

Nosocomial infections – influence of gender

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Nosocomial infections (NI)

- „nosocomial“ – greek „nosos - disease“ and „komeo - care“
- „hospital-acquired infection“ – HAI
 - Within 48 hours after hospital admission
- „health-care associated infection“ – HAI
 - Hospitals, chronic healthcare (in- AND outpatient care), long-term care facilities, ambulatory care, ...

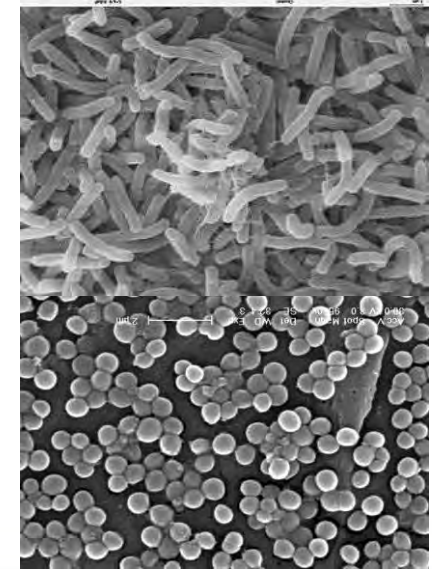
Nosocomial infections

- Clinical signs and symptoms of infection
- Examination
 - Chest x-ray
 - Microbiology
 - Chemistry



Nosocomial pathogens

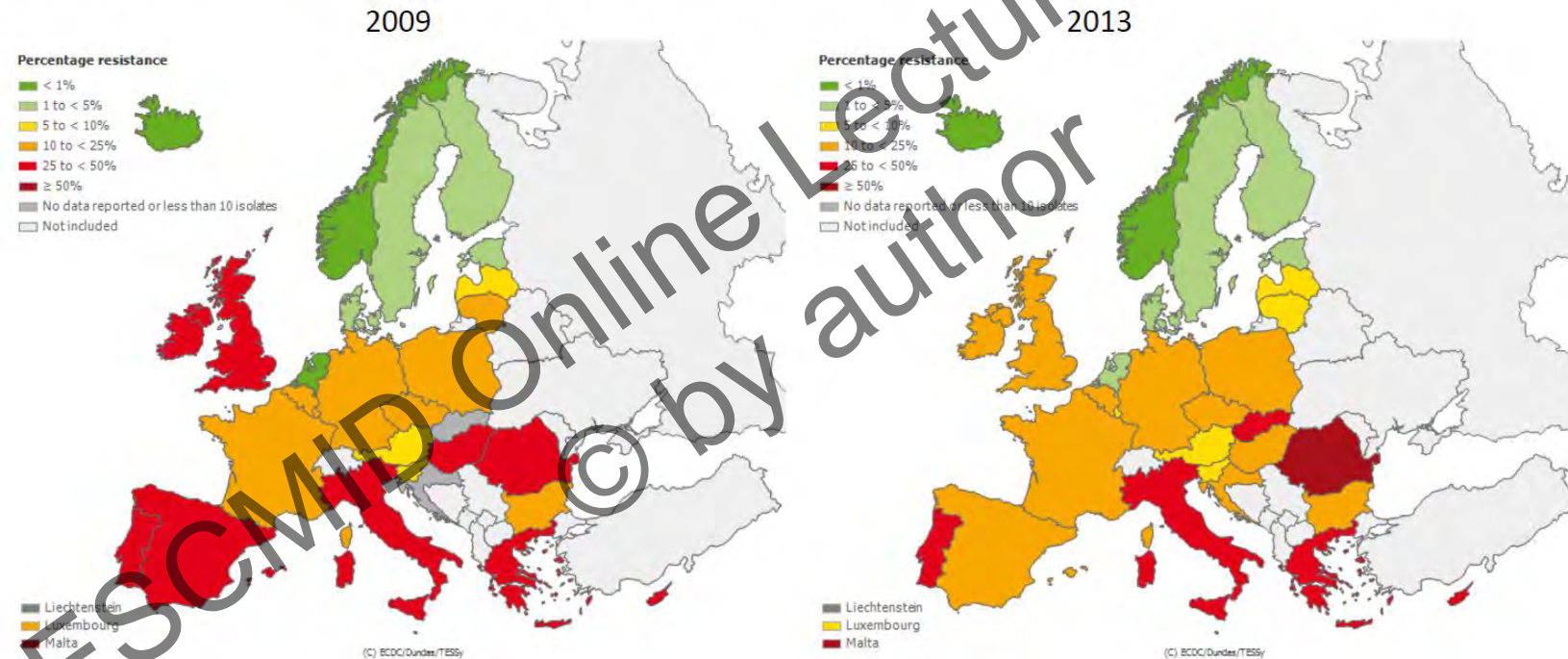
- Multi-resistant organisms
 - MRSA
 - Extended-Betalactamase-producing bacteria „ESBL“
 - Carbapenemase-producing bacteria
 - Clostridium difficile
 - Vancomycin-resistant enterococci VRE
 - Multi-resistant Acinetobacter
 - Fungi - Candida ?



