



**EU-IBIS :
Surveillance and epidemiology of invasive
meningococcal disease in Europe 1999 –
2006**

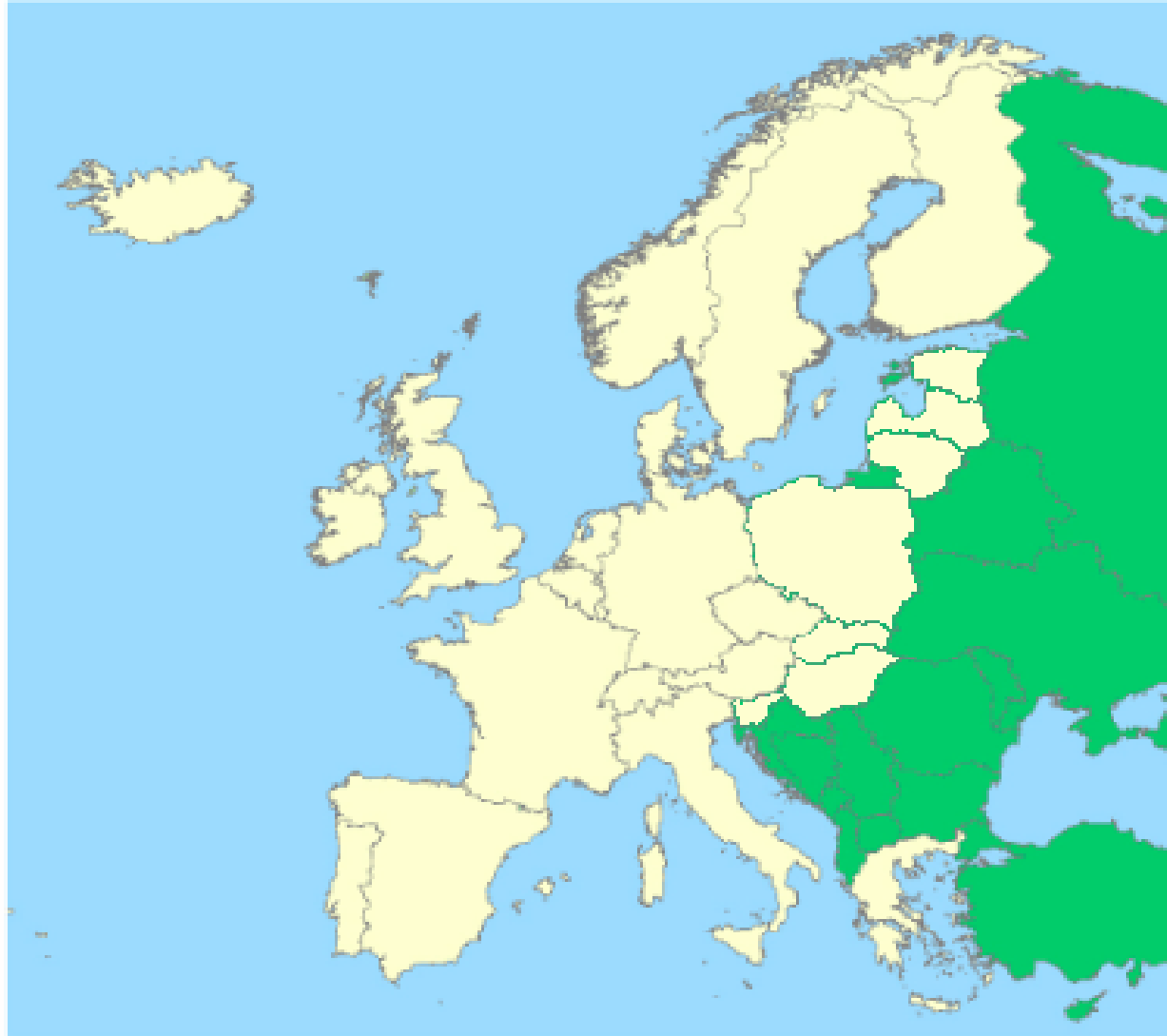
**Manny Chandra, Mary Ramsay on behalf of EU-IBIS
participants**



Invasive bacterial infection surveillance in the EU (EU-IBIS)

- European funding since October 1999
 - to Oct 2006 by DG Sanco (European Commission Public Health Directorate), then
 - to Oct 2007 by European Centre for Disease Prevention and Control (ECDC)
- Separate *H influenzae* and *N meningitidis* networks
 - 27 countries participate in *N meningitidis* (NM) network
 - includes 9 of countries admitted to EU in 2004
- Objectives of NM network
 - To collate and analyse epidemiological data on invasive disease
 - To assess the role and impact of vaccination on disease incidence
 - To produce an EU laboratory quality assurance programme

Participating countries



- Austria
- Belgium
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Iceland
- Ireland
- Italy
- Latvia
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Slovak Republic
- Slovenia
- Spain
- Sweden
- Switzerland
- UK

Variables collected

- Disaggregate data collected every six months
 - Around 6 -12 months after the end of the period

ID

Age or mth/yr of birth

Date of onset

Geographic location

Imported

Outcome

Clinical diagnosis

Method of confirmation

(Culture/PCR/Latex/Serology/Clinical diagnosis only)

Site of isolate

Epidemiological typing of the isolate

(Serogroup, serotype, PorA variants)

Vaccination status (if relevant)

Antibiotic sensitivities

EU-IBIS data 1999 - 2006

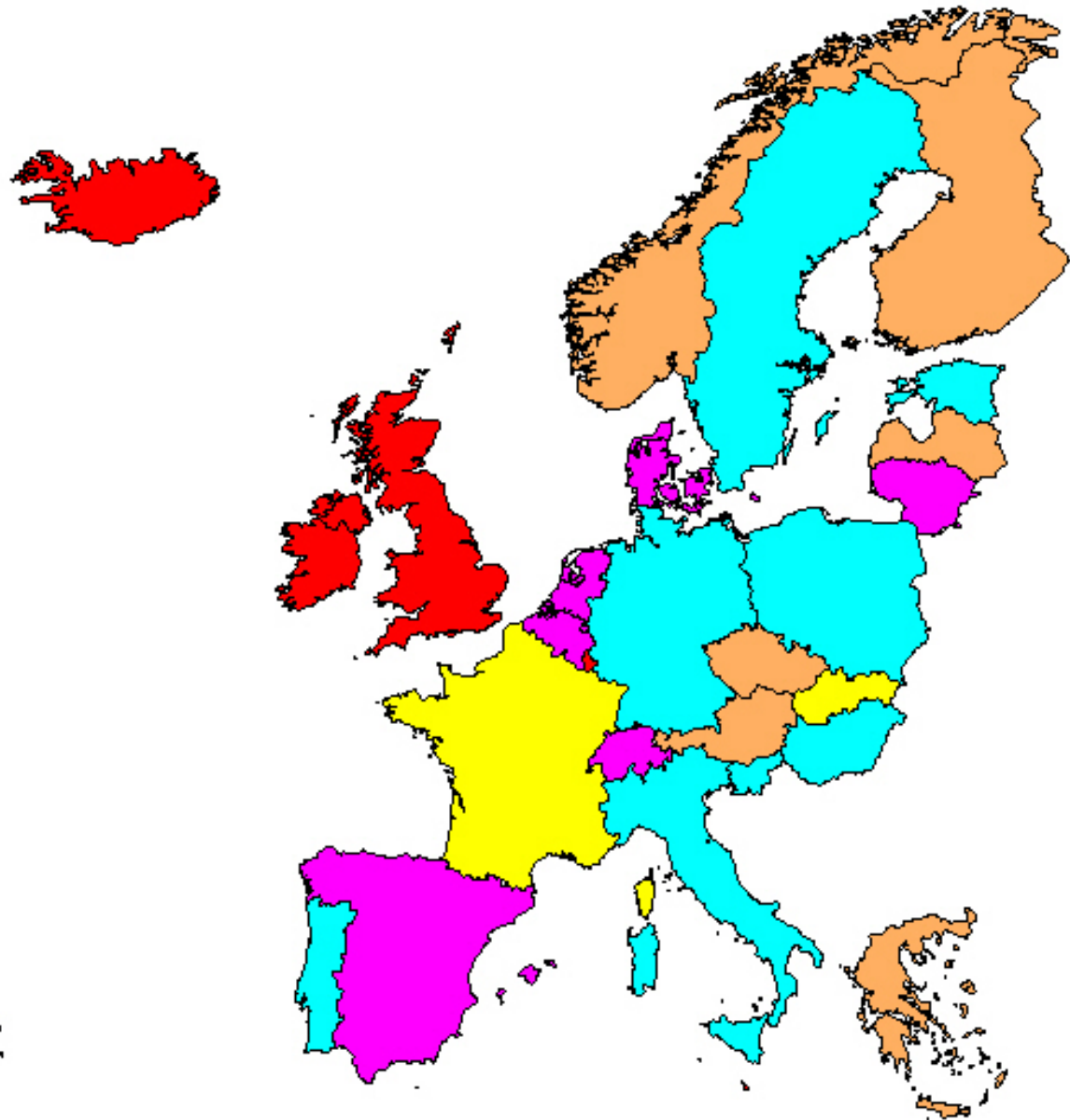
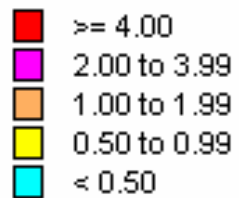
➤ Summary of total reports

- EU-IBIS holds data on over 63,000 cases of invasive meningococcal disease (IMD) from 27 countries
- Consistent data for 1999 to first half 2006 available from 20 countries, data to 2006 for 18 countries
- Three countries submit separate, unreconciled epidemiological and laboratory datasets

- ### ➤ In 2006, incidence of laboratory confirmed cases ranged from 0.29 (Italy) per 100,000 population to 4.37 (Ireland)
- Ranking of countries largely remains the same over time, but range in overall incidence appears to be decreasing

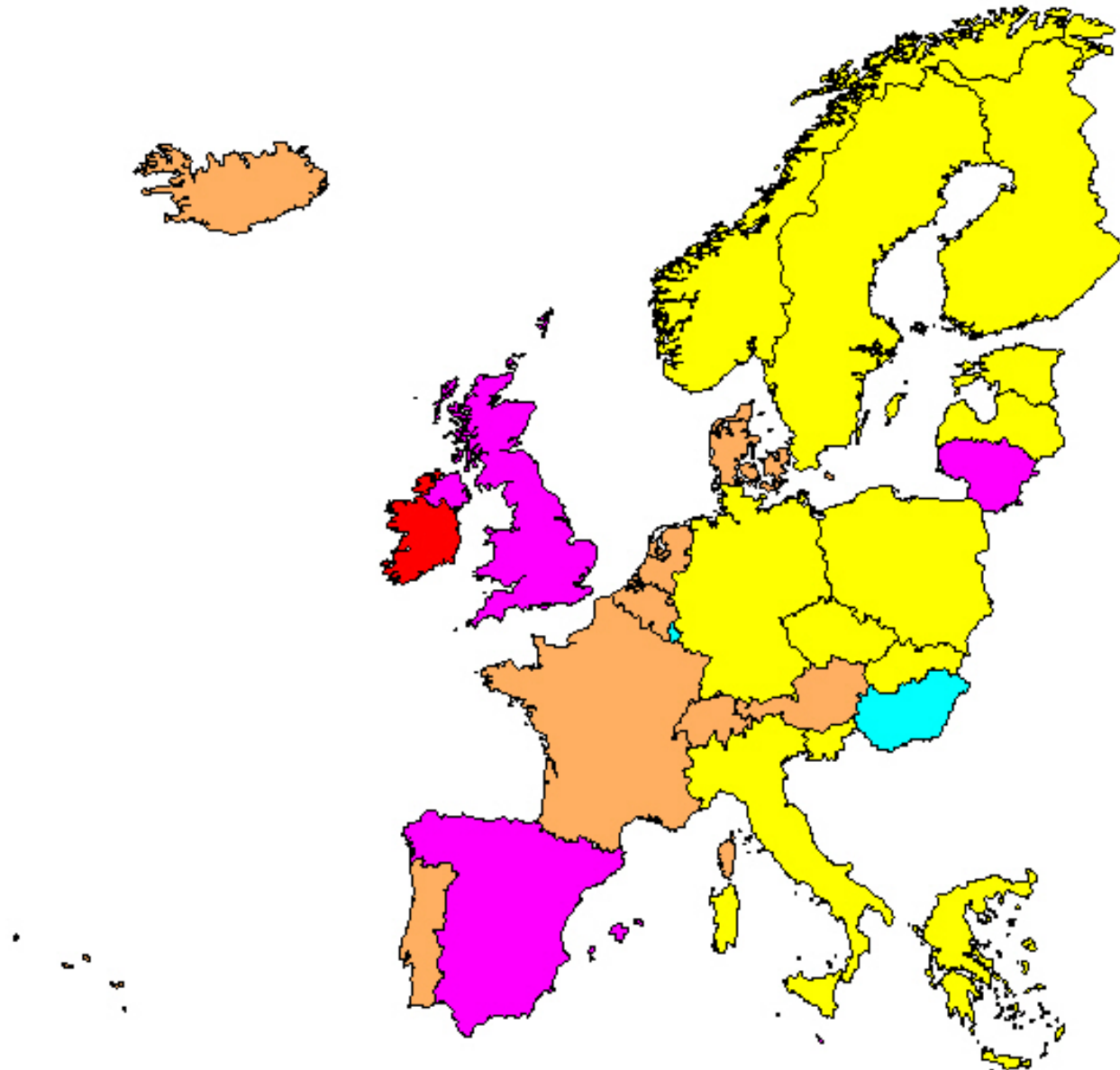
Incidence of IMD, 1999 or baseline year

Incidence (per 100,000 population)

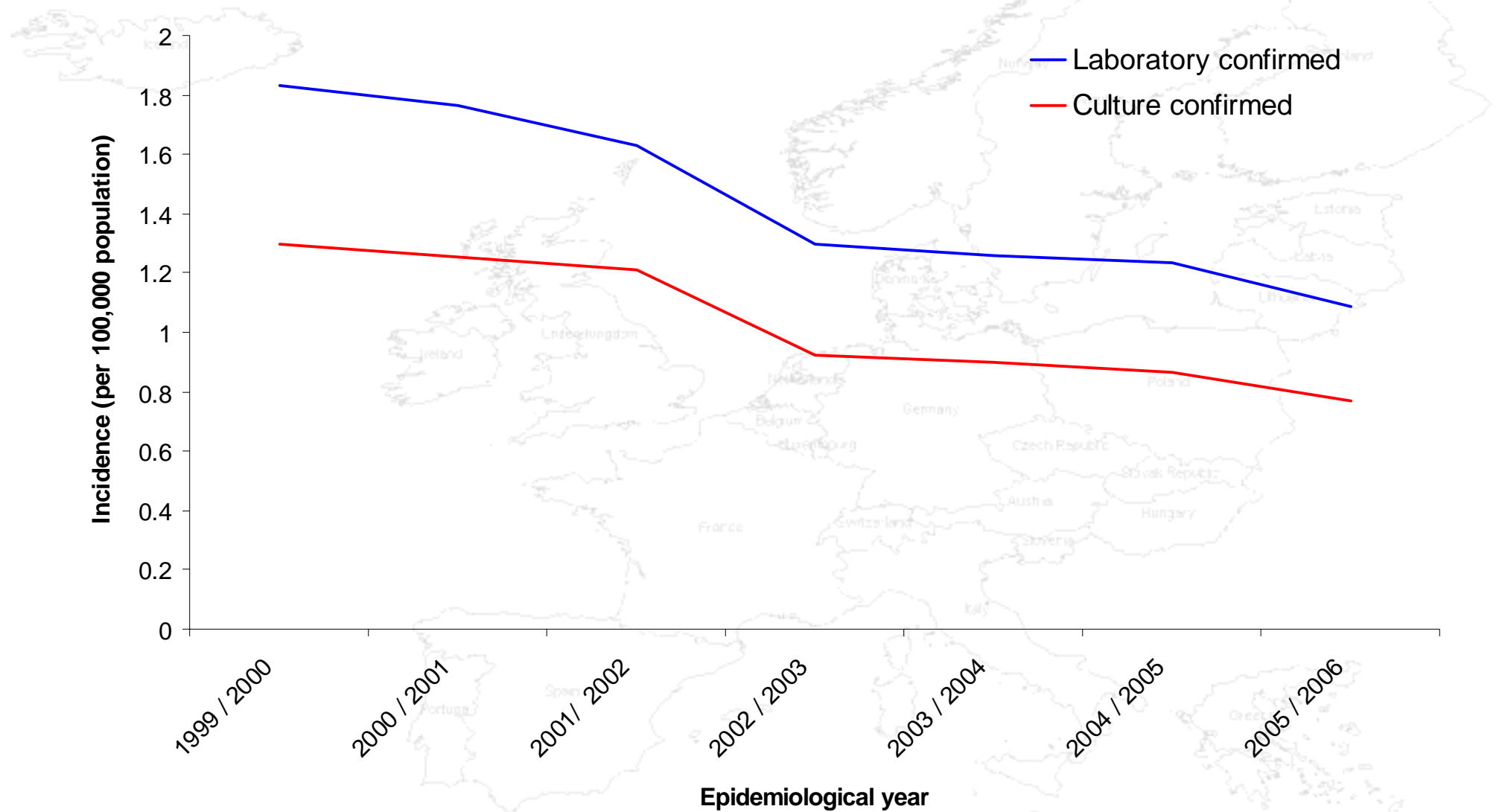


Incidence of IMD, 2005

Incidence (per 100,000 population)

