010-June 30, 2011 and discharged alive by July 31, 2011
- 1542 patients and 342 physicians
- iv-only therapy *vs.* iv-po therapy



LOS: length of hospital stay
ES: early switch
ED: early hospital discharge

Nathwani D et al. BMC Infect Dis 2014, 14:476

Patient and disease characteristics

Diabetes: 31.3%
peripheral vascular disease: 23.8%
Sepsis: 17.2%

242 physicians

	Primary study population (*N* = 1502)
	60.9 ± 16.5
	917 (61.1)
n (%)	1395 (92.9)
Charlson Comorbidity Index, mean ± SD	2.3 ± 2.2
Infection characteristics	
Primary reason for hospitalization is treatment of MRSA cSSTI, *n* (%)	1214 (80.8)
Timing of cSSTI index diagnosis, *n* (%)	
At hospital admission	1246 (83.0)
1–3 days after admission	48 (3.2)
≥4 days after admission	208 (13.8)
Type of cSSTI, *n* (%)	
Surgical site infection or post-traumatic wound	390 (26.0)
Major abscess	265 (17.6)
Infected ulcer	371 (24.7)
Deep/extensive cellulitis	392 (26.1)
Other (including infected burn)	84 (5.6)

Antibiotic selection by line of treatment during hospitalization and at discharge

	First MRSA-active antibiotic (*N* = 1468)		Last inpatient MRSA-active antibiotic (*N* = 1468)		Discharge MRSA-active antibiotic (*N* = 480)	
	n	%[a]	*n*	%	*n*	%
Vancomycin	737	50.2	609	41.5	11	2.3
Linezolid	222	15.1	310	21.1	202	42.1
Clindamycin	159	10.8	141	9.6	95	19.8
Teicoplanin	153	10.4	158	10.8	14	2.9
Ciprofloxacin	101	6.9	105	7.2	58	12.1
Daptomycin	87	5.9	98	6.7	1	0.2
Rifampicin	62	4.2	60	4.1	34	7.1
Tigecycline	48	3.3	54	3.7	2	0.4
TMP-SMX	45	3.1	56	3.8	57	11.9
Fusidic acid	21	1.4	26	1.8	16	3.3
Doxycycline	14	1.0	25	1.7	21	4.4

Nathwani D et al. CMI 2014

Patient and treatment

	Treatment patterns and healthcare resource utilization
Only IV MRSA-active treatment	1224 (81.5%)
IV to PO MRSA-active treatment	161 (10.7%)
Discharge from hospital	32.7%
Treatment not confirmed to MRSA-active	34 (2.3%)
Mean LOS (from diagnosis to discharge)	24.6 ± 17.4
Mean±SD time to start treatment	1.2 ± 2.7
Mean±SD length of treatment	14.8 ± 9.9
Single MRSA-active antibiotic	101 (81%)
Changed at least one MRSA-active	261 (17.8%)
Surgical procedures	582 (38.7%)

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Duration IV therapy – *IV only vs. IV to PO*

	IV-only n= 1228	IV to PO n= 197	Reduction (day)	p
Mean ± SD duration therapy	14.6 ± 9.9	9.3 ± 6.5	5.3	< 0.001
Mean ± SD hospital LOS	21 ± 18.2	19.1 ± 12.9	1.9	0.162

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Early switch (ES) - *Criteria*

At minimum, the following key criteria needed to be met prior to actual IV discontinuation:

- Stable clinical infection
- Afebrile/temperature of <38°C for 24 h
- WBC count normalizing, WBC count not <4 × 10^9/L or >12 × 10^9/L
- No unexplained tachycardia
- Systolic blood pressure of ≥100 mm Hg
- Patient tolerates PO fluids/diet and able to take PO medications with no gastrointestinal absorption problems

Additional criteria related to ES that were assessed, but not required to be documented, included:

