

Klinikum Stuttgart – Medizin fürs Leben

**Osteosarcoma treatment in Europe and elsewhere is far from being centralized:  
Lessons from EURAMOS-1 (NCT00134030)**

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Sigbjørn Smeland<sup>5</sup>, Matthew R Sydes<sup>3</sup>, Jeremy Whelan<sup>6</sup>, Mark Bernstein<sup>7</sup>**

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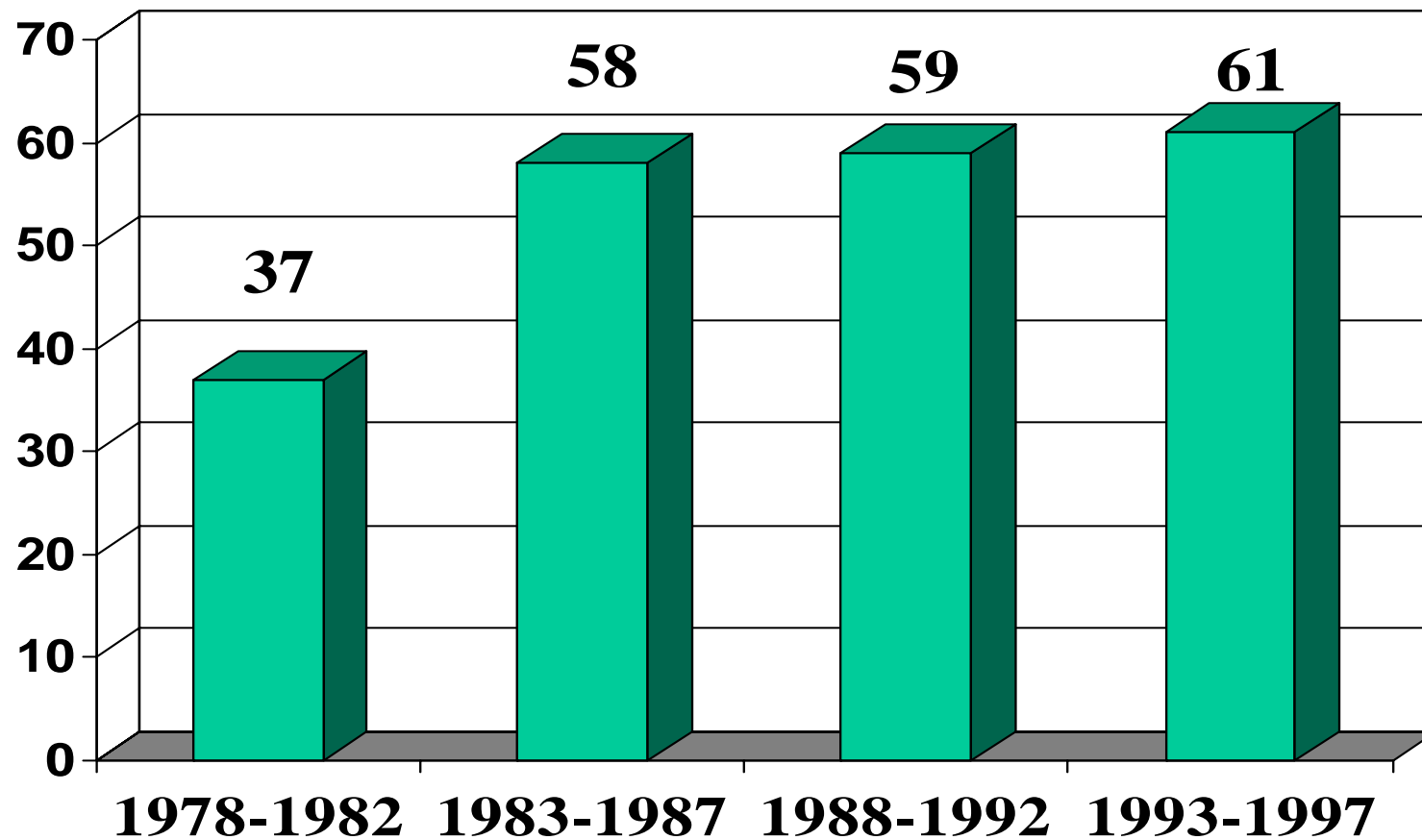
Supported by the European Science Foundation (ESF) under the EUROCORES Program European Clinical Trials (ECT), through contract No. ERASCT-2003-980409 of the European Commission, DG



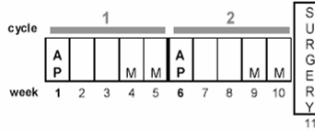
## Bone tumours in European children and adolescents, 1978-1997. Report from the Automated Childhood Cancer Information System project

C.A. Stiller<sup>a,\*</sup>, S.S. Bielack<sup>b,c</sup>, G. Jundt<sup>d</sup>, E. Steliarova-Foucher<sup>e</sup>

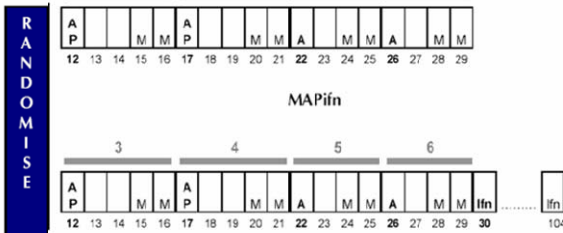
EUROPEAN JOURNAL OF CANCER 42 (2006) 2124-2135



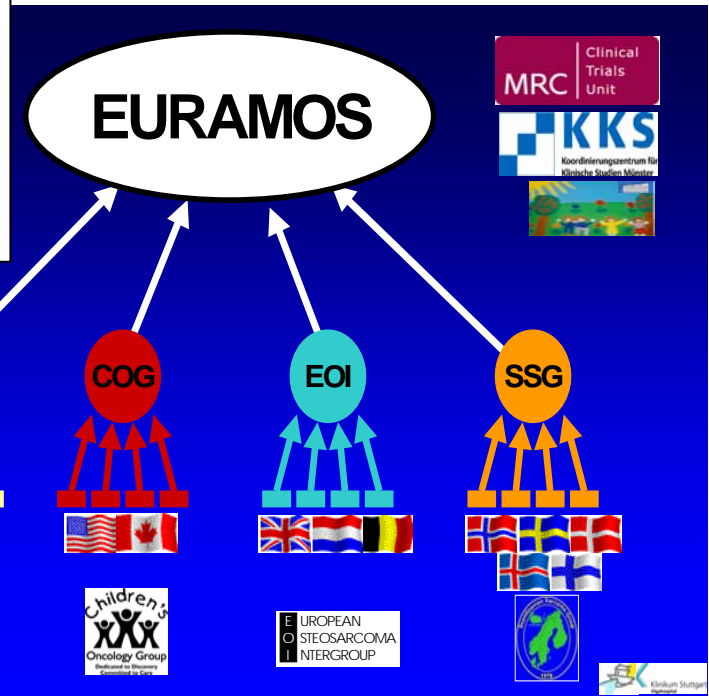
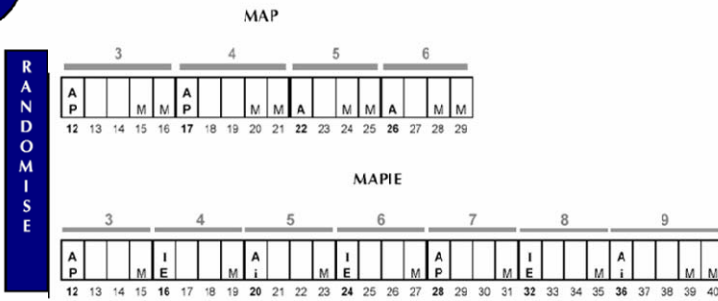
A = Doxorubicin 75mg/m<sup>2</sup>/course  
 P = Cisplatin 120mg/m<sup>2</sup>/course  
 M = Methotrexate 12g/m<sup>2</sup>/course  
 E = Etoposide 500mg/m<sup>2</sup>/course  
 I = Ifosfamide 14g/m<sup>2</sup>/course  
 i = Ifosfamide 9g/m<sup>2</sup>/course  
 Ifn = Interferon- $\alpha$  0.5-1.0 $\mu$ g/kg weekly