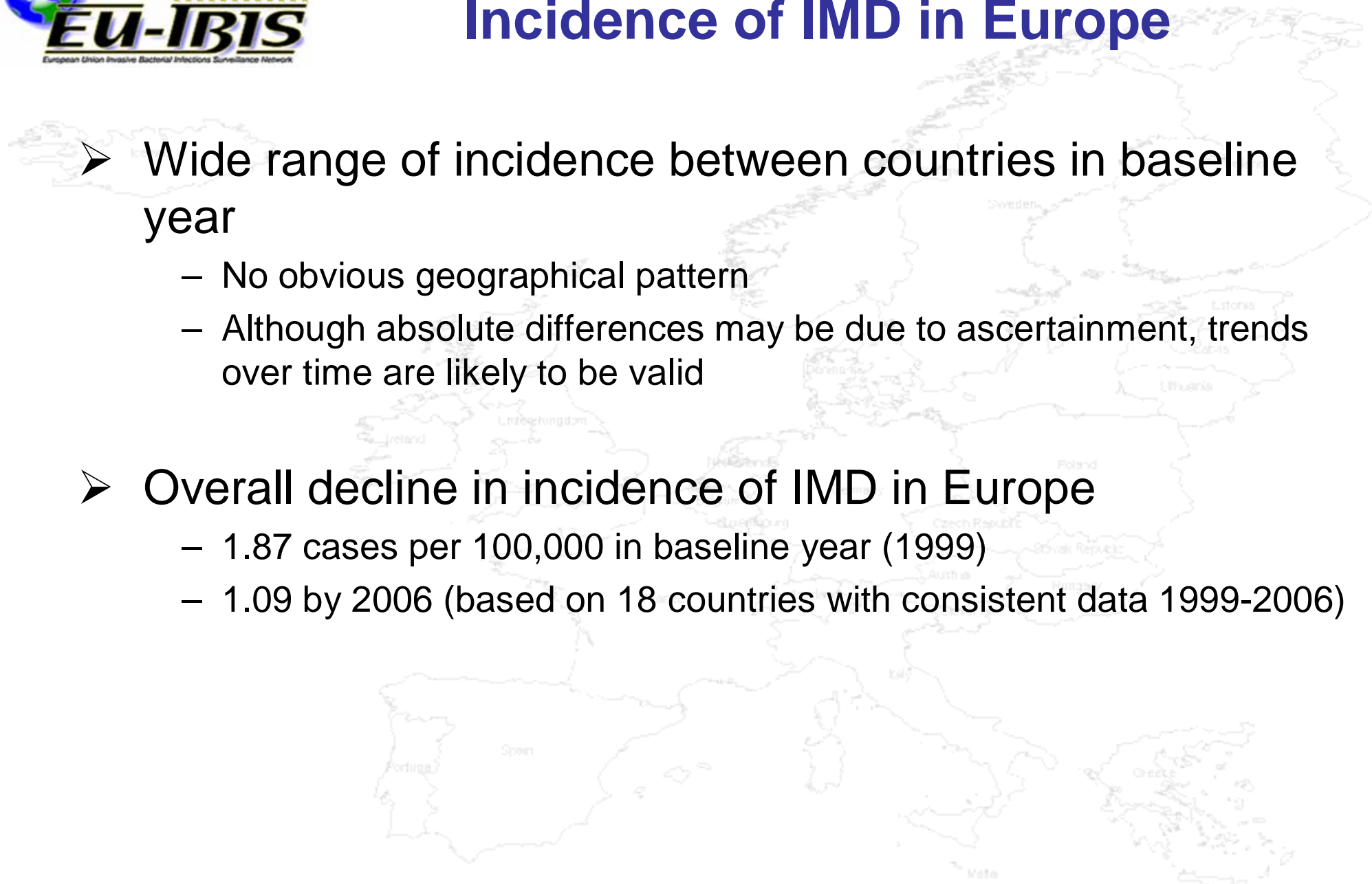


Overall incidence of IMD in Europe By epidemiological year 99/00 – 05/06

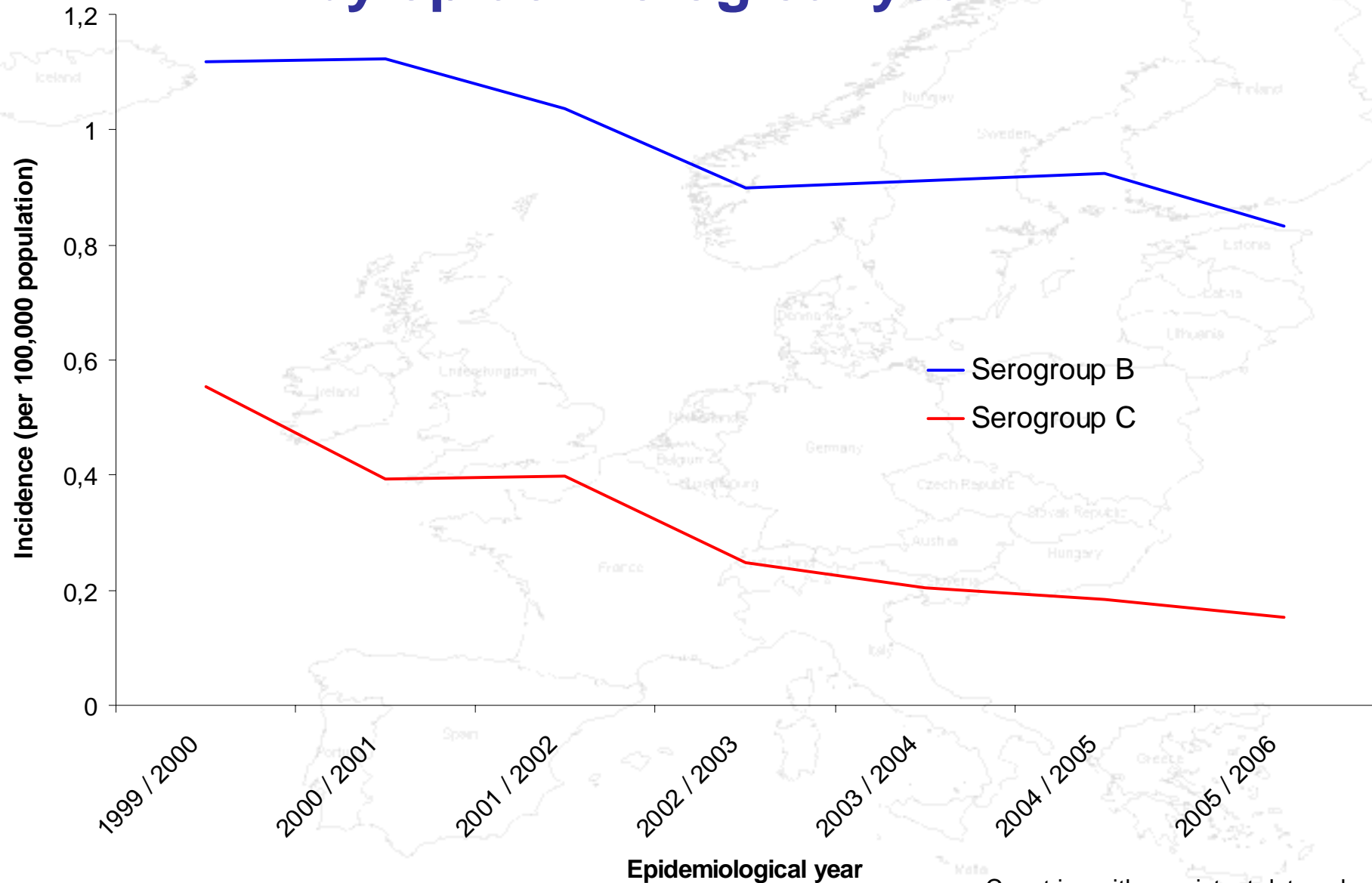


Countries with consistent data only

Incidence of IMD in Europe

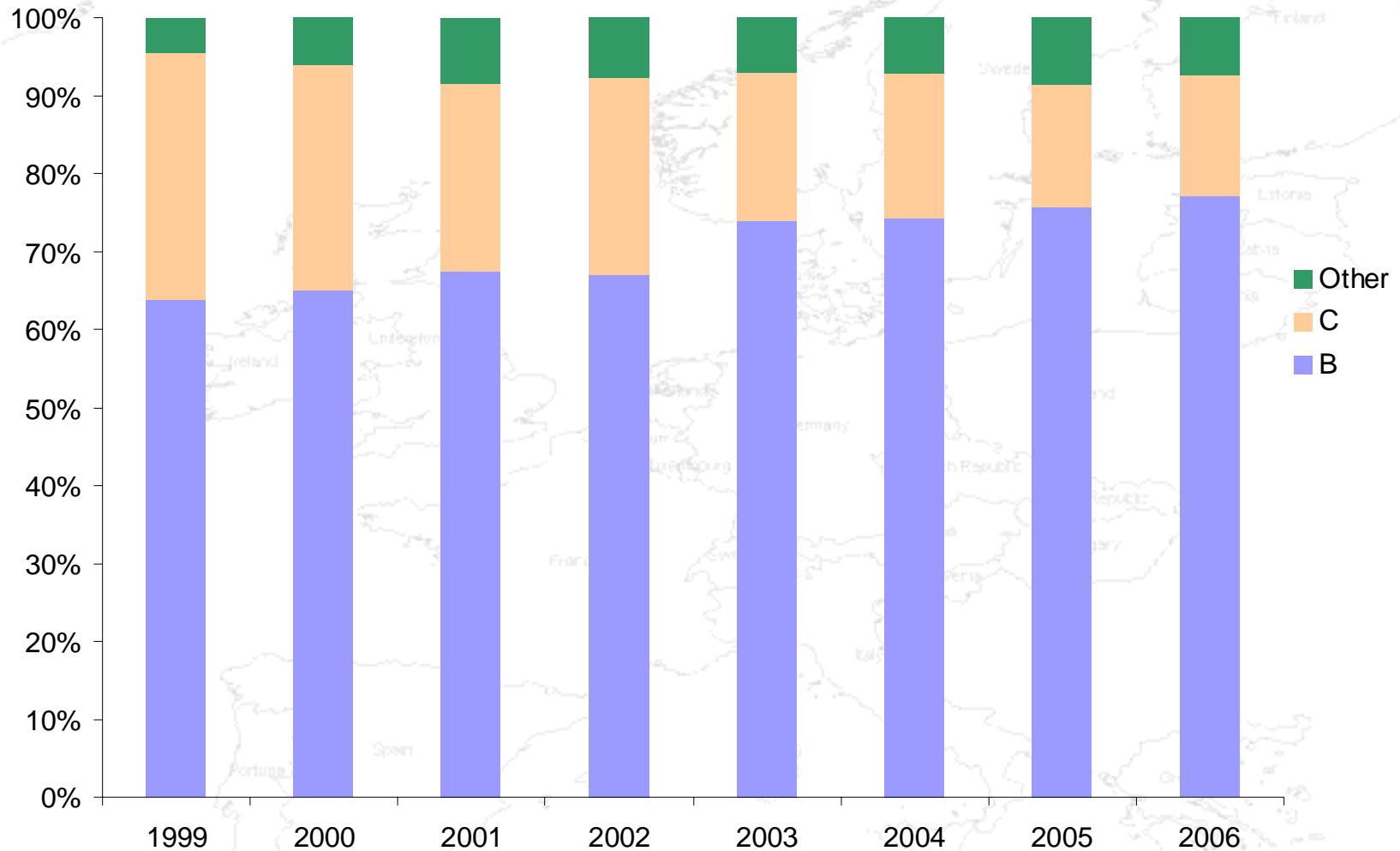
- 
- Wide range of incidence between countries in baseline year
 - No obvious geographical pattern
 - Although absolute differences may be due to ascertainment, trends over time are likely to be valid
 - Overall decline in incidence of IMD in Europe
 - 1.87 cases per 100,000 in baseline year (1999)
 - 1.09 by 2006 (based on 18 countries with consistent data 1999-2006)

