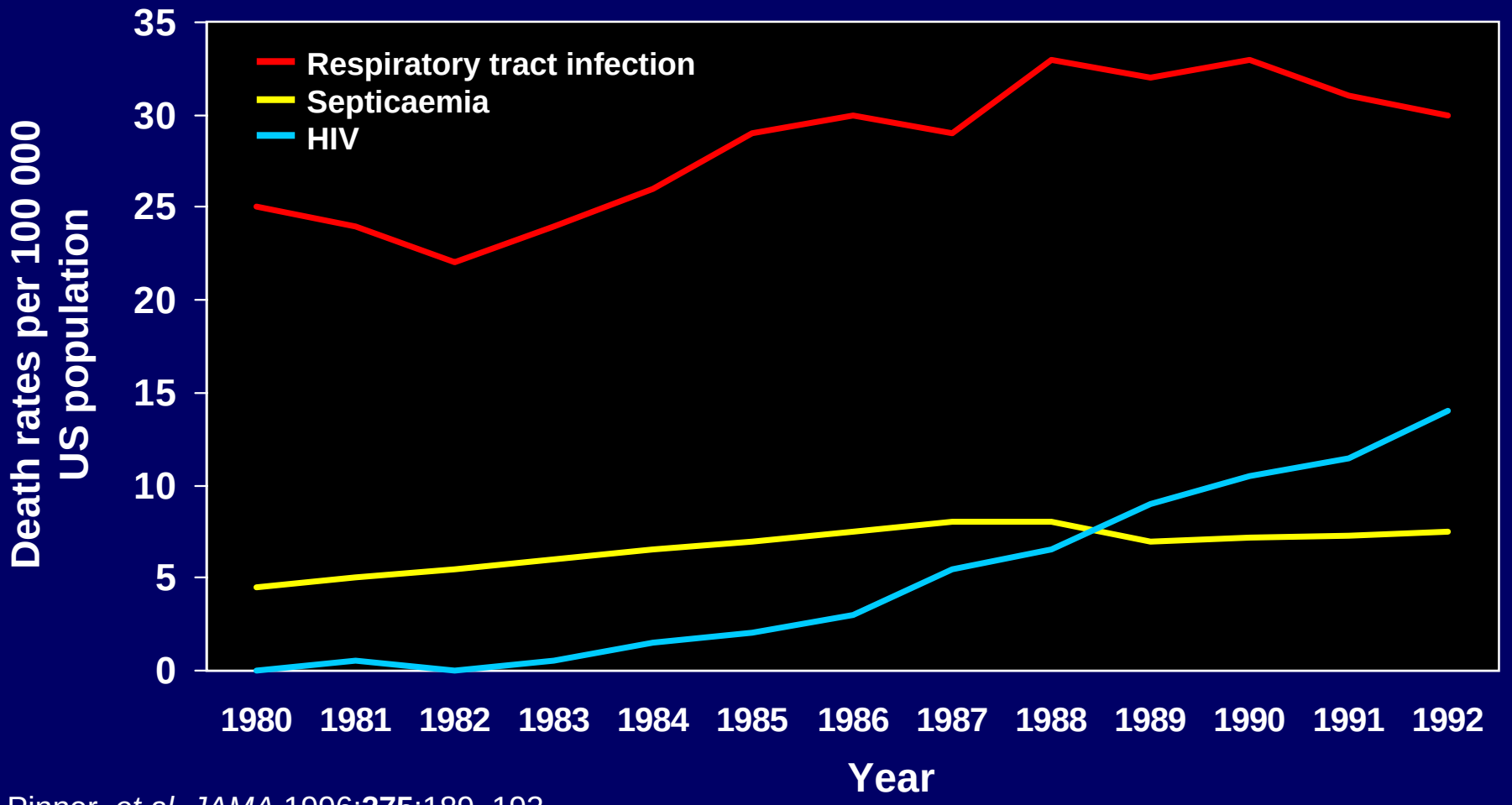
Infectious disease syndromes



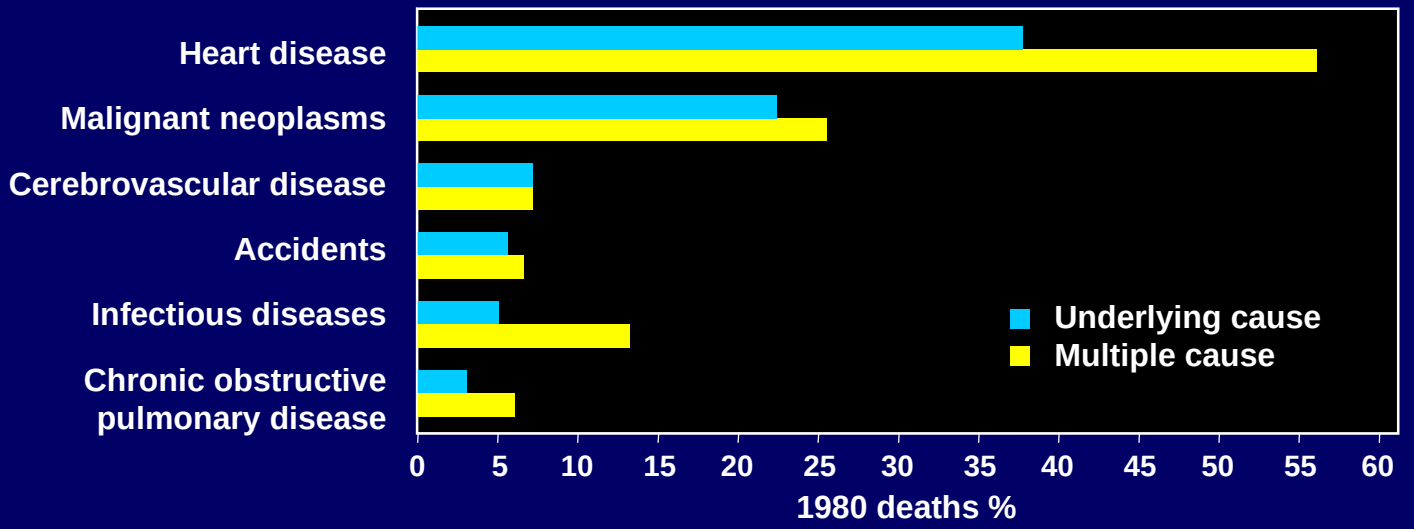
Pinner, *et al*. *JAMA* 1996;**275**:189–193