GOOD RESPONSE

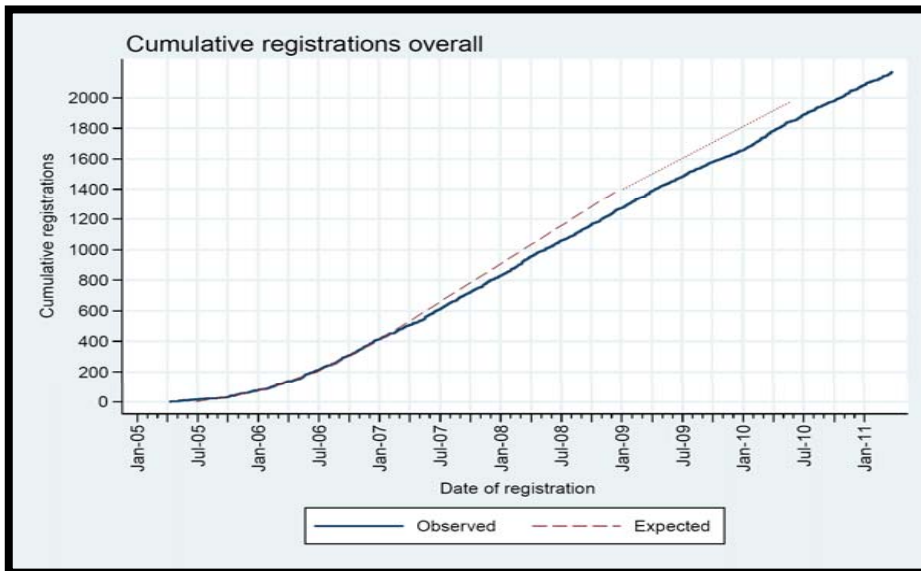


POOR RESPONSE



# EURAMOS Recruitment as of March 31, 2011

**2,169 patients**  
from **328 institutions**  
in **17 countries\***



COG	1,108	51.08
COSS	506	23.33
EOI	439	20.24
SSG	116	5.35
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Total	2,169	100.00