- Available bacteriology for cSSTI caused by MRSA that is sensitive to PO treatment
- Available bacteriology for cSSTI caused by MRSA that is sensitive to OPAT
- No surgery scheduled within the next 36 h
- No requirement for IV line other than administration of IV antibiotic therapy

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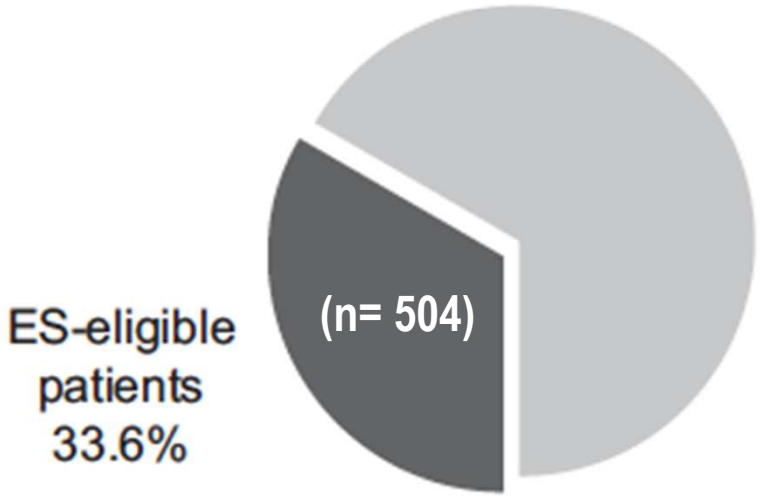
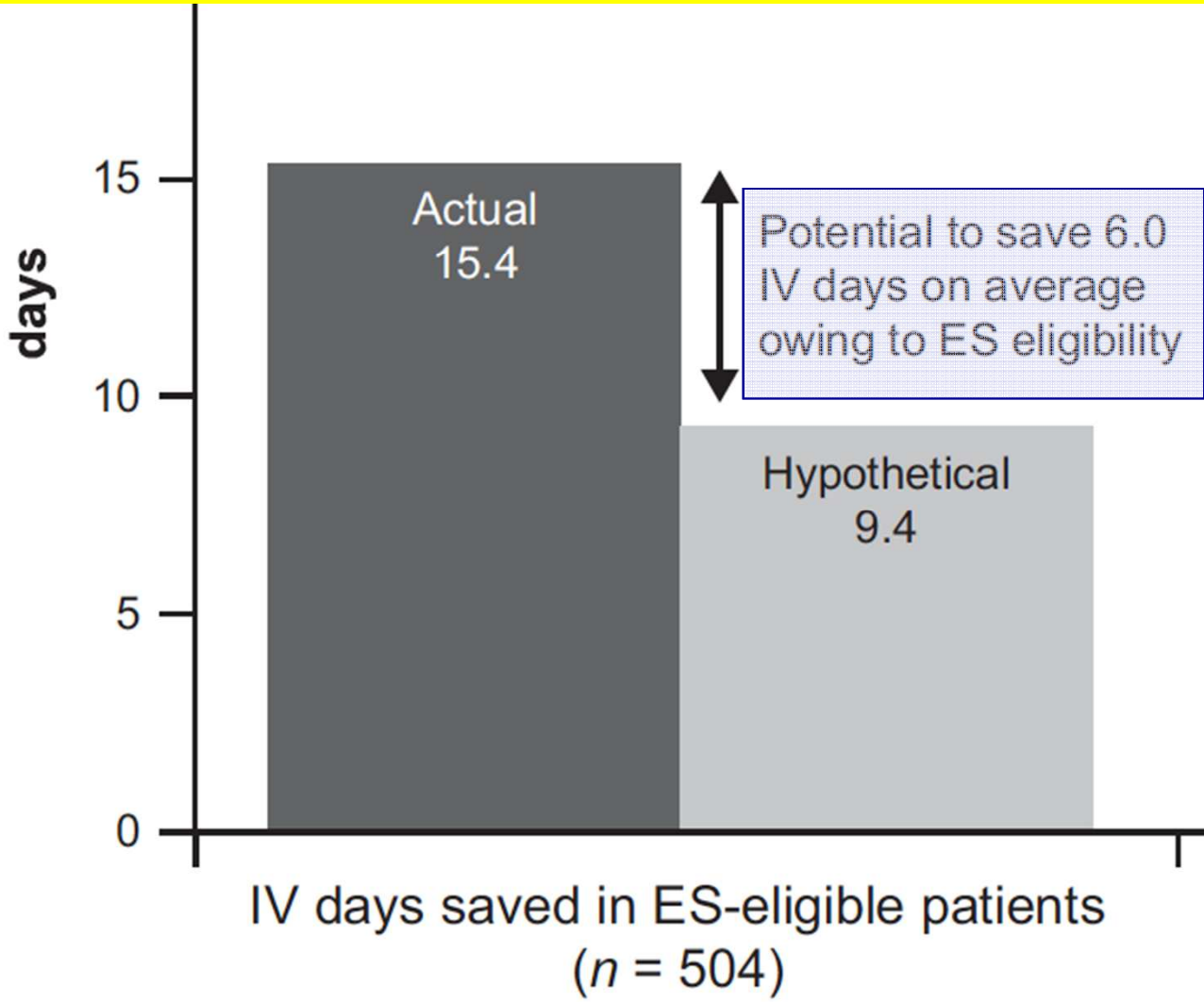
Comparison of actual and hypothetical intravenous (IV) days in early switch (ES)-eligible