Serogroup specific incidence of IMD, by epidemiological year

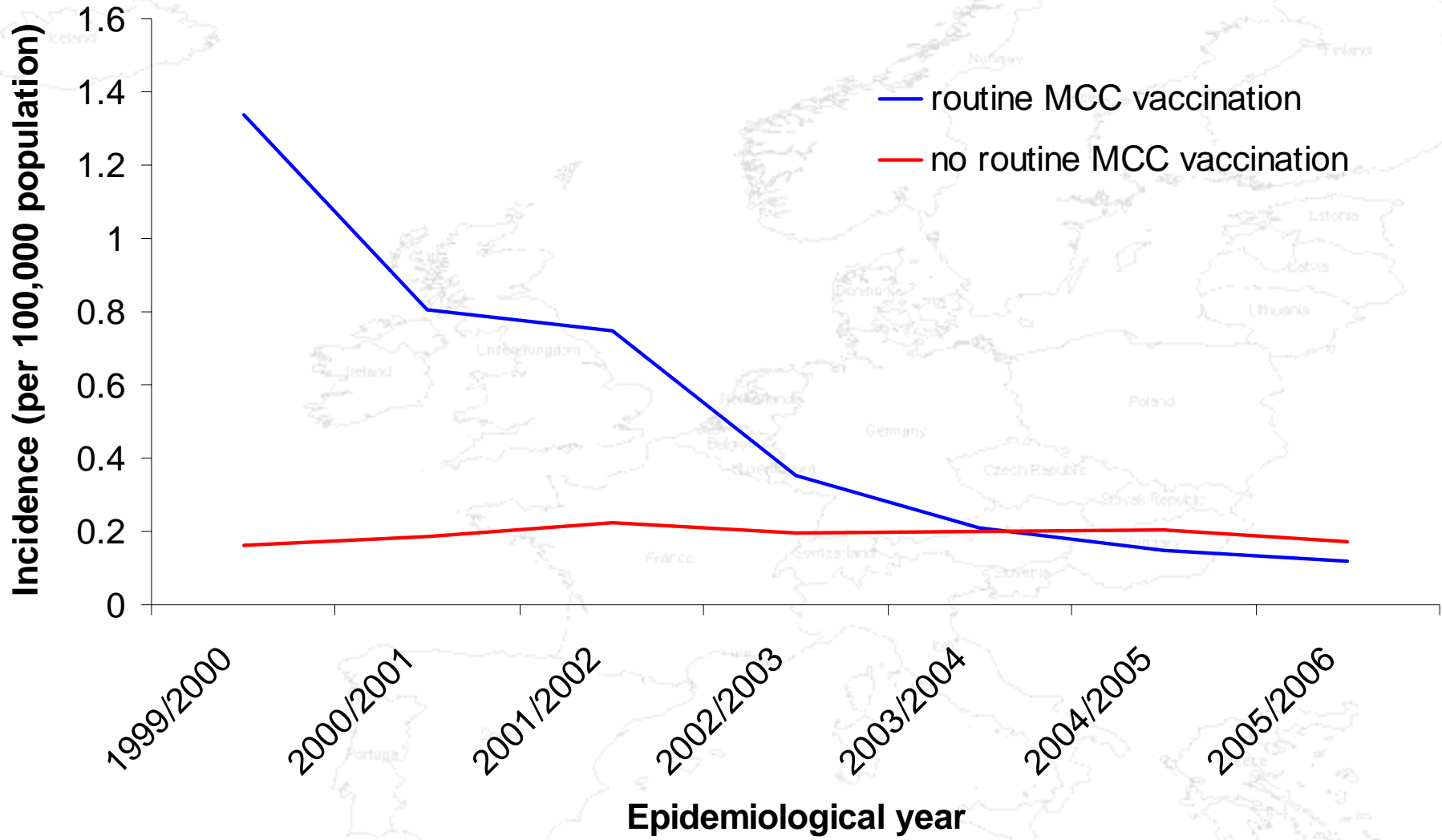


Countries with consistent data only

Serogroup distribution of IMD by year, all countries combined

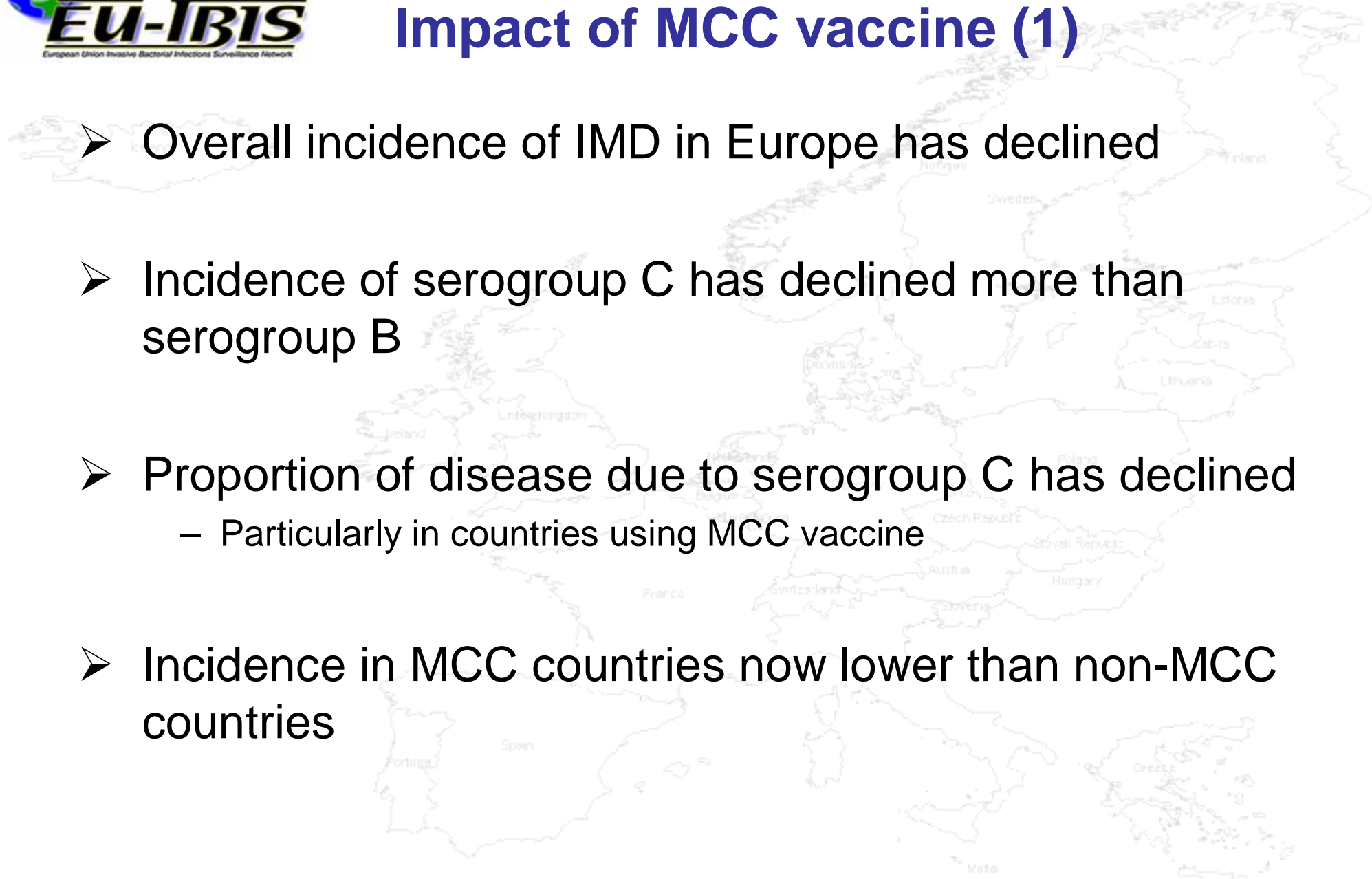


Incidence of serogroup C IMD by routine MCC vaccine use and epidemiological year

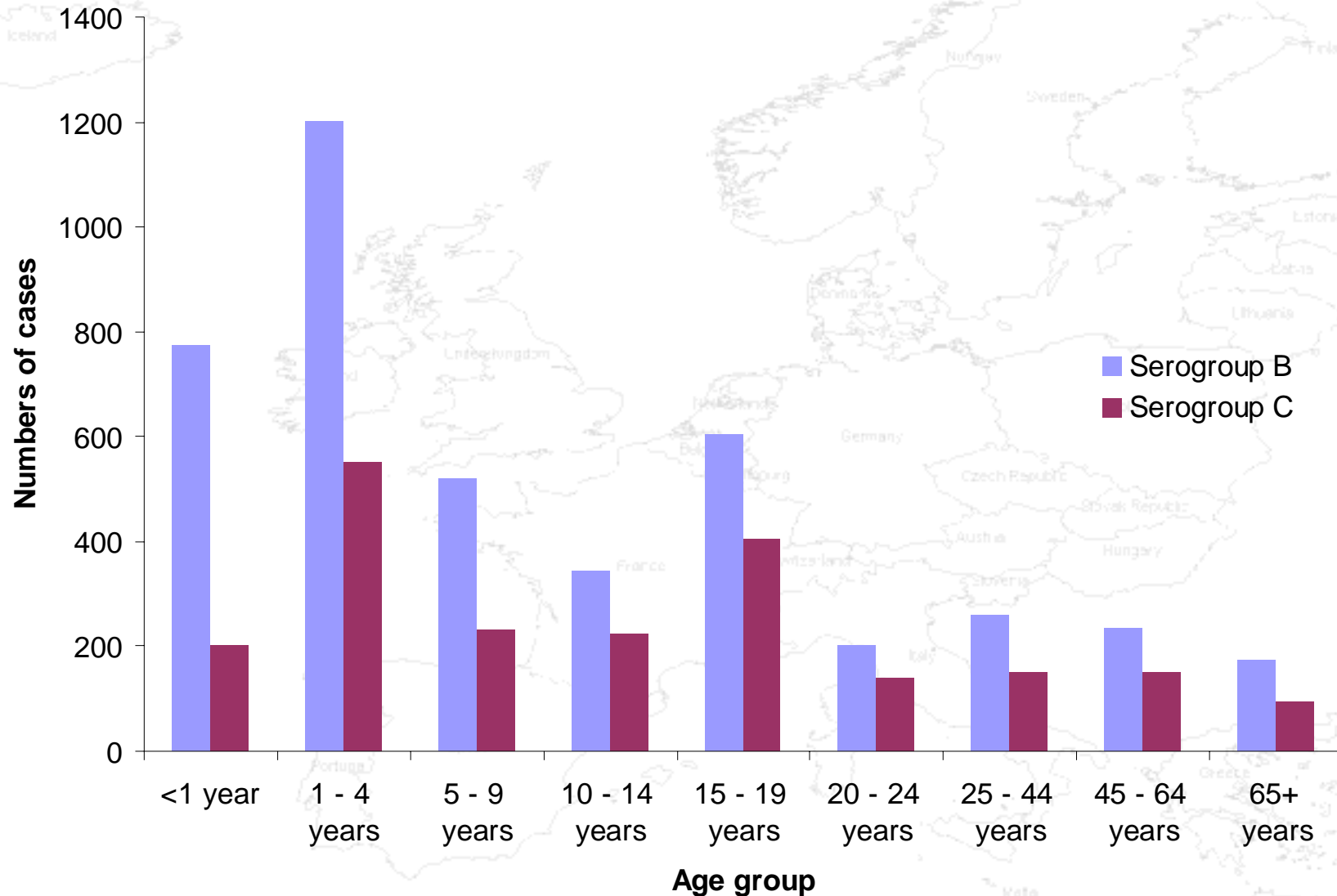


Countries with consistent data only

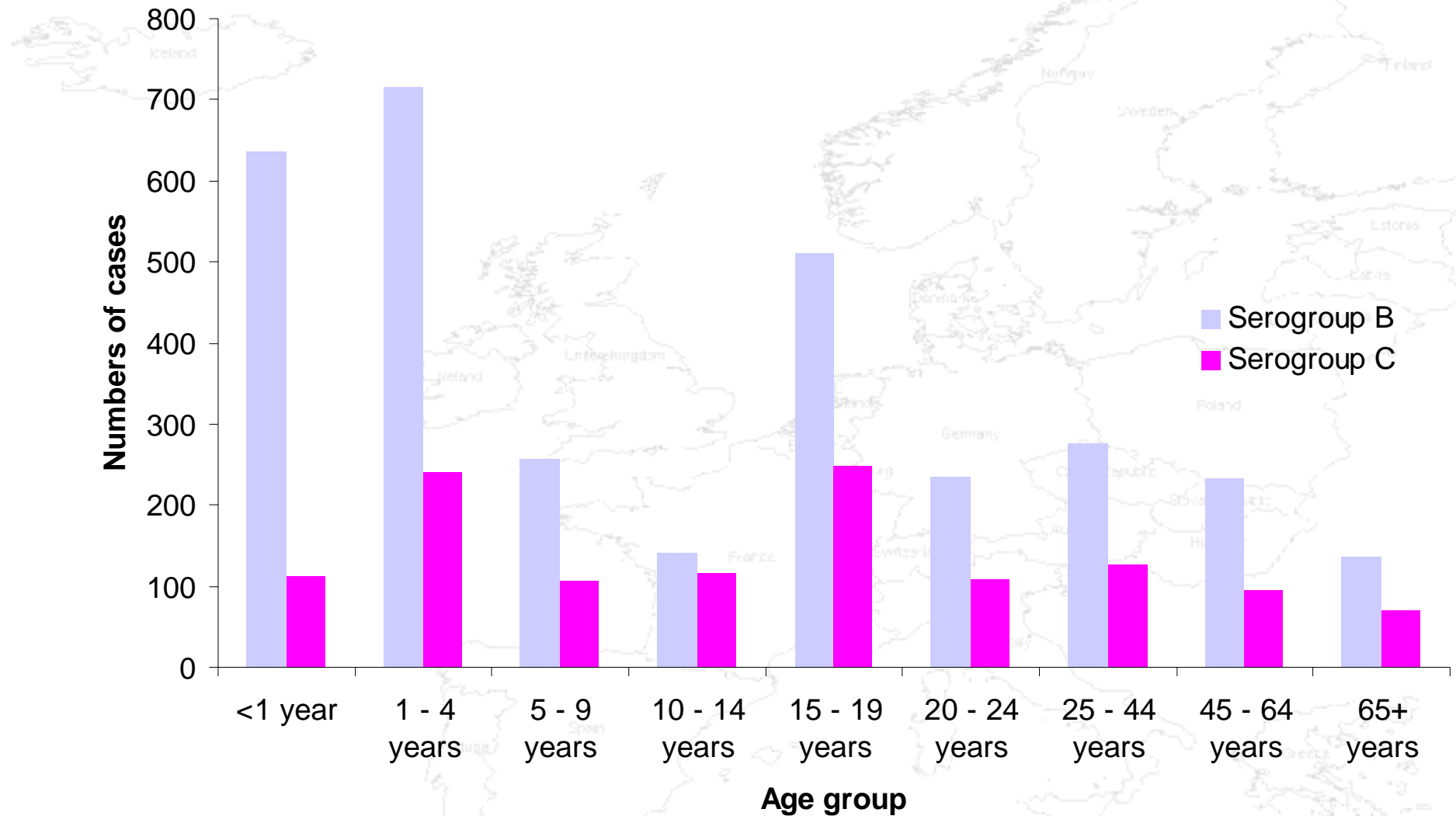
Impact of MCC vaccine (1)

- 
- Overall incidence of IMD in Europe has declined
 - Incidence of serogroup C has declined more than serogroup B
 - Proportion of disease due to serogroup C has declined
 - Particularly in countries using MCC vaccine
 - Incidence in MCC countries now lower than non-MCC countries

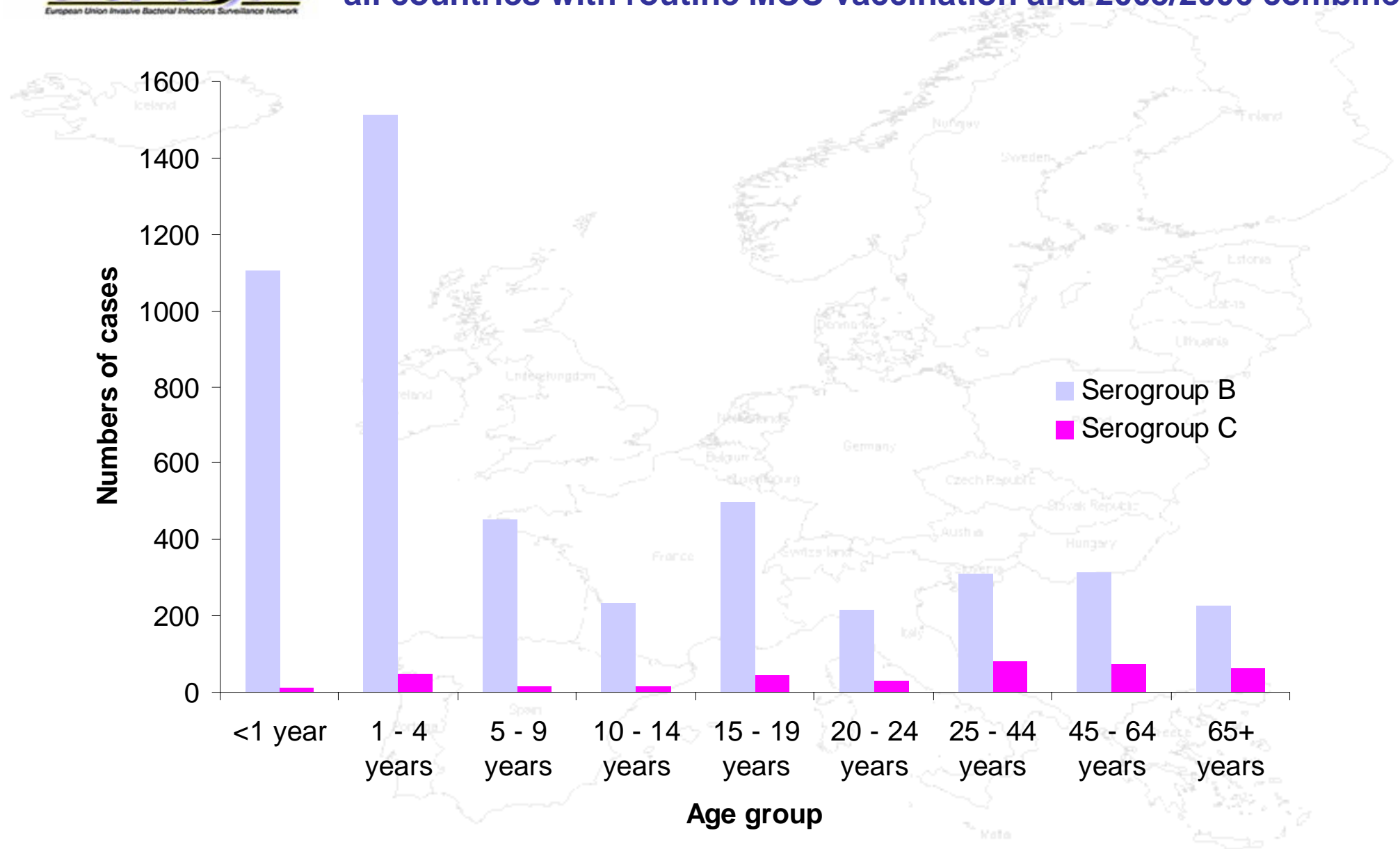
Age specific distribution of IMD by serogroup, all countries combined, 1999 or baseline year



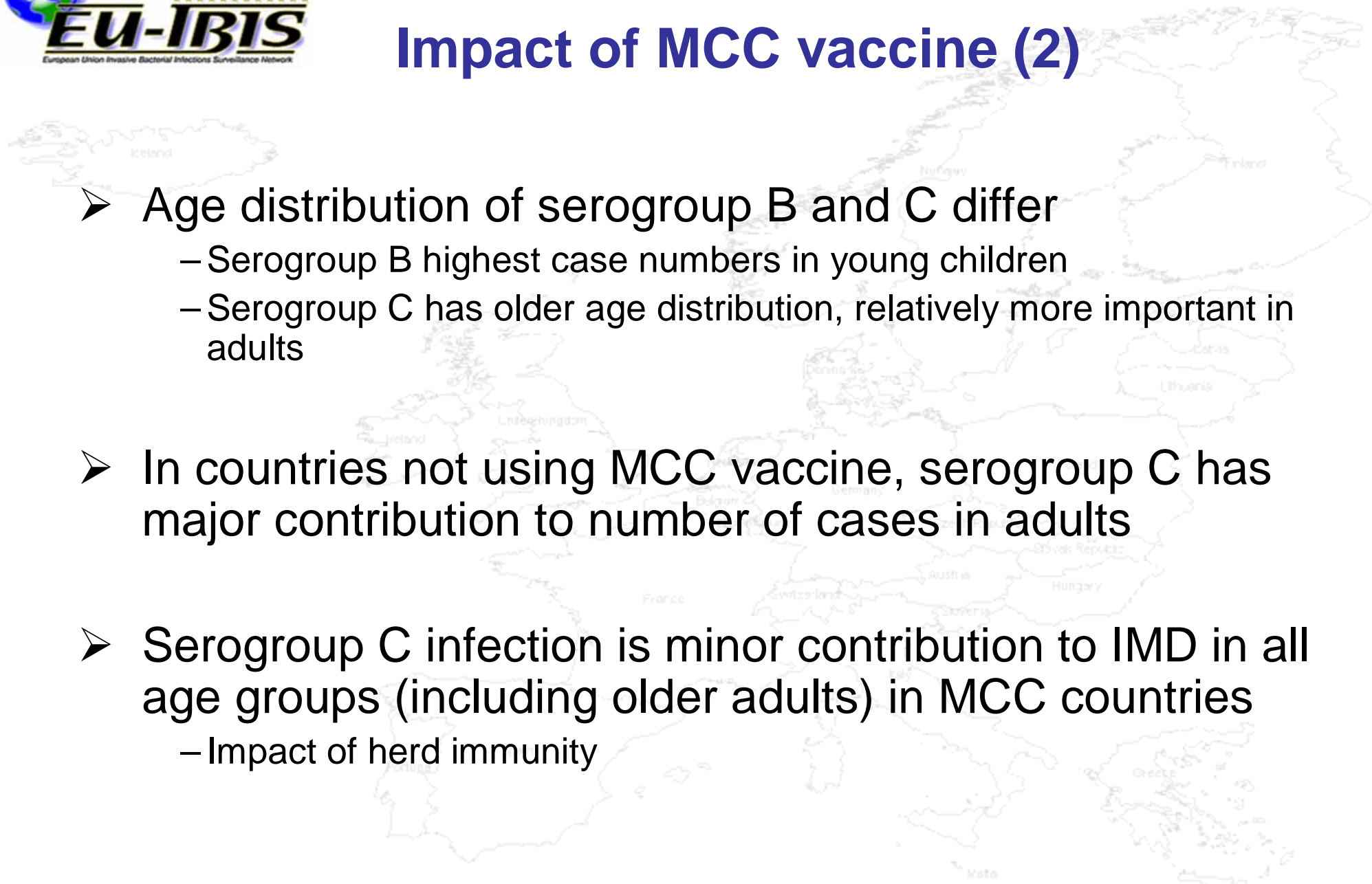
Age specific distribution of IMD by serogroup, all countries without routine MCC vaccination and 2005/2006 combined



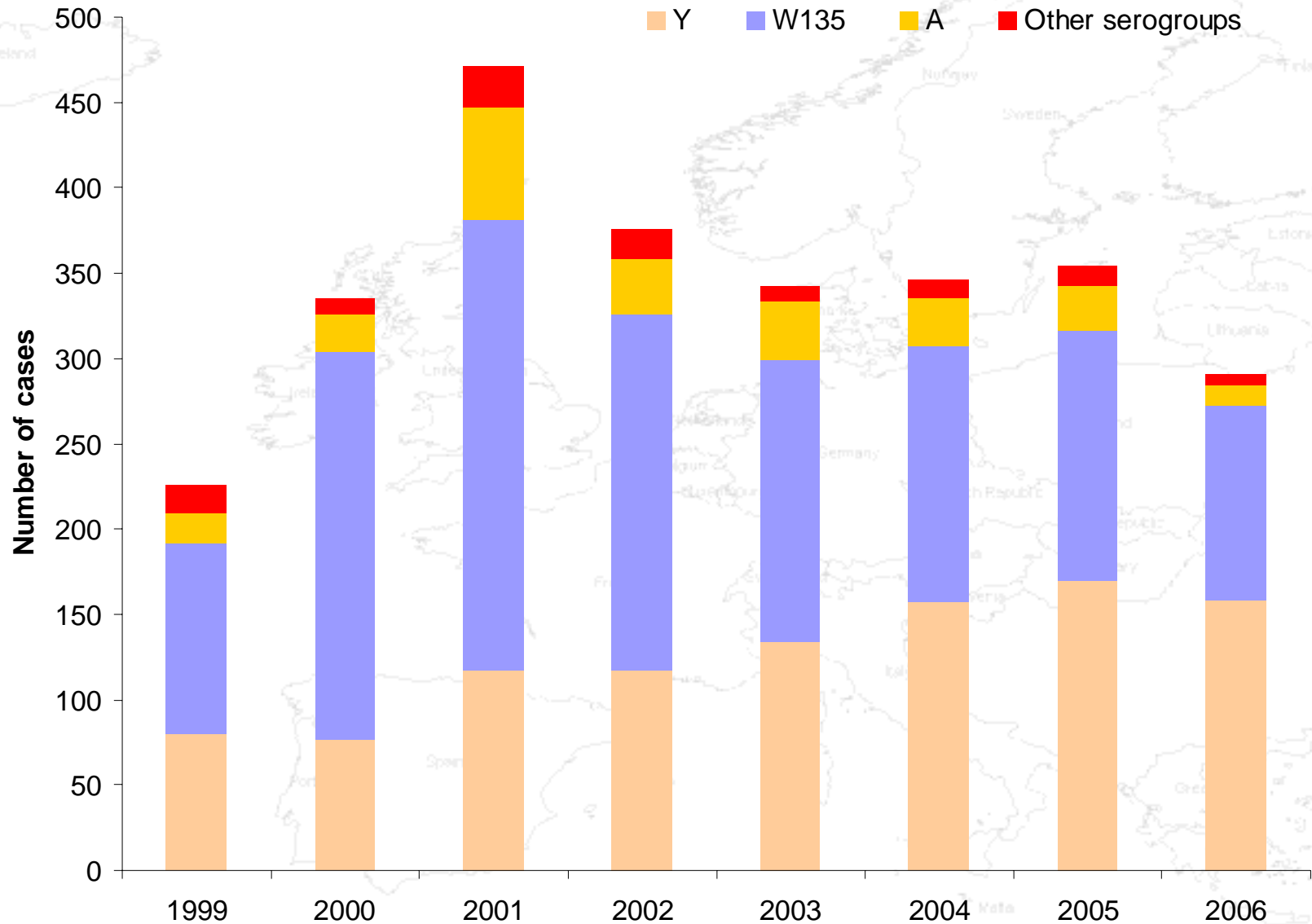
Age specific distribution of IMD by serogroup, all countries with routine MCC vaccination and 2005/2006 combined