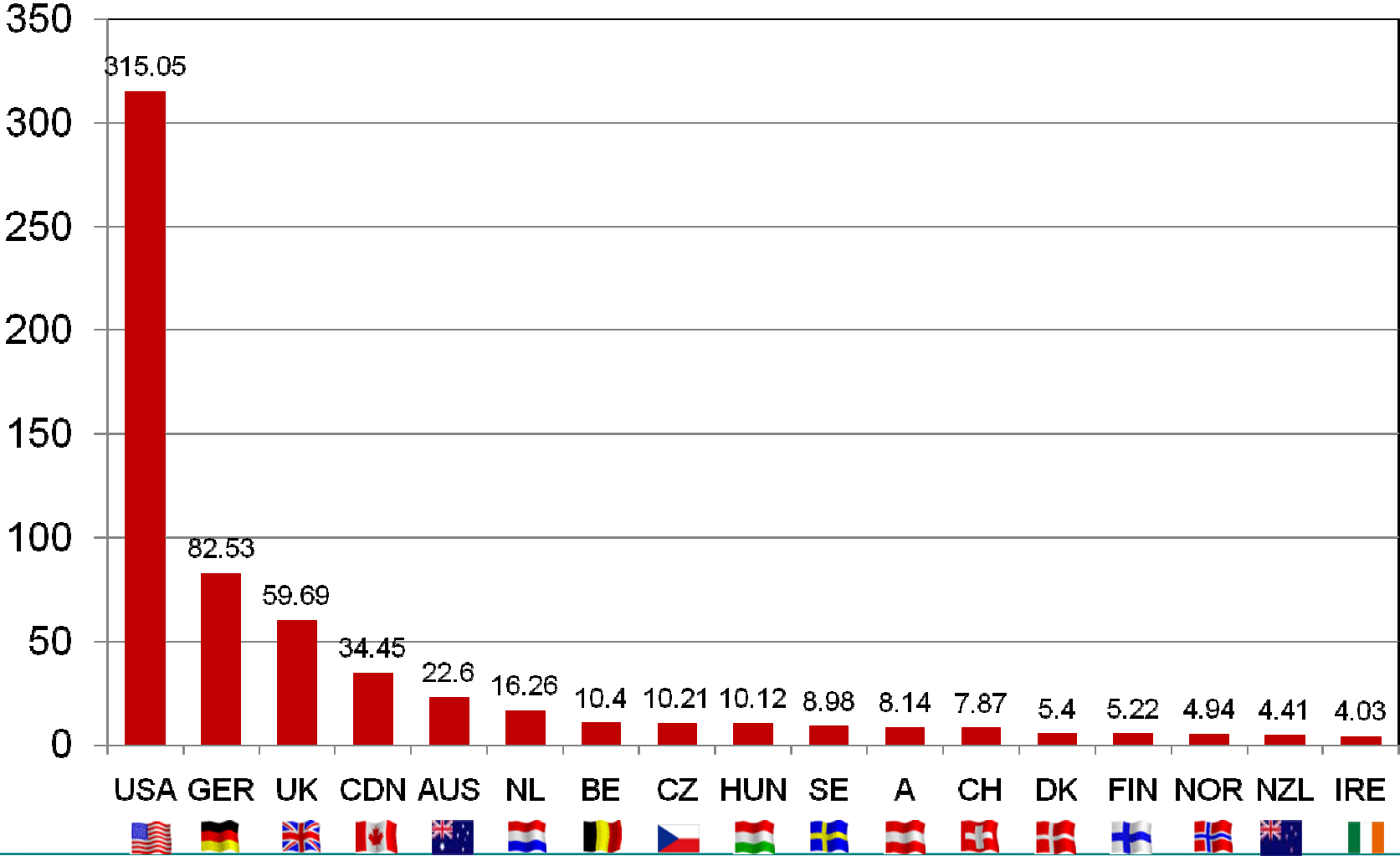
Thanks to EURAMOS-CDC,  
MRC London

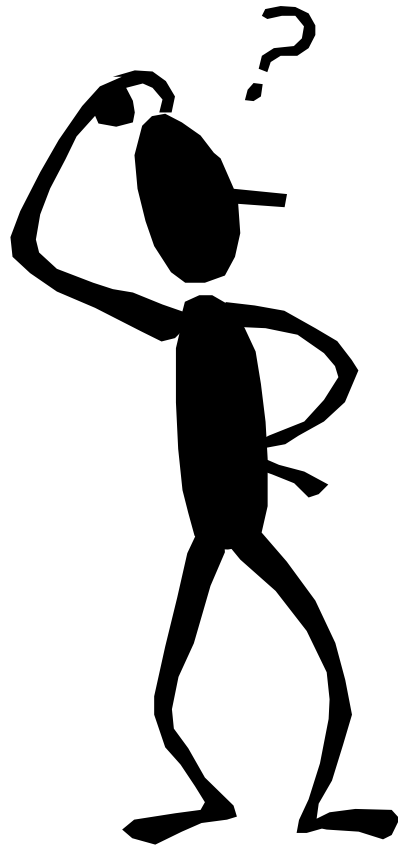


# EURAMOS target population **606.57 million**

ca. 8.7% of world

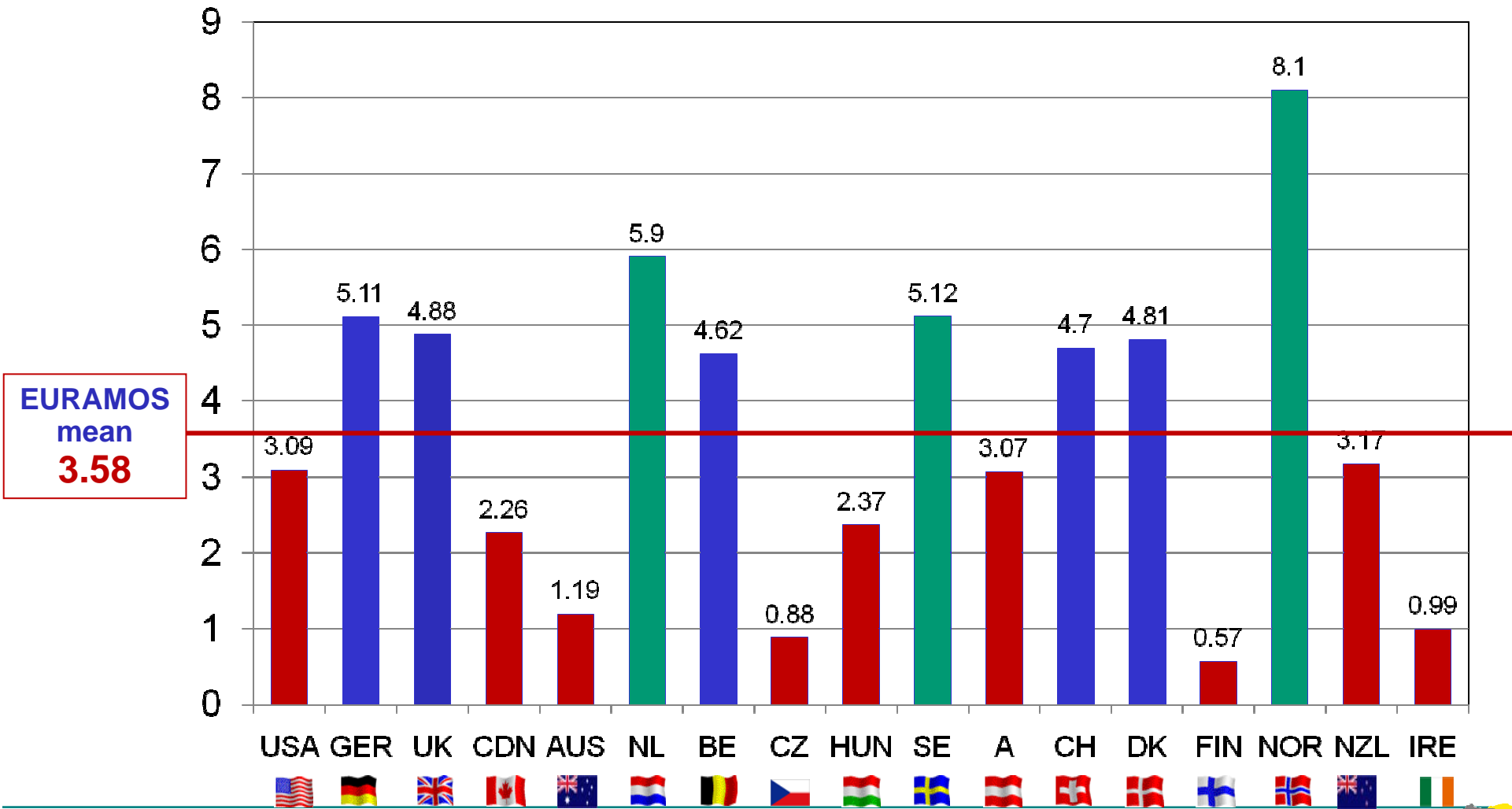
population





Do countries  
achieve similar  
*population-adjusted*  
recruitment  
rates?

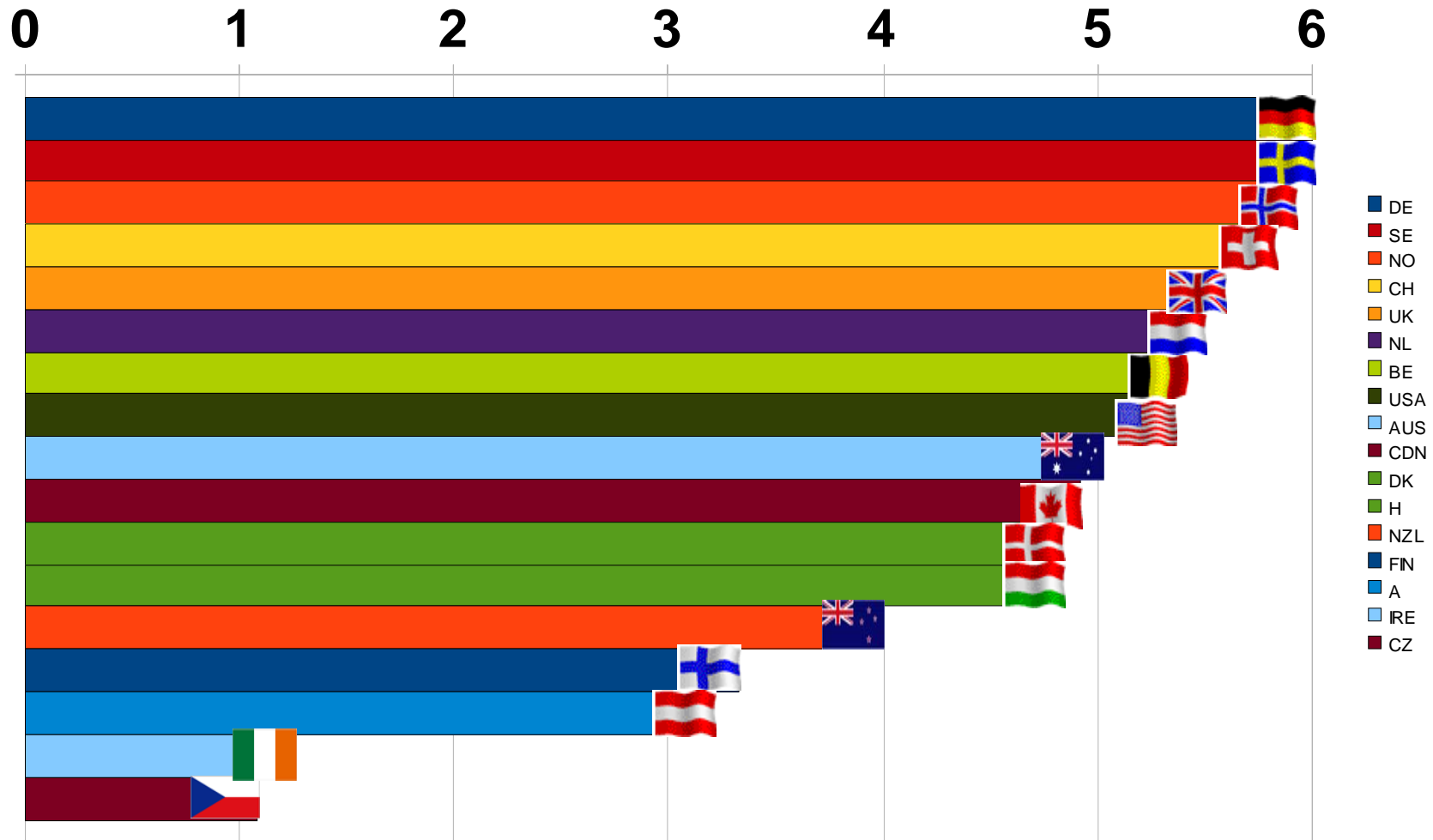
# Recruitment / Country / Million population