Methicillin-resistenter *Staphylococcus aureus*

MRSA

Abbildung 17: MRSA-Raten im europäischen Vergleich 2009 und 2013

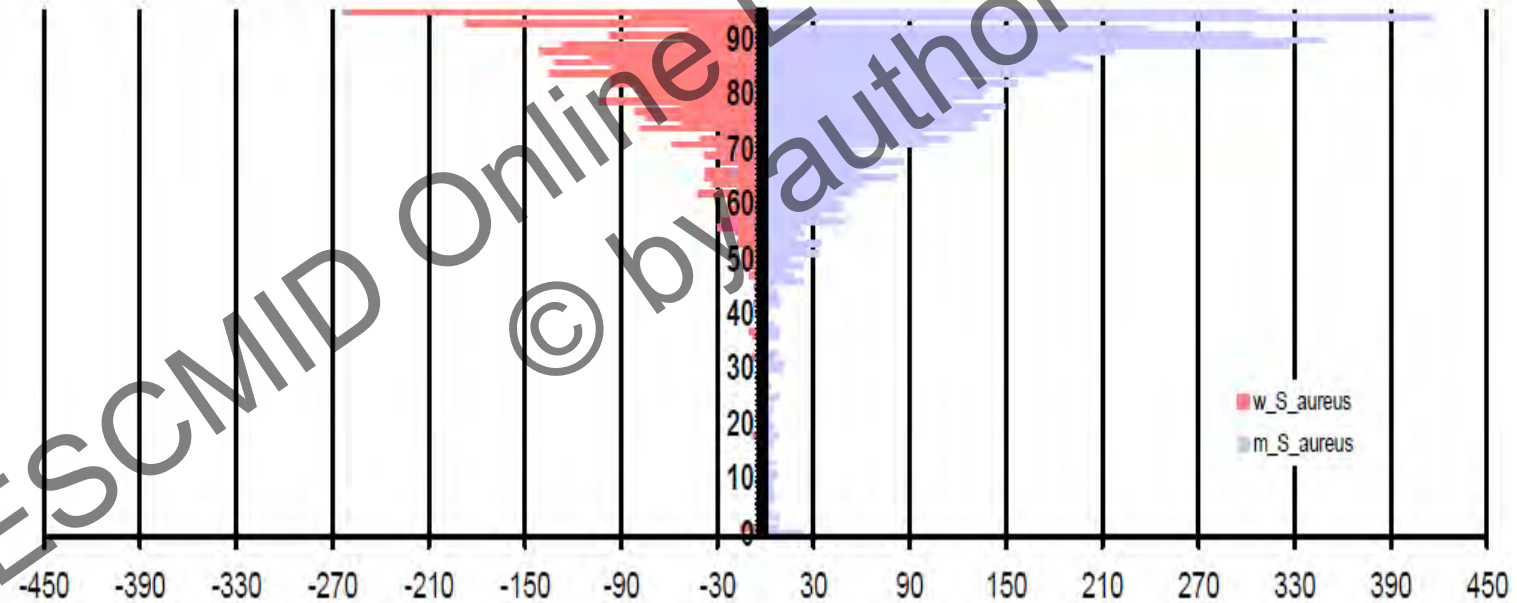


Quelle: TESSy – The European Surveillance System, Stand: 14. 08. 2014

MRSA in Austria

EARSS – EUROPEAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

Abbildung 16: Staphylococcus aureus nach Geschlecht und Lebensalter bezogen auf die österreichische Bevölkerung in den jeweiligen Lebensjahren im Jahr 2009



Skalierung: Fälle pro 100.000 Einwohner; Kategorie 95 ist >=95 Jahre

MRSA Infection – community vs. hospital acquired 1999 - 2009

- 72 hours in-hospital, MRSA n=724, 384 patients with MRSA infection
 - CA-MRSA: SCC*mec* type IV element (phenotype: susceptible to gentamicin, clindamycin, and trimethoprim-sulfamethoxazole), 30%
 - HA-MRSA: resistant, 70%
- Failure at day 14: HA-MRSA 60/267 (30%)
CA-MRSA 18/117 (18%), n.s.

Eels at al., Epidemiol Infect 2013

MRSA Infection – community vs. hospital acquired 1999 - 2009

- 30 mortality: HA-MRSA 51/267 (19%)
CA-MRSA 19/117 (16%), n.s.
- Associated factors:
 - Female gender (OR 2.28)
 - Old age (OR 1.05), MRSA bloodstream infection (OR 5.37), MRSA pneumonia (OR 7.91), HIV (OR 6.0), higher Charlson comorbidity index (OR 1.2), higher APACHE II score (OR 1.07)
 - Predictors of death : All above + „never been treated with active antibiotic“ (OR 4.99)