Early discharge (ED) - *Criteria*

At minimum, the following criteria needed to be met prior to discharge:

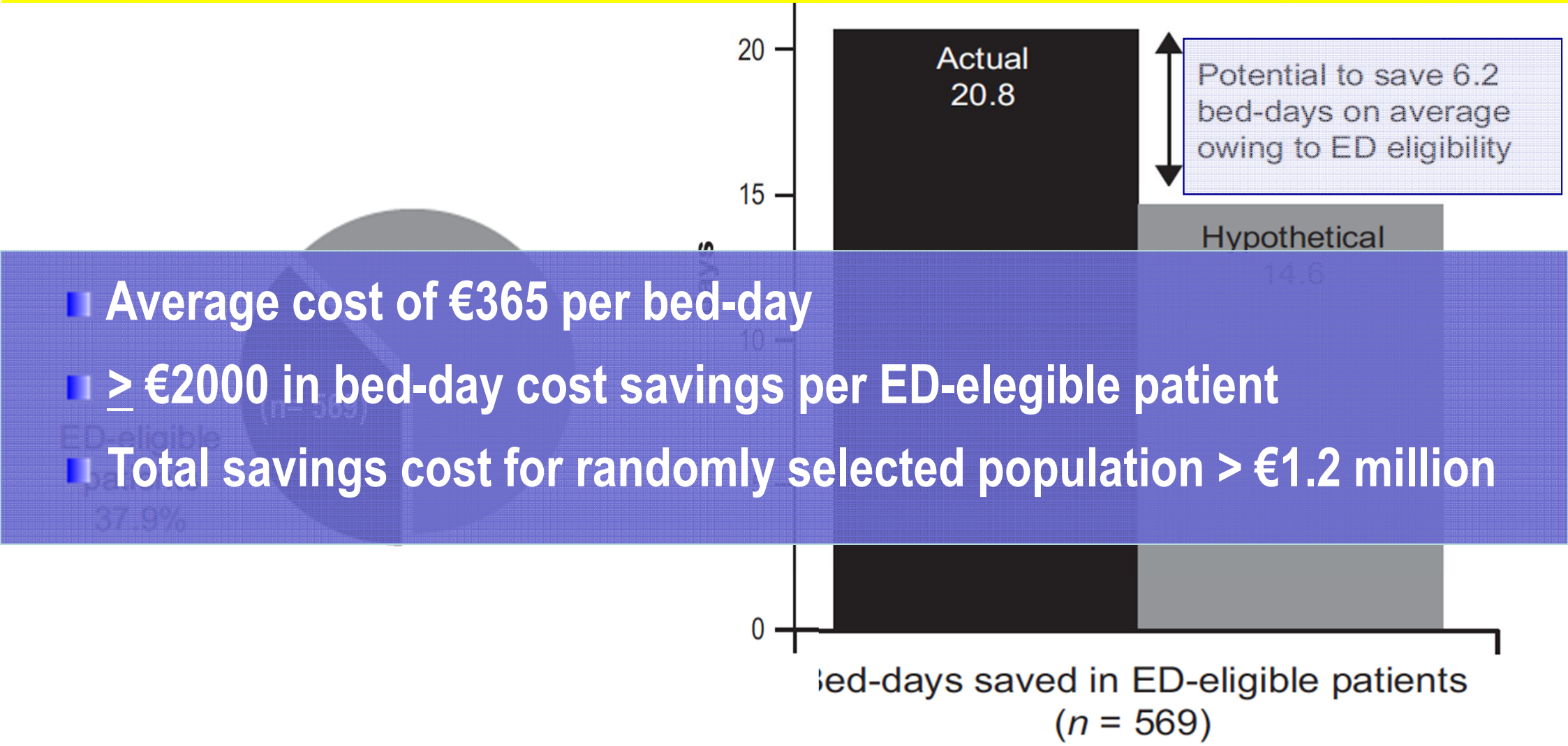
- All key ES eligibility criteria listed above
- No other reason to stay in hospital except infection management

