

Clostridium difficile infection in the elderly

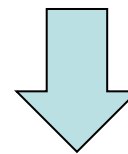
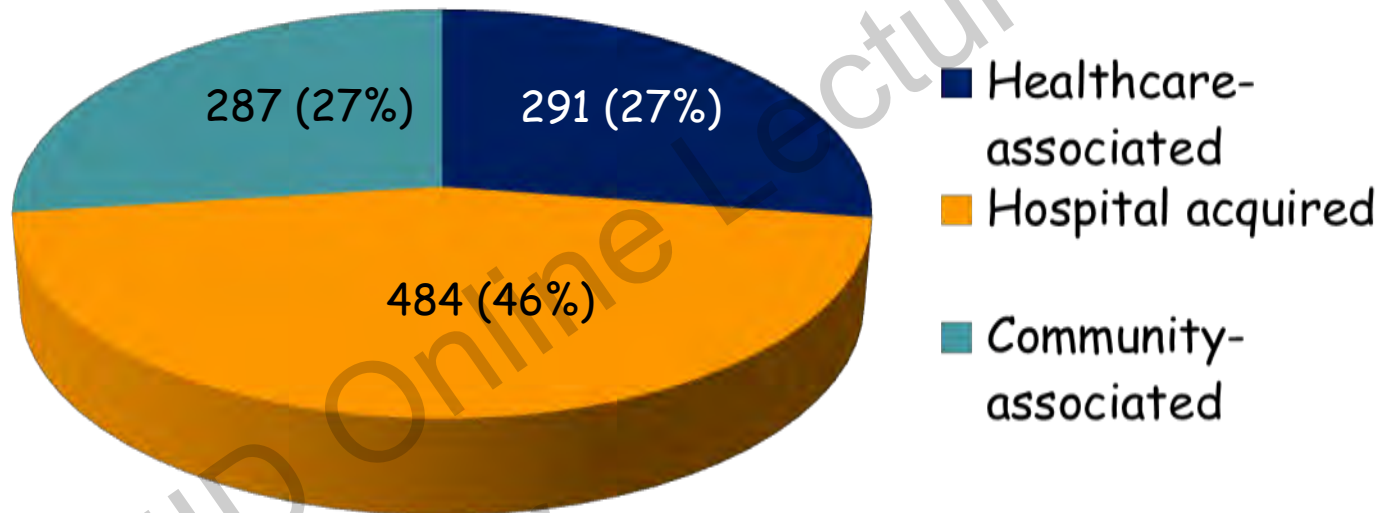
Infection prevention and management in long-term care facilities

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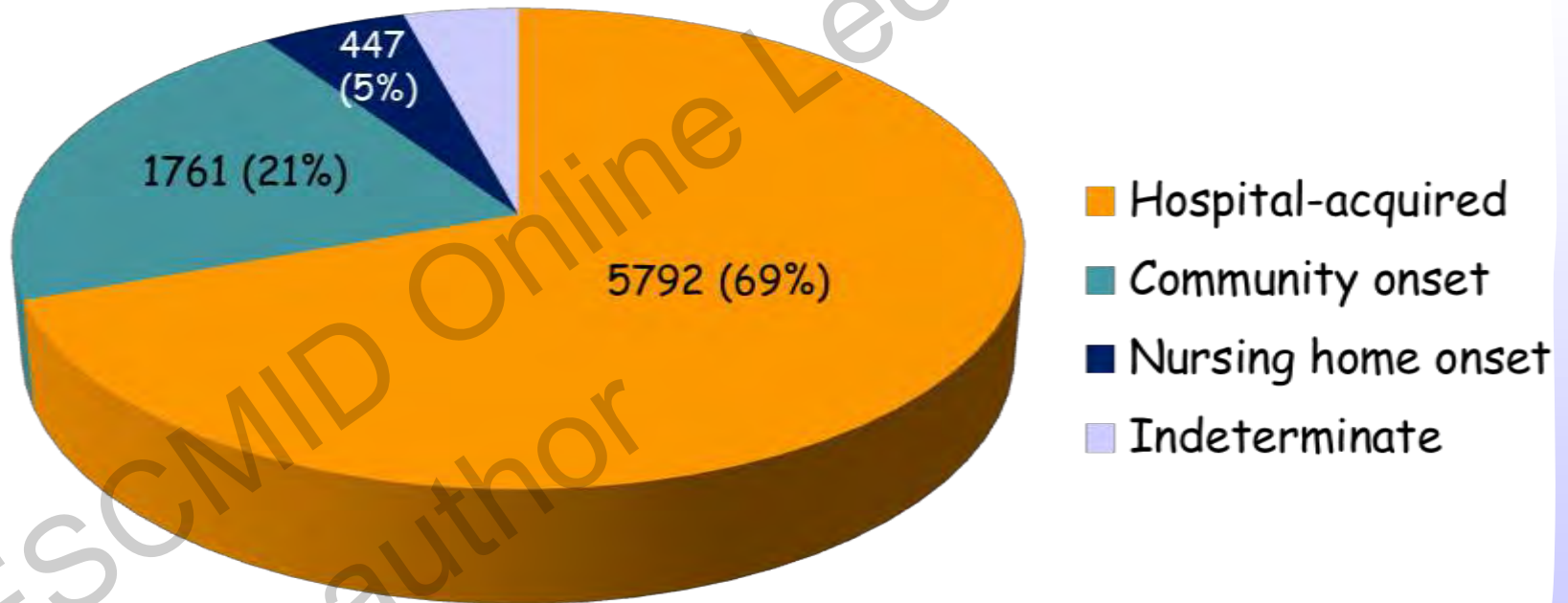
Epidemiology of hospitalized CDI