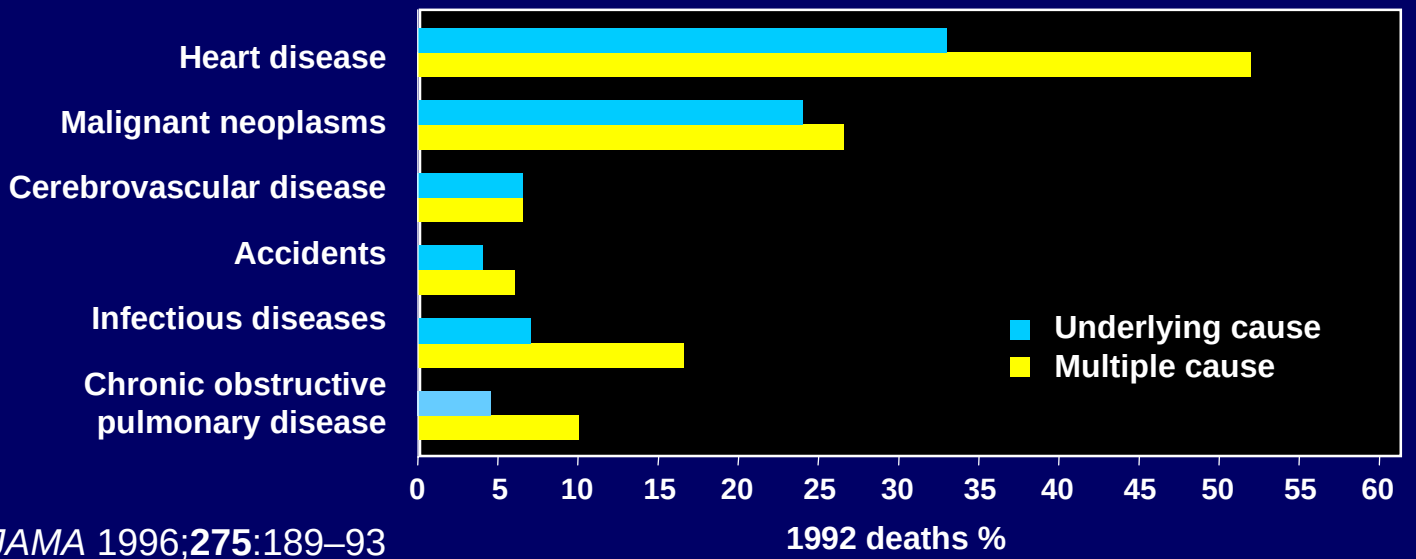
COPD, the clinical problem

- Affects 52 million worldwide
- 2.74 million deaths in 2000
- in the USA 4th leading cause of death
- 16 million office visits and 500.000 admissions yearly
- Total costs $ 30.4 billion in 1995

Koller NEJM, 2002; 346: 988-94

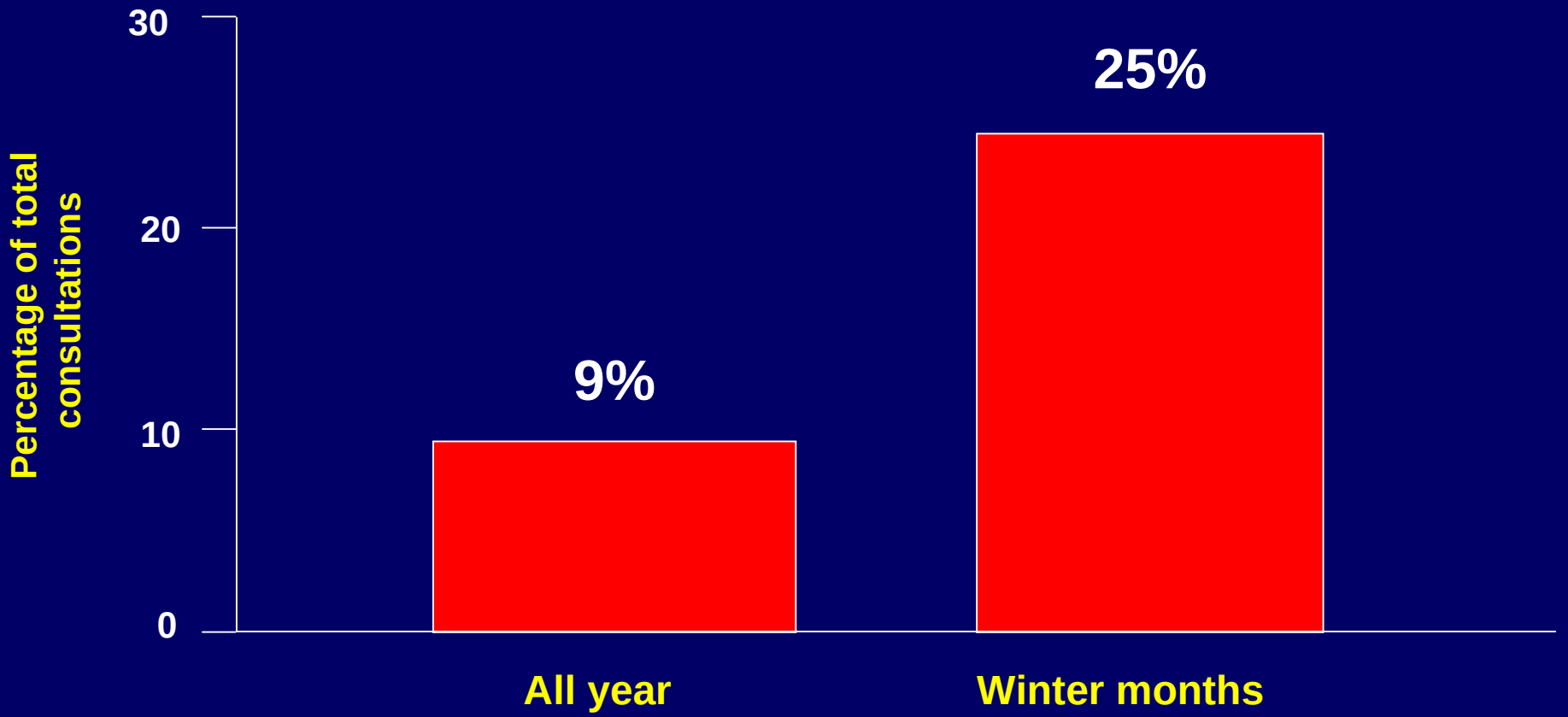
Leading cause of death as percentages of total deaths in 1980 and 1992