Impact of MCC vaccine (2)

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- Age distribution of serogroup B and C differ
 - Serogroup B highest case numbers in young children
 - Serogroup C has older age distribution, relatively more important in adults
 - In countries not using MCC vaccine, serogroup C has major contribution to number of cases in adults
 - Serogroup C infection is minor contribution to IMD in all age groups (including older adults) in MCC countries
 - Impact of herd immunity

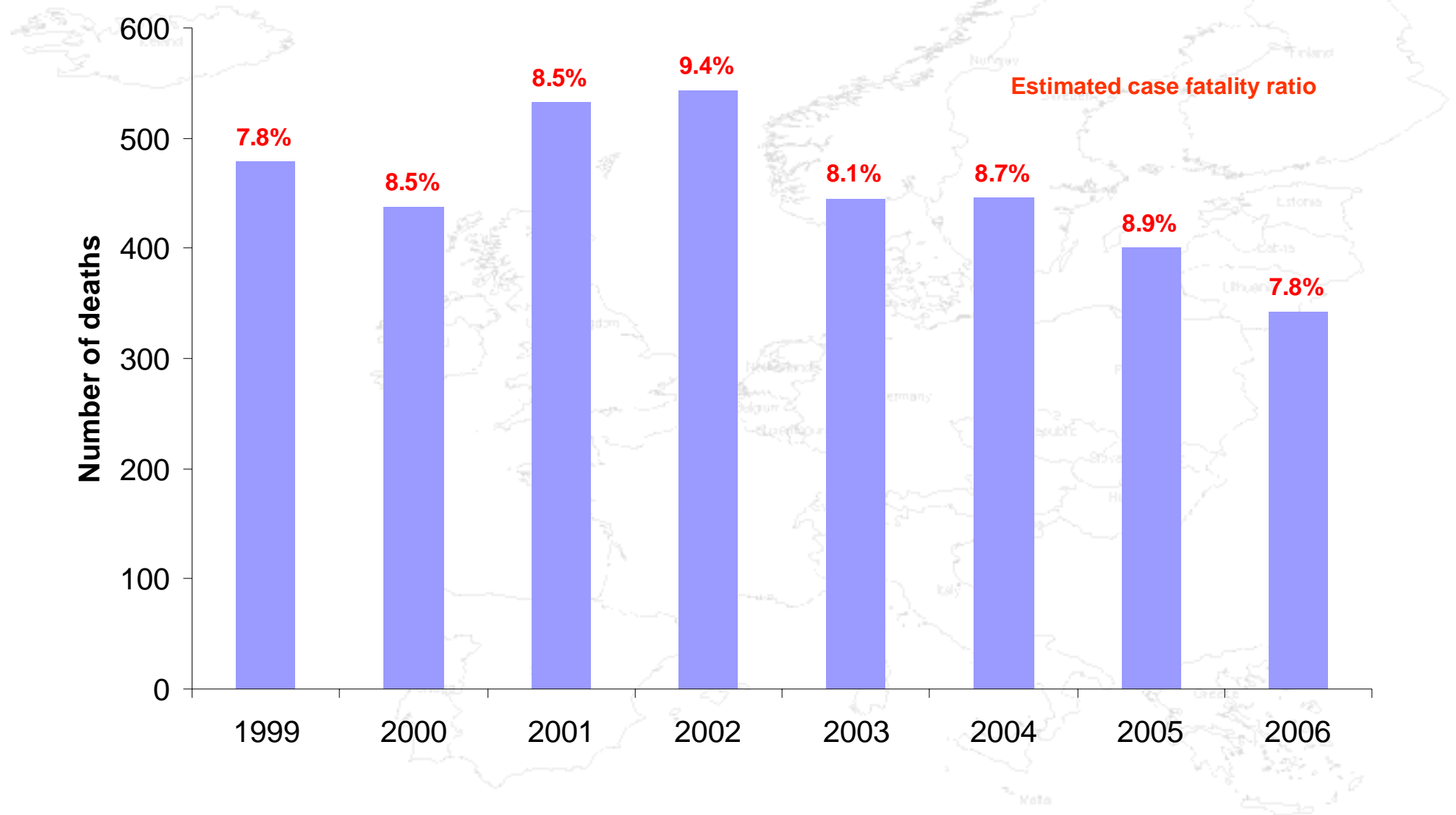
Non B, C serogroup distribution, by year, all countries combined



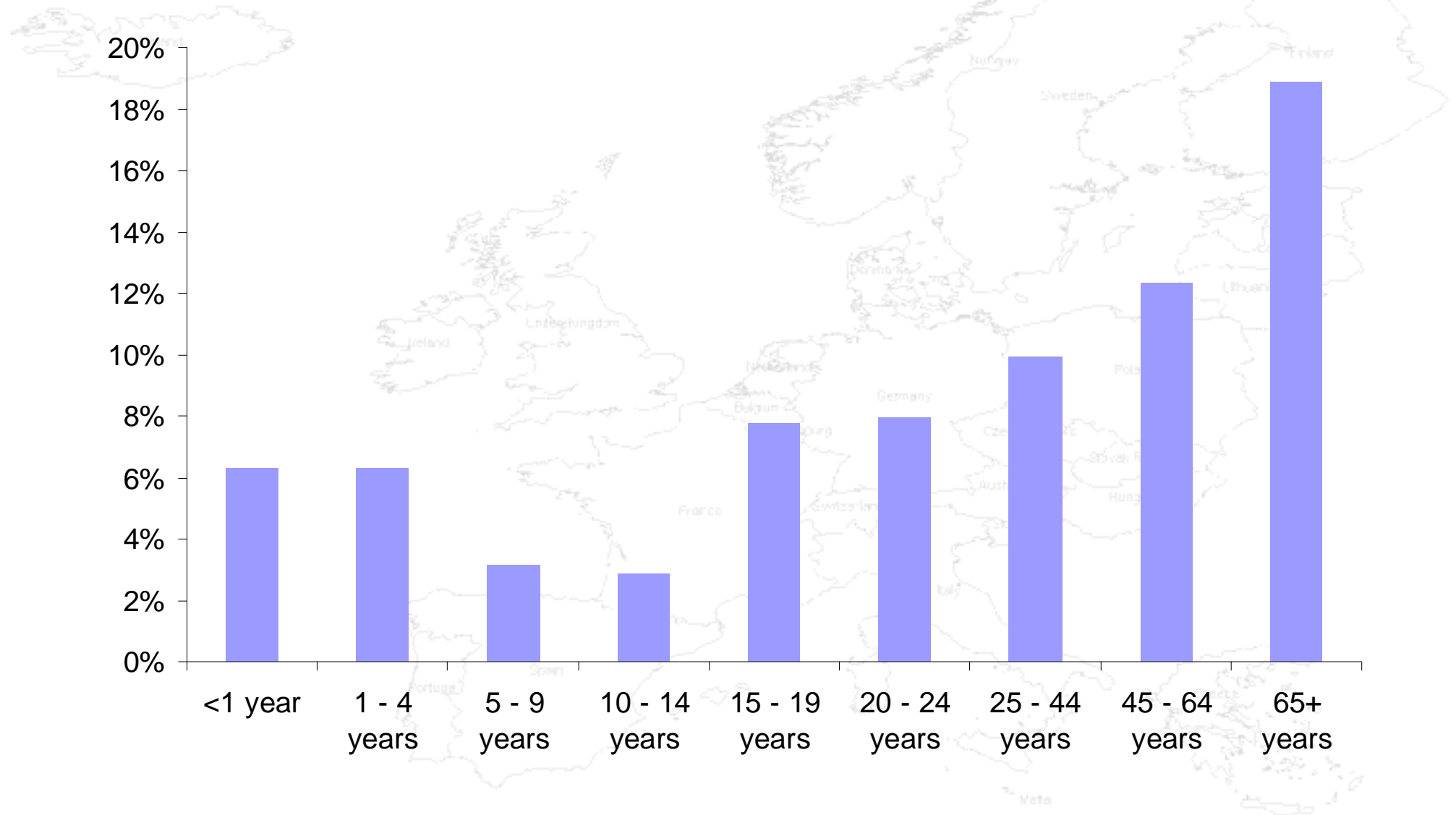
Serogroup distribution of IMD across Europe

- Small contribution of serogroups other than B and C
 - Around 300-400 of total annual number of approx 5,000
- Overall trends in number of non-B and C cases are fairly stable
- Relative importance of W135 and Y similar over time
 - W135 became increasingly important in 2001 and 2002
 - Following importation in association with Hajj
 - Successful impact of using quadrivalent vaccine for Hajj
- In 2006, serogroup Y is the major non-B, non-C serogroup causing IMD

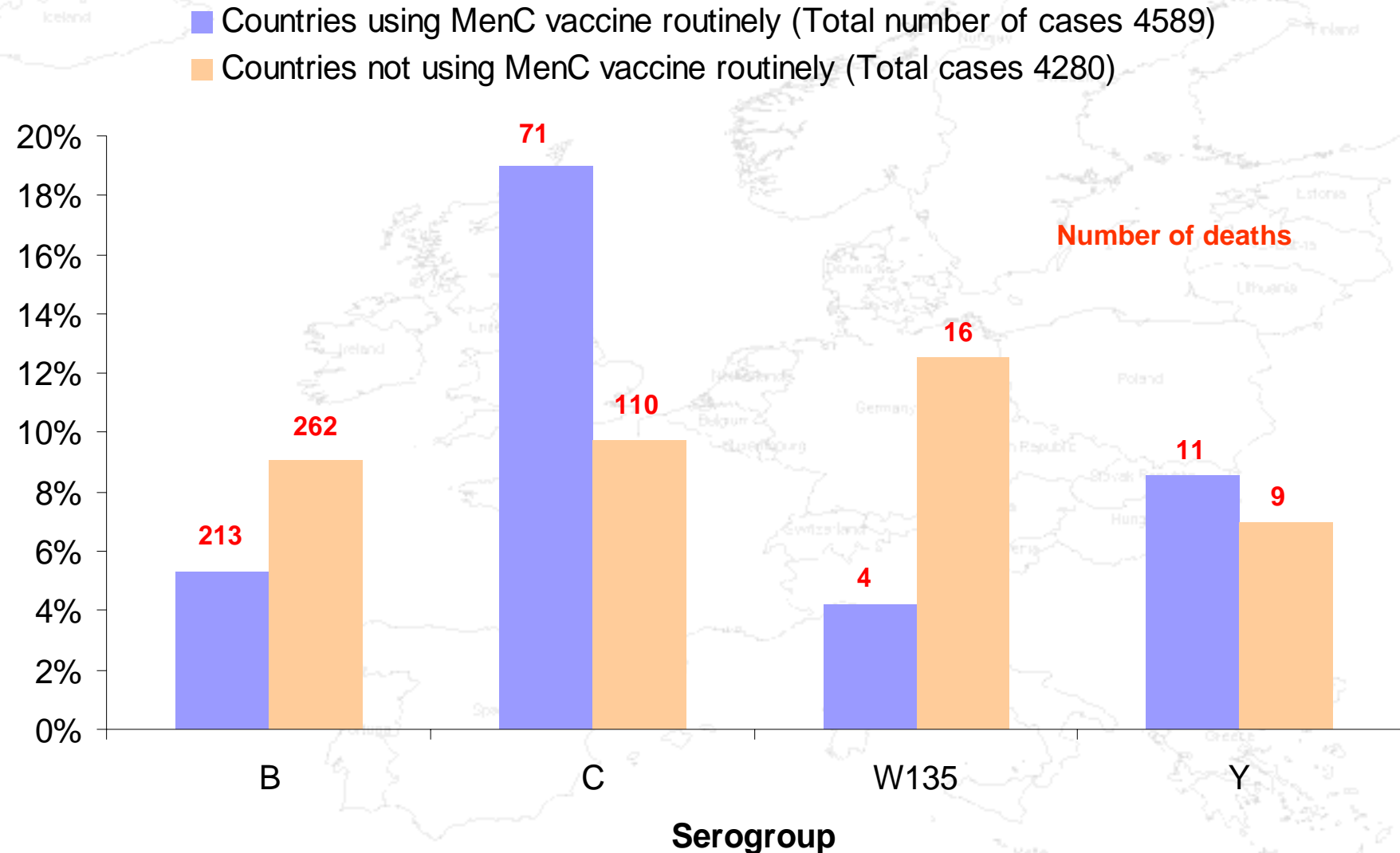
Deaths from confirmed IMD cases, by year, all countries combined



Case fatality ratio for confirmed IMD, 2005/2006 and all countries combined



Case fatality ratio for confirmed IMD, 2005/2006 and all countries combined



Case fatality ratio

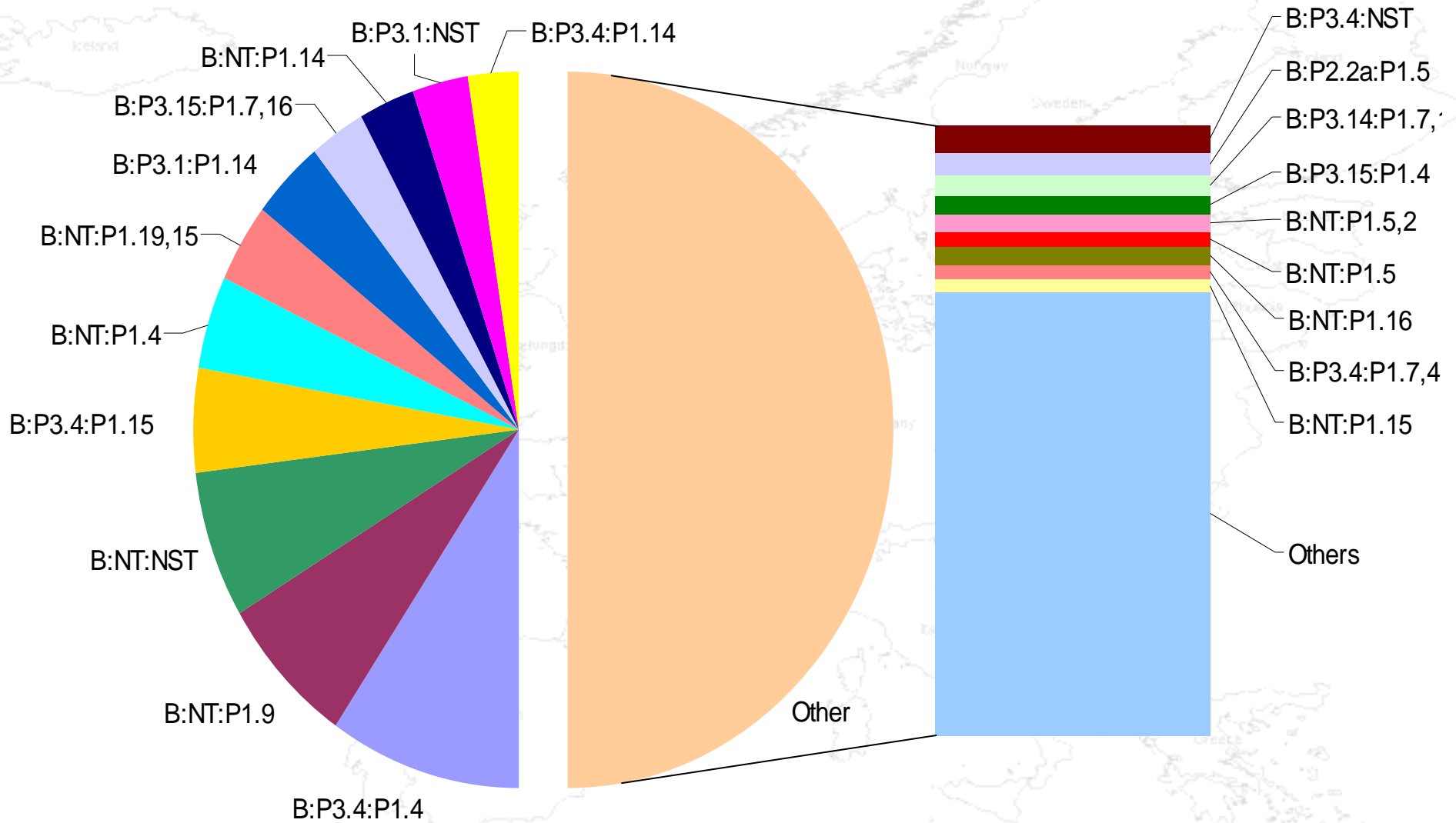
- Fewer deaths caused by IMD with time,
 - slightly reduced CFR and
 - reduced IMD incidence

- CFR increases with age, lowest in the 5 to 15 year age group, high in elderly

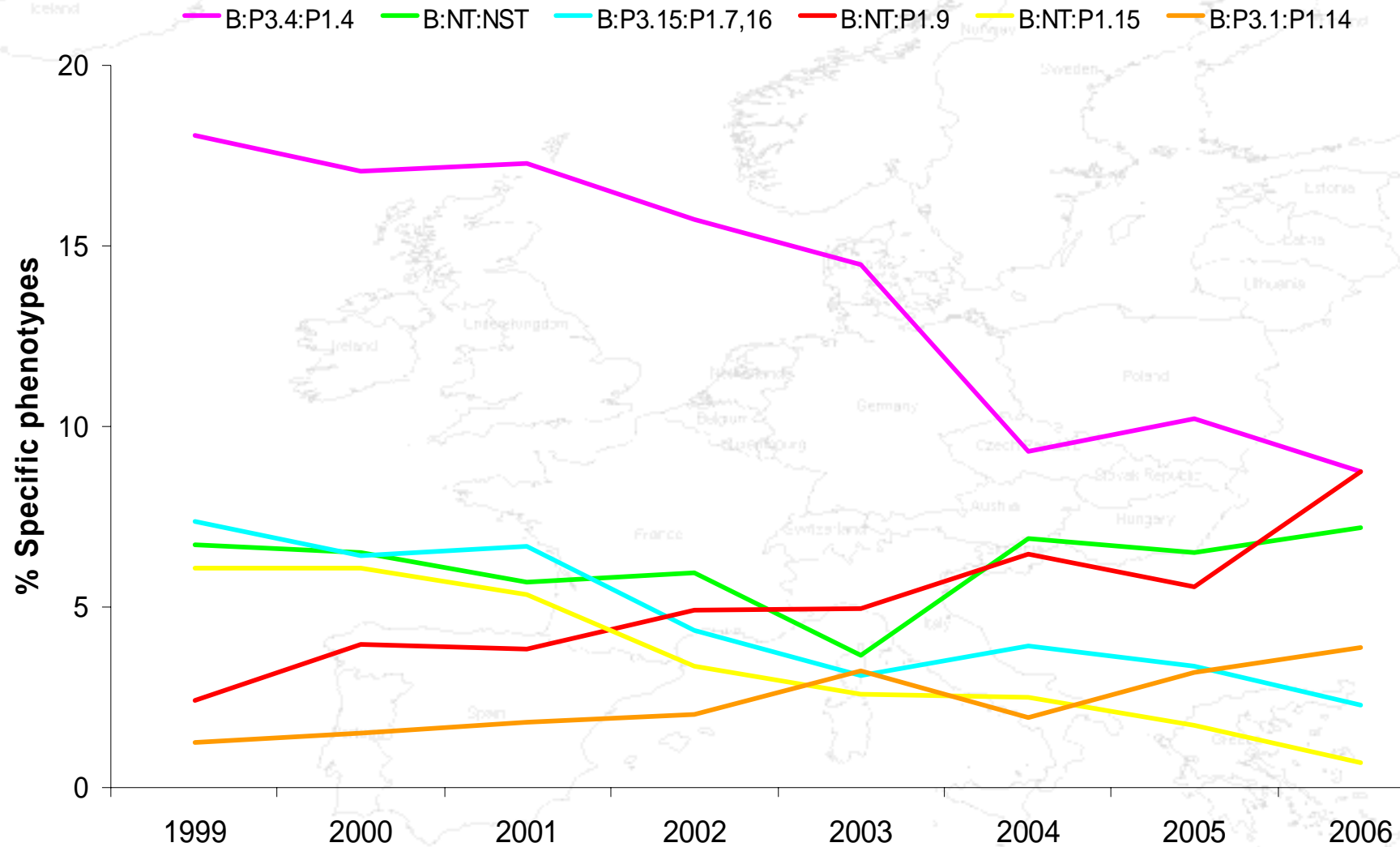
- CFR remains high for serogroup W135 and C