54.4% detected <48hr after admission

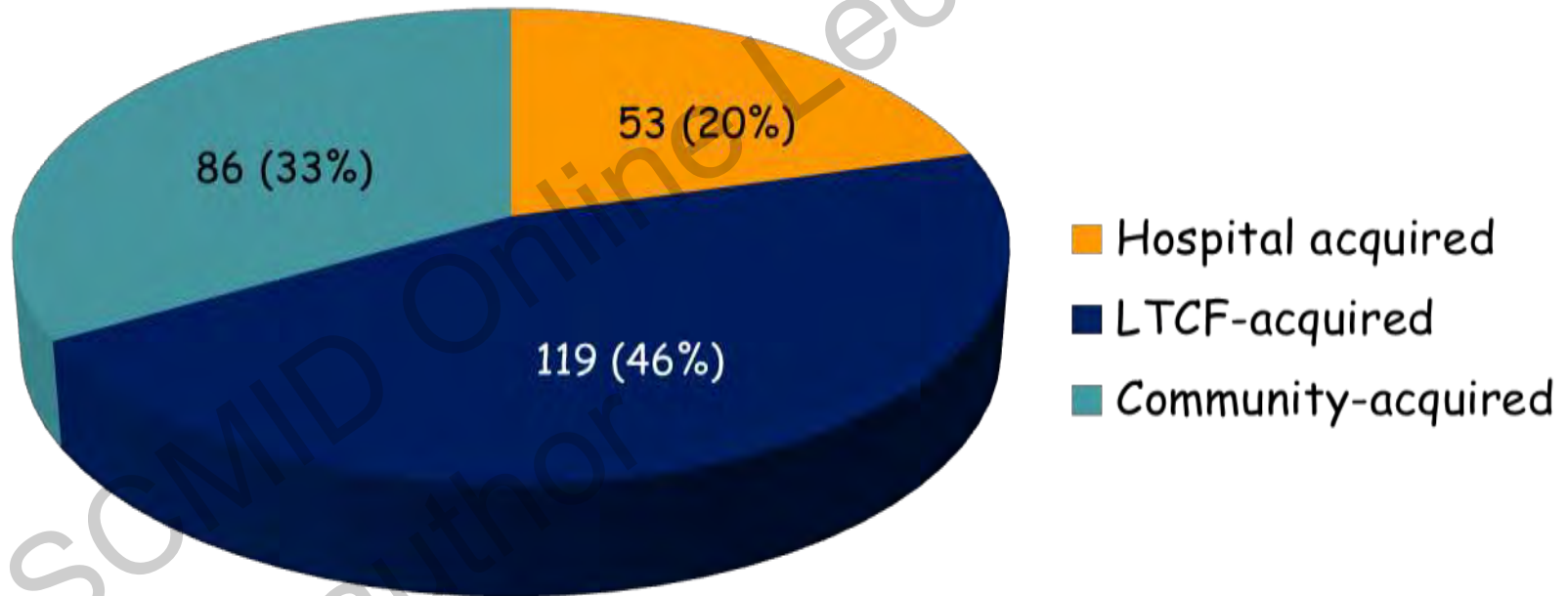
Jarvis, et al. Am J Infect Control. 2009 May;37(4):263-70. US, national point prevalence survey of acute care hospitals

Epidemiology of hospitalized CDI



Viseur et al. Euro Surveill. 2011;16(43). Belgium, acute care hospitals, CDI definitions applied on compulsory surveillance data

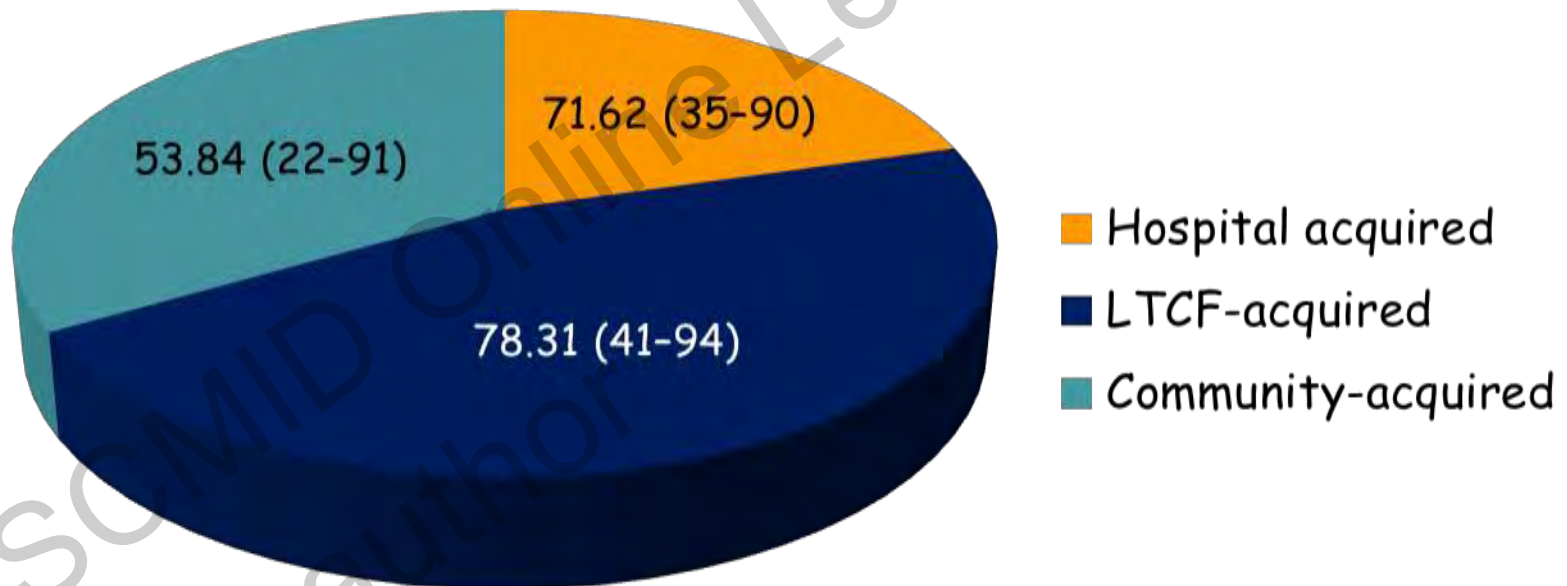
Epidemiology of hospitalized CDI



Garg et al. Dig Dis Sci 2013 58:3407-3412. US, Baltimore, Single hospital, cohort of inpatients with CDI