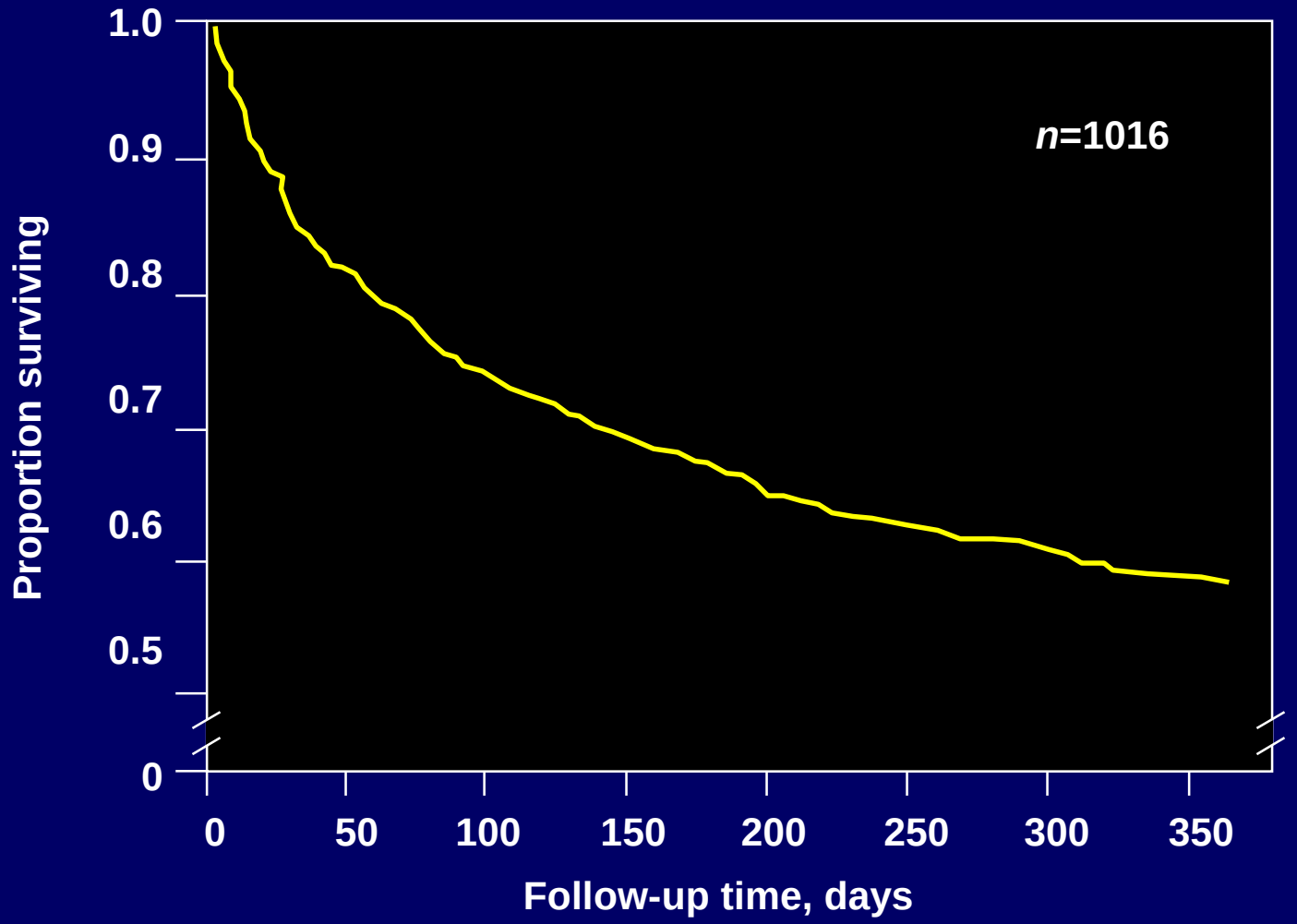


Pinner, *et al*. *JAMA* 1996;**275**:189–93

RTIs are one of the most common reasons for consulting a GP



One-year survival of patient with severe acute exacerbations of COPD



Connors, *et al. Am J Respir Crit Care Med* 1996;**154:**959–67

Cause of death in 200 COPD patients

Respiratory infection	20%
Neoplasm	7.3%
Pulmonary embolus	5.5%
Sudden death	4.6%
Suicide	1.9%

Burrows and Earl. *N Engl J Med* 1969;**280:**397–404

Zijn antibiotica geïndiceerd bij exacerbaties van chronische bronchitis?

ARE ANTIMICROBIAL AGENTS USEFUL

IN ACUTE EXACERBATIONS OF COPD?