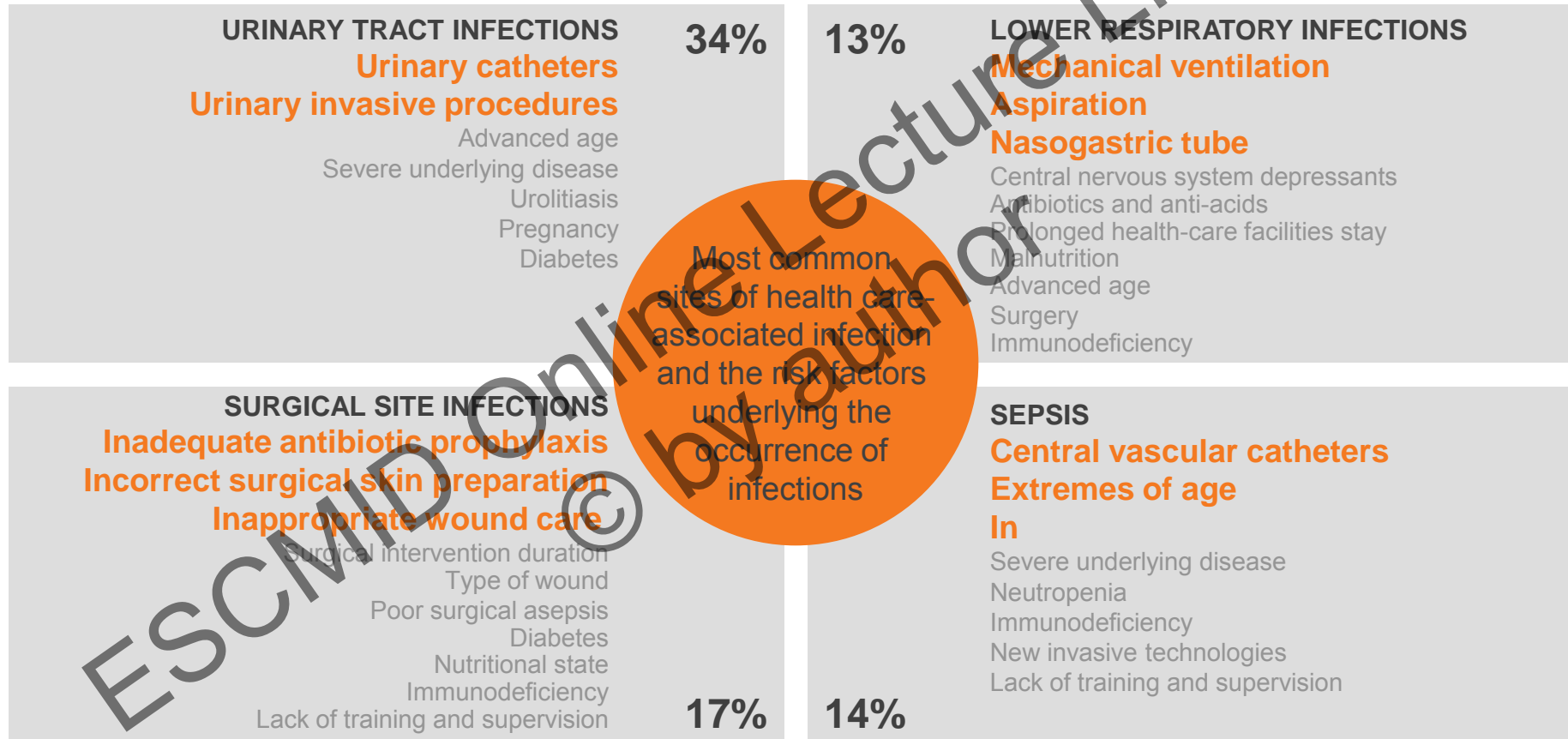
Eels at al., Epidemiol Infect 2013

Nosocomial infections



- Lead to increased
 - mortality
 - hospital stay
 - Costs
 - Loss of patients' trust and faith in modern medicine

Most frequent sites of infection and their risk factors



NI/HAI and patient safety –

- 2005 – 2011, n=62523, acute heart disease, pneumonia, major surgery
- Medicare Patient Safety Monitoring System
- 21 „adverse events“ (AE), 7 HAI
- Results:
 - Decline of AE, not for pneumonia and major surgery
 - Rates of HAI increased in patients with major surgery

Wang et al., NEJM 2014

Most common NI/HAI (all)

- Urinary tract infections - 40 %
- Pneumonia - 20 %
- Postoperative wound infections - 15 %
- Bacteremia/Sepsis - 8 %
- Other (catheter-related infections etc.) - 17 %

Gender differences in intensive care patients

	Women (n = 10,848)	Men (n = 15,150)	p Value
Age, mean (SD), yrs	66.0 (17.4)	59.3 (16.8)	<.001 ^a
Type of admission, no. (%)			<.001 ^b
Medical	4,077 (37.7)	6,692 (44.3)	
Scheduled surgical	3,953 (36.5)	4,887 (32.4)	
Unscheduled surgical	2,789 (25.8)	3,526 (23.3)	
Length of ICU stay, days (median, quartile)	3 (2-6)	3 (2-8)	<.001 ^c
TISS-28 score per patient and stay (median, quartile)	80 (47-182)	89 (51-233)	<.001 ^c
TISS-28 scores per patient per day (median, quartile)	27.8 (21.5-34.3)	29.0 (21.0-35.0)	<.001 ^c
SAPS II score (median, quartile)	28 (20-41)	26 (18-40)	<.001 ^c
SAPS II-predicted number of deaths, no. (%)	2,179 (20.1)	2,840 (18.7)	.003 ^b
SAPS II _{customized} -predicted number of deaths, no. (%)	1,986 (18.3)	2,579 (17.0)	.004 ^b
Observed number of deaths, no. (%)	1,960 (18.1)	2,610 (17.2)	.040 ^b
O/E ratio (95% CI)	0.90 (0.87-0.93)	0.92 (0.89-0.95)	
O/E ratio (95% CI)-SAPS II _{customized}	0.99 (0.95-1.02)	1.01 (0.98-1.04)	

- ... besides finding a higher frequency of male admissions, ... men had a significantly higher probability of receiving several invasive procedures.