Additional criteria related to ED that were assessed, but not required to be documented, included:

- Stable mental status
- Stable comorbid illnesses
- Stable social situation

Nathwani D et al. CMI 2014

Comparison of actual and hypothetical intravenous (IV) bed-days in early discharge (ED)-eligible



- Average cost of €365 per bed-day
- ≥ €2000 in bed-day cost savings per ED-elegible patient
- Total savings cost for randomly selected population > €1.2 million

Nathwani D et al. CMI 2014

Limitations of study

- Retrospective medical chart review
- Influency by a disease severity bias
- Applicability ES/ED criteria needs to be validated prospectively
- Several cost drivers for the treatment
- Increased LOS is the key cost driver

Antibiotic treatment patterns across Europe in patients with complicated skin and soft-tissue infections due to meticillin-resistant *Staphylococcus aureus*: A plea for implementation of early switch and early discharge criteria

Intern J Antimicrob Agents 2014; 44:56–64

Christian Eckmann[a], Wendy Lawson[b], Dilip Nathwani[c], Caitlyn T. Solem[d], Jennifer M. Stephens[d,*], Cynthia Macahilig[e], Damien Simoneau[f], Petr Hajek[g], Claudie Charbonneau[f], Richard Chambers[h], Jim Z. Li[i], Seema Haider[j]