VIRAL INFECTIONS IN ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS

- 14 studies range 4–63%
- 1621 exacerbations
  – mean 26%

PLACEBO CONTROLLED STUDIES OF ANTIBIOTIC THERAPY IN AECB

Meta-analyse I (9 studies)

- **SMALL BUT SIGNIFICANT EFFECT OF AB THERAPY**
- **ESPECIALLY IN PATIENTS WITH LOW PEAK EXPIRATORY FLOW RATES**

SAINT et al. JAMA, 1995, 273:957-960

PLACEBO CONTROLLED STUDIES OF ANTIBIOTIC THERAPY IN AECB

Meta-analyse II (11 studies)

- **Antibiotics are beneficial**
- **Patients with more severe exacerbations are more likely to benefit**

McCrory et al. CHEST, 2001, 119:1190-1209
SAINT et al. JAMA, 1995, 273:957-960

ROLE OF ANTIBIOTICS IN AIECBs

Results of double-blind study

- Success rate:
  - placebo 55%
  - antibiotic 68%

  } $P<0.01$

- Deterioration:
  - placebo 19%
  - antibiotic 10%

  } $P<0.05$

- Peak flow recovered more rapidly with antibiotic
- Response to treatment earlier with antibiotic

Anthonisen, *et al. Ann Intern Med* 1987; 106: 196–204

WINNIPEG STAGING CRITERIA FOR AIECBs

Type	Criteria
I	Increased sputum volume, purulence, and dyspnea
II	Two of the above
III	One of the above, plus: preceding upper respiratory tract infection; fever; cough; wheeze; 20% rise in respiratory or cardiac rate

Anthonisen, *et al. Ann Intern Med* 1987; 106: 196–204

Outcome of exacerbations of COPD by Type

	All-PI	Type-1P	Other-P	All-AB	Type-1 AB	Other AB
Success	55%	52%	72%	68%	60%	83%
No resolution	42%	28%	22%	34%	23%	14%
Deterioration	34%	30%	6%	18%	16%	3%

Anthonisen et al Ann Intern Med 1987; 106: 196-204

VIRAL AND ATYPICAL PATHOGENS IN Type-1 AECB

Author	Viral	Atypical	Type (no)	Period
Rademaker JAC, 1990	6 %	6 %	Influenza A (2) C.pneumoniae (4) M.pneumoniae (1) RS (1)	April 89- March 90
Mertens AAC, 1992	4 %	4 %	Influenza A (2) C.pneumoniae (1) L.pneumophila (1)	Dec 88- June 89
Hoepelman JAC, 1993	1 %	5 %	C.pneumoniae (1) L.pneumophila (1) Chlamydia spp. (2) RS (1)	Jan 91- Nov 91
Hoepelman CMI,1998	9 %	2 %	Influenza A/B (6) Parainfluenza (3) RS (3) L.pneumophila (1) Chlamydia spp. (1)	Nov 92- Febr 94
	6 %	4 %		

Infectious AE-COPD : role of bacteria

- Prospective, longitudinal cohort study
- n = 81 ; t = 56 months
- sputum culture with molecular typing :
  monthly
  during exacerbation

Acquisition of a new strain of a pathogenic bacterial species in a COPD patient significantly increases the risk of an exacerbation

Sethi et al. N Engl J Med 2002;347:465-471

Relative risk of an exacerbation according to whether a NEW STRAIN was isolated

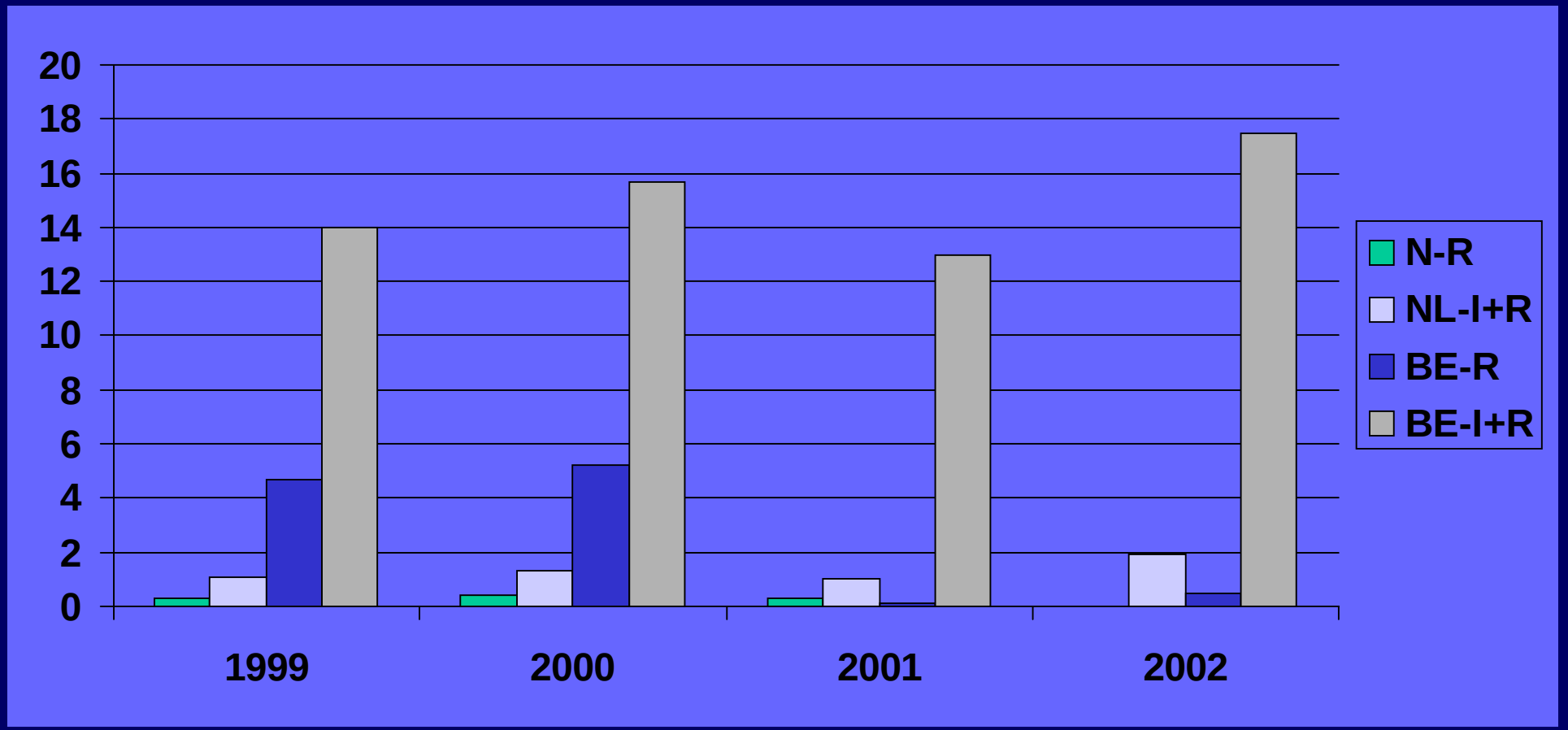
New strain	Frequency of exacerbation		P	RR
	New strain	No new strain		
Any	89/270 (33%)	213/1385(15 %)	<0.001	2.15
H.influenzae	38/145 (26)	257/150 (17)	<0.001	1.7
M. catarrhalis	41/84 (49)	261/1571 (17)	<0.001	3
P.aeruginosa	3/22 (14)	297/1631 (18)	0.38	0.61
S.pneumoniae	8/25 (14)	294/1630 (18)	0.01	1.8