Gender differences in outcome after treatment of infection in hospitalized patients

- N=892; 1470 infectious episodes; 782 in men, 688 in women

Table 3. Stepwise Logistic Regression Analysis of Factors Associated With Mortality for All Infections*

Characteristic	Odds Ratio (95% Confidence Interval)	P Value
Increasing APACHE II score	1.15 (1.11-1.18)	<.001
Transfusion	4.15 (2.46-6.99)	<.001
Increasing age	1.03 (1.02-1.05)	<.001
Malignancy	2.60 (1.62-4.17)	<.001
Temperature maximum	0.70 (0.58-0.85)	<.001
Admission to treatment >7 d	1.66 (1.05-2.61)	.03
Female	1.32 (0.90-1.94)	.16

Table 4. Infection Sites and Mortality Stratified by Gender*

Infection Site	Men		Women	
	No. (%) of Infection Episodes	Mortality, %	No. (%) of Infection Episodes	Mortality, %
Lung	282 (36)†	18†	144 (21)	34
Peritoneum	227 (29)	8	213 (31)	11
Bloodstream	203 (26)‡	18	131 (19)	20
Surgical site	156 (20)	5	138 (20)	8
Urinary tract	141 (18)†	10	227 (33)	18
Soft tissue	94 (12)	2‡	89 (13)	10
Catheter	78 (10)	22	62 (9)	30

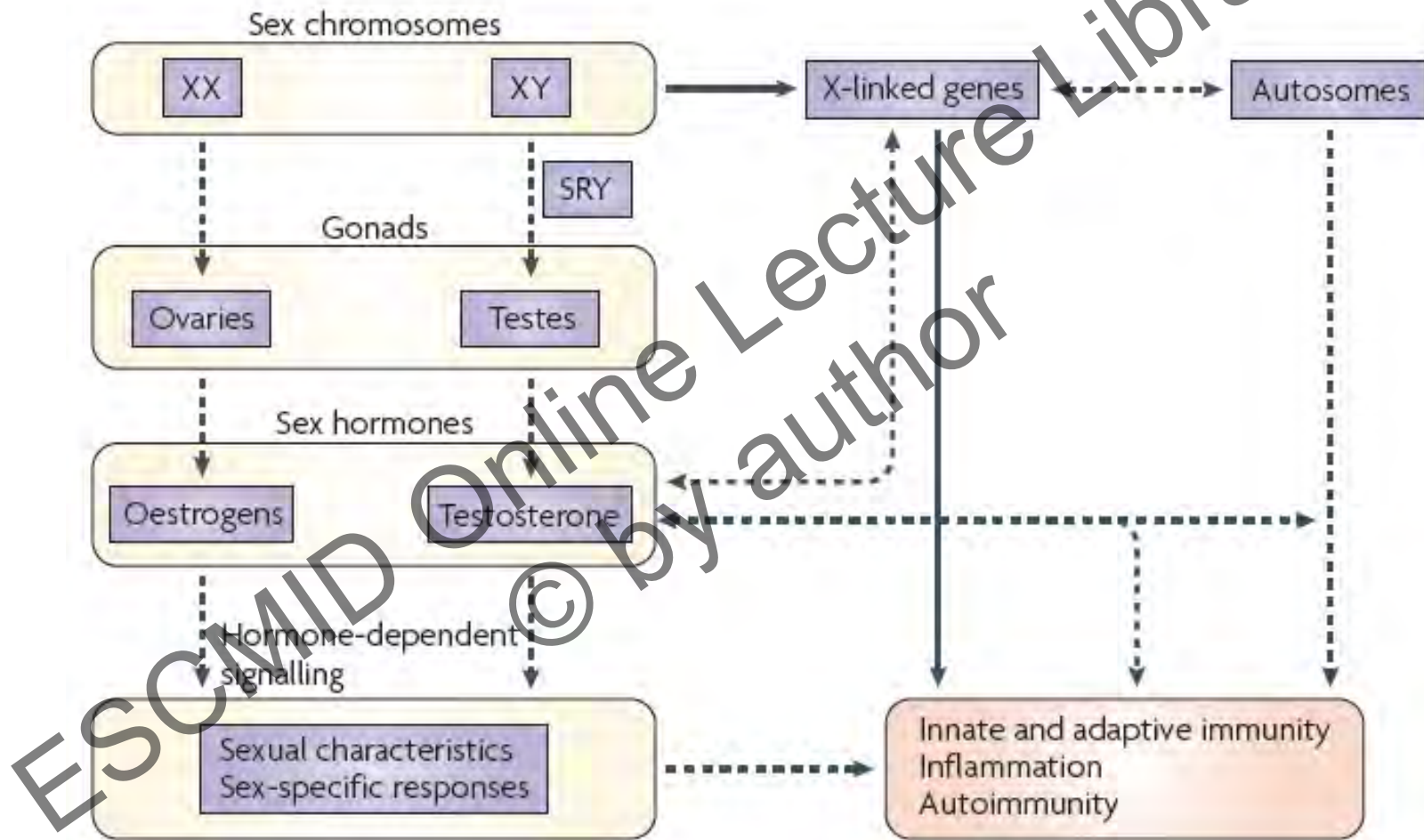
*Total percentage may exceed 100% because many patients had infections at more than 1 site during a single episode.