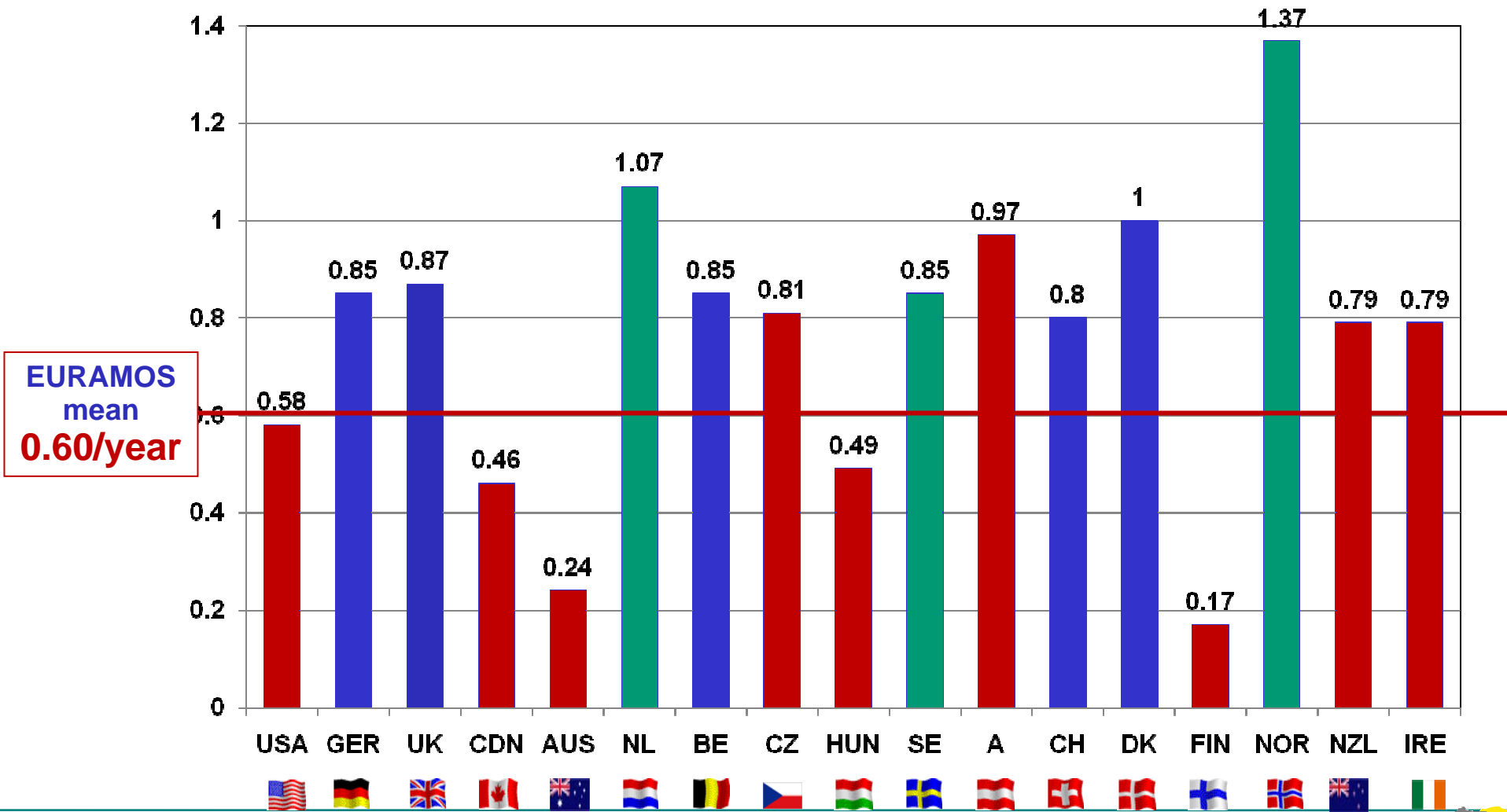
EURAMOS  
mean  
3.58



# Years recruiting



# Recruitment / Country / Million population per year with trial open





# EU-Clinical Trials Directive EC 2001/20

L 121/34

EN

Official Journal of the European Communities

1.5.2001

**DIRECTIVE 2001/20/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL  
of 4 April 2001**

**on the approximation of the laws, regulations and administrative provisions of the Member States  
relating to the implementation of good clinical practice in the conduct of clinical trials on  
medicinal products for human use**



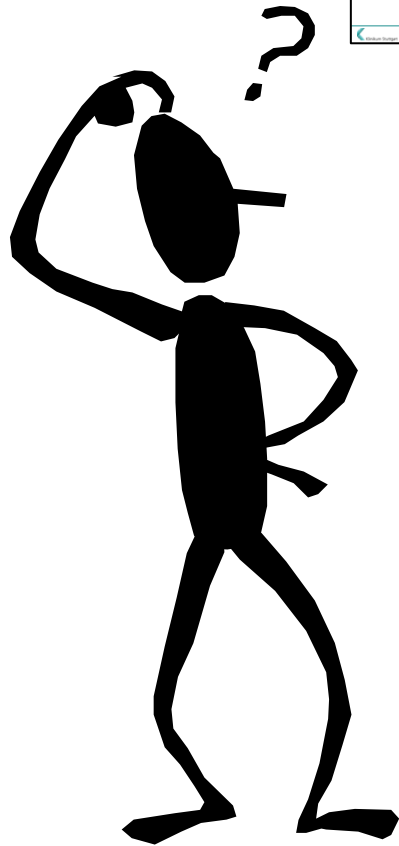
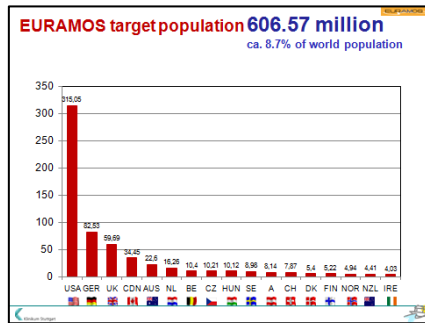
# Trial Approval

- National Competent Authorities
- Ethics Committees
  
- Regional Competent Authorities
- Science Funders
- Insurance Companies
- Learned Societies
- Drug evaluation bodies
- .....
- .....

