

Bloodstream Infection Epidemiology: Population- based Studies

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Objective

- Review the value of using population-based studies in defining the epidemiology of bloodstream infections (BSI)

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Bloodstream Infection

- Bacteremia-growth of an organism from one or more blood culture bottles
 - Contamination (not a true bacteremia)
 - Transient bacteremia (bacteremia but of no significance)
 - Bloodstream infection (bacteremia associated with infection)

Surveillance

- Ongoing, systematic collection, analysis and interpretation of health data for public health purposes
(<http://www.cdc.gov/ncidod/osr/index.htm>).
 - Define burden of disease
 - Evaluate risk factors
 - Monitor temporal trends in occurrence and resistance
 - Emerging pathogens
 - Assessment of preventive interventions

Population-based studies

- All residents within a defined geographical region represent the base study population (denominator)
- May be restricted (ie age, gender, organism)
- May include all cases or infer from unbiased random sampling
- But NOT all patients presenting a selected hospital, clinic etc

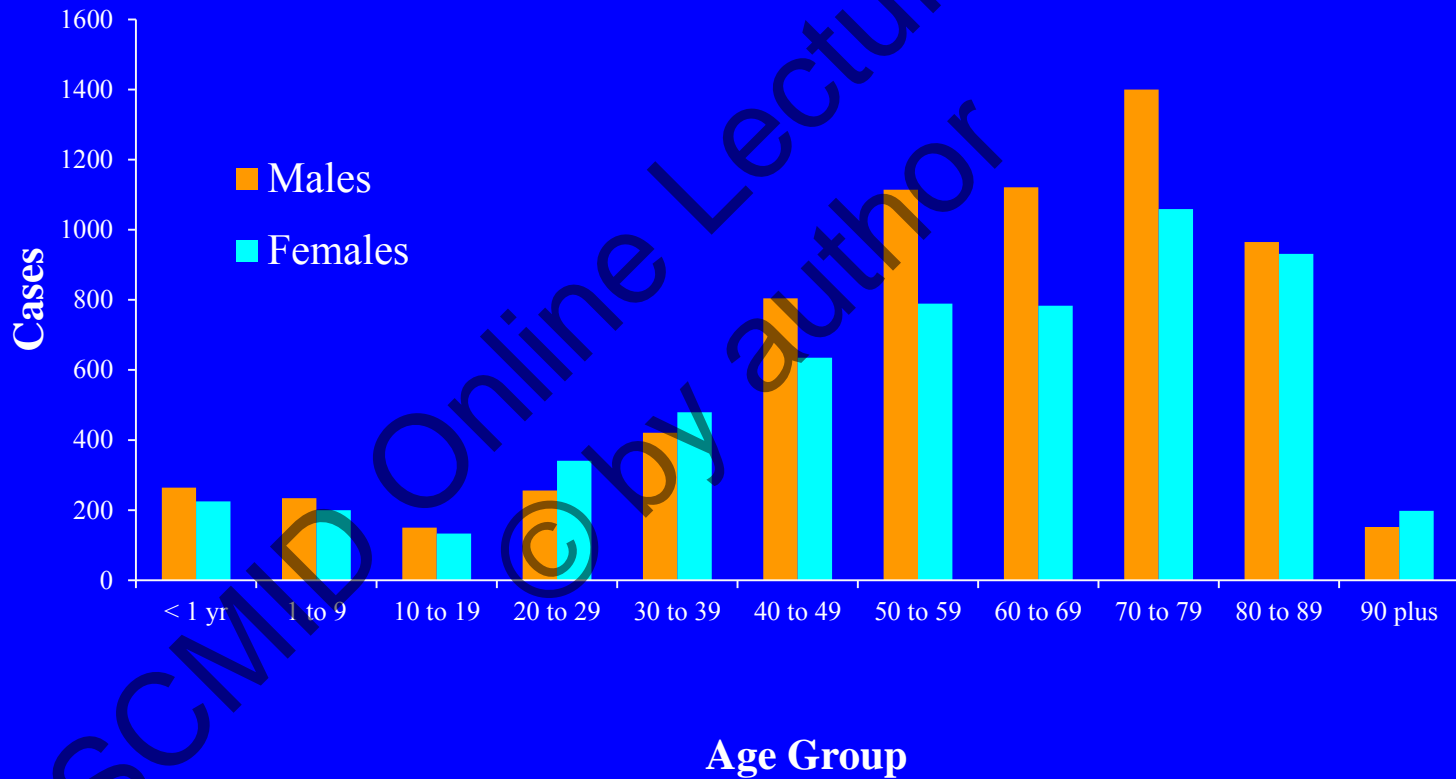
Filice et al. *Am J Epidemiol* 1986; 123:128-136.