†P≤.002 vs female incidence or mortality by χ^2 .

‡P≤.05 vs female incidence or mortality by χ^2 .

Sex-related differences of immune response

- Females have better survival rates from illnesses due to infectious diseases, sepsis, trauma or injury
- Immune system is influenced by
 - Sex-chromosomes X and Y
 - Sex hormones:
 - Testosteron
 - Estrogen
 - Progesteron



Nosocomial infections and prevalence studies

- Scottish prevalence study 2005 – 2006
- N=13 754 patients;
acute care: N=11 608
- HAI n=1103; 11.4% > 1 HAI
acute care 9.5%
non-acute care 7.3%

Reilly et al., J Hosp Infect 2008

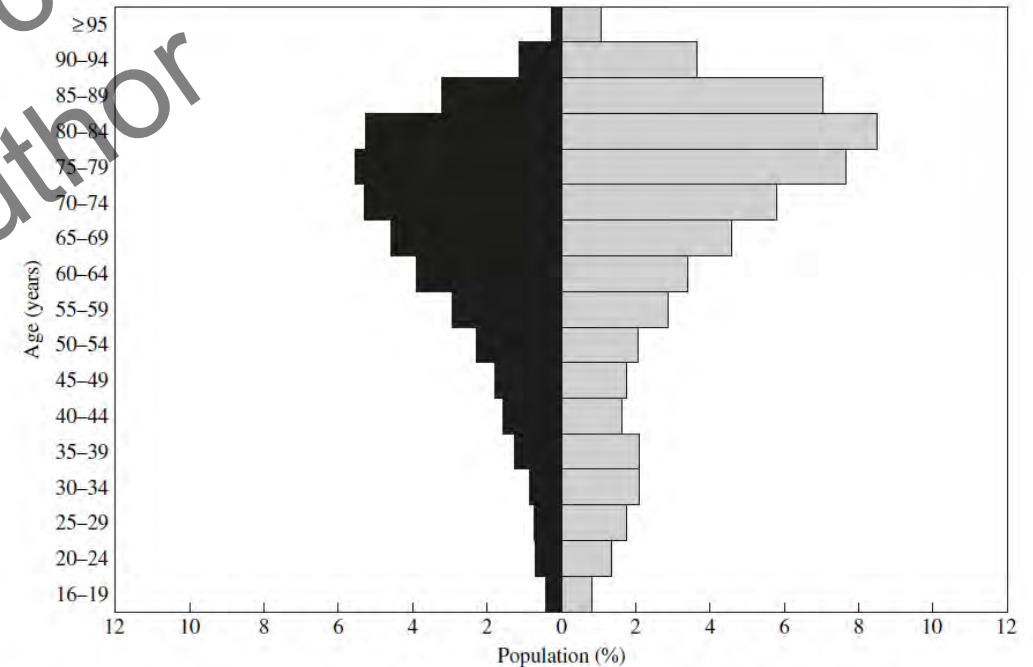


Figure 1 Acute hospitals: inpatients surveyed by age group and sex (N = 11 608). Black bars, males; grey bars, females.

Nosocomial infections and prevalence studies

- No difference in the incidence of gender
- Admittance F > M
- No adjustment for age or other covariates

Table I Acute hospitals: number and percentage of healthcare-associated infection (HAI) cases by HAI type

HAI type	Infections	
	No.	%
Bone and joint	6	0.5
Blood stream	55	4.4
Central nervous system	2	0.2
Cardiovascular system	11	0.9
Eye, ear, nose, throat or mouth	155	12.5
Gastrointestinal	191	15.4
Lower respiratory tract infection other than pneumonia	139	11.2
Pneumonia	109	8.8
Reproductive	17	1.4
Systemic	2	0.2
Surgical site	197	15.9
Skin and soft tissue	137	11.0
Urinary tract	222	17.9
Total	1243	100.0

Table II Acute hospitals: prevalence of healthcare-associated infection (HAI) in eligible inpatients by specialty

Specialty	Inpatients with HAI N	HAI prevalence within specialty %	95% CI	
			Lower	Upper
Care of the elderly	199	11.9	10.0	13.7
Dentistry	2	12.5	4.1	20.9
Gynaecology	10	4.8	1.2	8.4
Haematology	8	6.7	2.0	11.3
Medicine	491	9.6	8.5	10.7
Obstetrics	4	0.9	0.0	1.9
Oncology	12	8.8	2.0	15.7
Orthopaedics	105	9.2	7.3	11.1
Other	0	0.0	—	—
Psychiatry	9	3.5	0.3	6.7
Surgery	247	11.2	9.5	12.9
Urology	16	6.3	3.0	9.5
Total	1103	9.5	8.8	10.2

CI, confidence interval.