Sethi et al NEJM 2002; 347: 465-71

Antibacterial therapy for AECB (5–10 days)

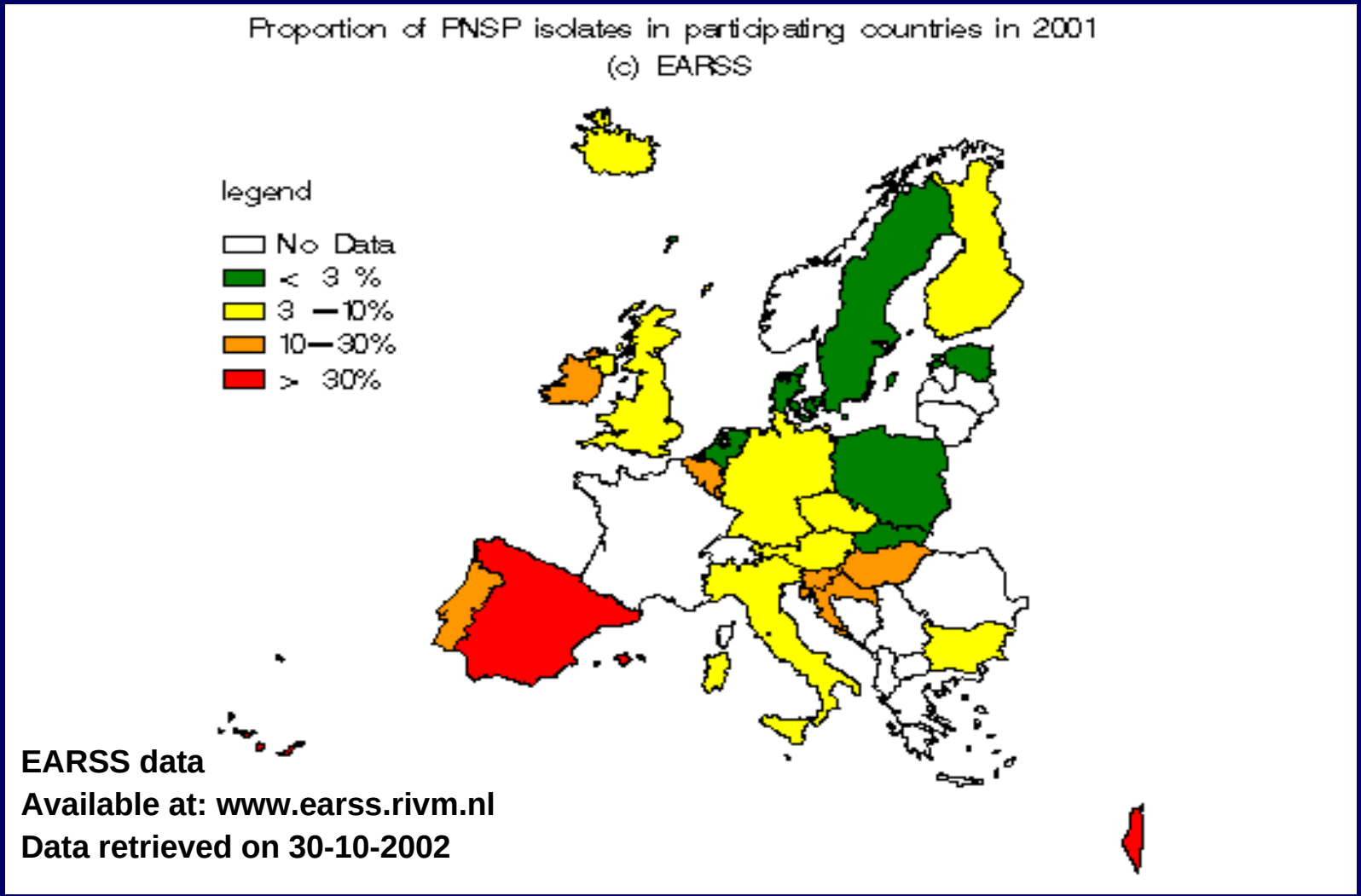
- Amoxicillin
- Co-amoxiclav
- Trimethoprim-sulfamethoxazole
- Doxycycline
- Erythromycin
- Clarithromycin
- Cefuroxime
- Azitromycin
- Cefaclor
- Levofloxacin
- Ciprofloxacin
- Moxifloxacin
- Telithromycin