- Residents of Charleston County, South Carolina during 1974-1976
- Captive population isolated from other major metro areas
- All six microbiology labs serving community and nine hospitals
- 80 per 100,000/year; most common *E.coli*, *S. aureus*, *Klebsiella*, and *S. pneumoniae*

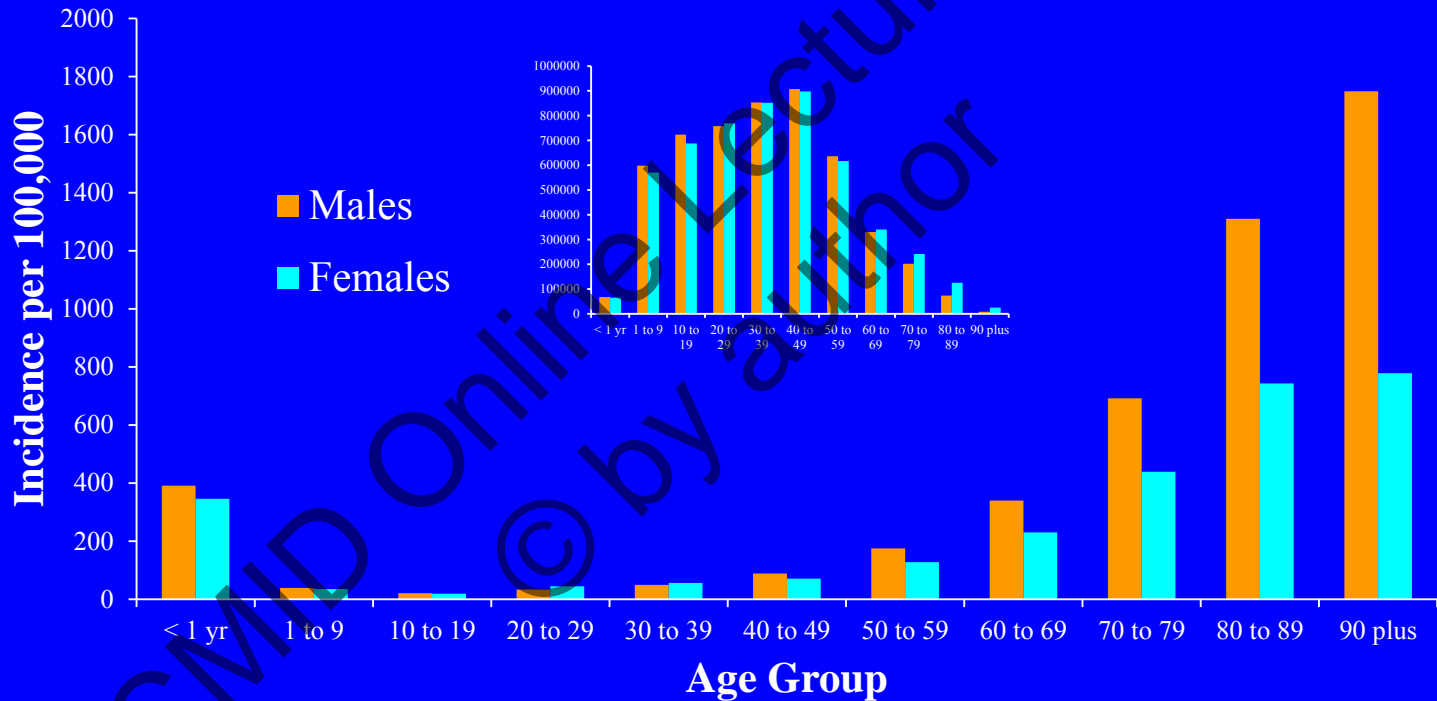
But why do population based studies?