# Documentation to be held by investigator / institution for clinical trials

Detailed guidance for the principles of GCP in the conduct in the EU of clinical trials on medicinal products for human use. ENTR/6416/01, July 2002

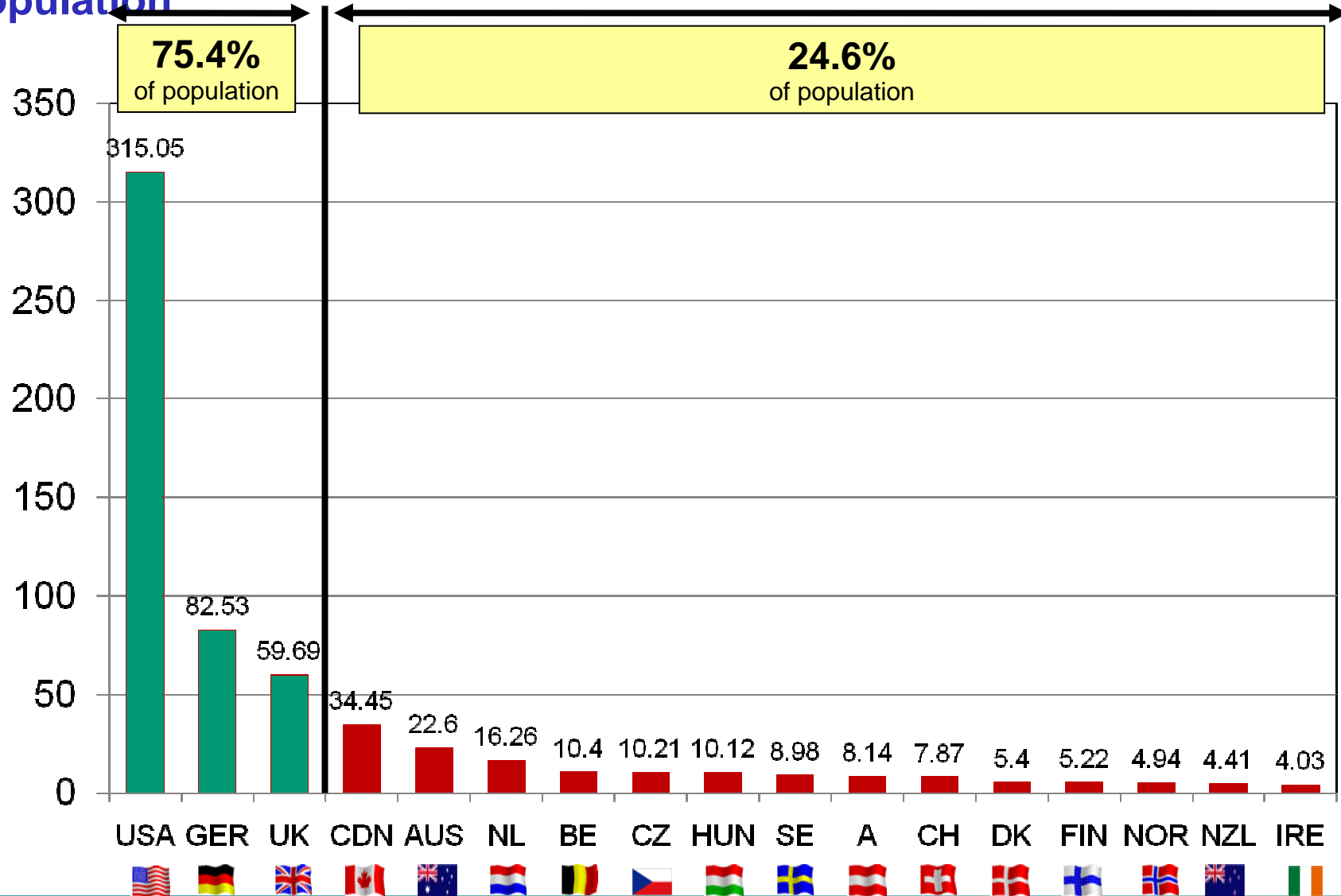
- Investigators brochure (+ updates) or SmPC
- Protocol and amendments (signed)
- Information sheet and consent form (+ updates)
- Financial aspects
- Insurance statements
- Signed agreements between parties
- EC opinion and composition
- MRHA authorisation
- Investigators CVs
- Medical and laboratory tests, including normal ranges
- Medicine labels
- Instructions for medicine use
- Shipping records
- Certificates of analysis
- Decoding procedures
- Master randomisation list
- Monitoring reports (pre-trial, initiation, close-out etc)
- List of persons responsibilities delegated to (+ updates)
- CRFs and corrections
- SAE notifications from investigators and to EC and MRHA
- EC/MRHA annual reports and final reports
- Subject screening log
- Subject identification code list
- Subject enrolment log
- IMP accountability at site
- Record of retained tissues
- Documentation of IMP destruction
- Completed subject identification code list
- Audit certificate
- Clinical study report

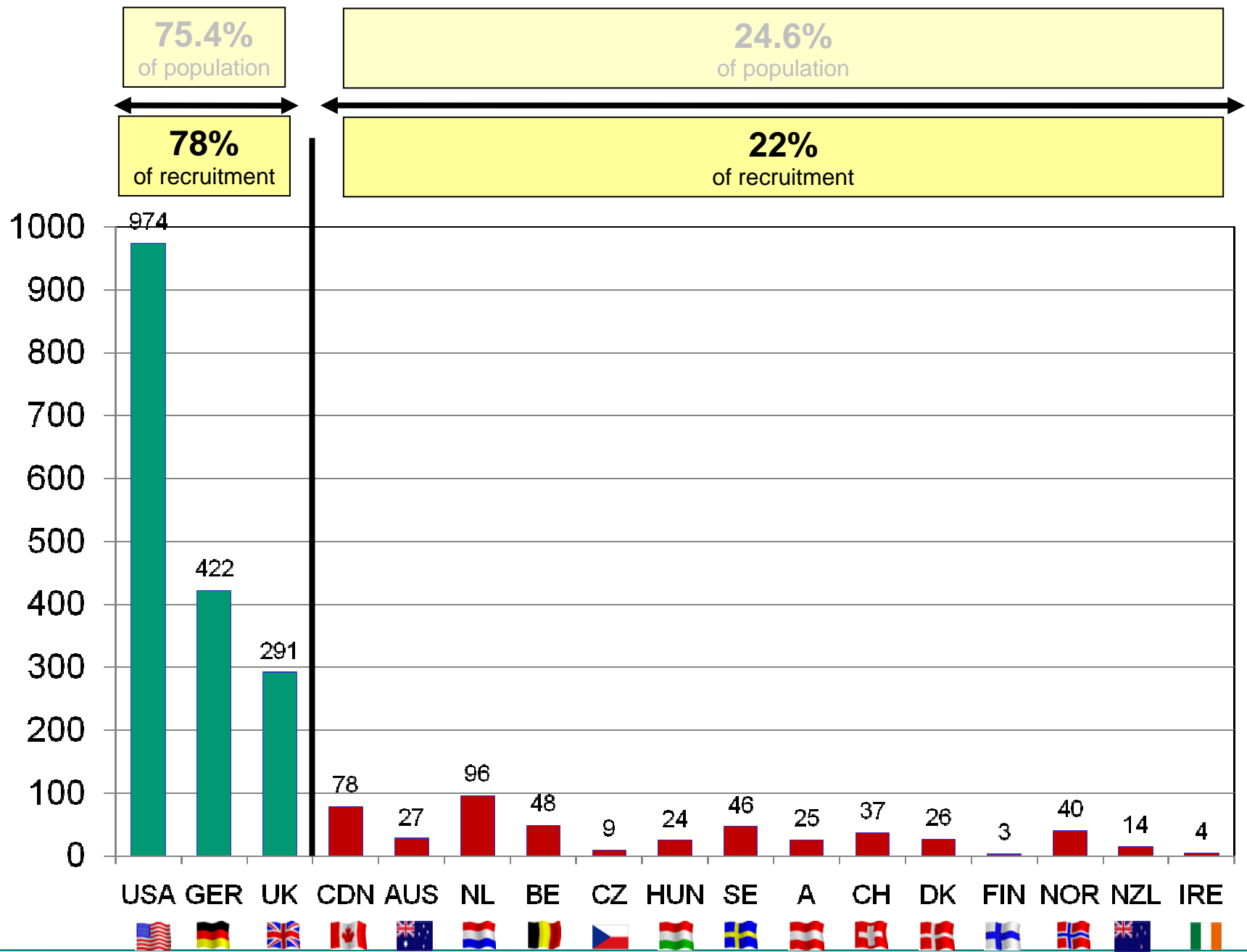


Would it be feasible  
to limit  
the number of centers  
by performing the trial  
in selected  
large countries only?