Patient and treatment

	Treatment patterns and healthcare resource utilization
Only IV MRSA-active treatment	1224 (81.5%)
IV to PO MRSA-active treatment	161 (10.7% -2% Greece to 20% Spain-)
Discharge from hospital	32.7% -18% Portugal to 49% Greece-
Treatment not confirmed to MRSA-active	34 (2.3%)
Mean LOS (from diagnosis to discharge)	24.6 ± 17.4
Mean±SD time to start treatment	1.2 ± 2.7
Mean±SD length of treatment	14.8 ± 9.9
Single MRSA-active antibiotic	101 (81%)
Changed at least one MRSA-active	261 (17.8%)
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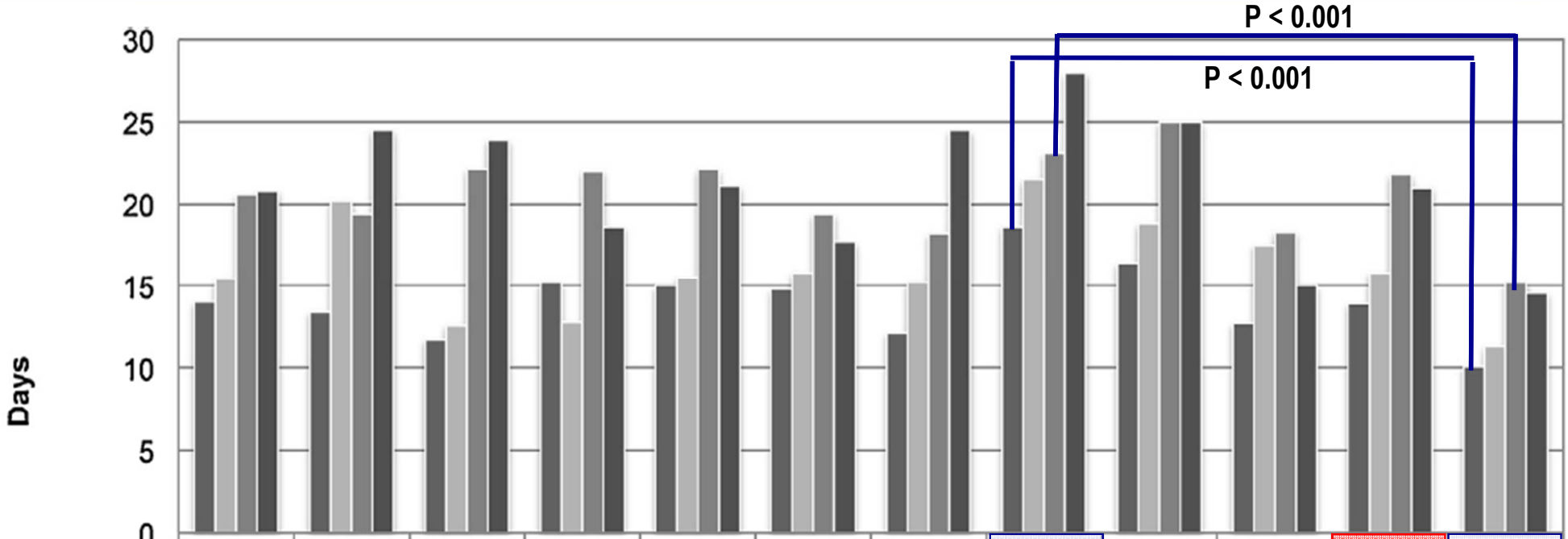
Hospitals - *antibiotic subcommittees and ES/ED protocols*

	Antibiotic subcommittee or steering committee (%)	I.v.-to-oral antibiotic switch protocol (%)	ED protocol for MRSA cSSTI (oral or OPAT) (%)
All hospitals ($N = 341$)[a]	82.9	23.7	12.9
Austria ($n = 24$)	87.5	4.1	4.1
Czech Republic ($n = 10$)	80.0	10.0	0
France ($n = 48$)	91.6	20.8	4.1
Germany ($n = 50$)	66.0	18.0	12.0
Greece ($n = 33$)	96.9	12.1	9.0
Italy ($n = 39$)	43.5	12.8	7.6
Poland ($n = 19$)	94.7	47.3	5.2
Portugal ($n = 20$)	85.0	0	25.0
Slovakia ($n = 7$)	100.0	71.4	14.2
Spain ($n = 32$)	96.8	37.5	28.1
UK ($n = 58$)	93.1	43.1	22.4