- A key feature of these designs is that *the population at risk is known*
- Measure of burden of a disease (incidence, mortality)
- Establish actual risk factors for acquiring disease in general population

BSI Cases Calgary 2000-2008



BSI Incidence Calgary 2000-2008



Minimize Bias

- Bias may be defined as systematic errors that may occur in *collecting* or *interpreting* data
- If all cases are included selection bias minimized

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Admitted/non-admitted

Factor	Admitted	Non-Admitted	P-value
Male	55%	51%	0.002
Age	63 years	54 years	<0.0001
Poly-microbial	7%	5%	0.0003
Isolate			<0.001
30-day Mortality	17%	6%	<0.0001

Admitted (adult) hospital

Factor	Hospital A	Hospital B	Hospital C	P-value
Male	56%	53%	55%	0.04
Age	64	65	71	<0.0001
Charlson score	2	1	1	<0.001
Isolate				<0.001
30-day mortality	20%	16%	15%	<0.001

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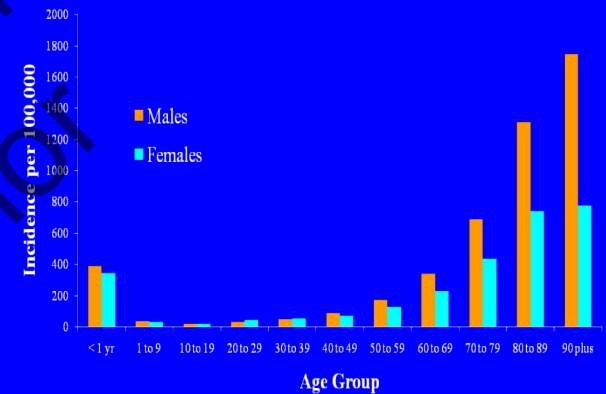
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Referral Bias

- Steckelberg JM, *et al Am J Med.* 1990;88(6):582-8
- Olmsted County USA comparison of population-based and referral cohort
 - **Referral cohort of left sided endocarditis**
 - **Under-represents elderly patients**
 - **Lower proportion of cases due to *S aureus* and higher rate of enterococcal endocarditis**
 - **Longer symptom duration prior to diagnosis**

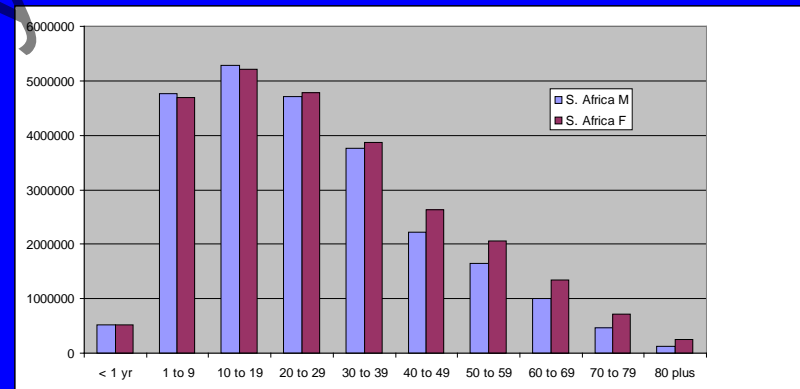
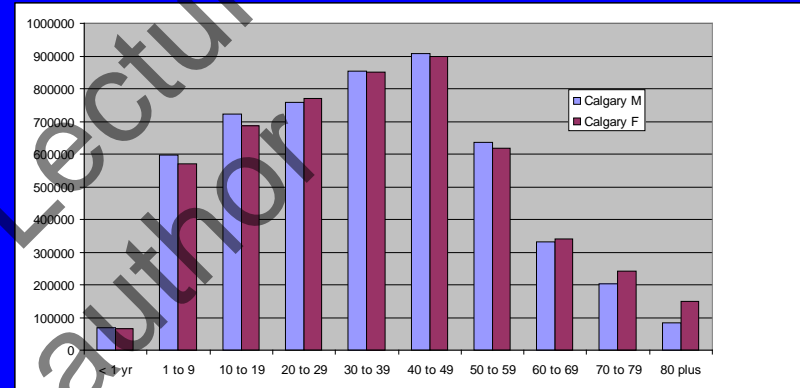
Age and gender standardize