# EURAMOS target population **606.57 million** ca. 8.7% of world

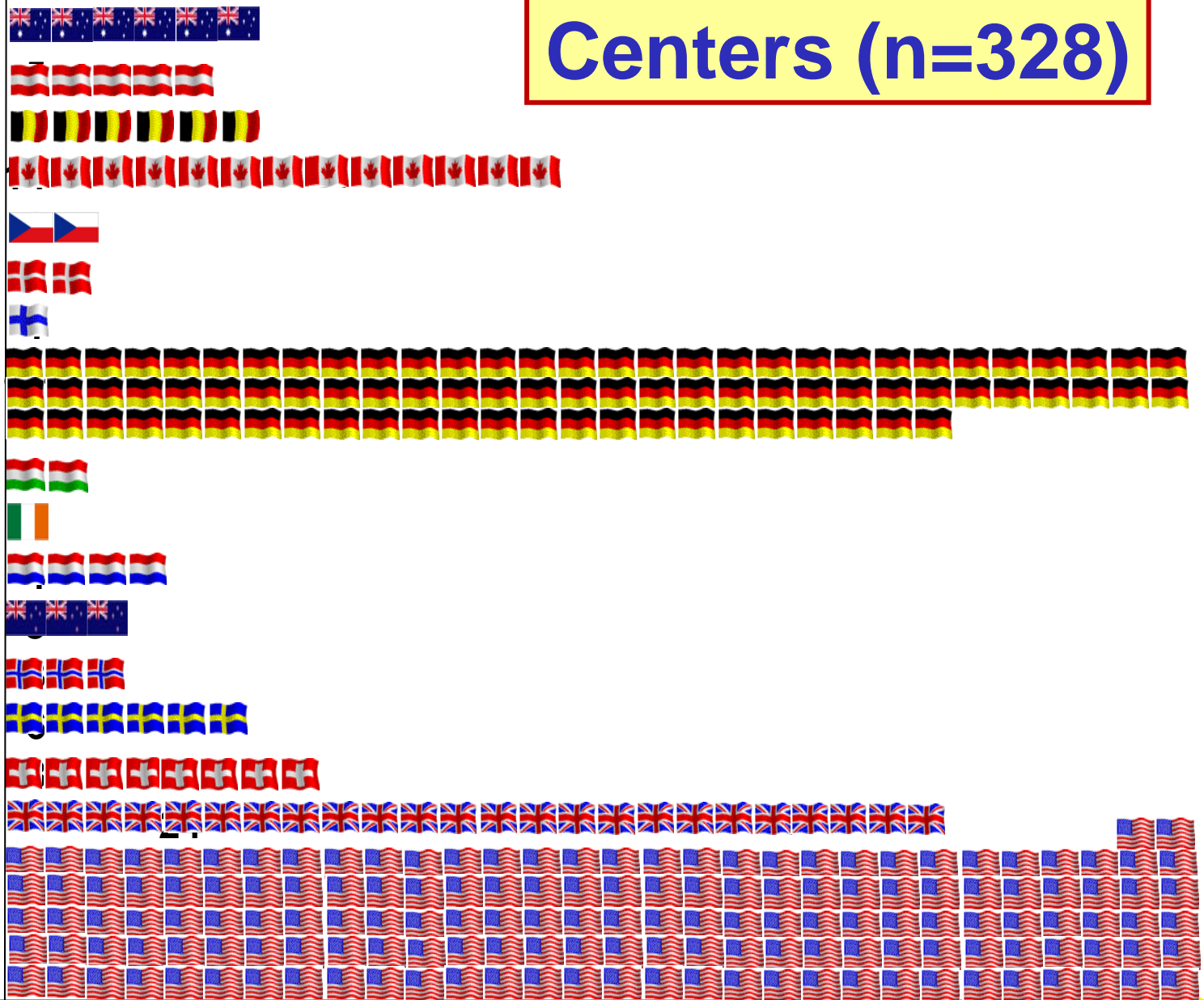
population





# Centers (n=328)

- Australia
- Austria
- Belgium 6
- Canada
- Czech Rep.
- Denmark
- Finland
- Germany
- Hungary
- Ireland
- Netherlands
- New Zeald.
- Norway
- Sweden
- Switzerland
- UK
- USA 152

