HIV-infection associated with increased risk of meningococcaemia and higher case-fatality rates in Gauteng Province, South Africa

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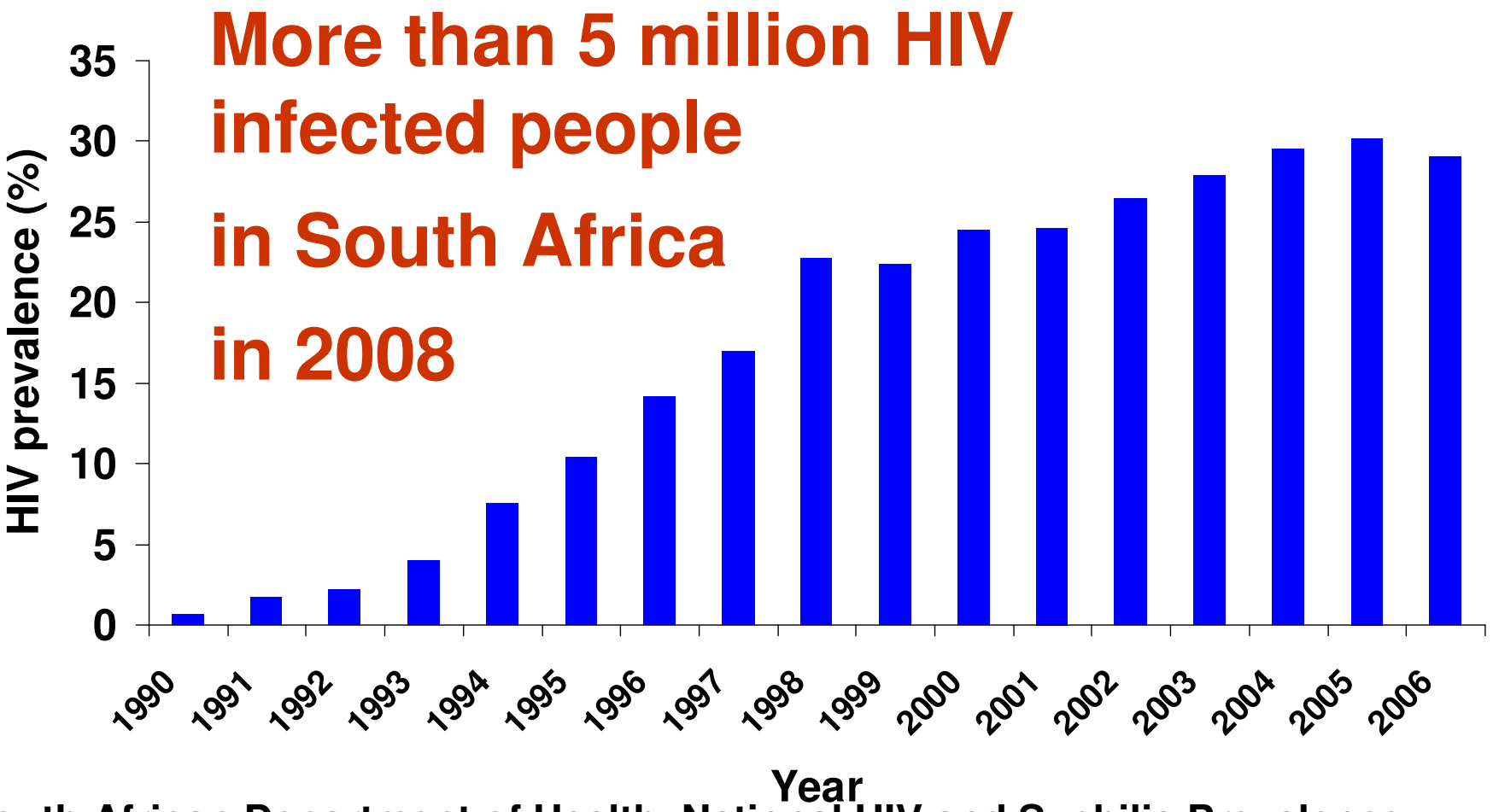
NICD

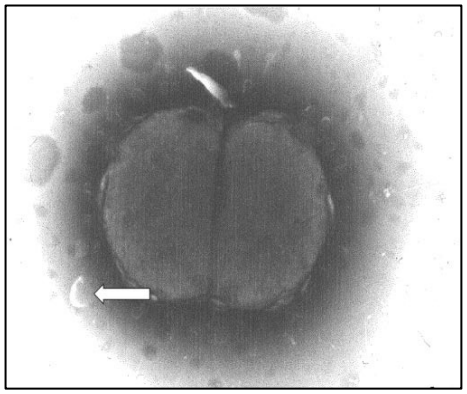
HIV seroprevalence amongst antenatal clinic attendees South Africa, 1990-2006



South African Department of Health. National HIV and Syphilis Prevalence Survey: South Africa 2007.