- Occurrence of BSI related to age and gender
- Demographic profile of a population will influence incidence rates
- Age- and gender-standardization facilitates like-comparison across time and location



Calgary/South Africa

- The incidence in Calgary 122 per 100,000
- After age and gender standardization to South Africa 85 per 100,000



The literature

Study	Location	Incidence
Filice et al, 1986	Charleston County, USA 1974-1976	80 per 100,000/year
Madsen, et al. 1999	North Jutland County, Denmark 1981-1994	76 per 100,000 in 1981 to 153 per 100,000 in 1994
Skogberg, et al. 2008	Finland 1995-2002	125 per 100,000/year
Uslan et al. 2007	Olmsted County USA 2003-2005	189 per 100,000

International Bacteremia Surveillance Collaborative

- Surveillance of bloodstream infections is important
- Population-based surveillance approaches are optimal
- The approaches between these regions have not been coordinated use of different definitions and surveillance periods
- Inter-regional comparisons are limited

Core minimal requirements

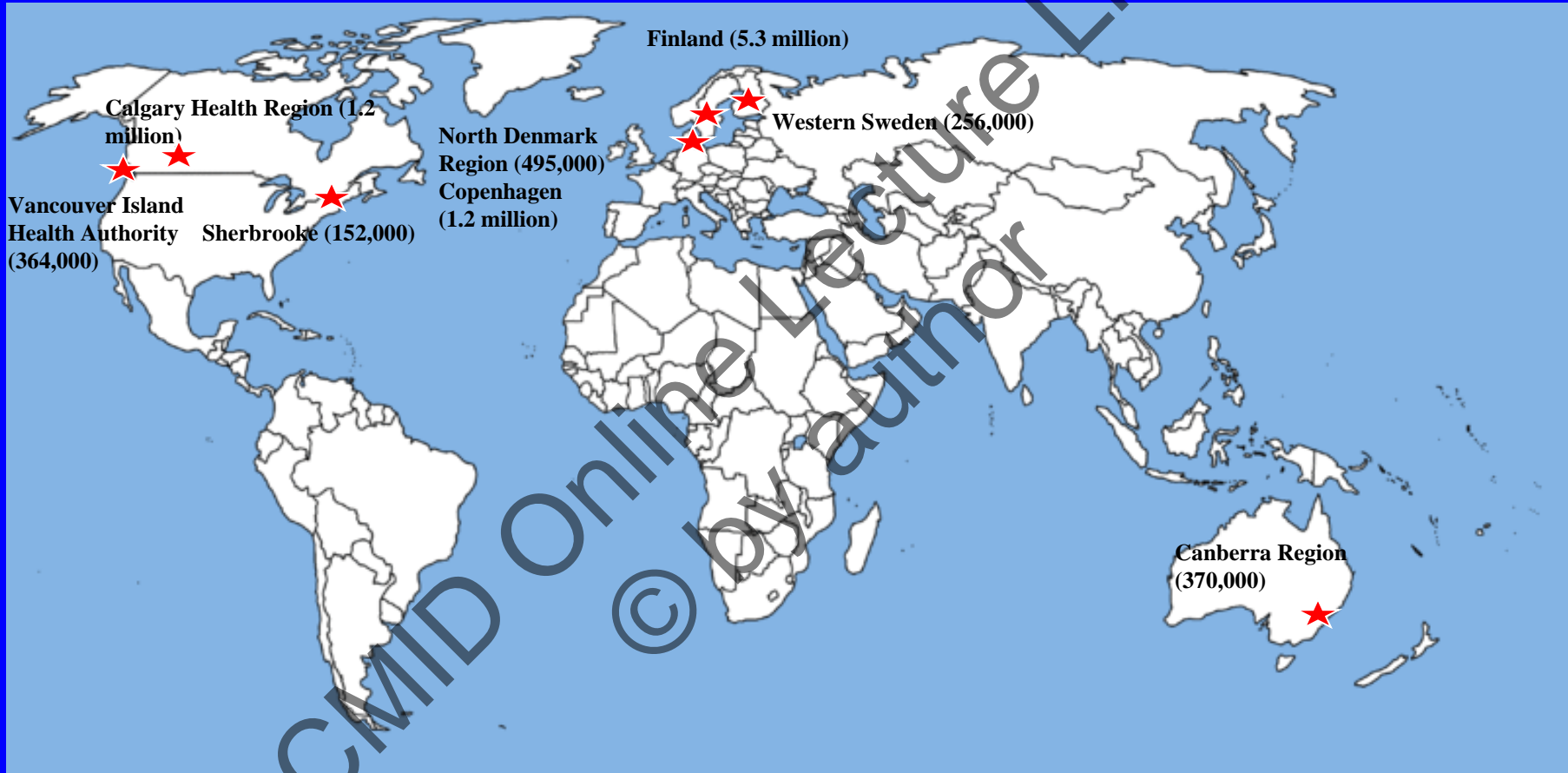
- 1. Surveillance region must be geographically and demographically (age and gender distribution known or estimated) definable.
 - incidence calculations
 - age and gender standardization