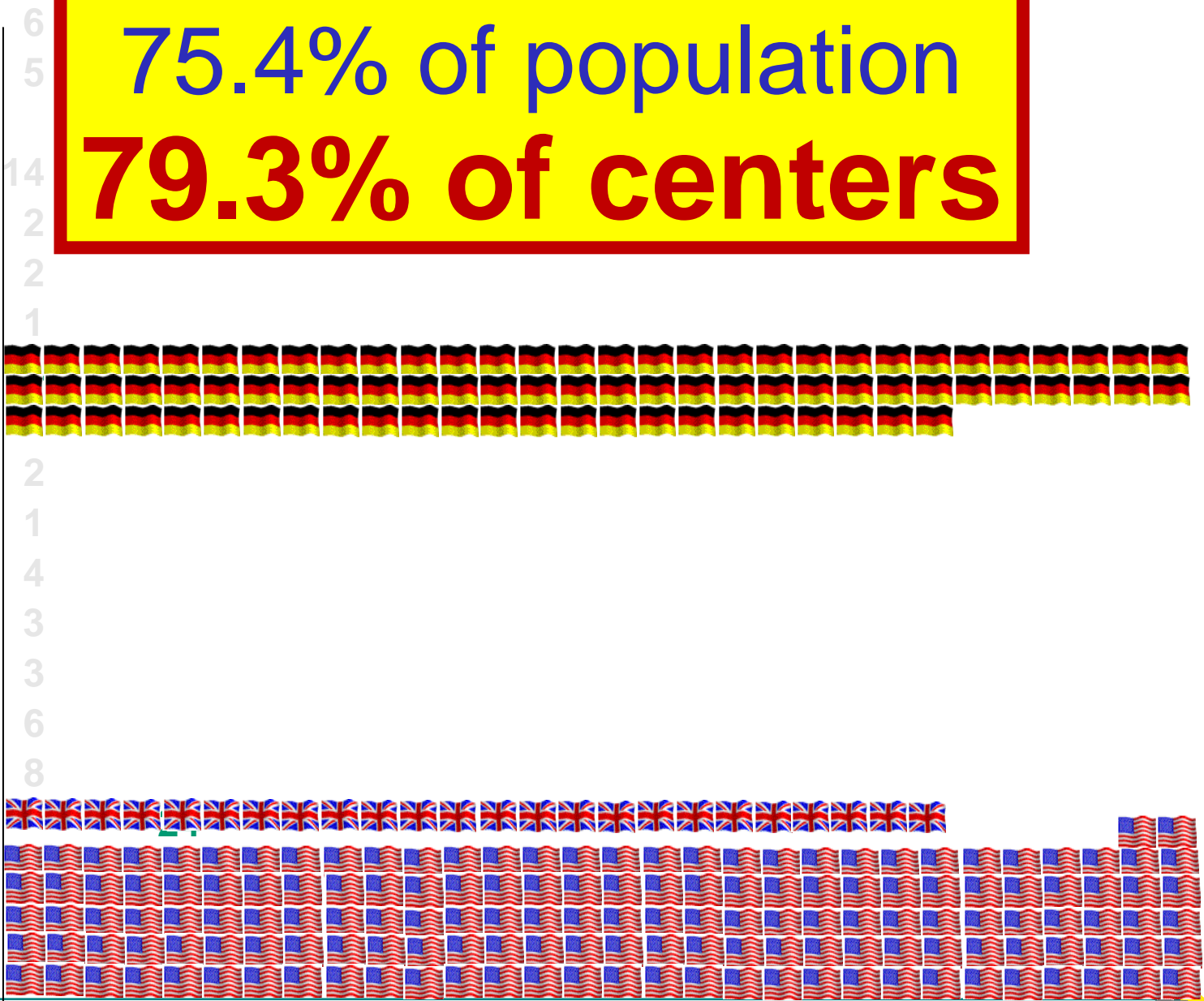


USA incl. Puerto Rico. 4 COG centers in 3 other countries



75.4% of population  
**79.3% of centers**

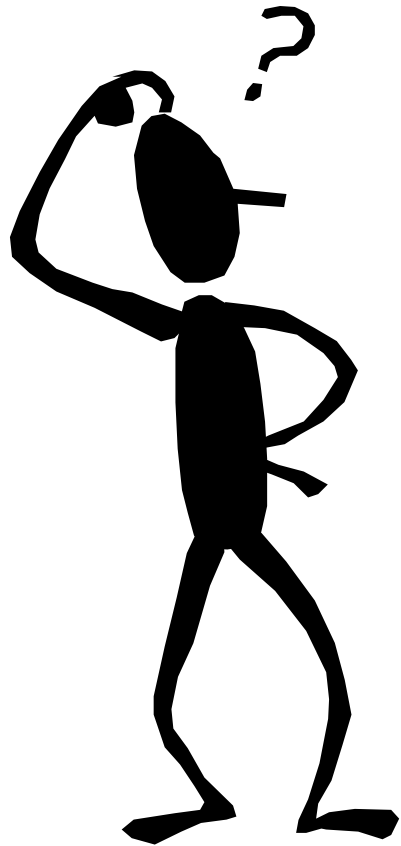
- Australia
- Austria
- Belgium 6
- Canada
- Czech Rep.
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- Hungary
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- Netherlands
- New Zeald.
- Norway
- Sweden
- Switzerland
- UK**
- USA 152**



# Limiting the trial to a few large countries

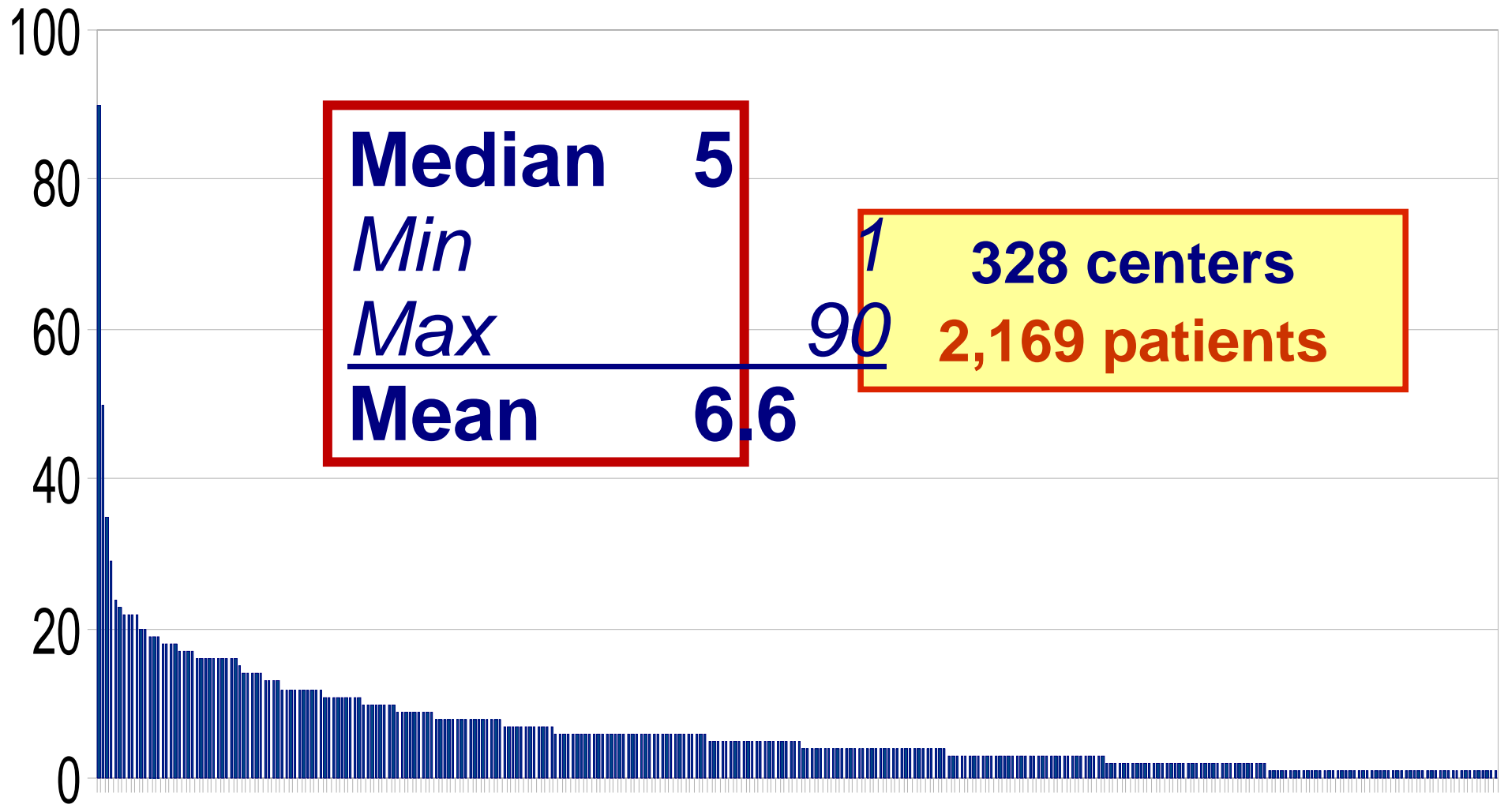
would reduce national regulatory and ethical submissions, but