Eckmann C et al. Intern J Antimicrob Agents 2014

iv Days and mean hospital stay - *Country*



	All Countries (n=1502)	Austria (n=54)	Czech Republic (n=41)	France (n=261)	Germany (n=217)	Greece (n=151)	Italy (n=190)	Poland (n=43)	Portugal (n=141)	Slovakia (n=50)	Spain (n=183)	UK (n=169)
IV days- Full Cohort	14.0	13.4	11.7	15.2	15.0	14.8	12.1	18.6	16.4	12.7	13.9	10.1
IV days- ES Eligible Patients*	15.4	20.2	12.6	12.8	15.5	15.8	15.2	21.5	18.8	17.5	15.8	11.3
LOS- Full Cohort	20.6	19.4	22.1	22.0	22.1	19.4	18.2	23.1	25.0	18.3	21.8	15.2
LOS- ED Eligible Patients*	20.8	24.5	23.9	18.6	21.1	17.7	24.5	28.0	25.0	15.0	21.0	14.6

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ES eligibility and potential savings in iv days

	Patient opportunities for ES	
	ES-eligible (%)	Potential i.v. days saved by ES-eligible patients (mean ± S.D.)
All countries ($n = 1502$)[c]	33.6	6.0 ± 5.5
Austria ($n = 54$)	25.9	6.9 ± 5.0
Czech Republic ($n = 41$)	22.0	3.3 ± 2.1
France ($n = 261$)	28.4	5.3 ± 4.1
Germany ($n = 217$)	46.5	6.7 ± 6.0
Greece ($n = 151$)	56.3	6.6 ± 6.0
Italy ($n = 190$)	25.3	5.7 ± 4.3
Poland ($n = 43$)	32.6	6.6 ± 5.5
Portugal ($n = 141$)	42.6	5.2 ± 4.2
Slovakia ($n = 50$)	12.0	2.7 ± 1.9
Spain ($n = 183$)	26.2	7.2 ± 8.5
UK ($n = 169$)	26.6	5.0 ± 4.9

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ED eligibility and potential savings in hospital length of stay

	Patient opportunities for ED	
	ED-eligible (%)	Potential bed-days saved by ED-eligible patients (mean ± S.D.)
All countries ($n = 1502$)[c]	37.9	6.2 ± 8.2
Austria ($n = 54$)	33.3	6.1 ± 5.9
Czech Republic ($n = 41$)	46.3	5.3 ± 6.5
France ($n = 261$)	35.2	7.8 ± 10.6
Germany ($n = 217$)	47.0	4.2 ± 5.5
Greece ($n = 151$)	41.1	7.5 ± 10.6
Italy ($n = 190$)	34.2	7.0 ± 8.1
Poland ($n = 43$)	27.9	6.6 ± 6.4
Portugal ($n = 141$)	48.2	6.4 ± 7.1
Slovakia ($n = 50$)	10.0	1.2 ± 0.4
Spain ($n = 183$)	38.8	6.7 ± 9.1
UK ($n = 169$)	32.5	4.3 ± 5.9

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ED eligibility and potential savings in costs

	Potential cost savings due to bed-days saved	
	Average cost (€344.87 per bed-day)[a]	Country-specific costs (2012€)[a,b]
All countries ($n = 1502$)[c]	2135 ± 2829	2129 ± 2846
Austria ($n = 54$)	2088 ± 2023	2716 ± 2631
Czech Republic ($n = 41$)	1833 ± 2247	1495 ± 1832
France ($n = 261$)	2703 ± 3643	2864 ± 3861
Germany ($n = 217$)	1454 ± 1912	1683 ± 2214
Greece ($n = 151$)	2581 ± 3644	2317 ± 3272
Italy ($n = 190$)	2430 ± 2785	2642 ± 3028
Poland ($n = 43$)	2270 ± 2203	1235 ± 1199
Portugal ($n = 141$)	2216 ± 2445	1592 ± 1756
Slovakia ($n = 50$)	414 ± 154	320 ± 119
Spain ($n = 183$)	2327 ± 3136	2193 ± 2955
UK ($n = 169$)	1499 ± 2024	1872 ± 2528