- In countries with routine MenC vaccination, high CFR due to serogroup C strains
 - May be due to shift in age distribution following vaccination of younger age groups

Major phenotypes of serogroup B, all countries and 2005/2006 combined

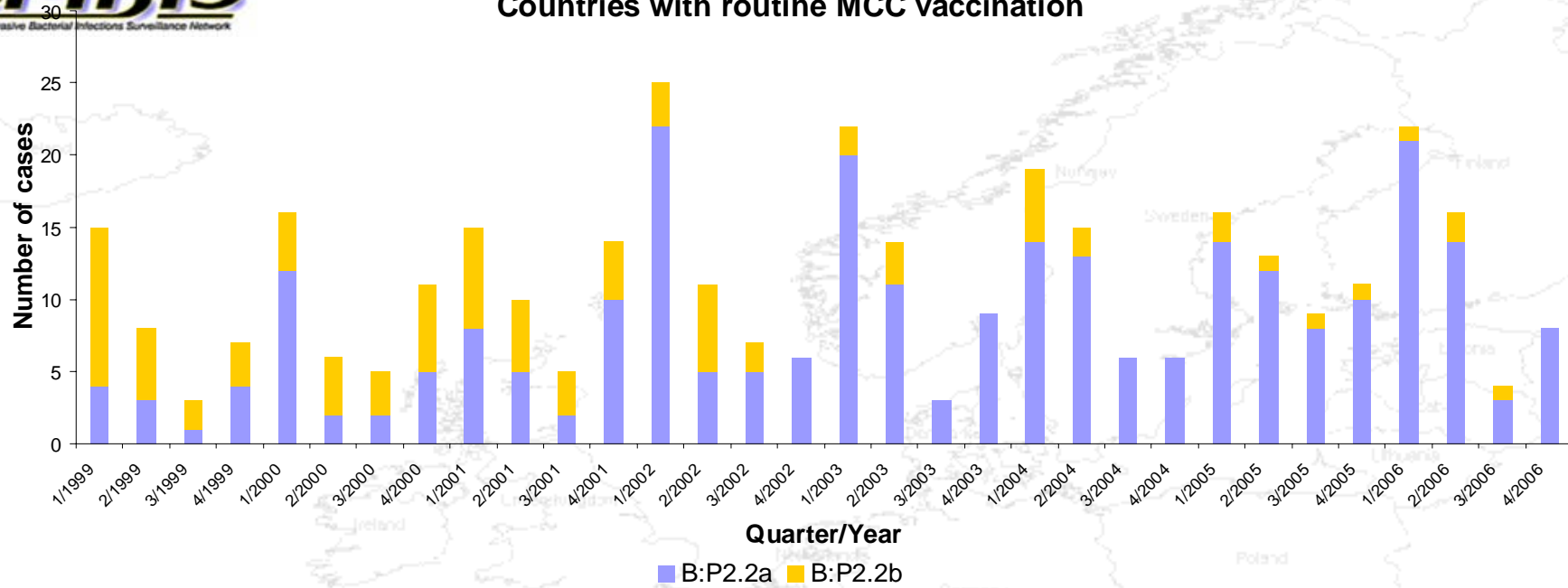


Trends in major phenotypes of serogroup B, by year, all countries combined

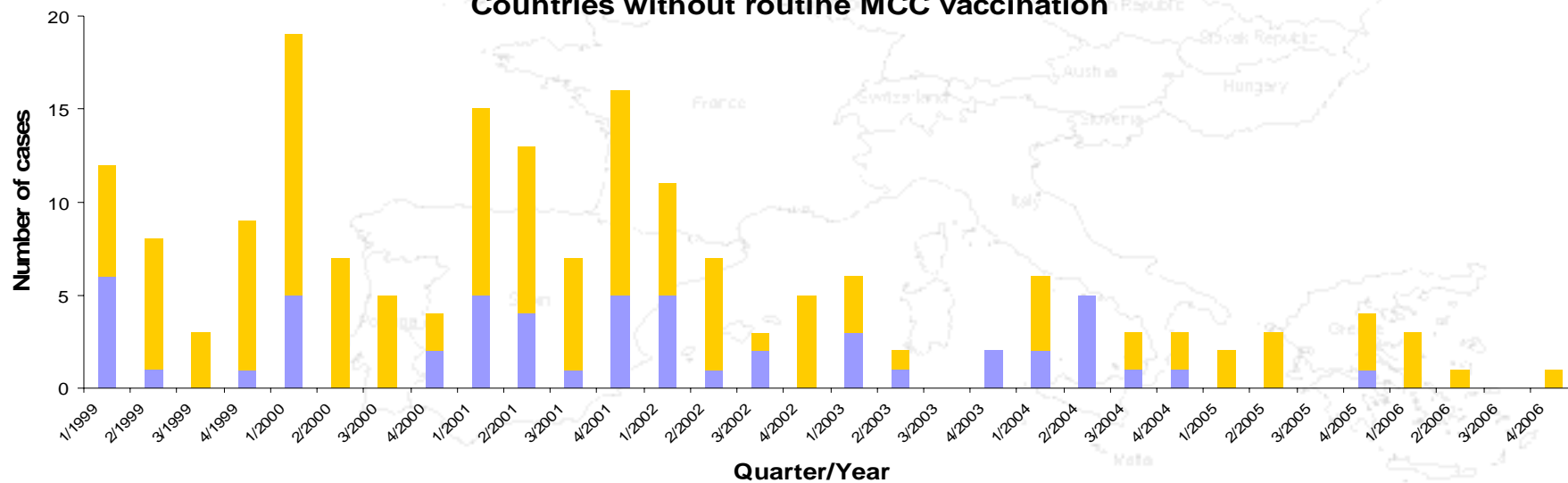


Sentinel monthly surveillance of B2a and B2b strains in Europe

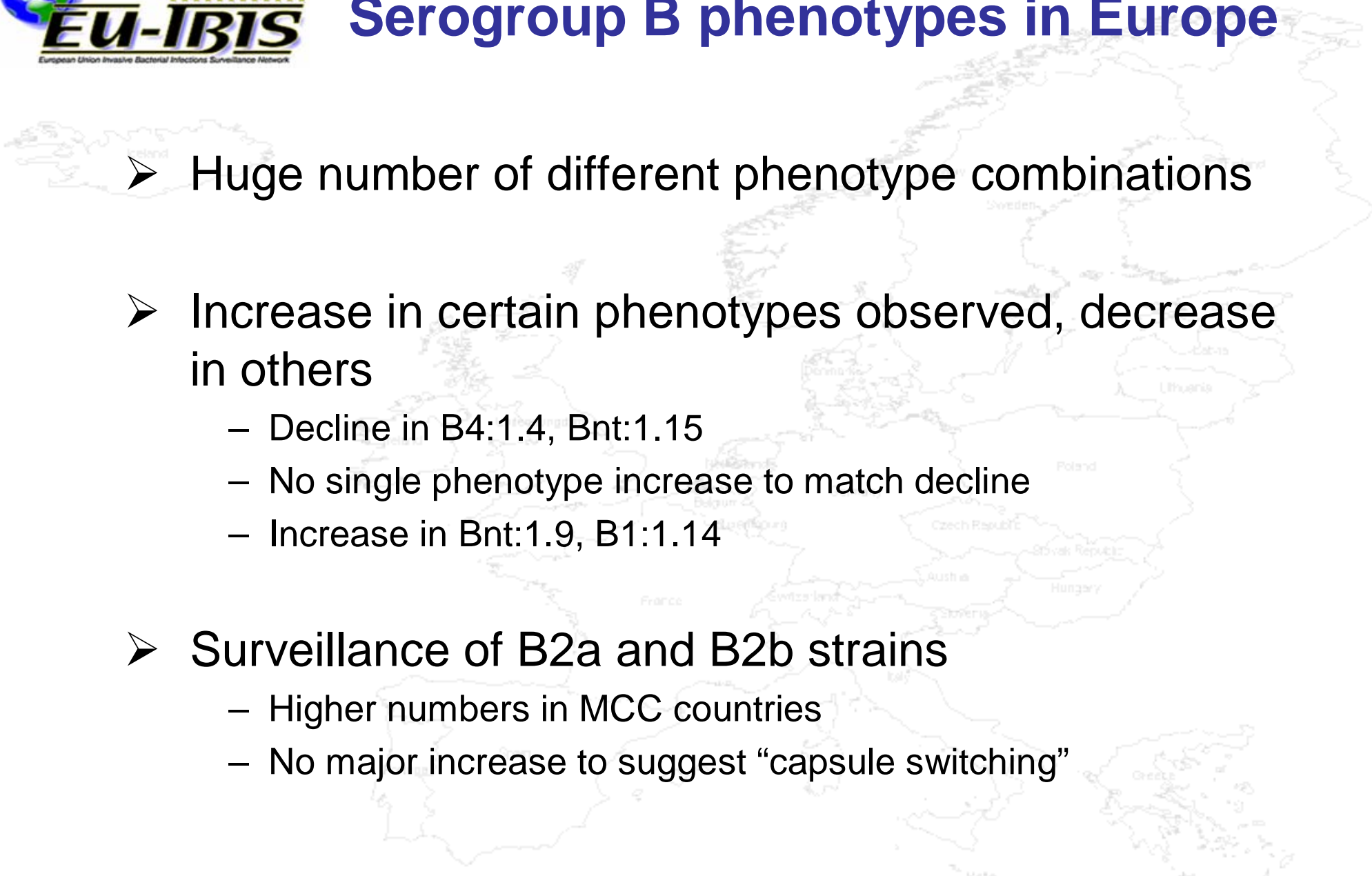
Countries with routine MCC vaccination



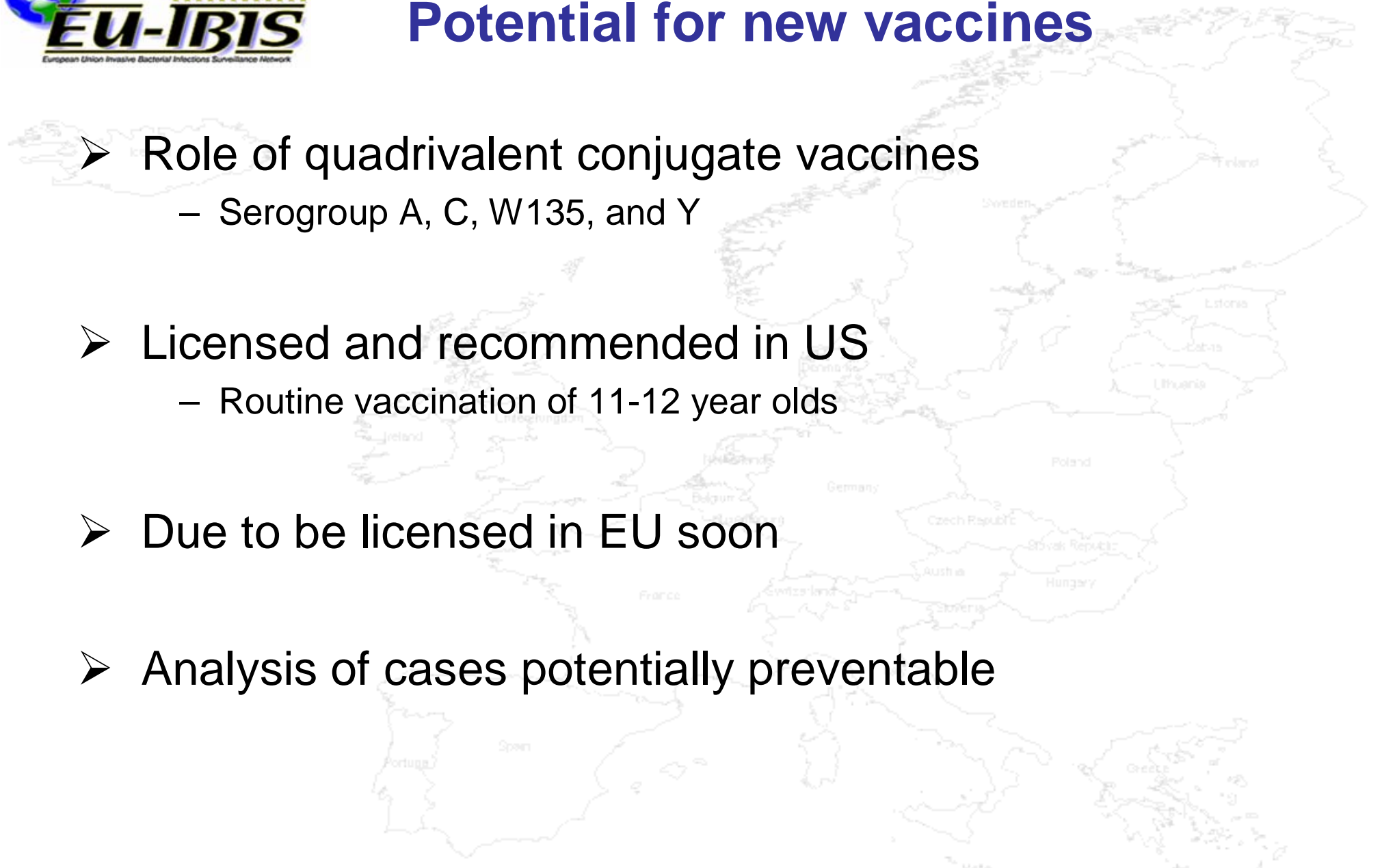
Countries without routine MCC vaccination



Serogroup B phenotypes in Europe

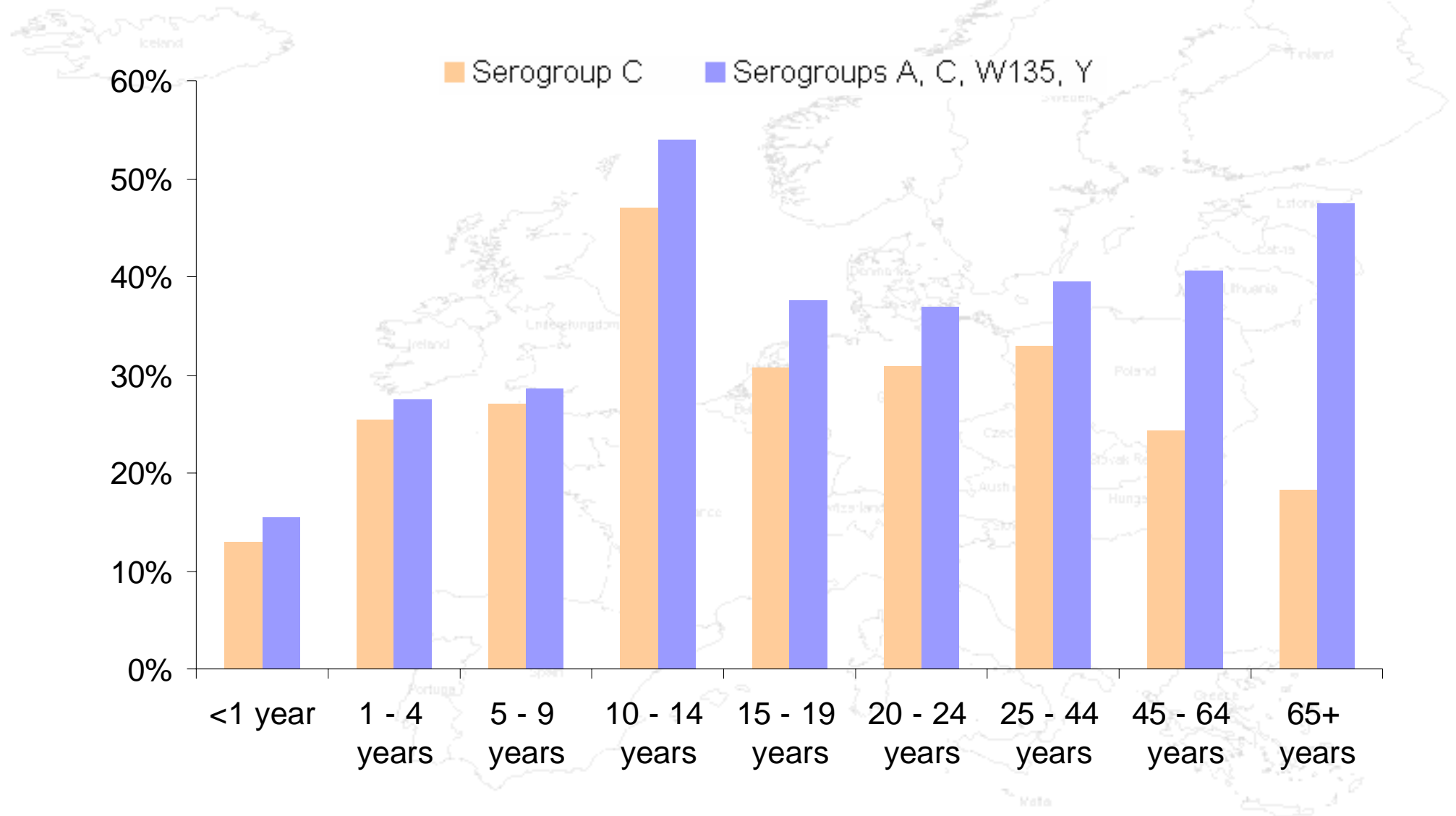
- 
- Huge number of different phenotype combinations
 - Increase in certain phenotypes observed, decrease in others
 - Decline in B4:1.4, Bnt:1.15
 - No single phenotype increase to match decline
 - Increase in Bnt:1.9, B1:1.14
 - Surveillance of B2a and B2b strains
 - Higher numbers in MCC countries
 - No major increase to suggest “capsule switching”