Reilly et al., J Hosp Infect 2008

Association of age, sex and HAI

- 2009-11; database Medicare Patient Safety Monitoring System, n=85 461
- Population: Patient groups at risk (Acute cardiovascular disease, pneumonia, major surgery)
- Primary aims:
 - Influence of gender/sex on HAI
 - Influence of age on HAI

Eckenrode et al., ICHE2014

Association of age, sex and HAI

- HAI:
 - Central line associated blood stream infection (CLABSI)
 - Postoperative pneumonia
 - Catheter associated urinary tract infection (CAUTI)
 - Sterile site hospital-acquired methicillin-resistant Staphylococcus aureus (MRSA)
 - Hospital-acquired Clostridium difficile
 - Ventilator-associated pneumonia

Eckenrode et al., ICHE2014

Association of age, sex and HAI demographic data

TABLE 1. Patient Characteristics

Characteristic	Aggregate (n = 85,461)	Female sex			Male sex		
		Age 18–44 years (n = 5,218)	Age 45–64 years (n = 12,988)	Age ≥65 years (n = 28,189)	Age 18–44 years (n = 2,789)	Age 45–64 years (n = 12,896)	Age ≥65 years (n = 23,381)
Percentage of aggregate patients	100.0	6.1	15.2	33.0	3.3	15.1	27.4
Condition							
Acute cardiovascular disease							
Proportion	35,270/85,461	507/35,270	3,521/35,270	12,908/35,270	985/35,270	6,090/35,270	11,259/35,270
Percentage	41.3	1	10	37	3	17	32
Pneumonia							
Proportion	25,034/85,461	1,229/25,034	3,403/25,034	8,486/25,034	1,122/25,034	3,176/25,034	7,618/25,034
Percentage	29.3	5	14	34	4	13	30
Major surgery							
Proportion	25,157/85,461	3,482/25,157	6,064/25,157	6,795/25,157	682/25,157	3,630/25,157	4,504/25,157
Percentage	29.4	14	24	27	3	14	18
Comorbidity, % of patients							
Cancer	19.3	6.2	14.8	21.2	5.7	13.4	27.3
Diabetes	35.2	12.7	34.4	36.7	19.5	36.2	40.2
Obesity	23.3	27.0	35.4	19.7	27.9	28.1	17.0
Cerebrovascular disease	16.2	2.3	8.8	21.6	3.5	9.9	21.9
CHF/pulmonary edema	40.9	8.5	24.4	51.9	21.3	30.9	51.7
COPD	30.6	7.1	26.2	33.7	10.3	26.2	39.6
Smoking	23.8	36.9	33.5	11.6	47.6	27.7	16.5
Renal disease	25.7	5.4	14.2	29.8	14.1	19.7	36.6

Association of age, sex and CAUTI

TABLE 2. Rates of Catheter-Associated Urinary Tract Infection (CAUTI)

Variable	No. of patients with CAUTIs/no. of patients at risk (% [95% CI])		
	Age 18–44 years	Age 45–64 years	Age ≥65 years
Pneumonia			
Male	5/156 (3.2 [1.2–7.5])	11/723 (1.5 [0.8–2.7])	81/2,113 (3.8 [3.1–4.7])
Female	7/142 (4.9 [2.2–10.0])	29/778 (3.7 [2.6–5.3])	115/2,663 (4.3 [3.6–5.2])
Acute cardiovascular disease			
Male	3/138 (2.2 [0.5–6.5])	33/1,208 (2.7 [1.9–3.8])	142/3,347 (4.2 [3.6–5.0])
Female	9/121 (7.4 [3.8–13.7])	55/1,099 (5.0 [3.9–6.5])	355/5,315 (6.7 [6.0–7.4])
Major surgery			
Male	8/577 (1.3 [0.7–2.8])	29/3,011 (1.0 [0.7–1.4])	103/3,809 (2.7 [2.2–3.3])
Female	16/3,242 (0.5 [0.3–0.8])	75/5,287 (1.4 [1.1–1.8])	218/5,632 (3.9 [3.4–4.4])

NOTE. CI, confidence interval.

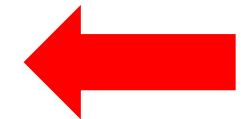
Eckenrode et al., ICHE2014

Association of age, sex and HAI

TABLE 3. Composite Rates of Other Hospital-Acquired Infections (HAIs)