Neisseria meningitidis

- 300 000 – 500 000 cases annually globally
- Potential for outbreaks



Electron microscopy of a pair of meningococci[1]

- Gram-negative encapsulated diplococcus
- Classified into 13 serogroups
- 5 serogroups A, B, C, Y and W135 are responsible for more than 90% of cases of disease

1. Baines et al , Br J Anaesth, 2003

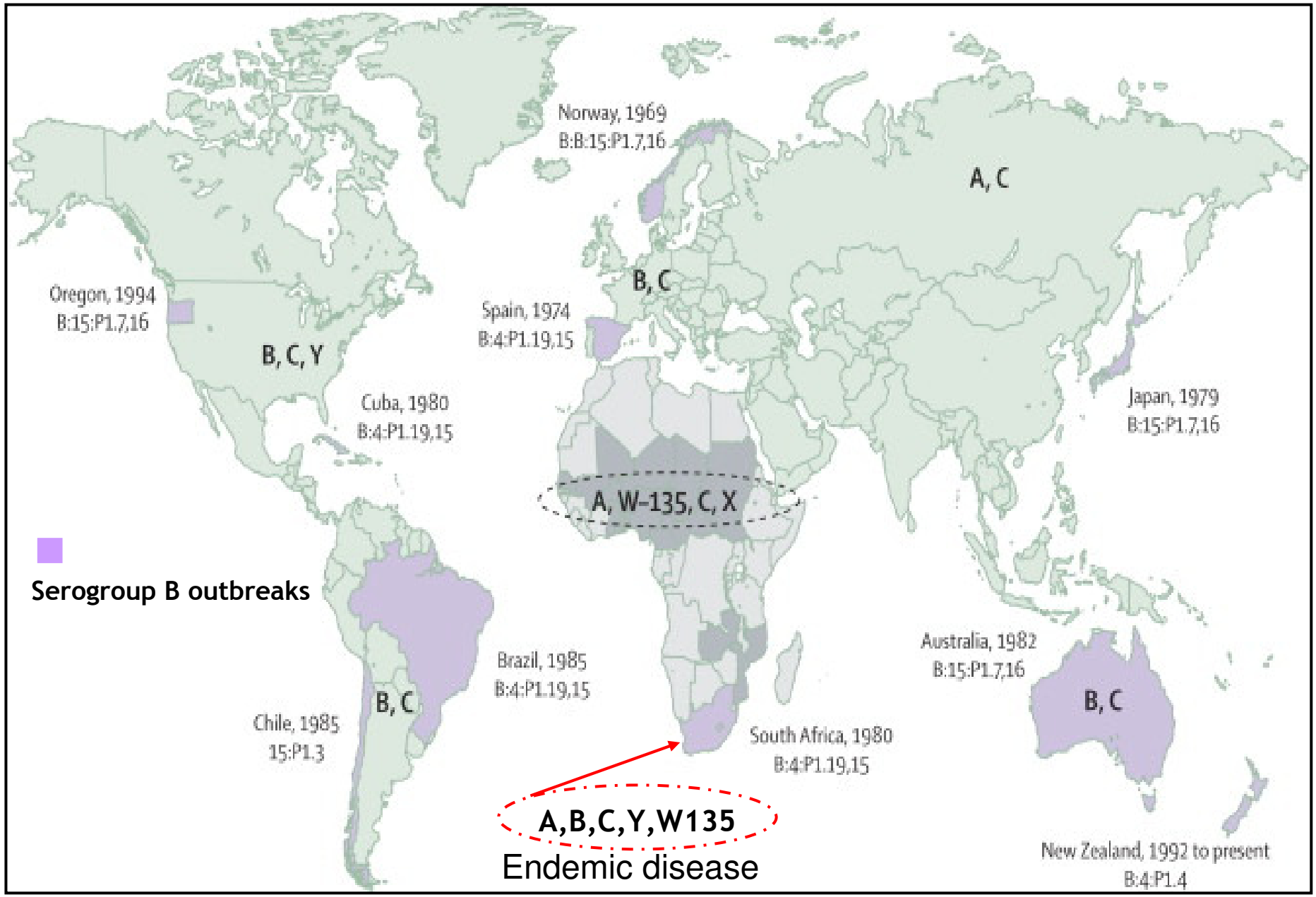
Meningococcal disease

- Case fatality rates: 2-13%[1]
- Sequelae: hearing loss, neurological complications, loss of a limb[2]
- Spectrum of disease: meningitis, meningococcaemia, pneumonia, septic arthritis, pericarditis, urethritis and conjunctivitis[1]
- Meningococcaemia:
  - severe disease
  - higher case fatality rates than meningitis[3]