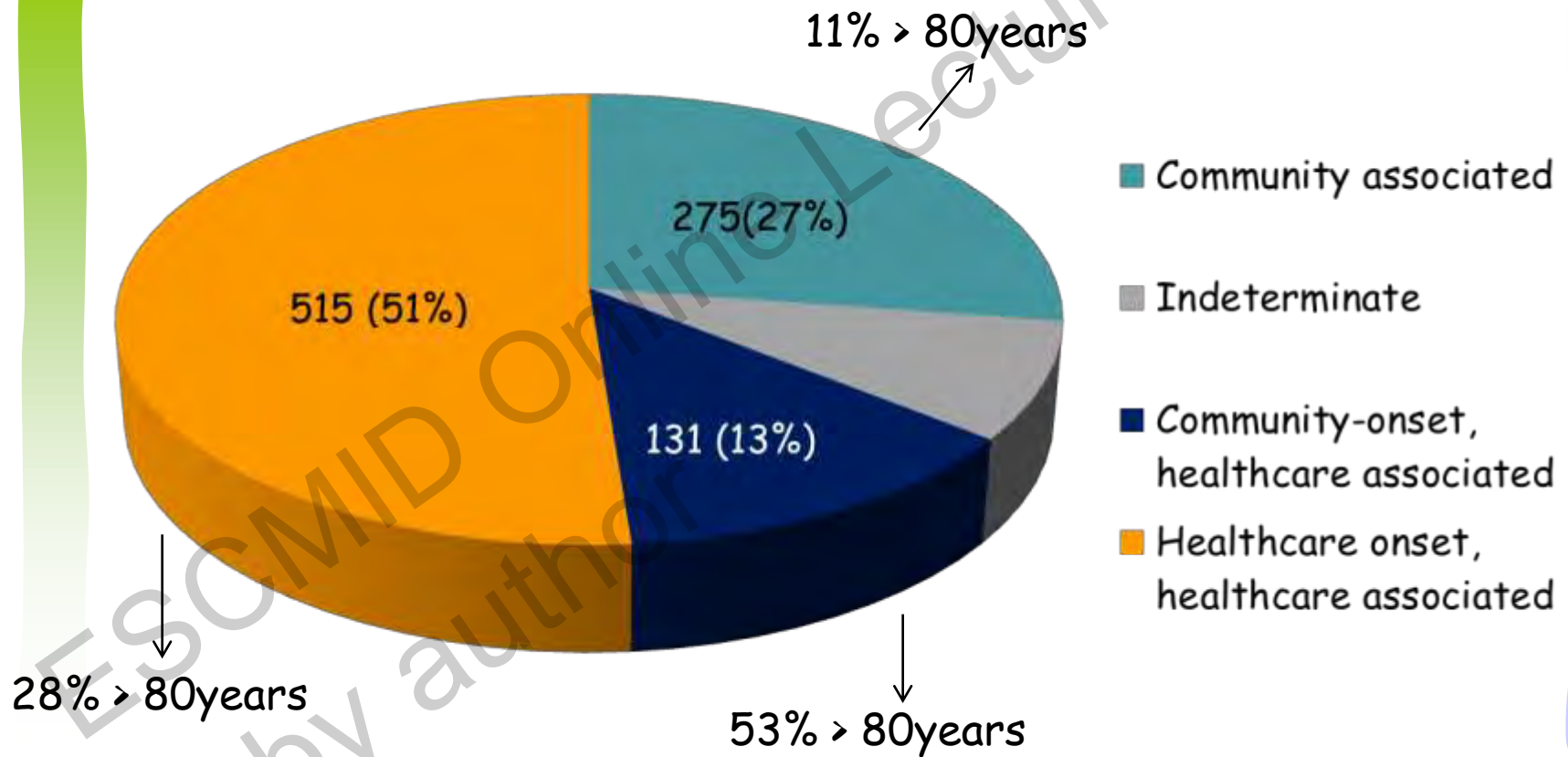
Epidemiology of hospitalized CDI

Age (mean, range) by place of acquisition



Garg et al. Dig Dis Sci 2013 58:3407-3412. US, Baltimore, Single hospital, cohort of inpatients with CDI

Epidemiology of hospitalized CDI

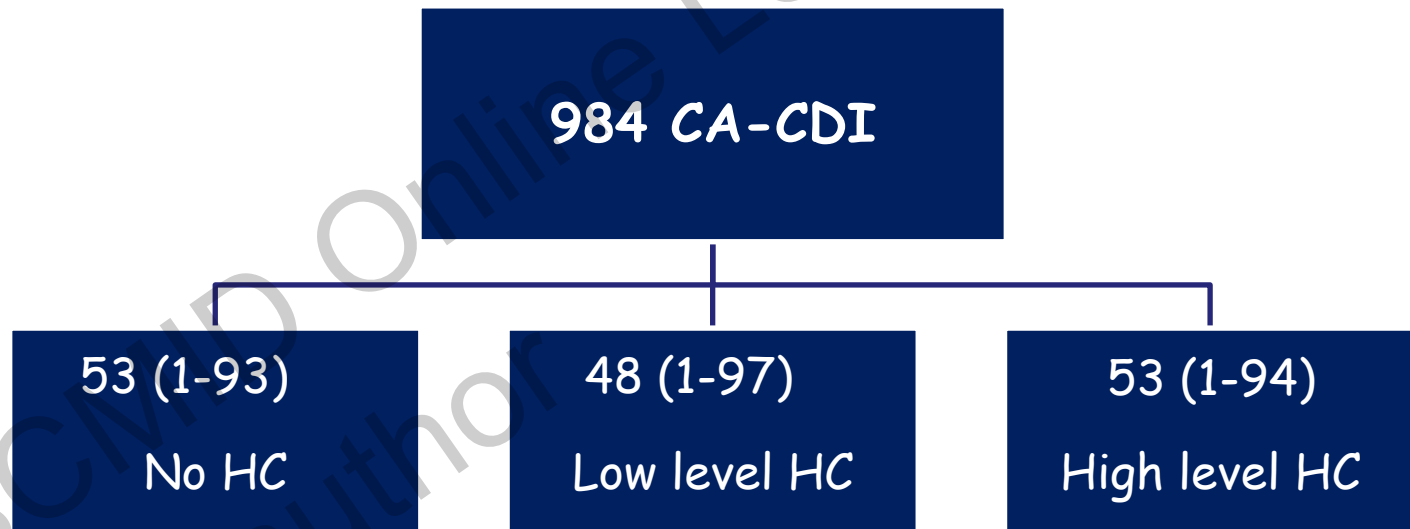


Lambert, et al. Infect Control Hosp Epidemiol. 2009 30(10):945-51. Canada, Manitoba, mandatory laboratory reporting

Who are the purely community-acquired cases?