Core minimal requirements

- 2. All ($\geq 90\%$) ascertainment
 - non-residents, duplicate specimens excluded
 - common contaminants two positive cultures required for inclusion

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Participating Centres



Total annual surveillance population >8 million residents

Output to date

- Study protocol (*BMC Res Notes* 2009)
- *Salmonella* Enterica (*BMC Infect Dis* 2010)
- *Haemophilus influenzae* (*J Infect* 2011)
- *Staphylococcus aureus* (submitted)

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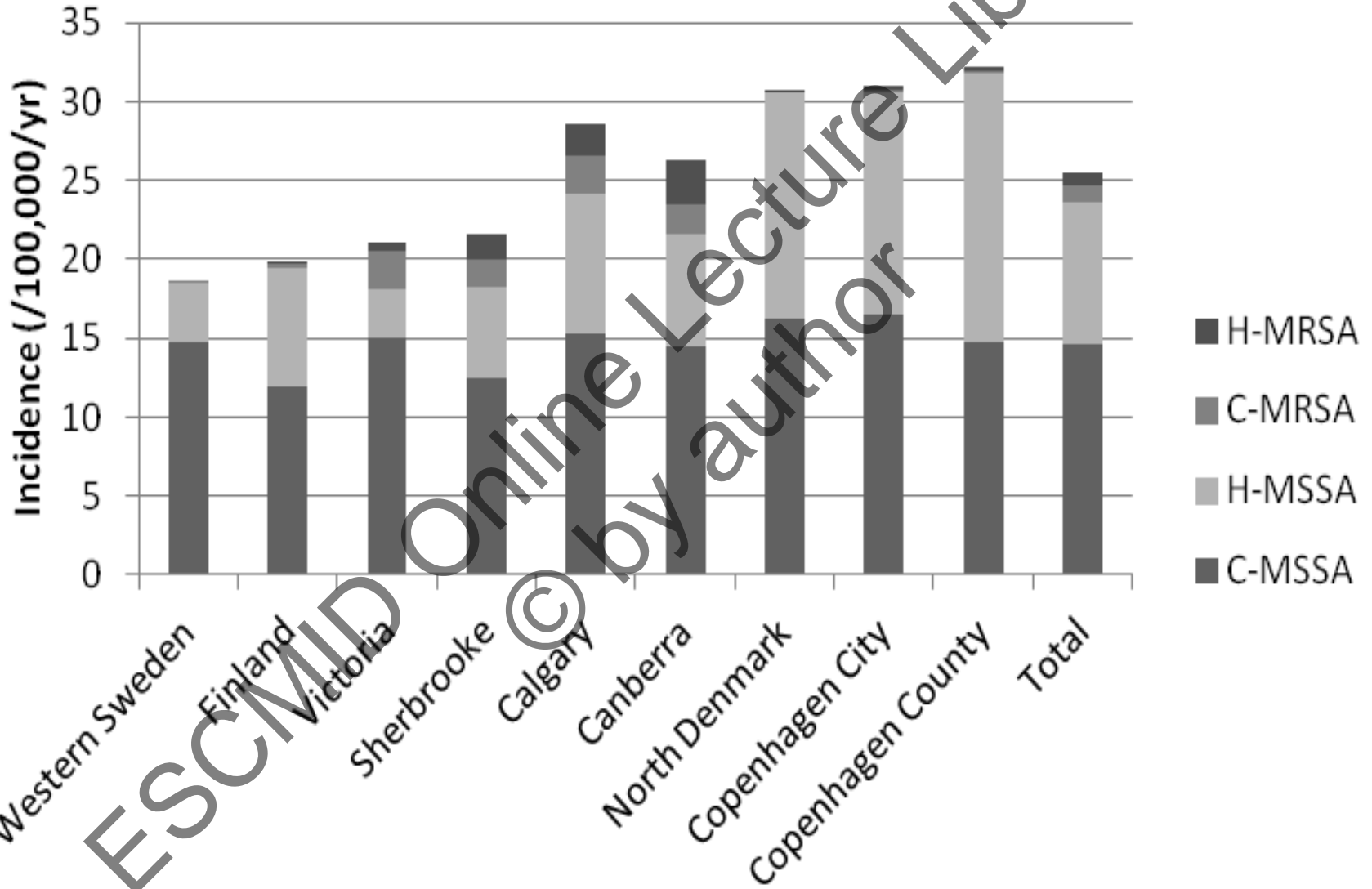
Staphylococcus aureus