Potential for new vaccines

- 
- Role of quadrivalent conjugate vaccines
 - Serogroup A, C, W135, and Y
 - Licensed and recommended in US
 - Routine vaccination of 11-12 year olds
 - Due to be licensed in EU soon
 - Analysis of cases potentially preventable

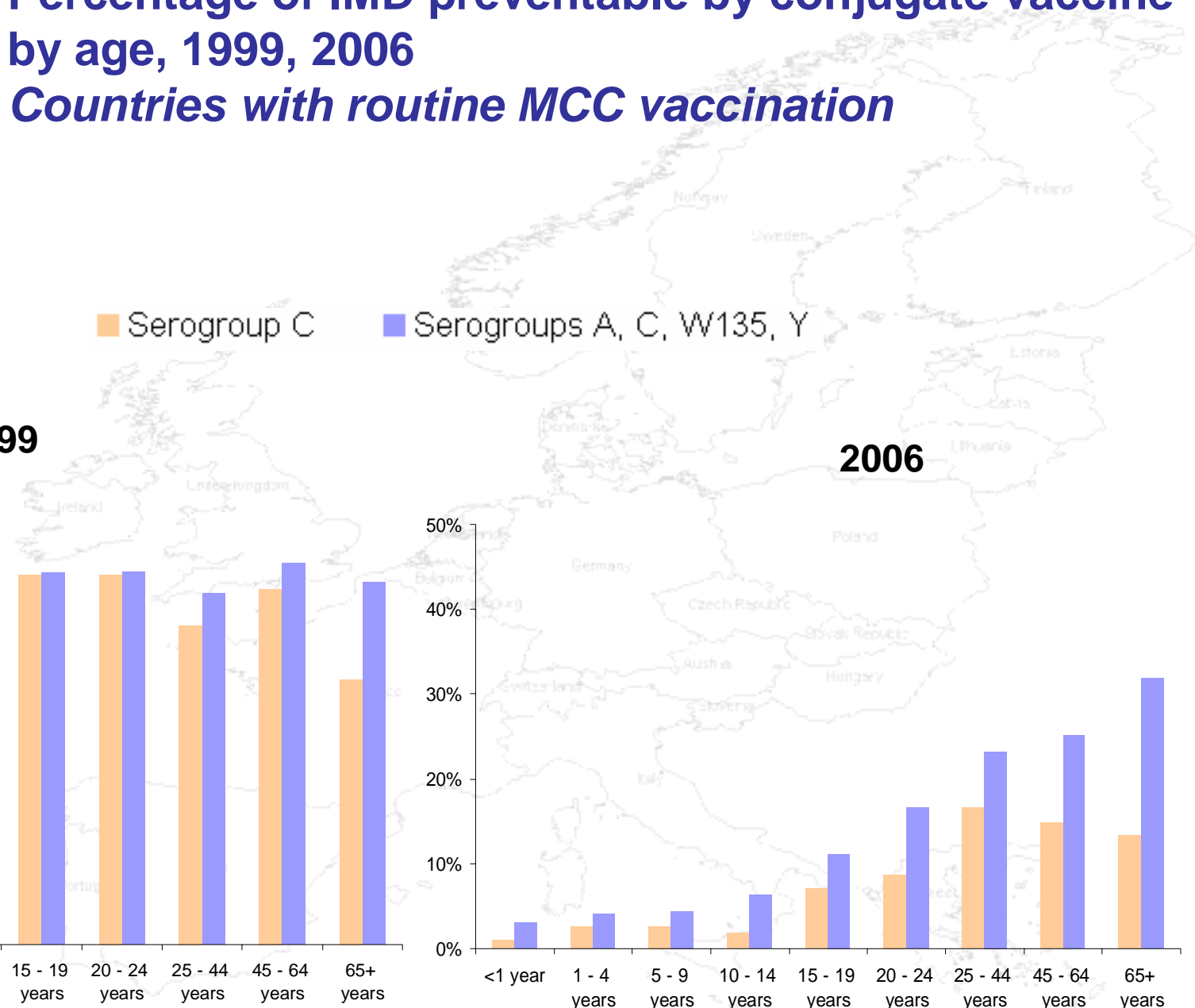
Percentage of IMD preventable by conjugate vaccine by age, 2006

Countries without routine MCC vaccination



Percentage of IMD preventable by conjugate vaccine by age, 1999, 2006

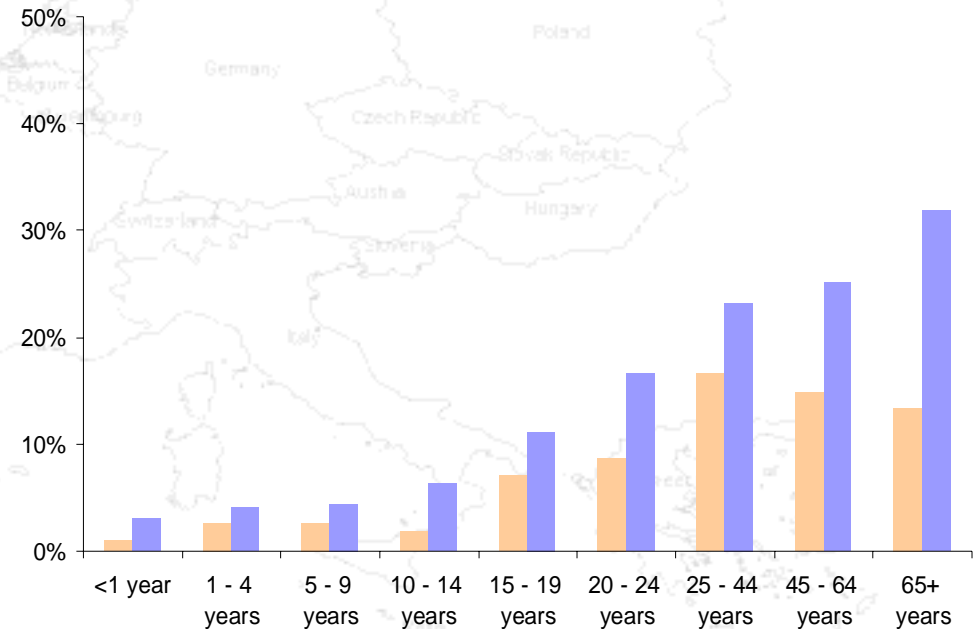
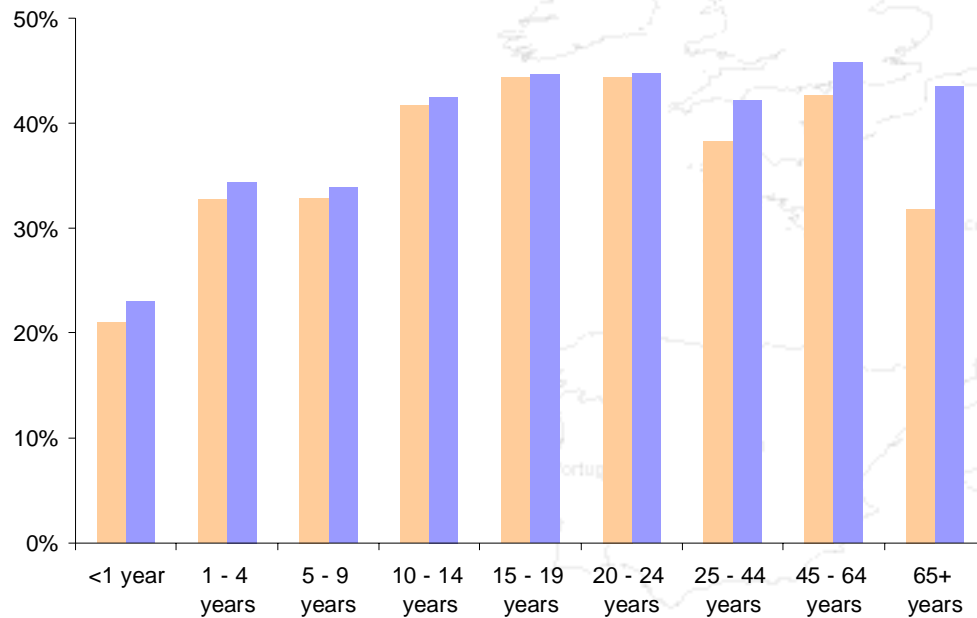
Countries with routine MCC vaccination



■ Serogroup C
 ■ Serogroups A, C, W135, Y

1999

2006



Potential for conjugate vaccines

➤ Countries without MCC vaccine

- Potential for MCC to prevent up to 40% of cases
- Additional benefit from quadrivalent increases with age group
- Benefit of quadrivalent vaccine would therefore increase if major herd immunity observed

➤ Countries already using MCC

- Potential minor benefit only in elderly population

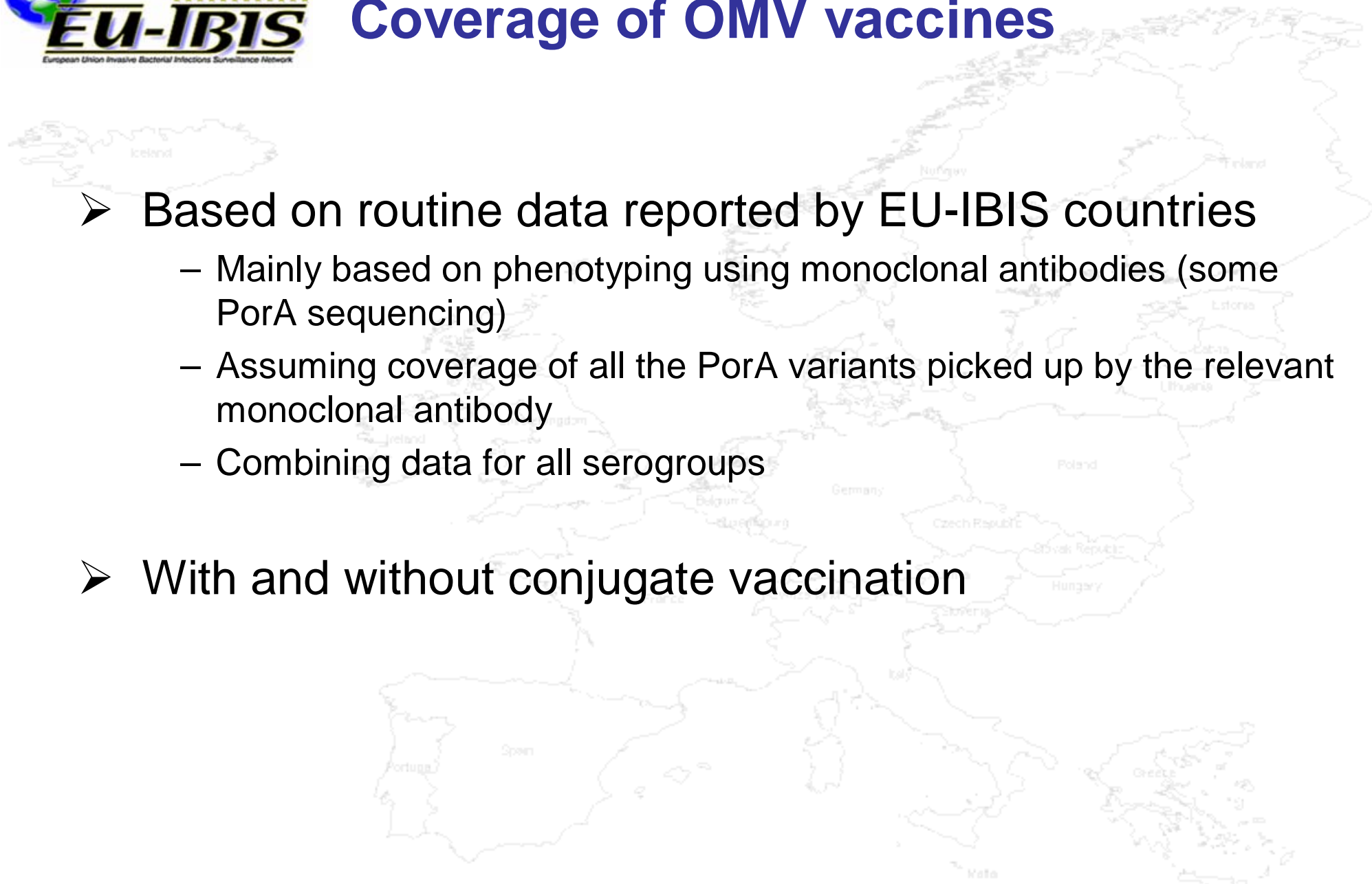
Potential for new vaccines

Role of nonavalent OMV vaccine – contains nine strains* that cover the following PorA types

VR1	VR2
P1.5-1, P1.5-2	P1.1
P1.7, P1.7-2, P1.7-1	P1.2-2
P12-1	P1.3
P1.18-1	P1.4
P1.19	P1.10
P1.22	P1.13
	P1.14
	P1.15-1
	P1.16

P1.7,16; P1.5-1,2-2; P1.19,15-1; P1.5-2,10; P1.12-1,13; P1.7-2,4, P1.22,14; P1.7-1,1; P1.18-1,3,6

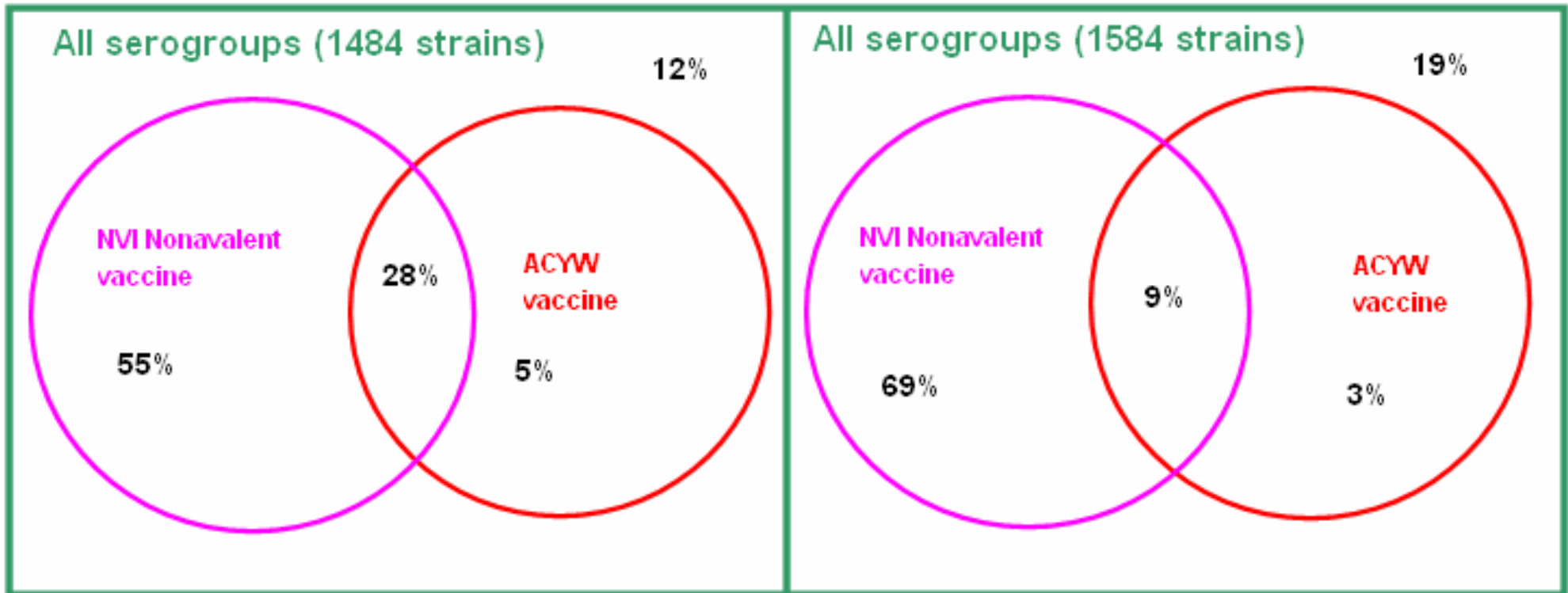
Coverage of OMV vaccines

- 
- Based on routine data reported by EU-IBIS countries
 - Mainly based on phenotyping using monoclonal antibodies (some PorA sequencing)
 - Assuming coverage of all the PorA variants picked up by the relevant monoclonal antibody
 - Combining data for all serogroups
 - With and without conjugate vaccination

Potential coverage of new vaccines in preventing cases, data from 2006

Countries not using MCC vaccine routinely

Countries using MCC vaccine routinely

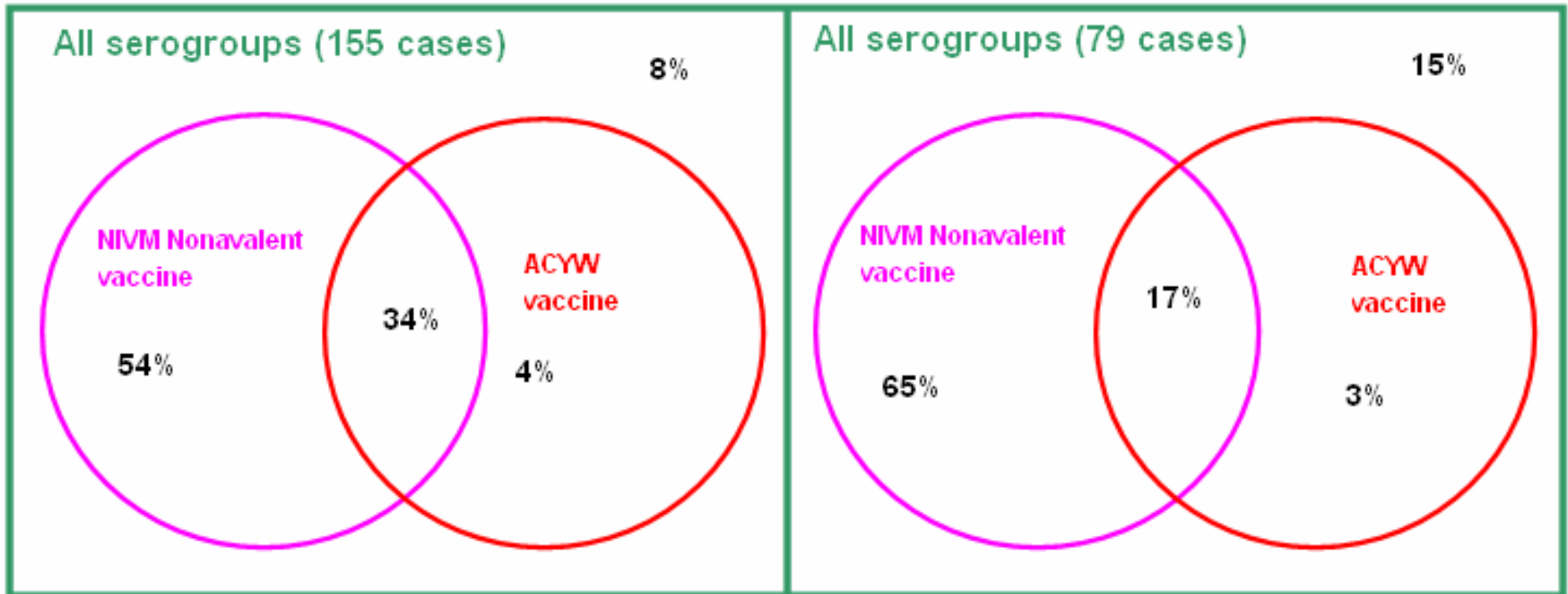


NB: Figures shown in actual presentation in Rome were incorrect; correct figures shown here