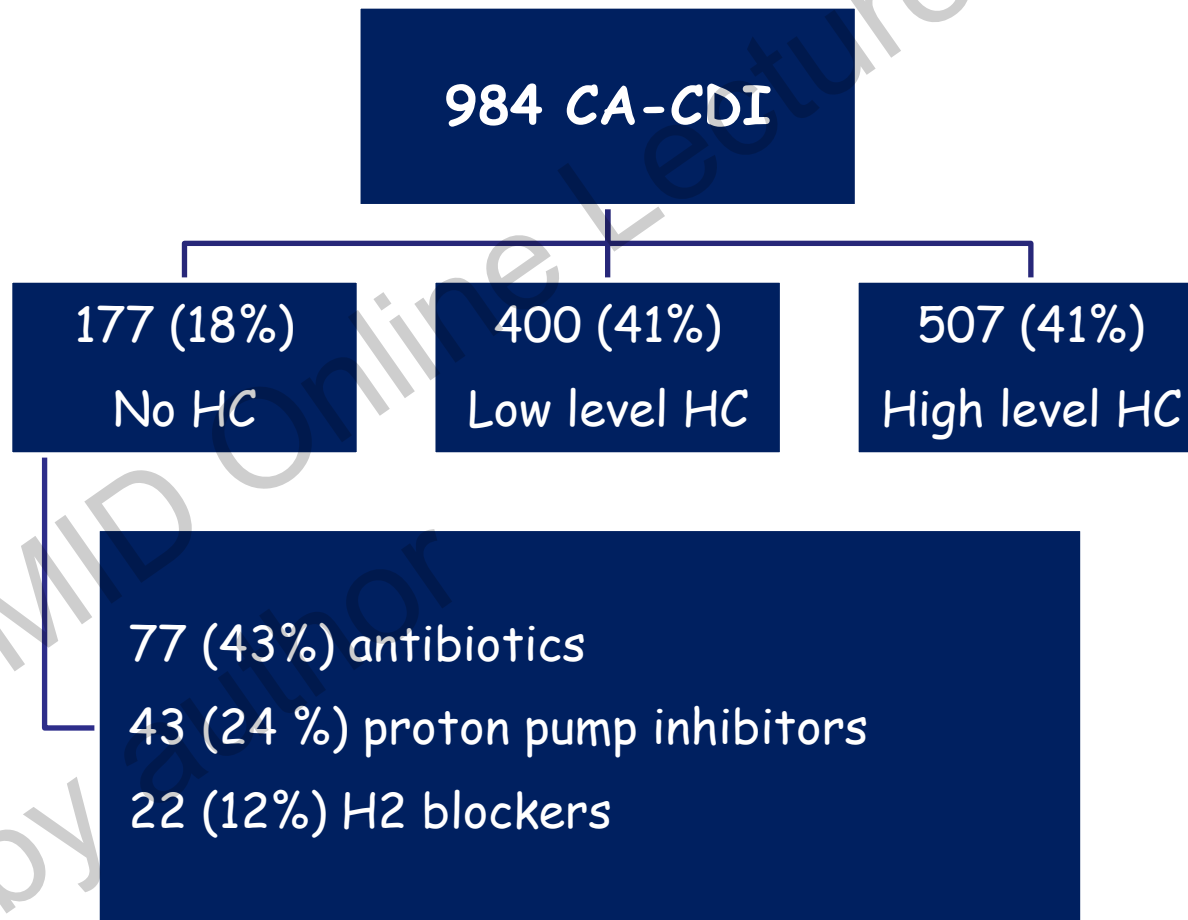
- Community-associated CDI, excluding overnight stay in long-term care facility or acute care hospital stay in the 12 weeks before infection
- Outpatient health care exposure classified:
 - None
 - Low-level: outpatient visit with physician or dentist
 - Higher level: hospital exposure without overnight stay or healthcare personnel

Factors associated with community-acquired CDI



Median patients' age young and not related to healthcare exposure

Factors associated with community-acquired CDI



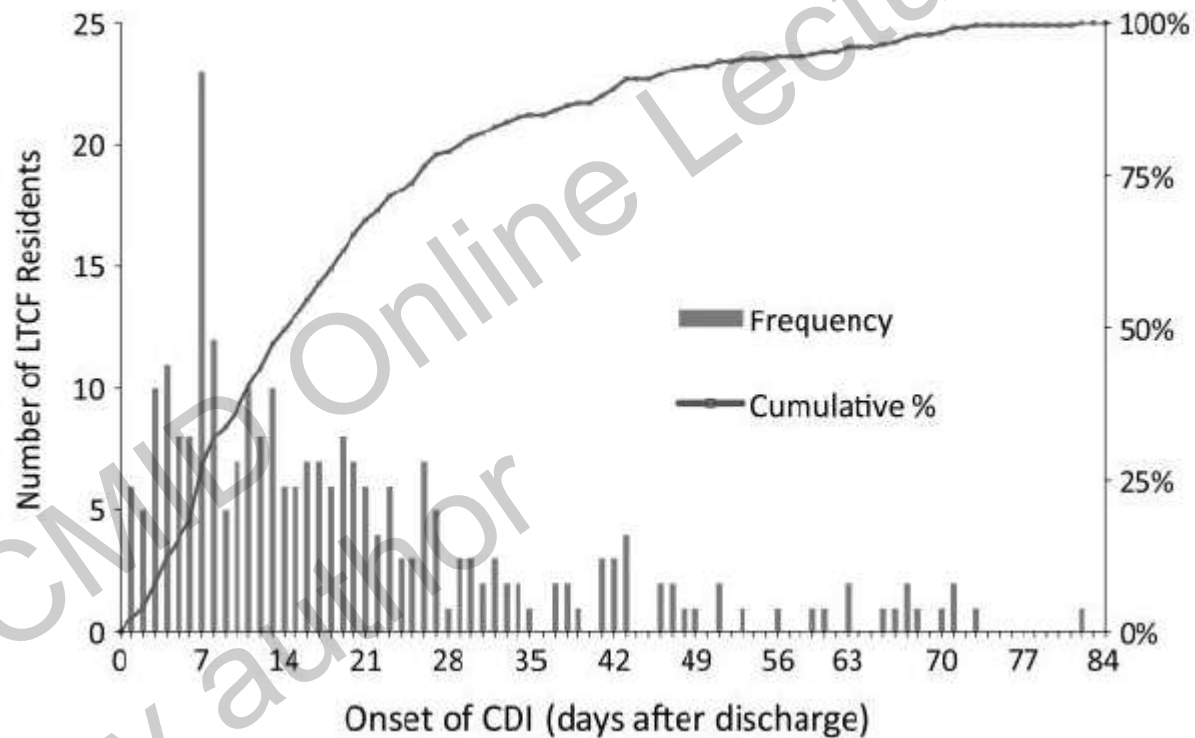
Independent risk factors for community acquired CDI with no or low level healthcare exposure

	No HC exposure	Low level HC exposure
Infant <1yr at home	1.8 (0.7-4.6)	2.1 (1.1-4.5)
Household member with CDI	6.8 (0.7-65.9)	6.9 (0.9-56.7)

Incidence in acute care hospitals vs. LTCFs

Location, design	Cases per 10,000 PD	
	Acute care	LTCF
France, MC survey	2.28	1.15
Monroe County, New York, population based surveillance	9.2 (10,125 cases)	3.3 (estimated 10,300 cases)

Time of CDI onset in LTCF



Pawar 2012. Infect Control Hosp Epidemiol. 2012 33(11):1107-12. Monroe County, New York., population-based surveillance.

Common knowledge

- Age associated with
 - Higher CDI incidence
 - More complications
 - Higher mortality
 - More frequent relapses



Common knowledge

- Age associated with
 - Higher CDI incidence?
 - More complications
 - Higher mortality
 - More frequent relapses



Is age a risk factor for CDI?