Thrombosis and gangrene of the fingers in a child surviving fulminant meningococcal septicaemia[4]

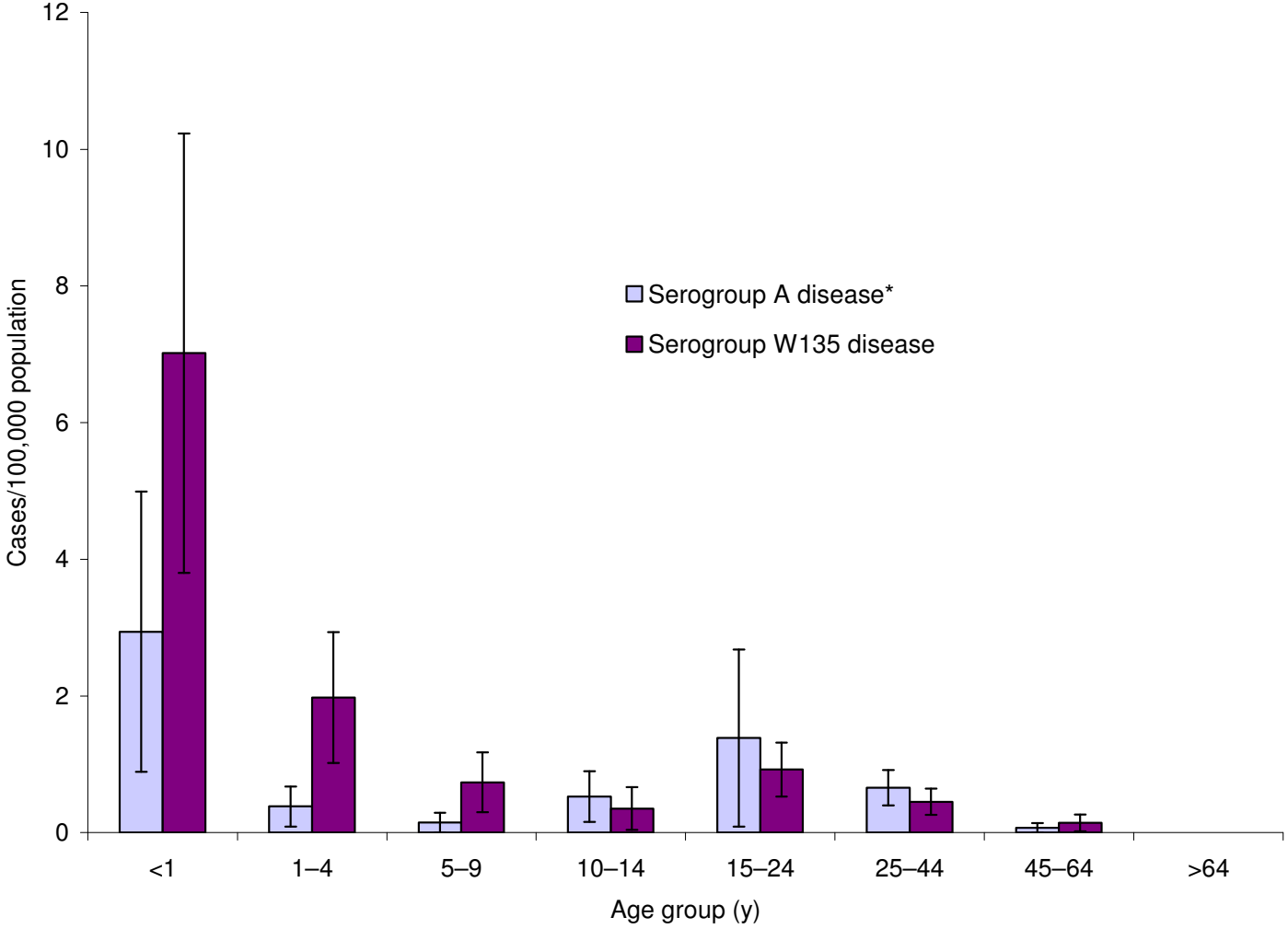
1. Scholten et al, Epi Infect, 1994 2. Rosenstein et al, NEJM, 2001 3. Baines et al, Br J Anaesth, 2003 4. Stephens et al, Lancet, 2007

Global distribution of serogroups causing invasive disease



Stephens et al, Lancet, 2007

Annual age-specific incidence rates for serogroup A and W135 invasive meningococcal disease in Gauteng Province, South Africa, as reported in 2004



*Serogroup-specific disease rates were calculated assuming that the distribution of serogroups for cases with missing serogroup data (n=31, 17% of total reported) was the same as the distribution for cases with serogroup information available.