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Influence of real-world characteristics on outcomes for patients with methicillin-resistant Staphylococcal skin and soft tissue infections: a multi-country medical chart review in Europe

Nathwani D et al. BMC Infectious Diseases 2014, 14:476

- Pan-European (12 countries) retrospective observational medical chart study
- Hospitalized patients ≥ 18 years with microbiologically MRSA cSSTIs
- To document real-world treatment patterns and healthcare resource and estimate opportunities for ES and ED
- Hospitalization July 1, 2010-June 30, 2011 and discharged alive by July 31, 2011
- 1542 patients and 342 physicians
- iv-only therapy *vs.* iv-po therapy
- **Logistic/linear regression models evaluated actual resource use:**
  - **Length of IV therapy, length of hospital stay, IV-to-oral antibiotic switch**
  - **ES and ED (using literature-based and expert-verified criteria) outcomes**

Predictive factors of length of IV therapy, LOS, IV-to-oral antibiotic switch

Clinical characteristics	IV-to-oral antibiotic switch (n = 1425) OR (95% CI)	Length of IV therapy (n = 1508) β (SE)	LOS (n = 1542) β (SE)
cSSTI type (vs deep/extensive cellulitis)			
Surgical site infection or posttraumatic wound	1.26 (0.77–2.07)	−1.39 (0.70)*	−2.07 (1.24)
cSSTI location (vs torso/abdomen)			
Upper extremity	1.90 (1.09–3.33)*	−1.62 (0.80)*	−4.97 (1.43)***
Hospital-acquired or healthcare-associated infection unknown/undocumented	0.98 (0.60–1.59)	−2.40 (0.68)***	−2.21 (1.20)
Days from admission to cSSTI index date (vs cSSTI at admission)			
≥4 days after admission		1.13 (0.64)	5.57 (1.13)***

*p < 0.05; **p < 0.01; ***p < 0.001.

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Predictive factors of length of IV therapy, LOS, IV-to-oral antibiotic switch

Treatment characteristics	IV-to-oral antibiotic switch (n = 1425) OR (95% CI)	Length of IV therapy (n = 1508) β (SE)	LOS (n = 1542) β (SE)
MRSA-targeted therapy patterns (vs IV-only)			
IV-to-oral antibiotic switch	–	−5.19 (0.74)***	−1.86 (1.32)
Discharged on OPAT	–	−2.64 (1.59)	−6.92 (2.85)*
No MRSA-active antibiotic	–	–	−7.52 (2.98)*
Initial antibiotic therapy was MRSA active (vs was not MRSA active)	0.41 (0.24 - 0.70)**	5.84 (1.01)***	
Time to initiating MRSA-active therapy (vs on or before cSSTI index date)			
1–2 days post cSSTI index date		−1.34 (0.39)***	−2.03 (0.66)**
≥3 days post cSSTI index date		2.20 (0.53)***	4.18 (0.80)***

*p < 0.05; **p < 0.01; ***p < 0.001.

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Predictive factors of length of IV therapy, LOS, IV-to-oral antibiotic switch

Physiscian speciality

	IV-to-oral antibiotic switch (n = 1425) OR (95% CI)	Length of IV therapy (n = 1508) β (SE)	LOS (n = 1542) β (SE)
Physician specialty (vs GP)[a]			
IM	2.26 (1.43–3.56)***	1.18 (0.64)	2.86 (1.13)*
Infectious disease	3.01 (1.88–4.82)***	2.39 (0.73)**	1.28 (1.30)
Surgeon	1.31 (0.70–2.45)	2.73 (0.87)**	5.78 (1.55)***
Any surgical procedures for cSSTI	1.46 (1.00–2.12)*	0.81 (0.54)	1.80 (0.96)

*p < 0.05; **p < 0.01; ***p < 0.001.