Penicilline resistentie S.pneumoniae



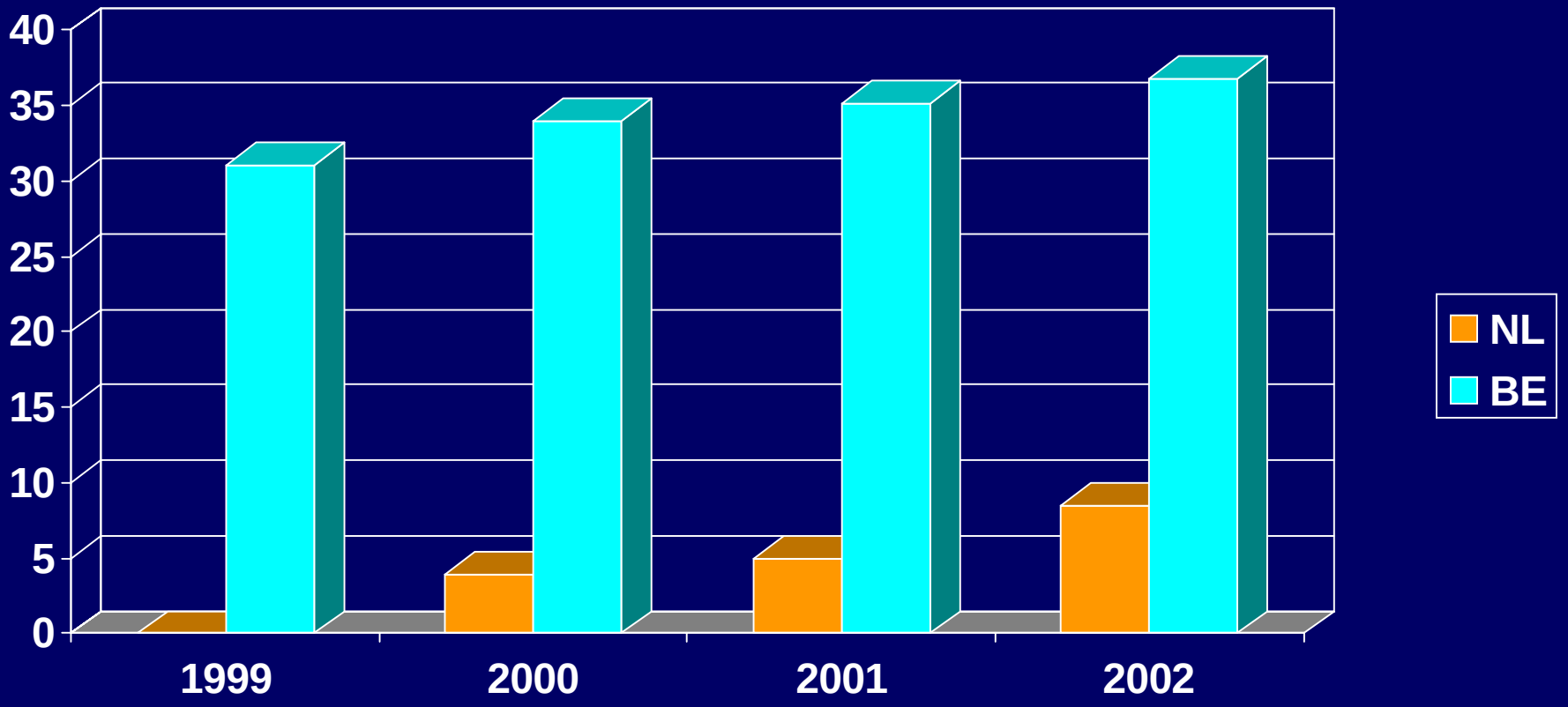
Earss.rivm.nl

Proportions of PNSP in 2001



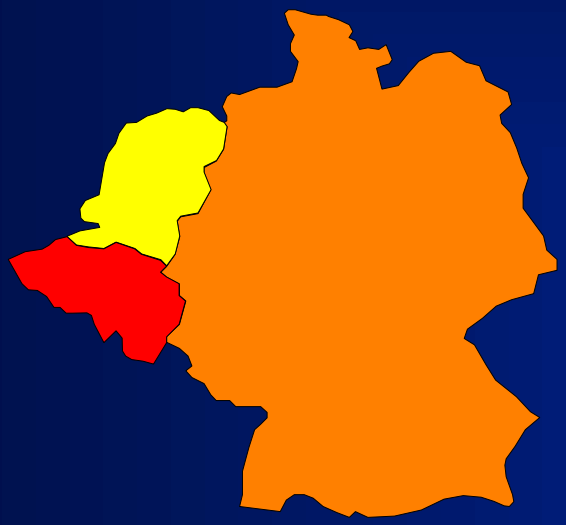
EARSS data
Available at: www.earss.rivm.nl
Data retrieved on 30-10-2002