HIV as a risk factor for meningococcal disease

- No large studies
  - Atlanta 1988 to 1993: 3 of 44 patients HIV[1]
  - France 1992: 15 patients with HIV and infection with *Neisseria* species[2]
  - Uganda 1992: 41 cases and 568 controls[3]

Sporadic Meningococcal Disease in Adults: Results of a 5-Year Population-Based Study

David S. Stephens, MD; Rana A. Hajjeh, MD; Wendy S. Baughman, MPH; R. Christopher Harvey, MPH; Jay D. Wenger, MD; and Monica M. Farley, MD

HIV as risk factor for mortality

- 1 publication[4]
  - Couldwell (2001) in Australia
  - Case series – 3 patients
  - Outcome uniformly poor

Invasive meningococcal disease and HIV coinfection

Deborah L Couldwell

Abstract

Three cases of meningococcal disease which occurred over a 3 year period in HIV-infected people living in the Wentworth Health Area of Sydney, Australia, are described. None of the 3 had ever received antiretroviral therapy which may have contributed to development of invasive meningococcal disease. *Commun Dis Intell* 2001;25:278-279.

Keywords: meningococcal; HIV; Neisseria meningitidis

1. Stephens et al, Ann Intern Med, 1995 2. Morla et al , J Clin Micro 1992 3. Kipp et al, AIDS, 1992 4. Couldwell DL, Comm Dis Intell, 2001

Objectives

- Prevalence of HIV amongst cases
- Case-fatality rate amongst HIV-infected and HIV-uninfected
- To determine if HIV is an independent risk factor for mortality amongst cases
- To determine if HIV is a risk factor for meningococcaemia

Methods

- Analytic cross sectional study
- Surveillance system
  - National laboratory-based surveillance system (120 laboratories)
  - Basic demographic data collected
  - Enhanced surveillance sites (additional demographic and clinical data)
- Study population: patients with laboratory confirmed invasive meningococcal disease from Gauteng Province from 2003 through 2007 with HIV status and outcome data

Case definitions

- Meningitis: patients for whom diagnosis made from a CSF specimen (with or without identification from blood cultures)
- Meningococcaemia: patients for whom diagnosis made from a blood culture specimen

Data analysis

- Comparison of patients tested and not tested for HIV
- HIV prevalence
- Univariate analysis
- Multivariable logistic regression analysis
  - Covariates evaluated age group, gender, underlying illness, appropriate antibiotics, penicillin non-susceptibility, year of infection, syndrome, Pitt bacteraemia score
- Independence of data assumed

***Neisseria meningitidis* cases reported, Gauteng**
n=1336

↓

Cases from enhanced surveillance sites
n=591
(44%)

↓

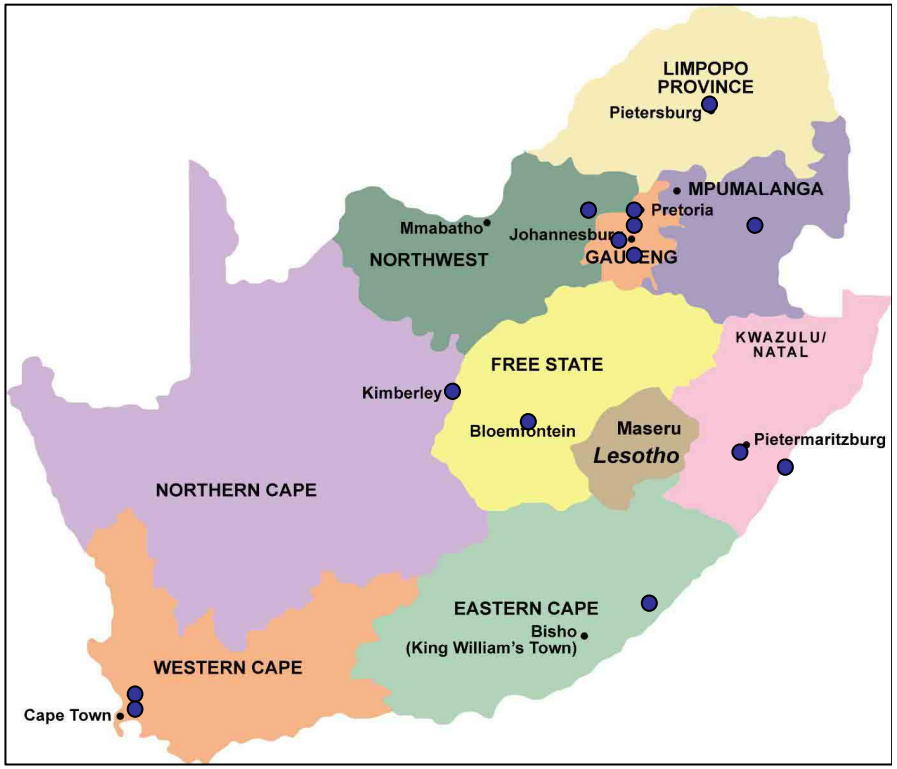
Case report forms
n=506
(86%)