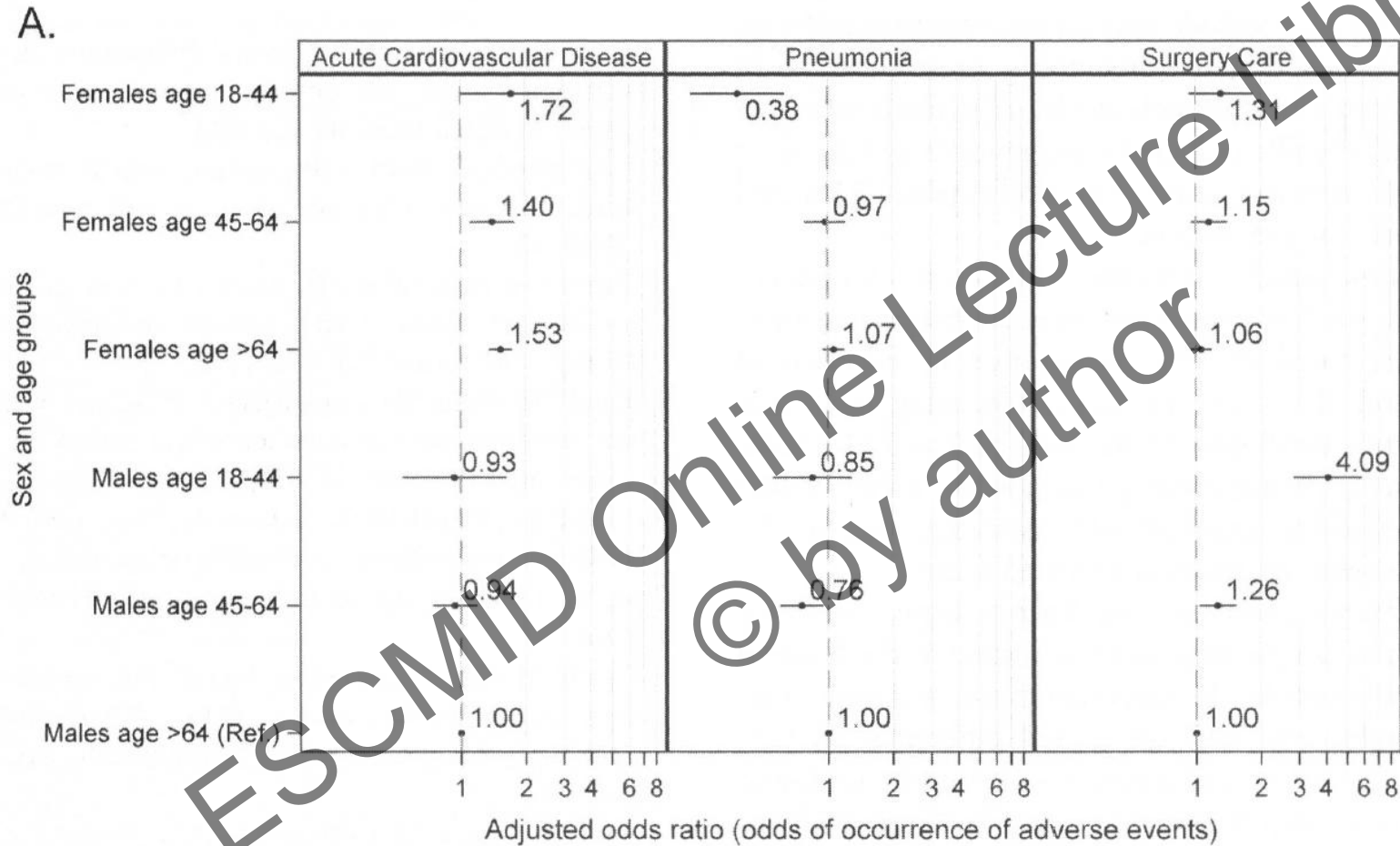
Variable	No. of patients with infection/no. of patients at risk (% [95% CI])		
	Age 18–44 years	Age 45–64 years	Age ≥65 years
Pneumonia			
Male	11/2,225 (0.5 [0.3–0.9])	39/6,294 (0.6 [0.5–0.9])	98/14,826 (0.7 [0.4–1.3])
Female	0/2,431 (0.0 [0.0–0.2])	36/6,771 (0.5 [0.4–0.7])	92/16,566 (0.6 [0.2–1.1])
Acute cardiovascular disease			
Male	6/1,361 (0.4 [0.2–1.0])	48/9,215 (0.5 [0.4–0.7])	101/17,632 (0.6 [0.3–1.1])
Female	1/750 (0.1 [0.0–0.8])	25/5,400 (0.5 [0.3–0.7])	58/20,234 (0.3 [0.1–0.7])
Major surgery			
Male	26/2,149 (1.2 [0.8–1.8])	99/11,451 (0.8 [0.4–1.6])	205/14,364 (1.4 [1.0–2.2])
Female	26/10,388 (0.2 [0.1–0.8])	81/18,493 (0.4 [0.2–0.9])	216/21,114 (1.0 [0.7–1.6])

NOTE. Includes the following HAIs: catheter-associated bloodstream infection, hospital-acquired *Clostridium difficile*, sterile site methicillin-resistant *Staphylococcus aureus*, postoperative pneumonia, and ventilator-associated pneumonia. CI, confidence interval.