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Predictive factors of length of IV therapy, LOS, IV-to-oral antibiotic switch

Hospital characteristics	IV-to-oral antibiotic switch (n = 1425) OR (95% CI)	Length of IV therapy (n = 1508) β (SE)	LOS (n = 1542) β (SE)
Overall hospital beds (vs ≥1000)			
10–249	2.37 (1.45–3.88)***	−2.17 (0.77)**	−2.17 (1.37)
Hospital had an IV-to-oral antibiotic switch protocol		0.88 (0.61)	−2.13 (1.08)*

*p < 0.05; **p < 0.01; ***p < 0.001.

Nathwani D et al. BMC Infect Dis 2014, 14:476

Predictive factors of length of IV therapy, LOS, IV-to-oral antibiotic switch

Country	IV-to-oral antibiotic switch (n = 1425) OR (95% CI)	Length of IV therapy (n = 1508) β (SE)	LOS (n = 1542) β (SE)
Country (vs Ireland/United Kingdom)			
Austria	0.17 (0.04–0.76)*	2.74 (1.49)	2.48 (2.64)
France	1.44 (0.81–2.57)	4.24 (0.93)***	6.23 (1.66)***
Germany	0.40 (0.21–0.78)**	4.16 (0.97)***	4.28 (1.74)*
Greece	0.05 (0.01–0.18)***	2.53 (1.14)*	1.25 (2.03)
Italy	0.23 (0.10–0.55)***	2.91 (1.04)**	4.69 (1.87)*
Poland	0.19 (0.04–0.90)*	7.65 (1.69)***	5.97 (2.93)*
Portugal	0.16 (0.06–0.40)***	4.41 (1.18)***	4.46 (2.12)*
Slovakia	0.67 (0.23–1.93)	5.29 (1.83)**	3.32 (3.14)
Spain	0.90 (0.49–1.65)	3.10 (1.01)**	5.26 (1.81)**

*p < 0.05; **p < 0.01; ***p < 0.001.

Nathwani D et al. BMC Infect Dis 2014, 14:476

Predictive factors of ES and ED

Infection/treatment characteristics	ES (n = 1542) OR (95% CI)	ED (n = 1542) OR (95% CI)
Hospital-acquired or healthcare-associated infection	1.75 (1.30–2.37)***	1.69 (1.25–2.27)***
Days to first MRSA culture (vs on or before cSSTI index date)		
No MRSA culture documented	0.46 (0.30–0.69)***	0.58 (0.40–0.85)**
Days from admission to cSSTI index date (vs cSSTI at admission)		
≥4 days after admission	0.47 (0.32–0.70)*	0.55 (0.38–0.79)
MRSA-targeted therapy patterns (vs IV-only)		
IV-to-oral antibiotic switch	0.49 (0.33–0.72)***	1.40 (1.00–1.96)
Time to initiating MRSA-active therapy (vs on or before cSSTI index date)		
1–2 days post cSSTI index date		1.20 (0.92–1.56)**
≥3 days post cSSTI index date		0.71 (0.51–0.99)**

*p < 0.05; **p < 0.01; ***p < 0.001.

Nathwani D et al. BMC Infect Dis 2014, 14:476

Predictive factors of ES and ED

Hospital characteristics	ES (n = 1542) OR (95% CI)	ED (n = 1542) OR (95% CI)
Hospital had an IV-to-oral antibiotic switch protocol		0.58 (0.43–0.80)***
Hospital had an ED protocol (IV-to-oral antibiotic switch or OPAT)		1.86 (1.31–2.64)***

*p < 0.05; **p < 0.01; ***p < 0.001.

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Conclusions

- Significantive variation across countries
- Association of IV-to-oral antibiotic switch therapy with shorter length of IV therapy days and LOS
- Rates of ES and ED

Many opportunities are available to optimize actual practice patterns, particularly through the identification and targeting of interventions to patient populations with greater eligibility and longer LOS and IV days

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