↓

Outcome recorded
n= 504
(99.6%)

↓

HIV status recorded
n= 308
(61%)



GERMS-SA
CASE REPORT FORM
FOR ENHANCED SURVEILLANCE SITES

National Microbiology Surveillance Unit (NMSU)
TEL: 011 386 6234 OR 011 555 0353
FAX: 011 386 6077

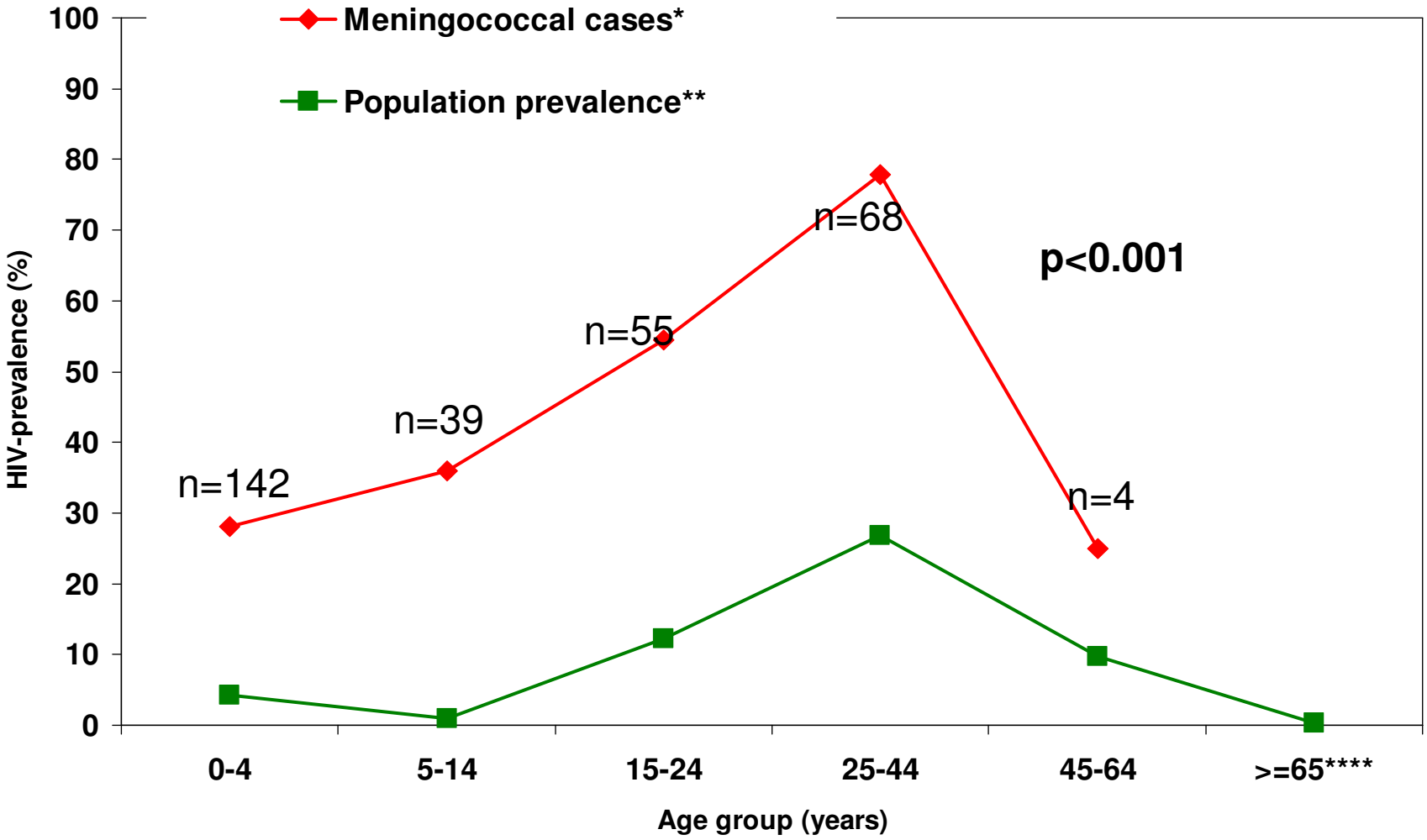
NICD

Surveillance officer name:			Signature:	Date:
Sources of data:	Patient/Guardian ☐	Clinician ☐	Medical records ☐	No record found ☐
Lab Specimen No:			Laboratory Name:	
Hospital Name:	Hospital Number:		Ward:	Adult Ward ☐ Paed Ward ☐
Gender: M ☐ F ☐ Unk ☐	Race: Asian ☐	Black ☐	Coloured ☐	White ☐ Unk ☐