Case control studies: No

	N patients	Matching criteria	CDI age	Non-CDI age
Hensgens 2012	564	Time, ward, diarrhea	61.8 ± 21.1	58.1 ± 21.4
Pakyz 2014	14,134	LOS, service	adjusted OR for age 0.98 (0.97-0.98)	
Modena 2005	250	AB Tx	57.5 ± 18.1	60.2 ± 16.9
Muto 2005	406	LOS, service, date	64 (17-95)	59 (16-93)
Søes 2013 (community)	714	Suspected Cdif	50 (2-94)	50 (2-90)
Leonard 2012	137	Suspected Cdif	60 ± 17	61 ± 20

Is age a risk factor for CDI?

Cohort studies: Yes

Study	N patients	Adjusted age association
Beaulieu 2007	827 MICU	Age ≥ 65 yrs. OR 2.33 (1.23-4.40) vs <65 yrs.
Carignan 2008	7,657 surgical	65-74 yrs. OR 2.4 (1.0 - 4.9); ≥ 75 yrs. OR 3.1 (1.4 - 6.8) vs. <65 yrs.
Dalton 2008	14,719 +antibiotics	OR per year 1.03 (1.01 - 1.04)
Garey 2009 *	41 224 +antibiotics	50-80 yrs. OR 1.5 (1.1 - 2.1); >80 yrs. OR 2.5 (1.7 - 3.7) vs. <50 yrs.
Dubberke 2011 *	35,350	OR per year 2.5 (1.9 - 3.3)
Chandra 2012 *	21,541	Age >65 yrs. received 3 points in a 16-point predictive score for CDI
Doernberg 2012	2,305 +antibiotics	HR per year 1.01 (0.99 - 1.03)
Ahyow 2013	93,190	65-84 yrs. OR 1.85 (1.11 - 3.09); >85 yrs. OR 2.14 (1.27 - 3.59) vs. <25 yrs.
Rodriguez 2014	12,026 >55 yrs.	OR per year 1.02 (1.01-1.03)

Where is the truth?

Cohort studies



Case-control studies

(Micro)biological risk?

The microbiota

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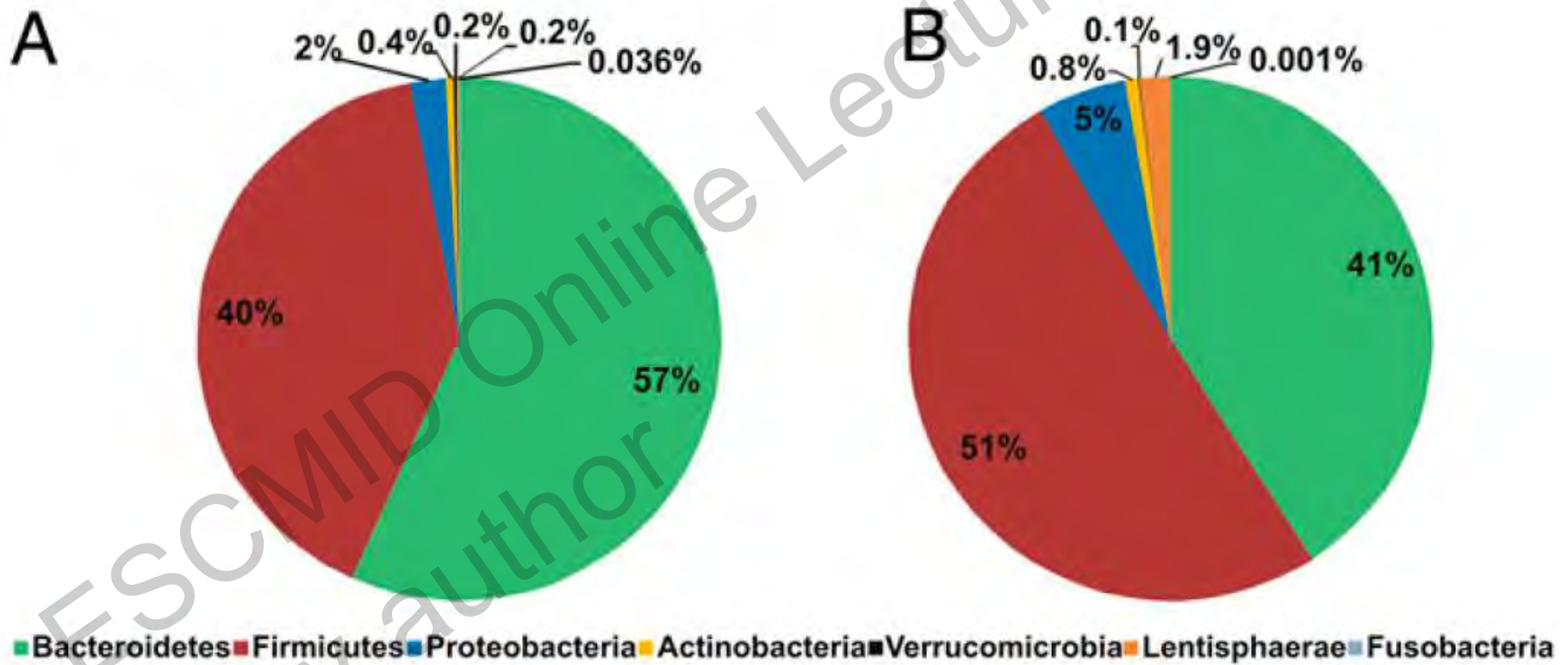
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Lecture Library

Microbiota of elderly vs. younger adults

- ELDERMET consortium, Ireland
- Comparison of the microbiota composition in elderly Irish people ≥ 65 yrs. and adults aged 28-46 yrs.
- People recruited in-hospital, some treated with antibiotics
- Composition of the fecal microbiota in each of the enrolled subjects was determined by sequencing over 40,000 16S rRNA gene V4 region amplicons
- Validated by comparison with a phylogenetic profiling microarray.