Potential coverage of new vaccines in preventing deaths, data from 2006

Countries not using MCC vaccine routinely

Countries using MCC vaccine routinely



NB: Figures shown in actual presentation in Rome were incorrect; correct figures shown here

Potential benefit of new vaccines

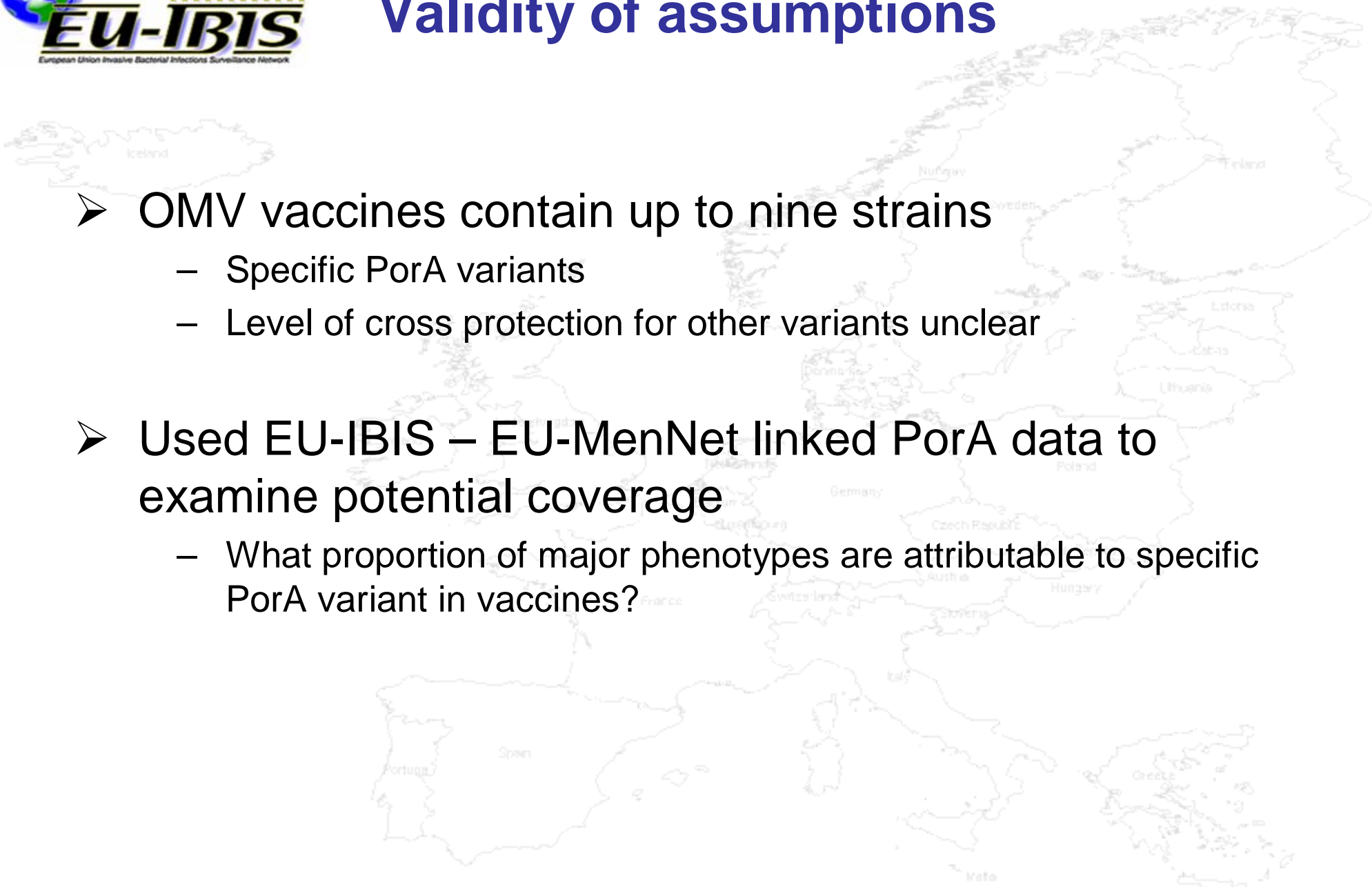
- Overall coverage of quadrivalent vaccine
 - 11% in MCC countries, 33% in non-MCC countries
 - Greater proportion of fatal cases

- Overall coverage of nonavalent OMV vaccine
 - 48% in MCC countries (as some common PorA types already removed by MCC vaccination)
 - 68% in non-MCC countries
 - Lower proportion of fatal cases

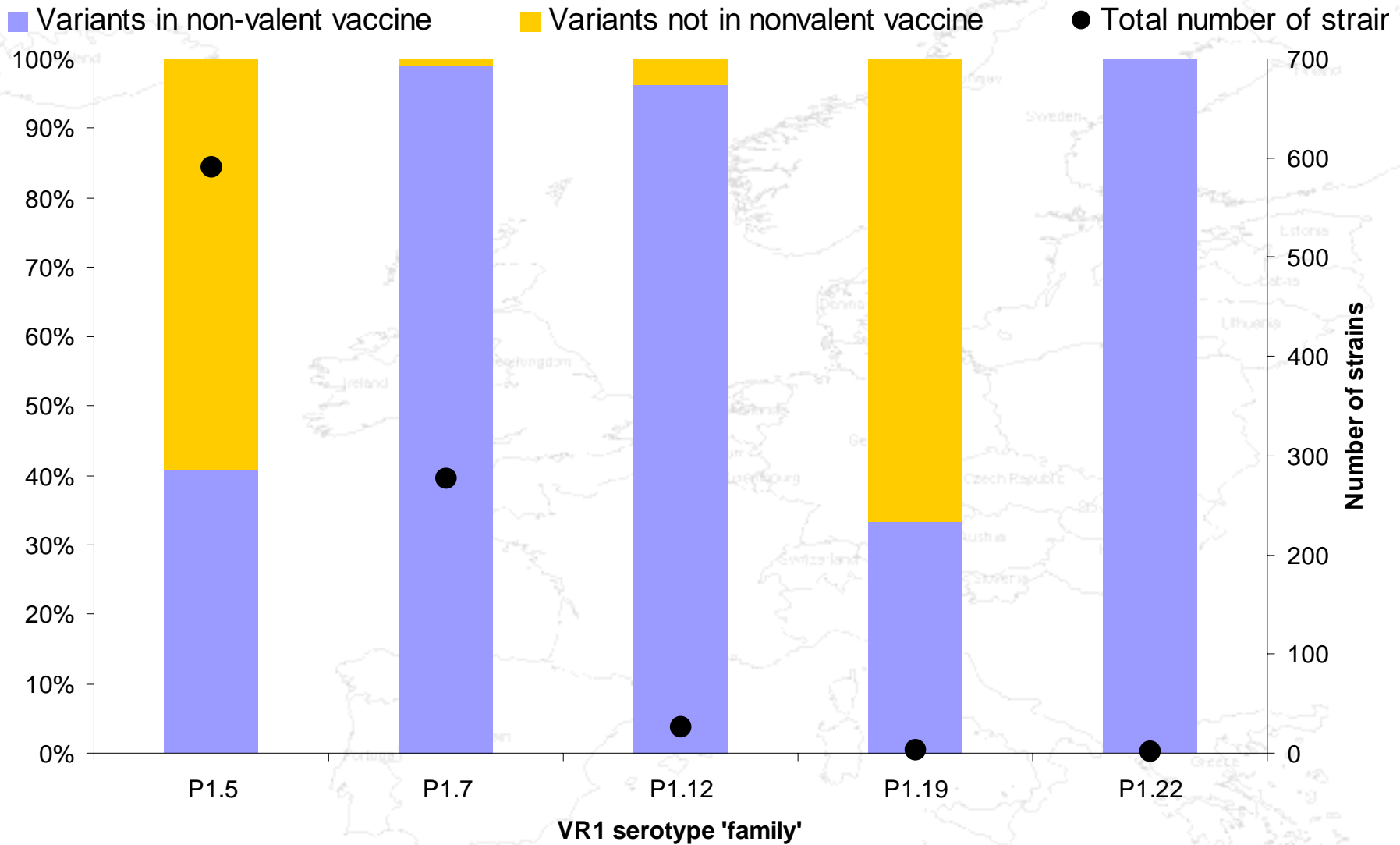
- Use of both vaccines has potential to prevent 78% of cases in non-MCC countries

- How valid are assumptions?

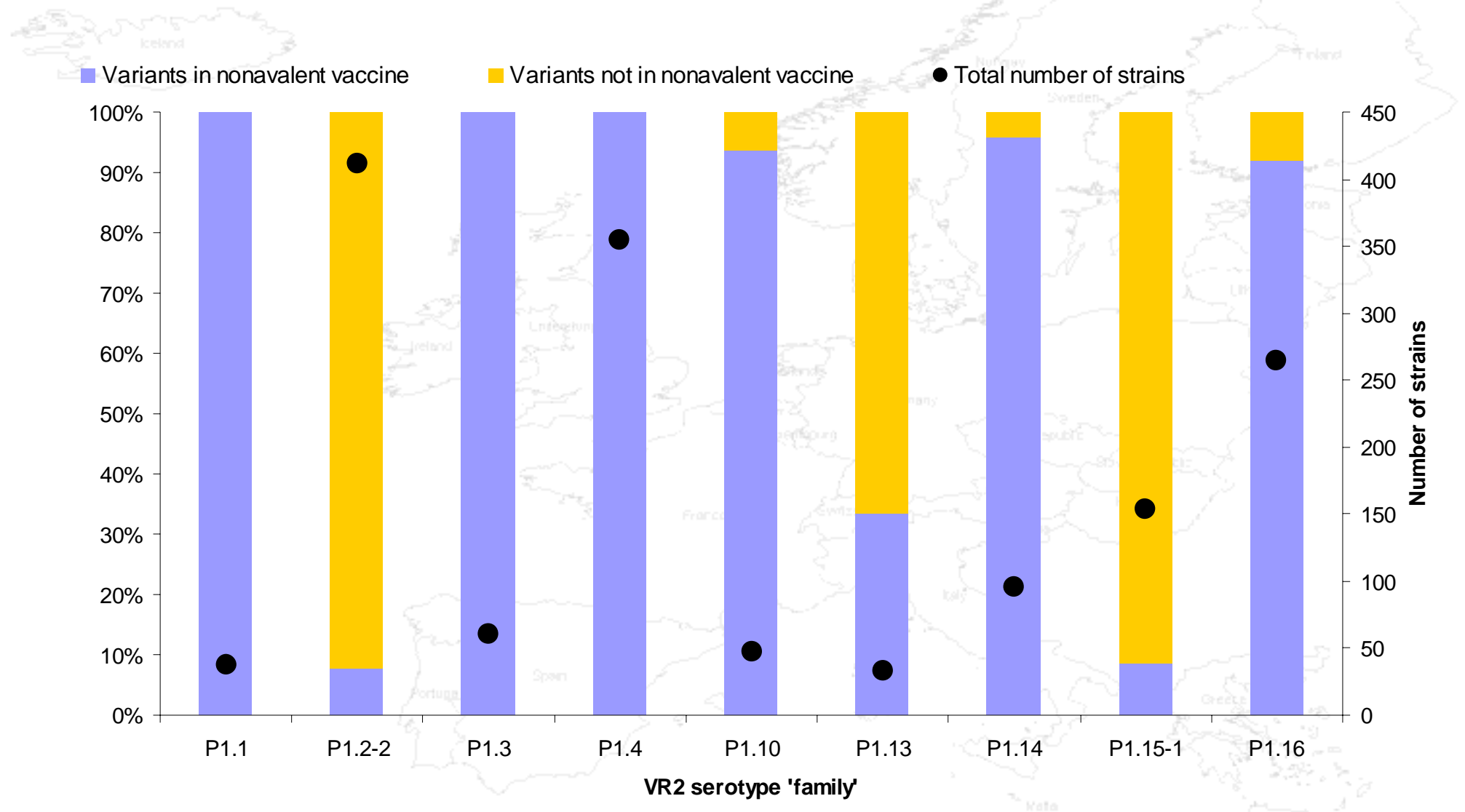
Validity of assumptions

- 
- OMV vaccines contain up to nine strains
 - Specific PorA variants
 - Level of cross protection for other variants unclear
 - Used EU-IBIS – EU-MenNet linked PorA data to examine potential coverage
 - What proportion of major phenotypes are attributable to specific PorA variant in vaccines?

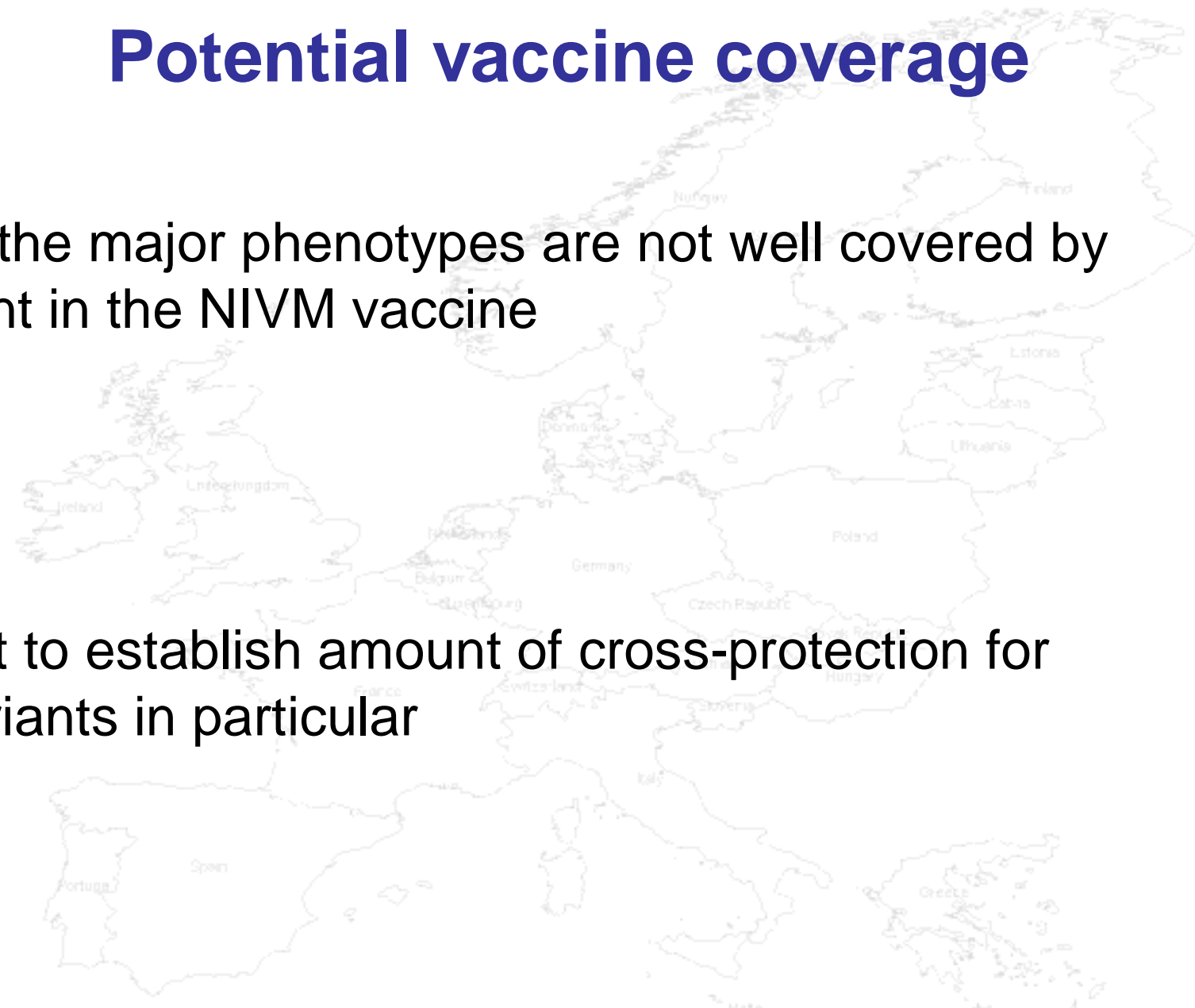
Coverage of VR1 variants present in NIVM nonavalent vaccine, EU-IBIS/EU-MenNet linked data, 1999 – 2002



Coverage of VR2 variants present in NIVM nonavalent vaccine, EU-IBIS/EU-MenNet linked data, 1999 – 2002