Date of Birth: D D M M Y Y Y Y	DOB Unk ☐	Age:	Unit: Days ☐ Months ☐ Years ☐	Age Unk ☐
Patient Surname:			Patient First Names:	
Address:			Town/City:	Province:
Tel no: (H)	(W)	(C)	(Neighbour)	

Comparison of patients tested for HIV vs those not tested

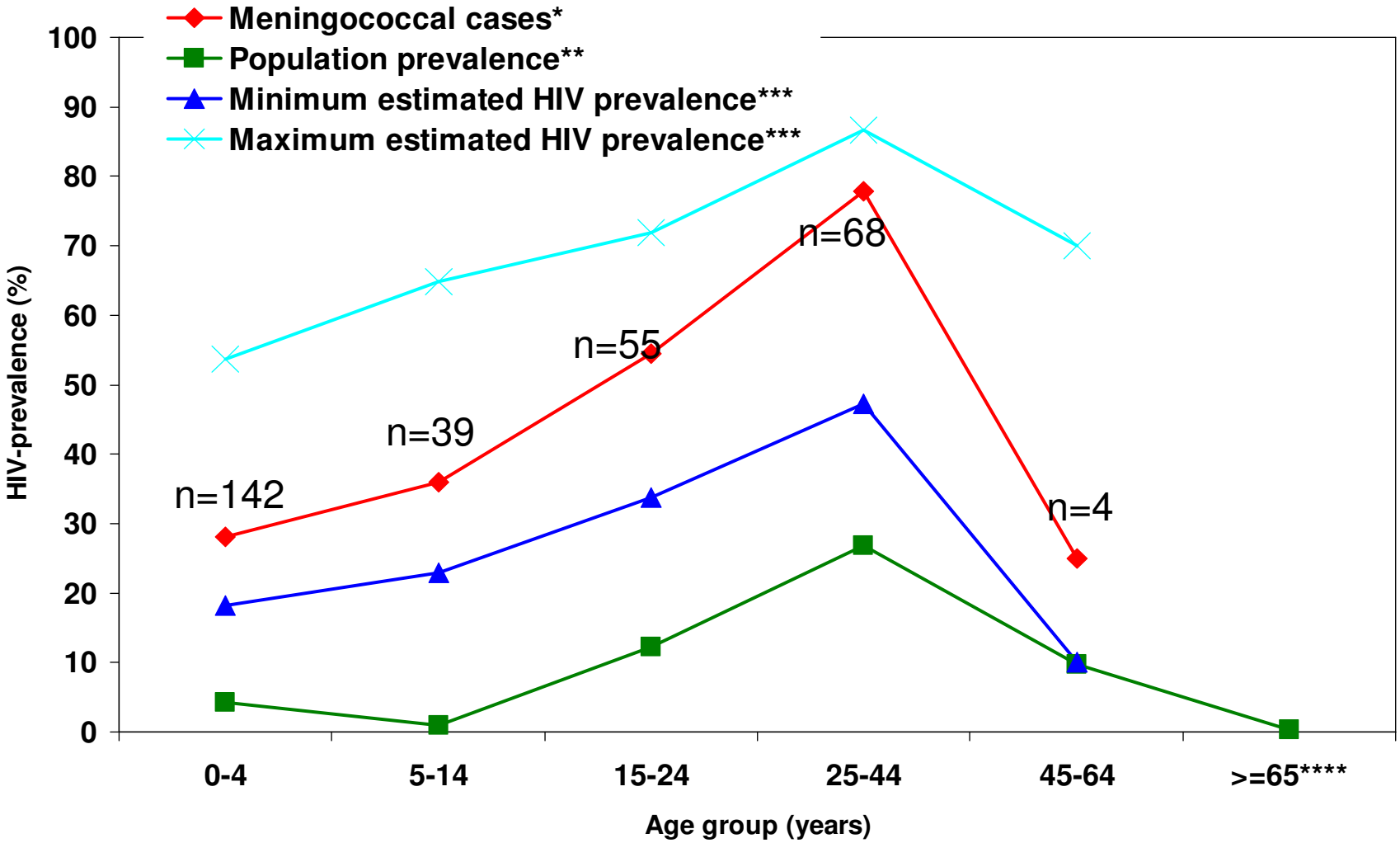
- No difference in age group, gender, syndrome, Pitt bacteraemia score, underlying illness or year of specimen collection
- Patients not tested had higher case-fatality rate (28% 54/196) than those tested (15% 45/308)($p<0.001$)