Erythromycine resistentie S.pneumoniae



Earss.rivm.nl

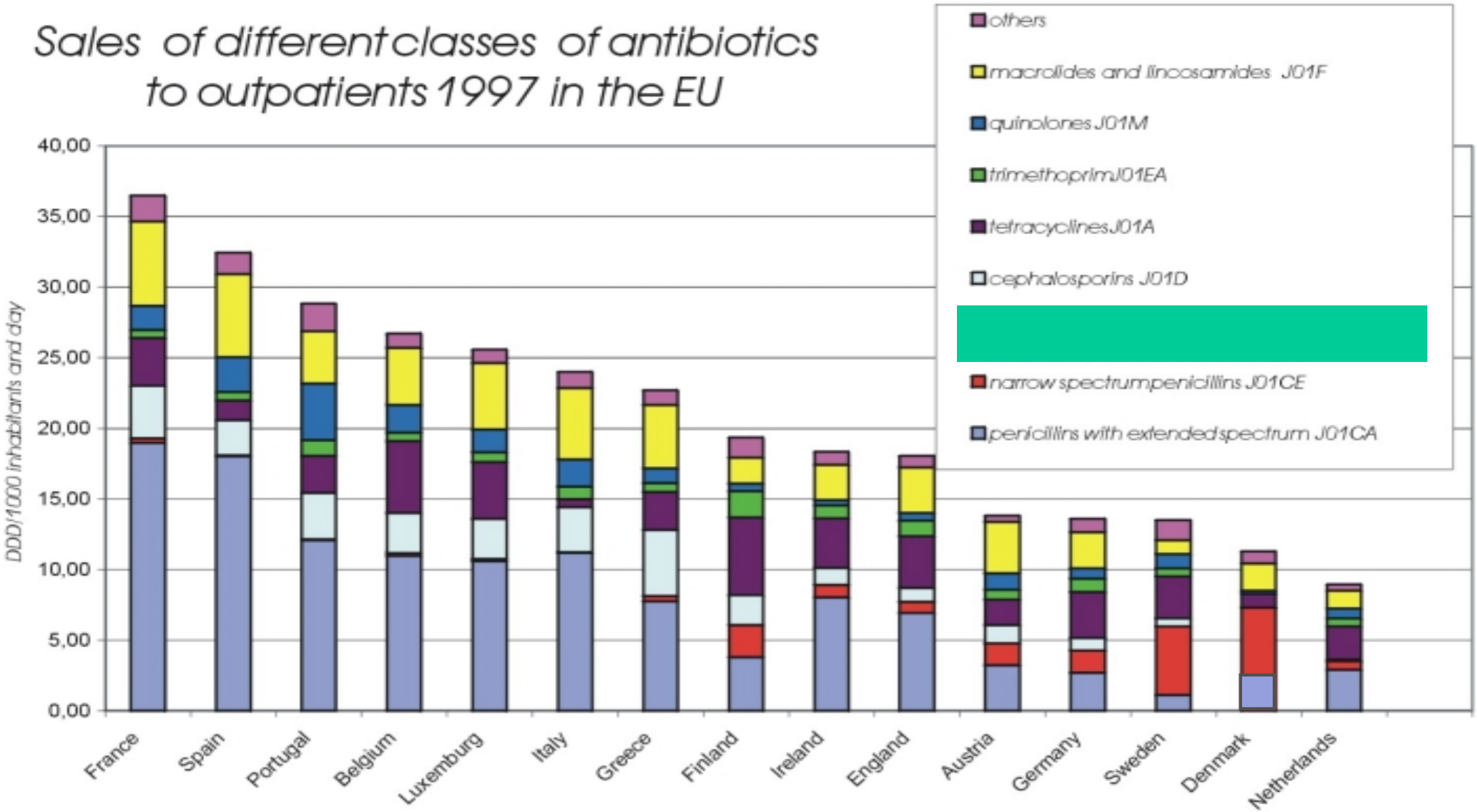
Antimicrobial Use in Hospitals in the Netherlands, Germany and Belgium



DDD/1,000 bed-days

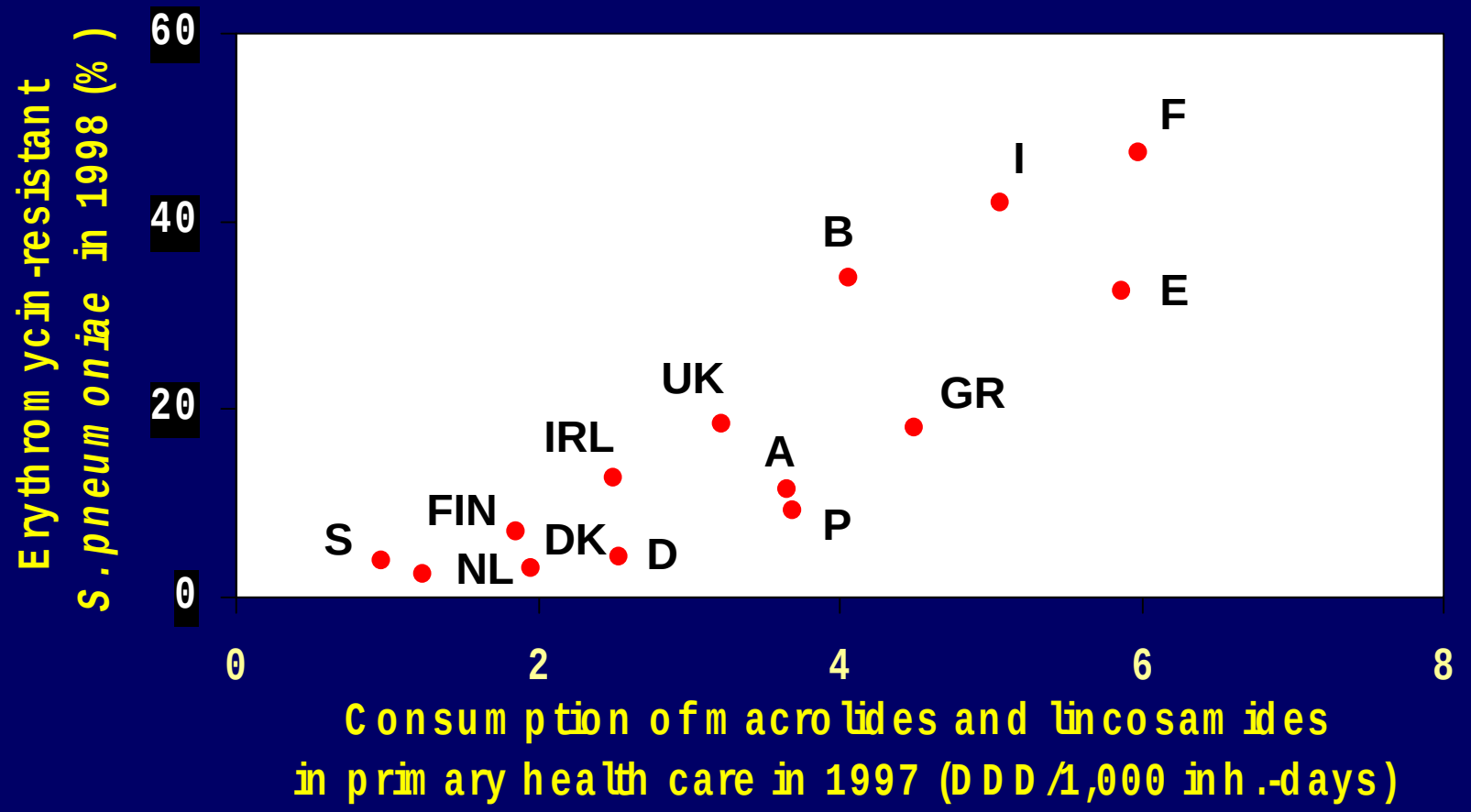
- 341
- 379
- 520-556

Source: Janknegt R, et al. Eur Clin Microbiol Infect Dis 1993;12:832-838.