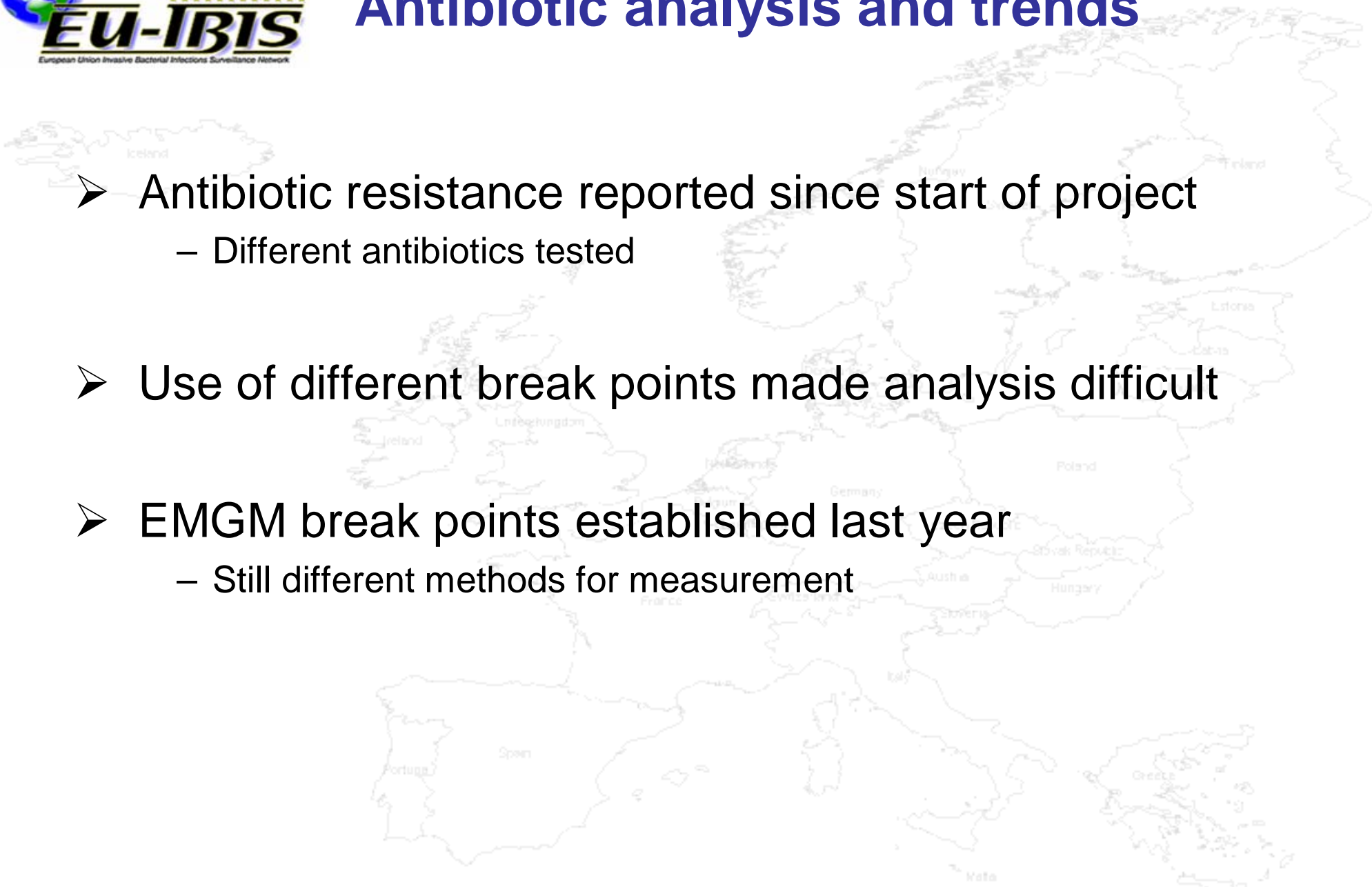


Potential vaccine coverage

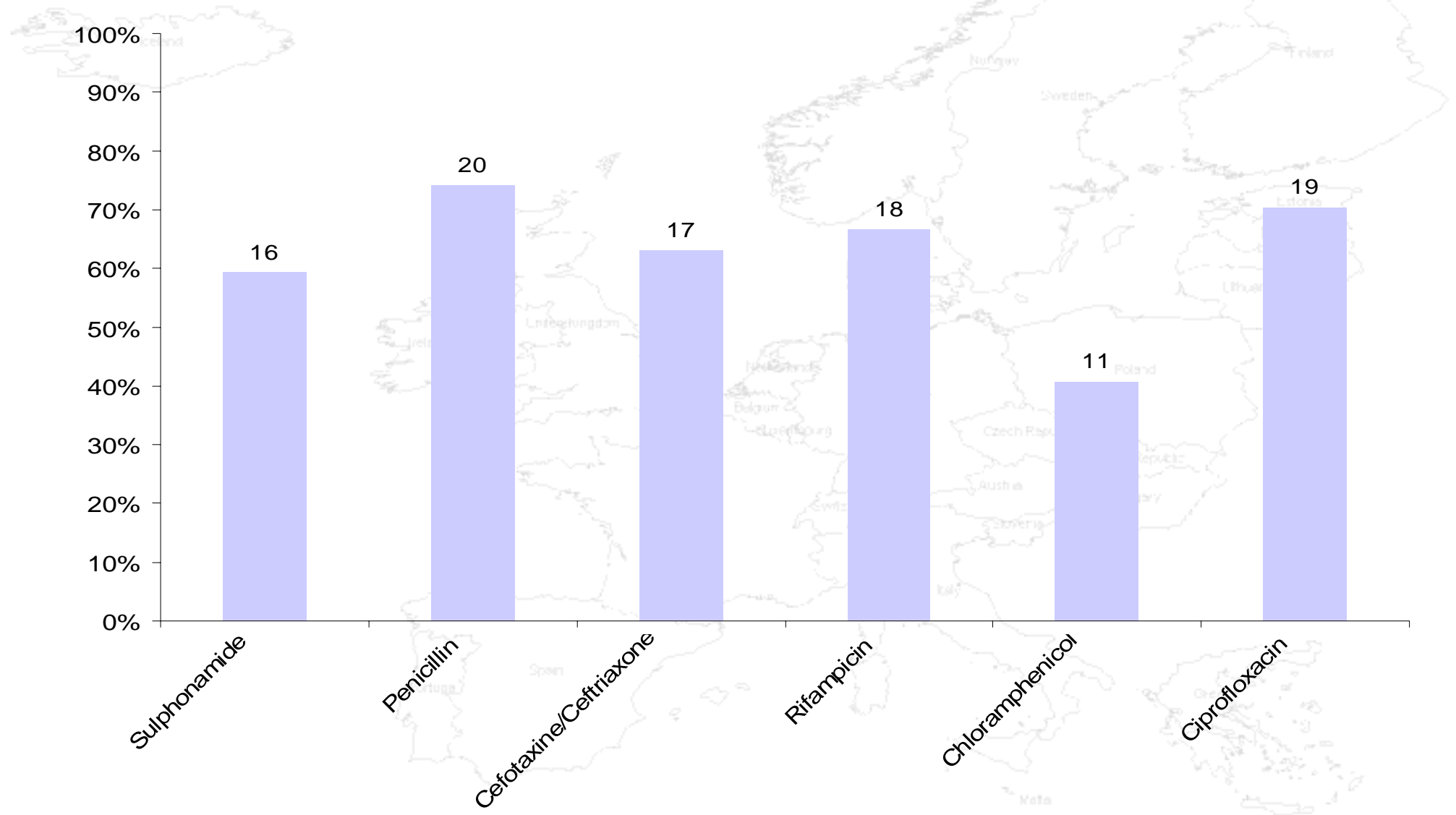
- 
- Some of the major phenotypes are not well covered by the variant in the NIVM vaccine
 - P1.5
 - P1.2
 - P1.15

 - Important to establish amount of cross-protection for these variants in particular

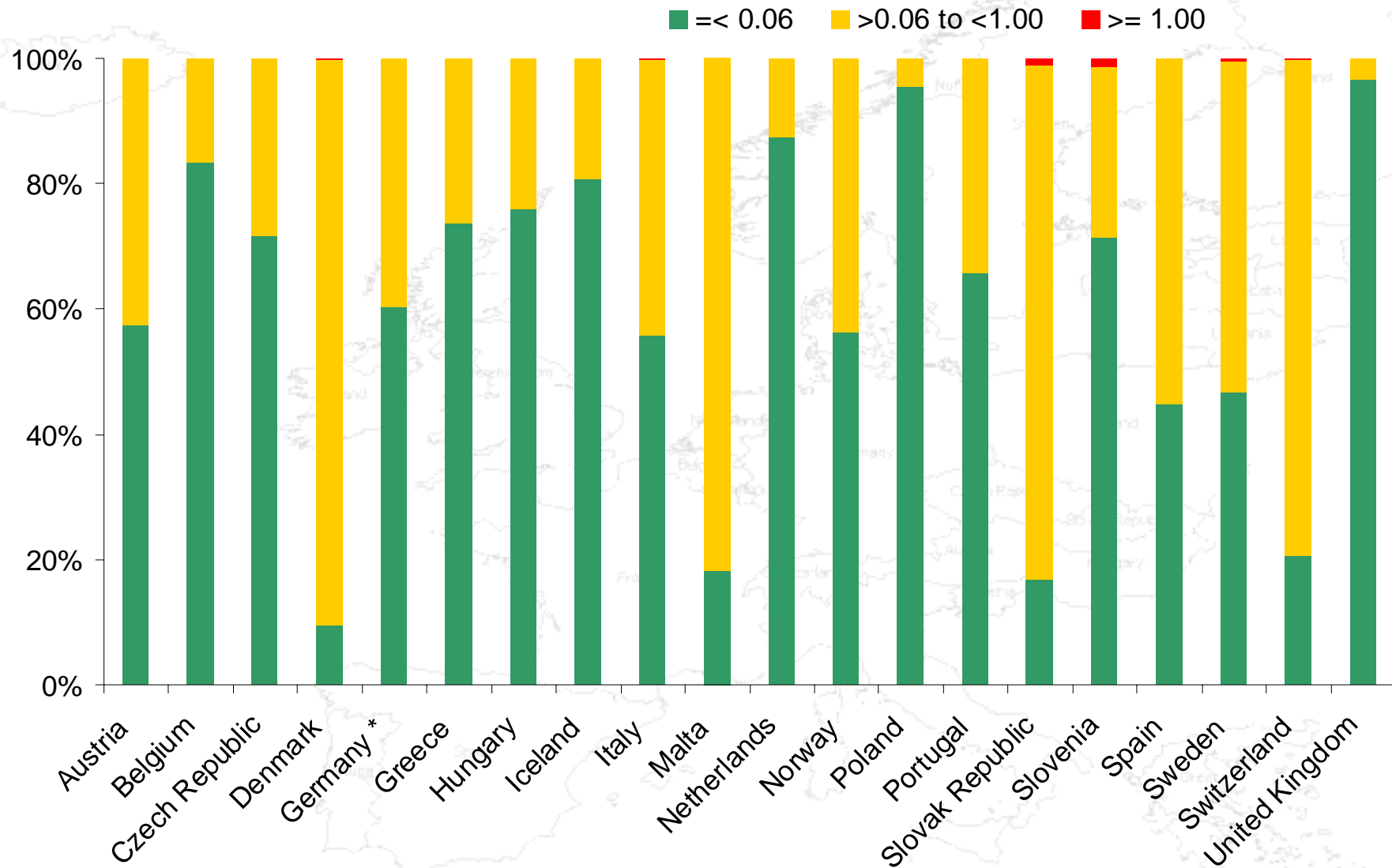
Antibiotic analysis and trends

- 
- Antibiotic resistance reported since start of project
 - Different antibiotics tested
 - Use of different break points made analysis difficult
 - EMGM break points established last year
 - Still different methods for measurement

Proportion of EU-IBIS countries reporting antibiotics testing, all years combined



Comparison of Pencillin MICs, by country, all years combined

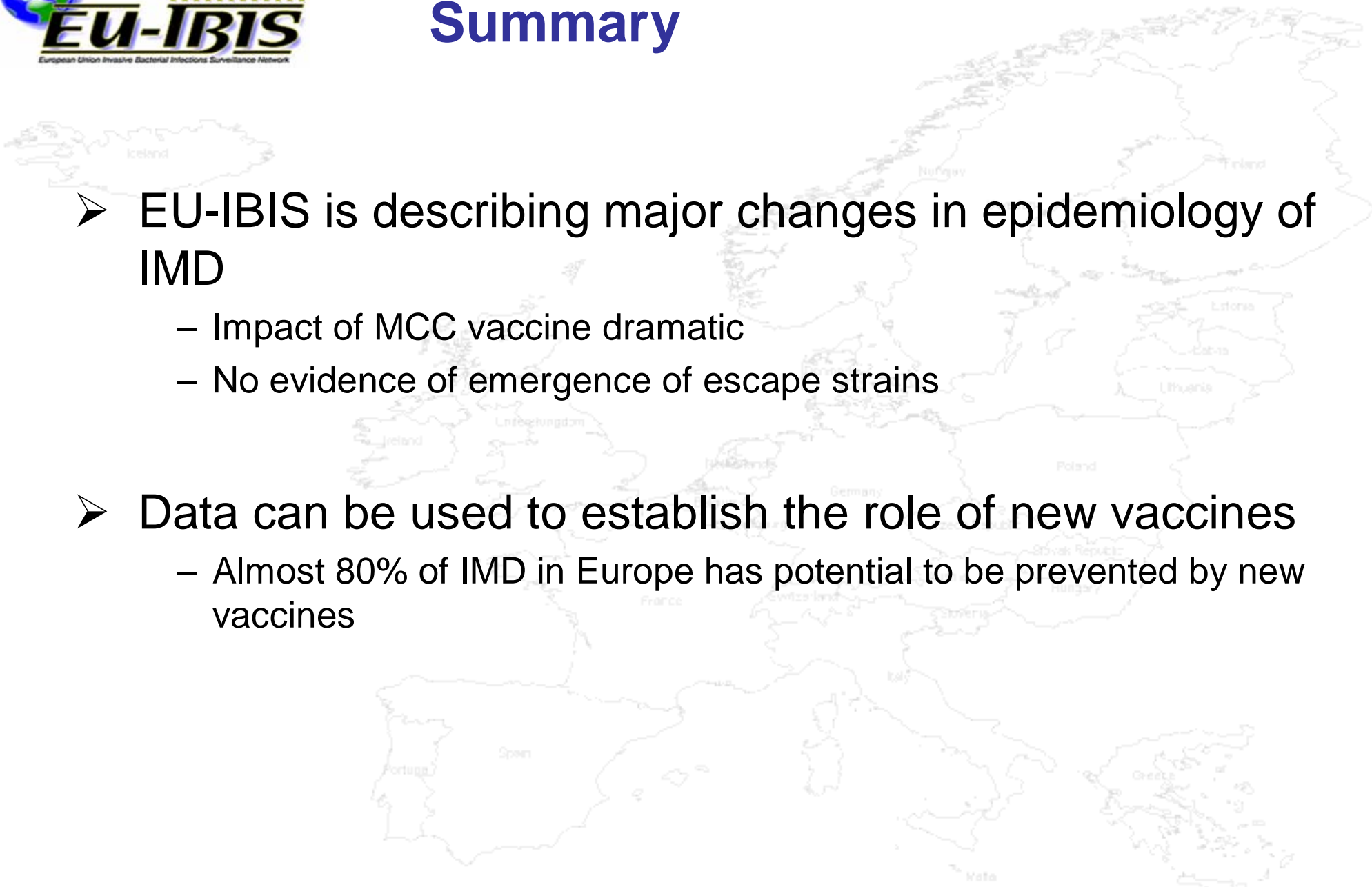


* German data 2002 - 2006

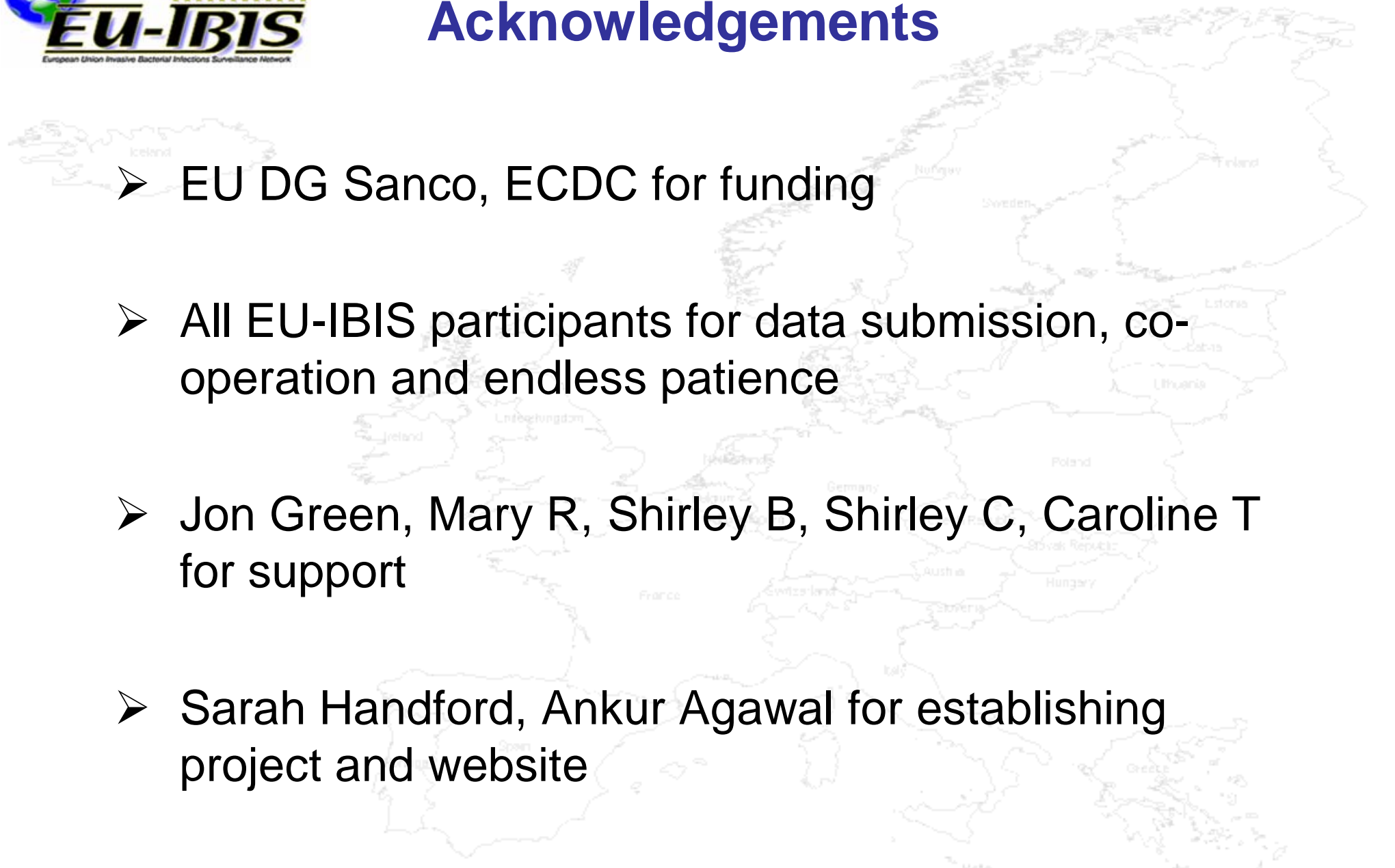
Antibiotic analysis

- 
- European countries differ as to which antibiotic tests are carried/reported
 - Penicillin and ciprofloxacin mostly commonly reported
 - Chloramphenicol least commonly reported
 - Virtually no penicillin resistance present in any EU-IBIS country
 - Proportion with intermediate resistance varies widely
 - high in Denmark, Slovakia, Switzerland
 - Low in UK, Netherland, Poland, Belgium
 - Clinical/ epidemiological relevance is not clear

Summary

- 
- **EU-IBIS is describing major changes in epidemiology of IMD**
 - Impact of MCC vaccine dramatic
 - No evidence of emergence of escape strains
 - **Data can be used to establish the role of new vaccines**
 - Almost 80% of IMD in Europe has potential to be prevented by new vaccines

Acknowledgements

- 
- EU DG Sanco, ECDC for funding
 - All EU-IBIS participants for data submission, co-operation and endless patience
 - Jon Green, Mary R, Shirley B, Shirley C, Caroline T for support
 - Sarah Handford, Ankur Agawal for establishing project and website