Phylum level microbiota composition: elderly vs. younger adults



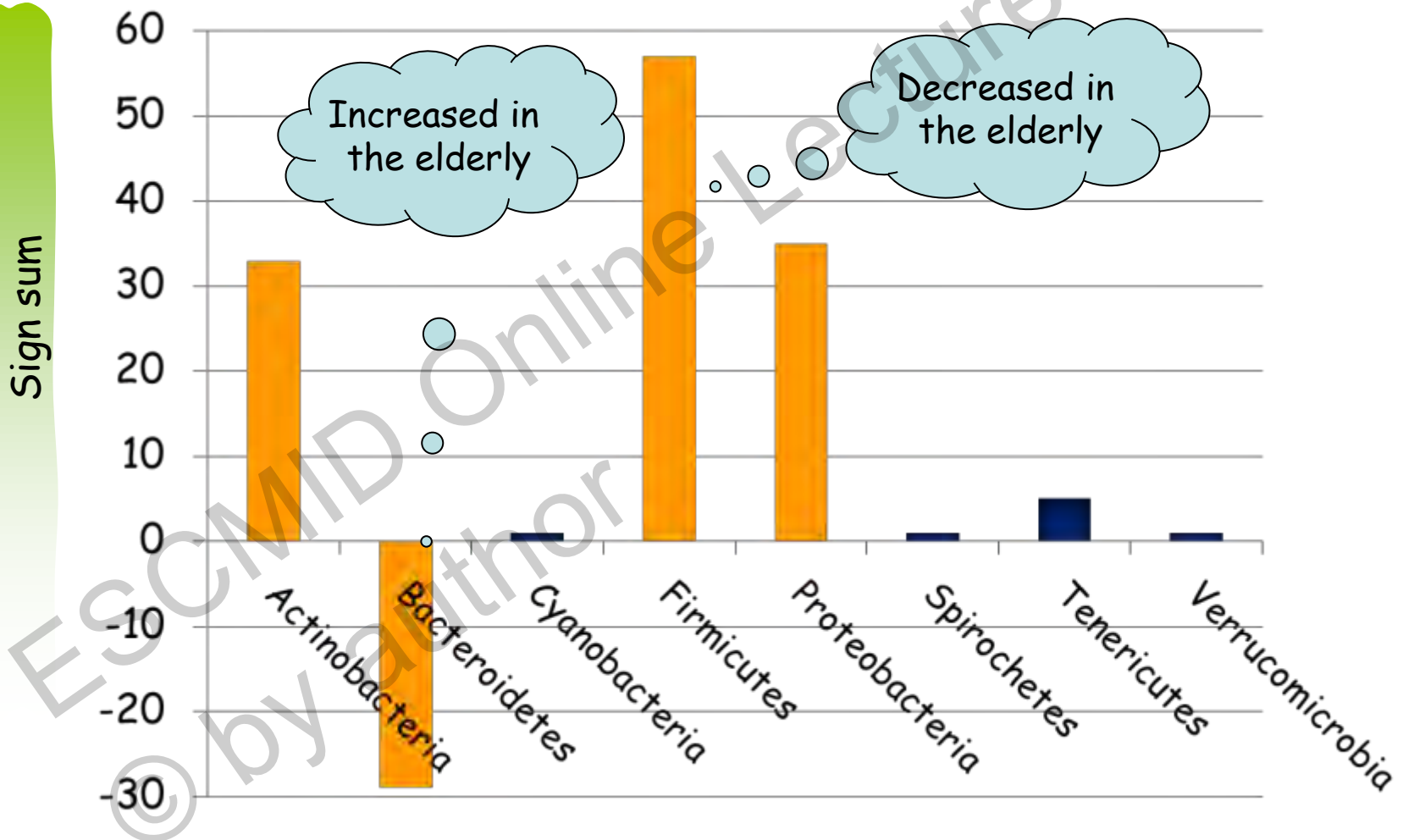
A. 187 elderly patients ≥ 65 yrs.

B. 9 younger adults 28 to 46 yrs.

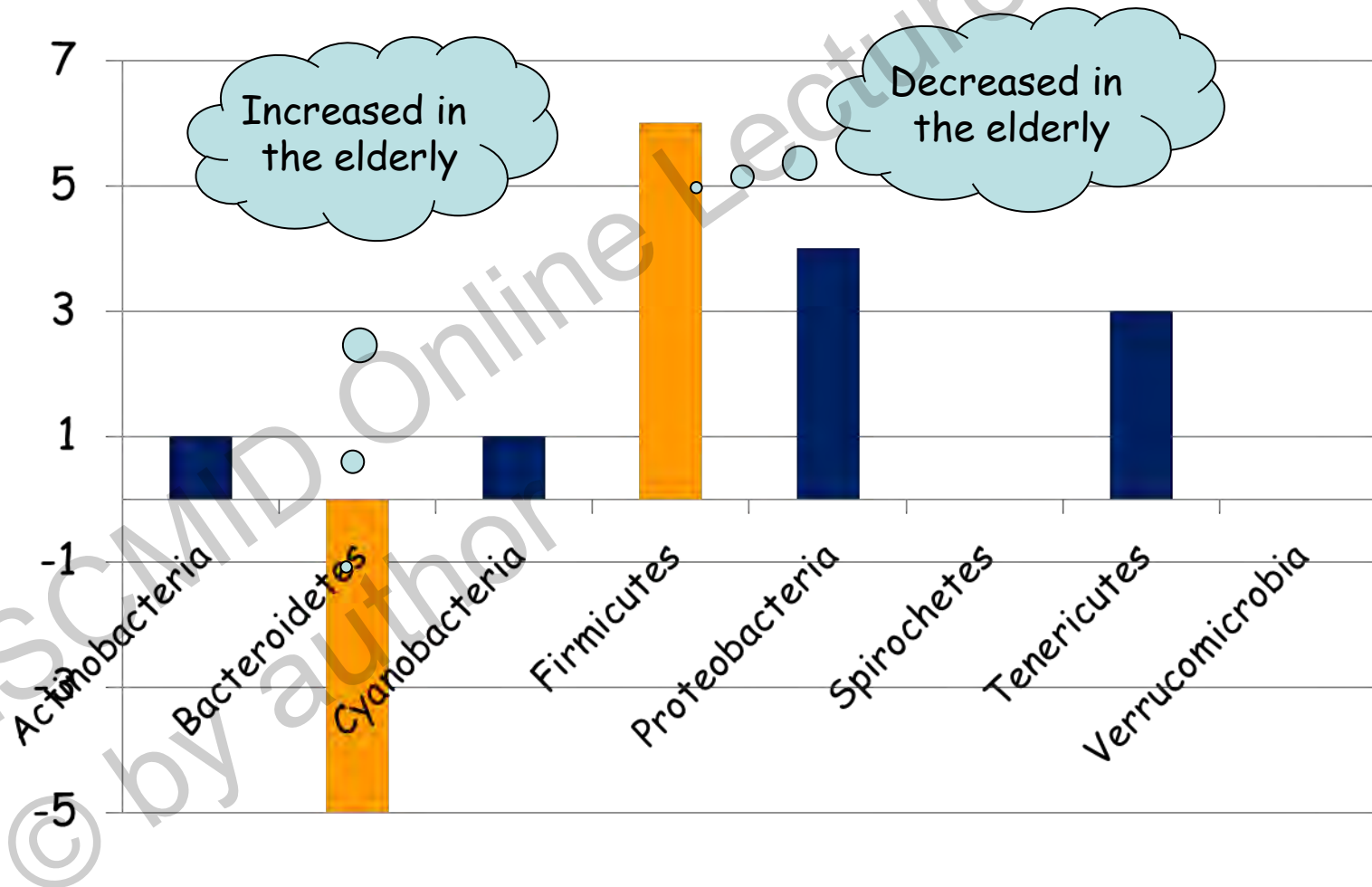
Who is prone to CDI microbiota-wise?