Source: Cars O, et al. Lancet 2001; 357: 1851-3.

Erythromycin-Resistant *Streptococcus pneumoniae* and Macrolide Consumption in EU Member States, 1997-1998



Sources: Alexander Project, FINRES, STRAMA, DANMAP, and Cars O

Beta-lactamase production in *H.influenzae* and *M.catarrhalis*

- ***H.influenzae* ± 11-19% Europe**
  - **Belgium 16-18%**
  - **Netherlands 3-6%**

- ***M.catarrhalis* ± 90%**

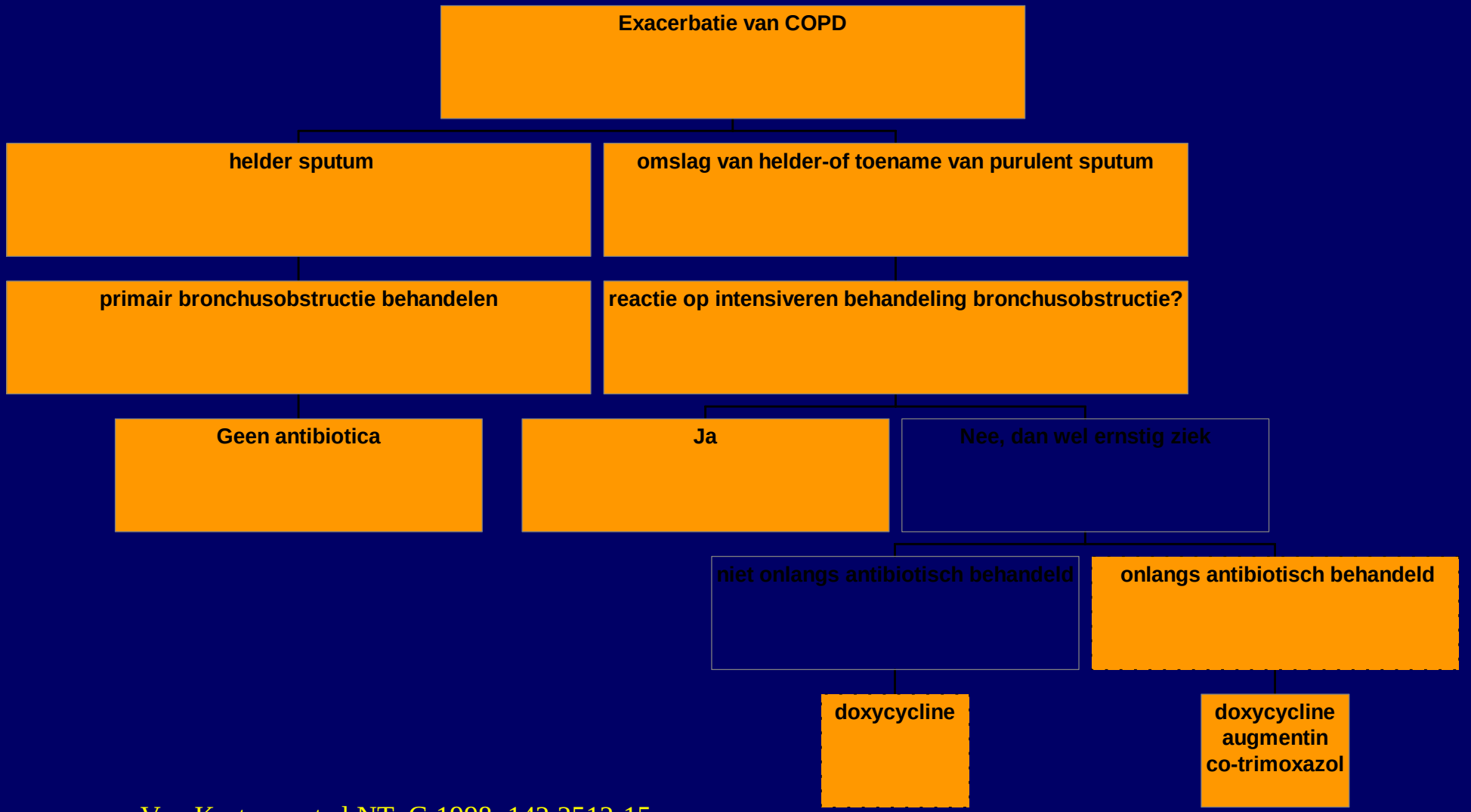
Felmingham et al CMI 2002;8 Suppl 2:12-42

Recommendations by professional societies regarding the usage of antimicrobial agents for AE of COPD

Organization	Statement	Type, route and duration
BTS 1997	Recommended for moderate or severe exacerbation;	Oral common antibiotic; broader spectrum if no response
ACCP, ACP, Am Soc Int Med 2001	Recommended	Optimal duration unclear
ERS 1995	Recommended	7-14 day of inexpensive antibiotic
ATS 1995	Recommended for abnormal mucus	simple antibiotic, unless severe
GOLD 2001	Recommended with increased sputum volume and purulence.	Choice should reflect local sensitivity for SP, HI and MC

Koller NEJM, 2002; 346: 988-94

SWAB richtlijn AECB in het ziekenhuis



Van Kasteren et al NTvG 1998; 142:2512-15

Conclusions

- Antibiotics are effective in severe forms of AECB
- Clinical criteria are useful in the determination of the indication
- Currently the “best” guidelines are the GOLD guidelines, although not restrictive enough
- Antibiotics should at least be effective against M. catarrhalis; H. influenzae and S.pneumoniae
- It is not clear at what resistance level (%) guidelines should leave out an antibiotic
- The Netherlands should probably revise their guidelines