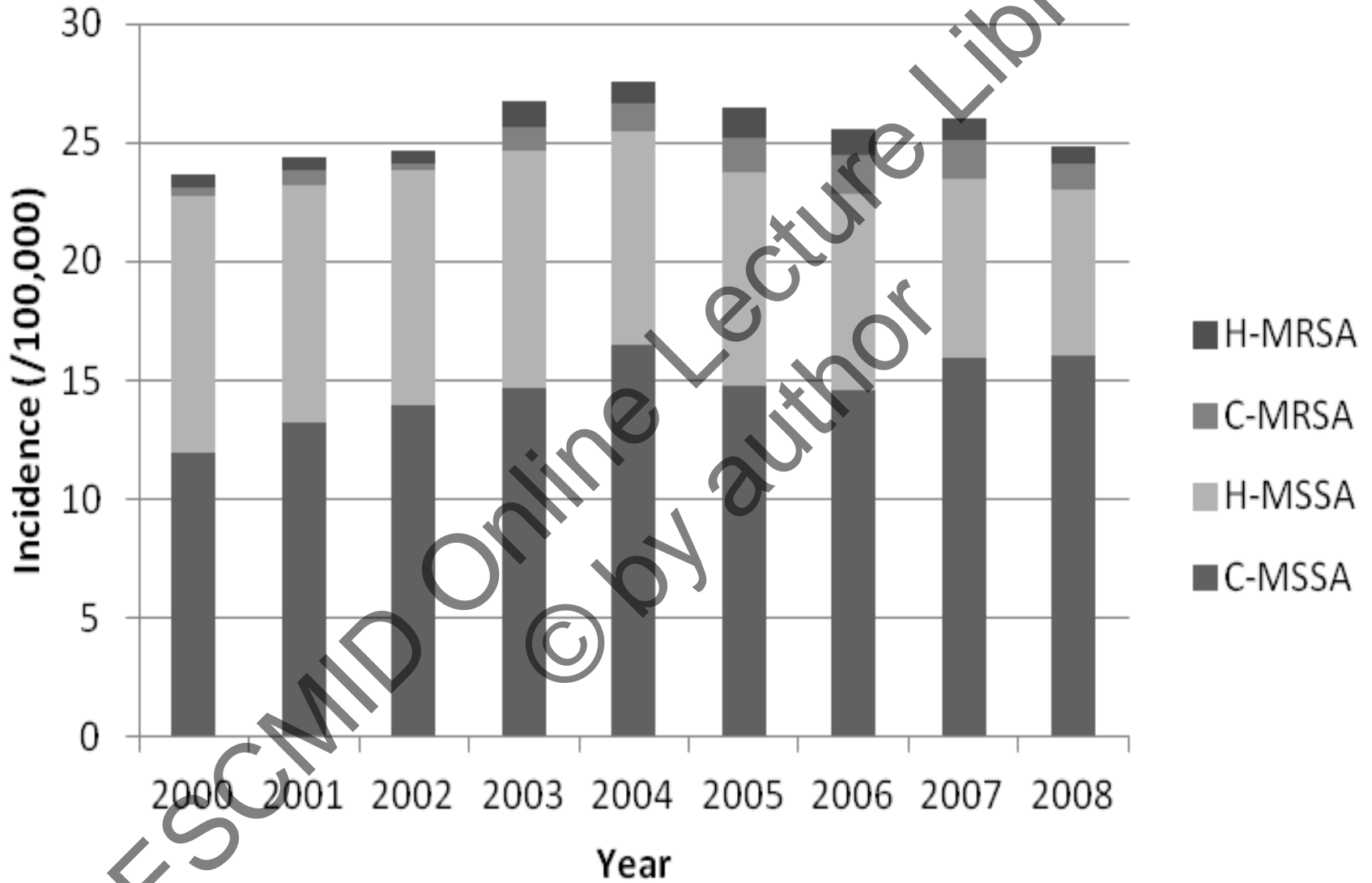
- Important (most) cause of BSI
- MRSA is rising
- Is the emergence of MRSA replacing or adding to the burden?

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Results

- 18,304 episodes of *S. aureus* BSI 17,492 (95.6%) were methicillin-sensitive (MSSA) and 812 (4.4%) were MRSA
- Age and gender standardized incidence
 - Overall 25.6 per 100,000
 - MSSA 23.7 per 100,000
 - MRSA 1.9 per 100,000





Staphylococcus aureus

- No overall change in disease burden
- Major changes in MRSA, and shifts between community vs hospital acquired disease that were region dependent and varied even within countries
- In some regions MRSA added to burden and in others it replaced the MSSA burden

Staphylococcus aureus

- The collaborative allows assessment of a large number of cases and facilitates comparison among regions
- This study demonstrates that care must be taken in broadly generalizing results from single region studies

Conclusions

- Population based studies include all cases occurring in known population
 - assess burden of disease
 - minimize bias
 - like-comparison among regions and among time periods
- The limitations of studies conducted in selected populations and population based studies in single regions should be generalized with caution

International Bacteremia Surveillance Collaborative

- Kevin B. Laupland, Deirdre L. Church, Daniel B. Gregson (Calgary)
- Mette Søgaaard, Henrik C. Schönheyder (Aalborg); Jenny Dahl Knudsen, Christian Ostergaard, Ulrich Jensen, Magnus Arpi (Copenhagen), Kim Gradel (Odense)
- Karina J. Kennedy, Peter Collignon (Canberra)
- Outi Lyytikäinen (Helsinki, Finland)
- Louis Valiquette (Sherbrooke)
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