- Nested case-control study
- Stool samples taken from all cohort patients within 72 h of hospital admission
- Cases (N=25) developed CDI
- Controls (N=50) without CDI matched for age, sex, date and LOS
- Fecal specimens taken at admission evaluated by 16S ribosomal RNA microarray

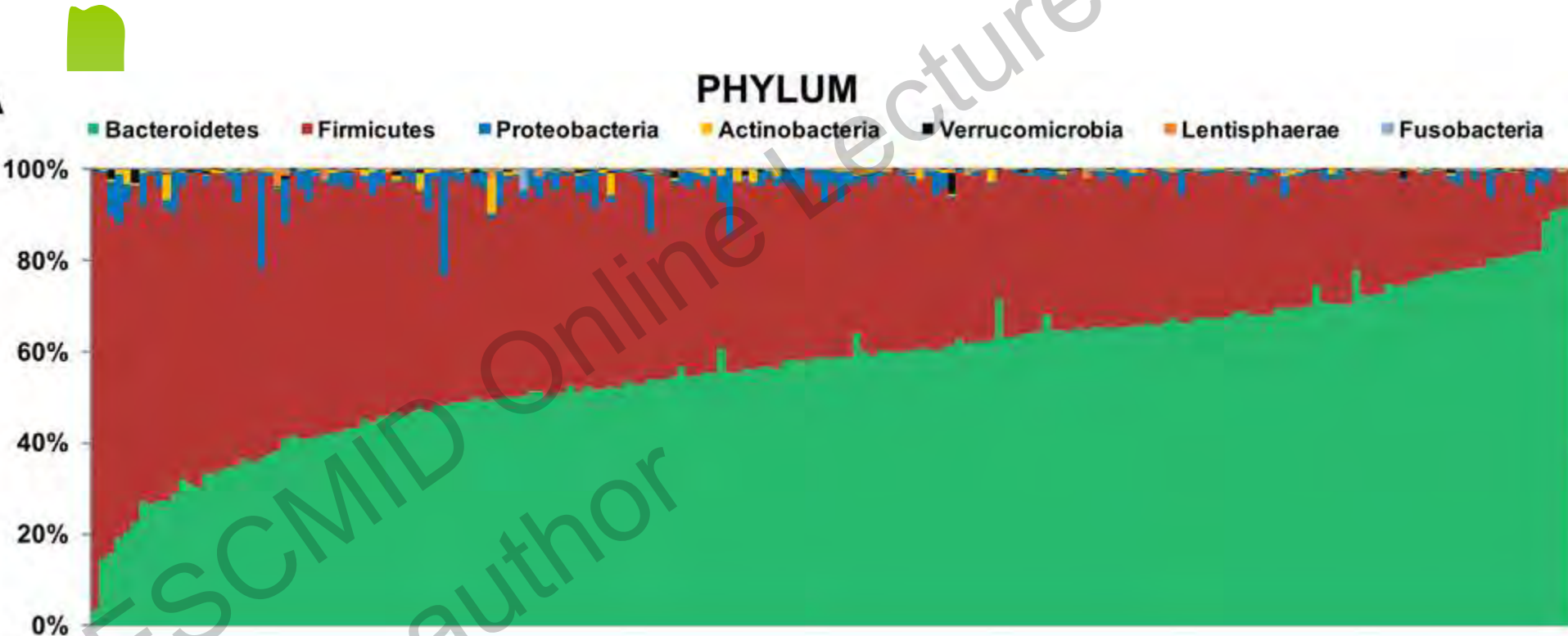
Unadjusted model: phyla level associations with subsequent CDI



Adjustment to epidemiological risk factors



Inter-individual microbiota variation: elderly people



Universal? No

- Cross sectional study of adults (20-50 yrs.) and elderly (>60 yrs.) in France, Germany, Italy, and Sweden
- Genus level analysis by 16S rRNA-targeted oligonucleotide probes
- Country-age interactions inverse for the predominant bacterial groups
- Bifidobacteria affected by country, not by age
- Enterobacteria more common in the elderly across countries

Common knowledge

- Age associated with
 - Higher CDI incidence
 - More complications
 - Higher mortality
 - More frequent relapses