Eckenrode et al., ICHE2014

Association of age, sex and HAI



Eckenrode et al., ICHE2014

Association of age, sex and HAI

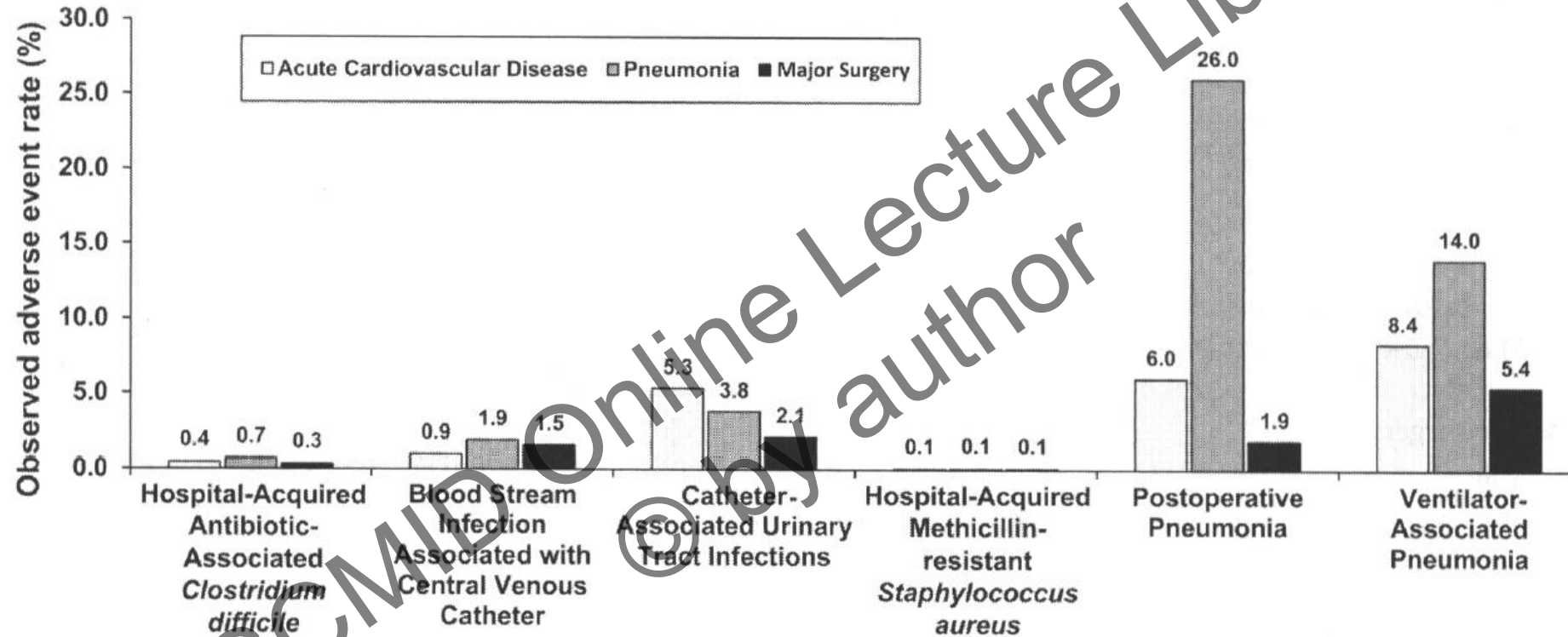


FIGURE 1. Observed adverse event rate, age 18 years and older, both sexes, by condition.

Eckenrode et al., ICHE2014

Association of age, sex and HAI conclusions

- HAI not age-associated but comorbidity-ass.
- HAI and gender/sex
 - CA-UTI: $F > M$
 - Cardiovascular disease: $F > M$
 - Pneumonia: $F = M$
 - Surgical patients: $F = M$
- Outcome of HAI similar in sex and age groups

Eckenrode et al., ICHE2014

HAI in long-term care facilities

gender aspects

- Netherlands, n=1429, HAI: n=40, prevalence 2.8%, female n=31, most common: UTI n=10, antibiotic use n=50, f=32

Potential determinant	Relative risk (95% CI)
Sex (men vs women)	0.43 (0.21–0.91)
Aged >85 years	1.62 (0.87–2.99)
Had a urinary catheter	1.62 (0.83–2.42)
Had pressure wounds*	2.58 (1.04–6.39)
Had other wounds*	5.70 (2.99–10.86)
Disorientated	0.58 (0.31–1.07)
Incontinent	0.96 (0.51–1.79)
Had an operation in the past 30 days	2.49 (0.80–7.79)
Wheelchair bound or bedridden	NA ^a

Eilers et al., Euro Surv 2011

HIV and HAI

- New York cohort, n=1911 (3877 discharges), 2006-2008
- UTI n=142, BSI n=106, RTI n=100,
- Incidence rate UTI 4.35, BSI 3.16, RTI 2.98

Predictors		Crude OR	Adjusted OR
UTI	Female sex	1.52 (1.06-2.59)	2.12 (1.28-3.51)
	Urinary catheter	4.06 (2.93-5.61)	2.54 (1.56-4.12)
	Steroids	2.38 (1.73-3.28)	1.75 (1.1-2.78)
	TMP-SMX	3.49 (1.76-6.91)	2.55 (1.22-5.34)
BSI	CVC	3.75 (2.37-5.92)	1.10 (0.53-2.27)
	Steroids	3.76 (1.70-8.32)	1.90 (1.08-3.32)
	TMP-SMX	3.49 (1.76-6.91)	3.19 (1.41-7.22)
RTI	ETT	9.58 (5.87-15.63)	7.06 (3.20-15.61)
	Steroids	4.16 (2.79-6.20)	2.53 (1.46-4.40)
	TMP-SMX	7.02 (2.46-20.01)	5.15 (1.70-15.62)

Mitha et al., J Infect Prev 2014

Point prevalence survey of HAI and antimicrobial use in European acute care hospitals

- 2011 – 2012, n=273 753, HAI prevalence 6%
 - Male gender 6.9%, Adjusted OR 1.1 (1.1-1.2)
- Gender/sex differences:
 - Antibiotic use: male gender 1.2 (1.1 – 1.2)

ECDC, 2013, Surveillance report „Point prevalence survey of HAI and antimicrobial use in European acute care hospitals 2011-12)



Conclusions

- Data on HAI and gender/sex are still limited
- Results are conflicting/controversial
 - Association varying
 - Why?
 - In depth analyses missing
- FUTURE ?
 - Prospective data on the gender aspect in large epidemiological studies
 - Research on sex influence in infections and immune response