Figure 1: HIV prevalence amongst meningococcal cases, 2003-2007 and population HIV prevalence 2005, Gauteng Province, South Africa



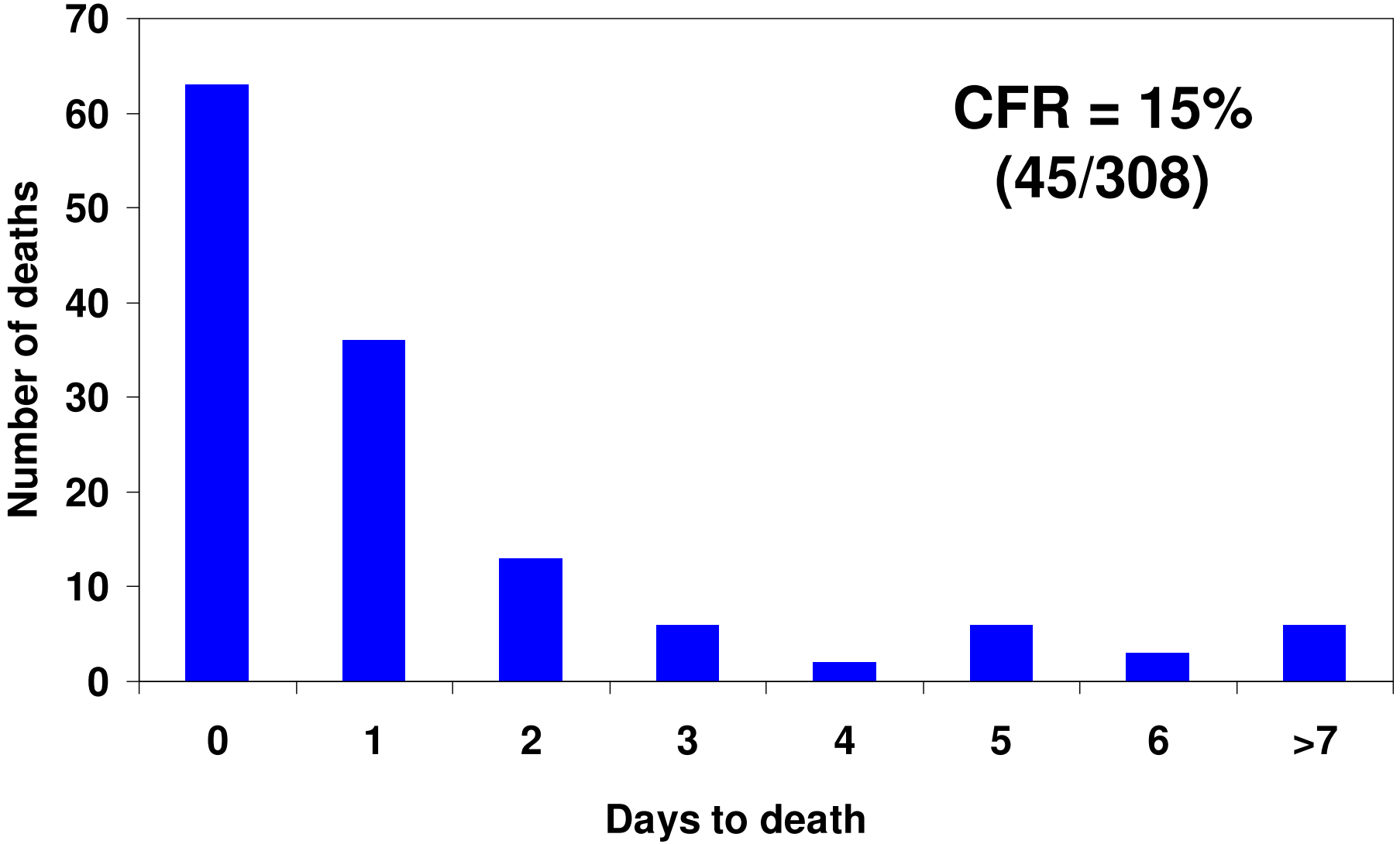
Note: *Only patients tested for HIV serostatus included, **Actuarial Society of South Africa (ASSA) model,****No cases >= 65 years of age were tested for HIV