Older age and mortality in CDI adjusted analysis

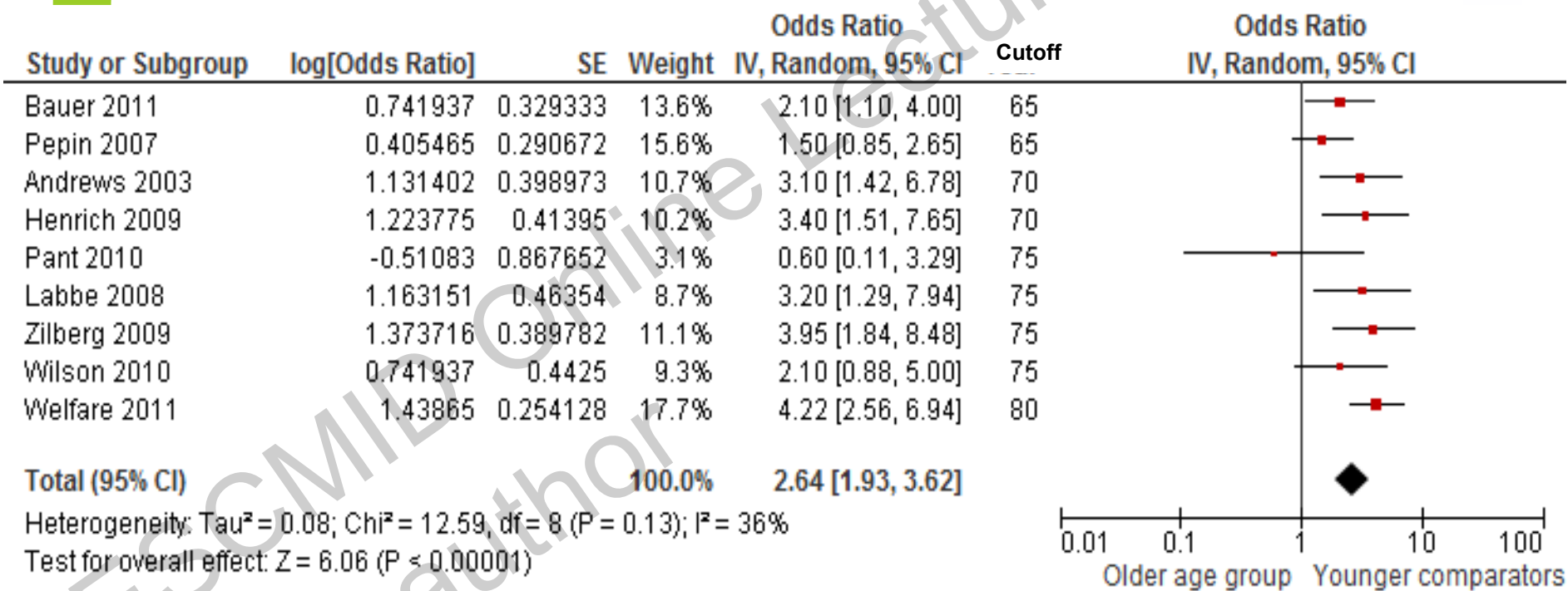
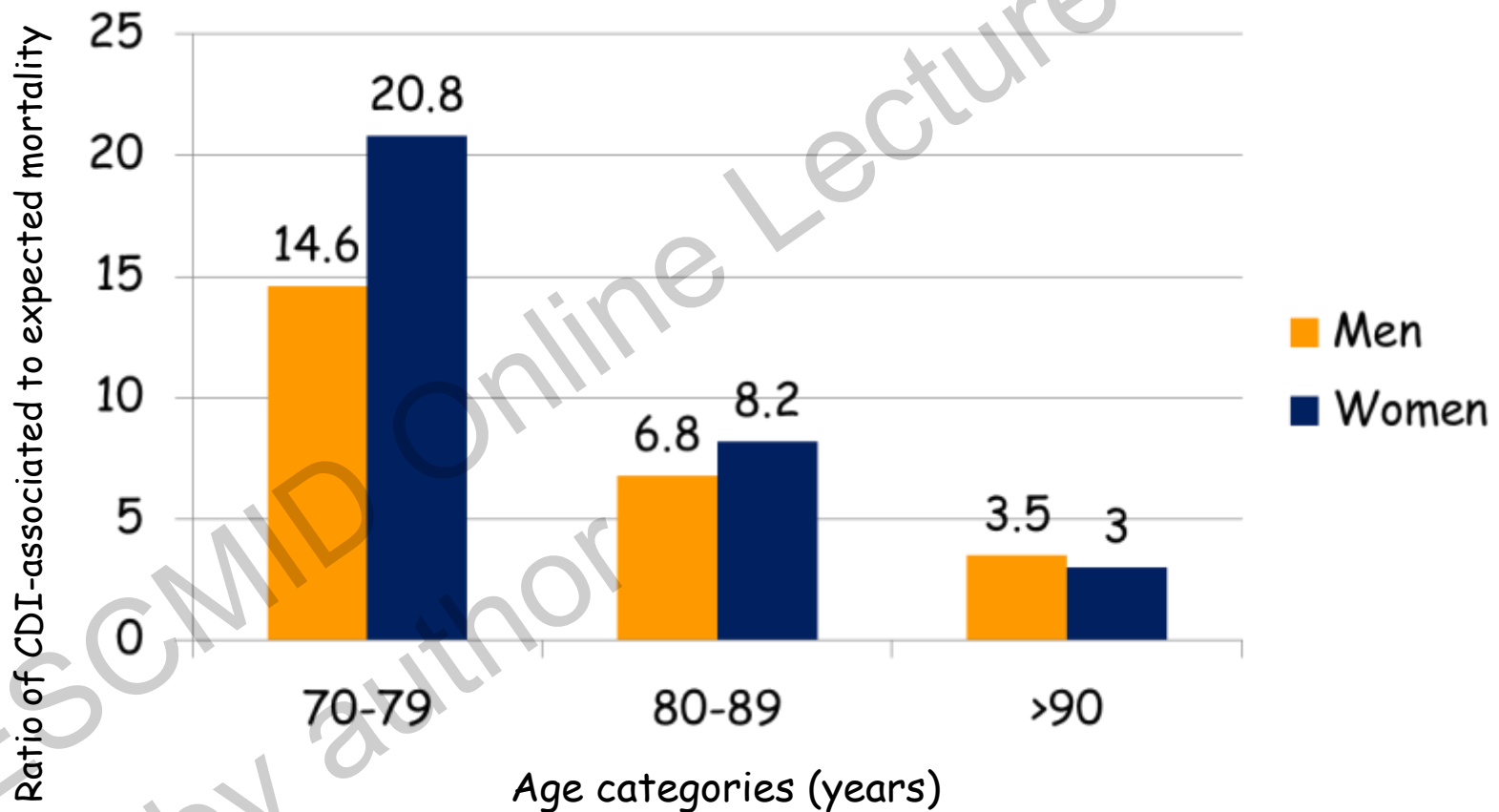


Figure taken from Bloomfield et al. J Hosp Infect. 2012; 82(1): 1-12 and additional studies

Standardized mortality rates in CDI

Ratios of CDI : population expected mortality



Age association with complicated CDI

Study	N patients	Association with complicated CDI	
Lungulescu 2011	255	No	No significant difference in mean age
Shivashanker 2013	1446	Yes	Adjusted OR 1.1 (95% CI 1.0-1.1), p=0.0029 for every 10-year increment
Hensgens 2014	395	Yes	Adjusted OR 5.15 (95% CI 1.66-16.0) for age >85 yrs. compared to <49 yrs. reference

Complicated CDI: ICU admission, colectomy, death due to CDI, prolonged hospital stay related to CDI, hypotension, shock, sepsis, ileus, megacolon, colon perforation.

Age association with CDI relapse

Study	N patients	Association with relapse	
Cadena 2010	128	No	Mean age with and without relapse 66.62 ±14.23 vs. 68.76± 13.86, NS, univariate
Freedberg 2013	894	Yes	Adjusted HR 1.02 (95% CI 1.01 - 1.03) per each additional year
D'Agostino 2014	922	Yes	Adjusted OR for age ≥75 yrs. 1.21, p=0.05 (vs. <75 yrs.). Age ≥75 yrs. assigned 1 point in a 4-point risk score
Zilberberg 2014	425	Yes	Adjusted OR 1.08 (95% CI 1.02-1.14) per 10 year increment

Summary

- Elderly patients probably do not have an inherent higher risk for CDI than other people
 - However, CDI is more common in the elderly due to healthcare and antibiotic exposure
- Complicated disease, relapse and mortality are more frequent in the elderly
 - Probably related to same exposures
 - Frailty, immune dysfunction, nutritional status

Opportunities for risk reduction

- Do not treat asymptomatic bacteriuria
 - Avoid redundant catheterization
- Infected decubitus ulcers respond to local treatment
 - Avoid decubitus ulcers
- Diarrhea usually does not necessitate antibiotic treatment
- Stop antibiotics, other than Cdif treatment, when treating CDI whenever possible
- Home > LTCF > Hospitalization

Thank you

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