Figure 1: HIV prevalence amongst meningococcal cases, 2003-2007 and population HIV prevalence 2005, Gauteng Province, South Africa



Note: *Only patients tested for HIV serostatus included, **Actuarial Society of South Africa (ASSA) model,***Predicted HIV prevalence amongst cases assuming that cases not tested were HIV-negative or –positive respectively,****No cases >= 65 years of age were tested for HIV

Days to death amongst patients with meningococcal disease who died: Gauteng, 2003 -2007



Univariate analysis of risk factors for death in meningococcal cases Gauteng, South Africa, 2003-2007

Characteristic	Mortality*		Univariate analysis	
	n/N	%	OR (95% CI)**	p
Syndrome				
Meningitis	16/226	7	1	<0.001
Meningococcaemia	29/82	35	7.2 (3.6-14.2)	
HIV co-infection				
HIV-negative	18/170	11	1	0.03
HIV-positive	27/138	20	2.1 (1.1-3.9)	
Pitt bacteraemia score				
<4	26/227	12	1	
≥4	12/27	44	6.2 (2.6-14.64)	<0.001

* Number of deaths /number of cases ** Odds ratio (95% confidence interval)

Multivariable analysis of risk factors for death in meningococcal patients Gauteng, South Africa, 2003-2007

Characteristic	Multivariable analysis*	
	OR (95% CI)**	p
Syndrome		
Meningitis	1	<0.001
Meningococcaemia	7.8 (3.4-17.7)	
HIV co-infection		
HIV-negative	1	0.78
HIV-positive	0.9 (0.4-2.1)	
Pitt bacteraemia score		
<4	1	<0.001
≥4	4.5 (1.6-12.3)	

*Controlling for age group ** Odds ratio (95% confidence interval)

Univariate analysis of risk factors for meningococcaemia (vs meningitis) Gauteng, 2003-2007

Characteristic	% meningococcaemia		Univariate analysis	
	n/N	%	OR (95% CI)**	p
Serogroup				
A	3/31	10	1	
B	4/14	29	3.7 (0.7-19.7)	
C	3/13	23	2.8 (0.5-16.2)	0.24
W135	59/201	29	3.9 (1.1-13.3)	
Y	4/16	25	3.1 (0.1-16.1)	
HIV co-infection				
HIV-negative	31/170	18	1	<0.001
HIV-positive	52/138	37	2.6 (1.6-4.4)	

** Odds ratio (95% confidence interval)

Multivariable analysis of risk factors for meningococcaemia (vs meningitis) Gauteng, 2003-2007

Characteristic	Multivariable analysis*	
	OR (95% CI)**	p
Serogroup		
A	1	0.17
B	4.4 (0.8-24.5)	
C	2.9 (0.5-17.8)	
W135	4.2 (1.2-14.8)	
Y	3.2 (0.6-17.5)	
HIV co-infection		
HIV-negative	1	0.001
HIV-positive	2.8 (1.5-5.1)	

*Controlling for age group ** Odds ratio (95% confidence interval)

Conclusions

- HIV-prevalence amongst meningococcal cases higher than population HIV prevalence
- CFR for HIV-infected was twice that for HIV-uninfected
- In the multivariable model, meningococcaemia was associated with increased odds of dying
- HIV-infected individuals were significantly more likely to be diagnosed with meningococcaemia than HIV-uninfected individuals

Limitations

- Laboratory based surveillance
  - Underestimate of patient numbers
  - Misclassification of syndrome
- Only 60% of patients with HIV status recorded
- Patients not tested for HIV had higher CFR
- Secondary analysis of data – not all risk factors available to be analysed

Discussion

- Common conditions → public health impact
- Further research needed - case-control study
- Clinician awareness
- Possible role of vaccination of HIV-infected patients

GERMS SOUTH AFRICA

All participating patients, laboratory, clinical and administrative staff for submitting case reports and isolates

NICD

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HIV stage of meningococcal cases

- CD4 count available for 82 HIV-infected individuals
  - 43 (52%) < 200 cell/mm^3
  - 21 (26%) > 500 cell/mm^3
- 5 cases receiving ART currently