would not reduce the  
number of centers  
considerably

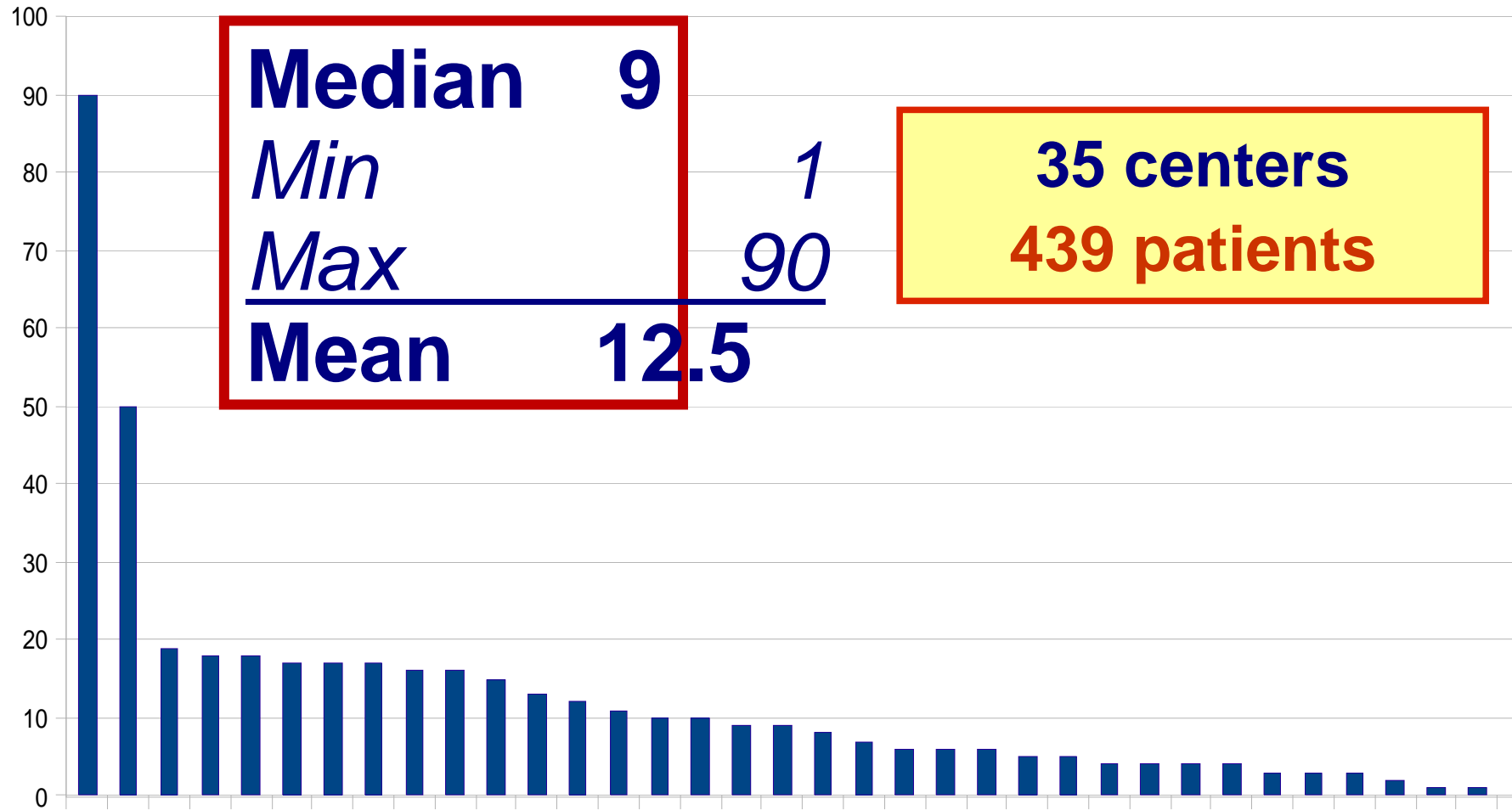


Would it be feasible  
to perform such  
trials in selected  
large centers only?

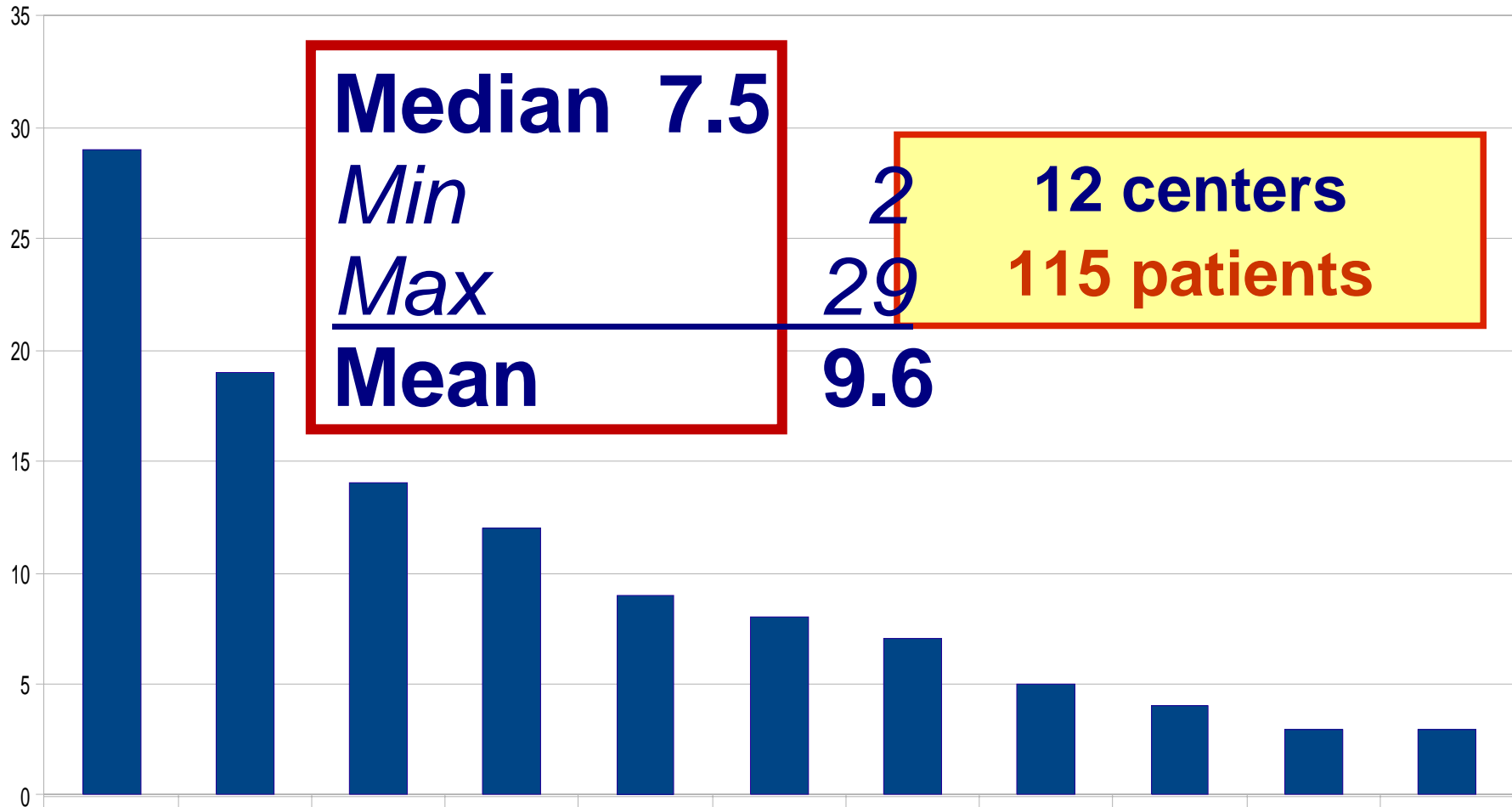
# EURAMOS Patients per center



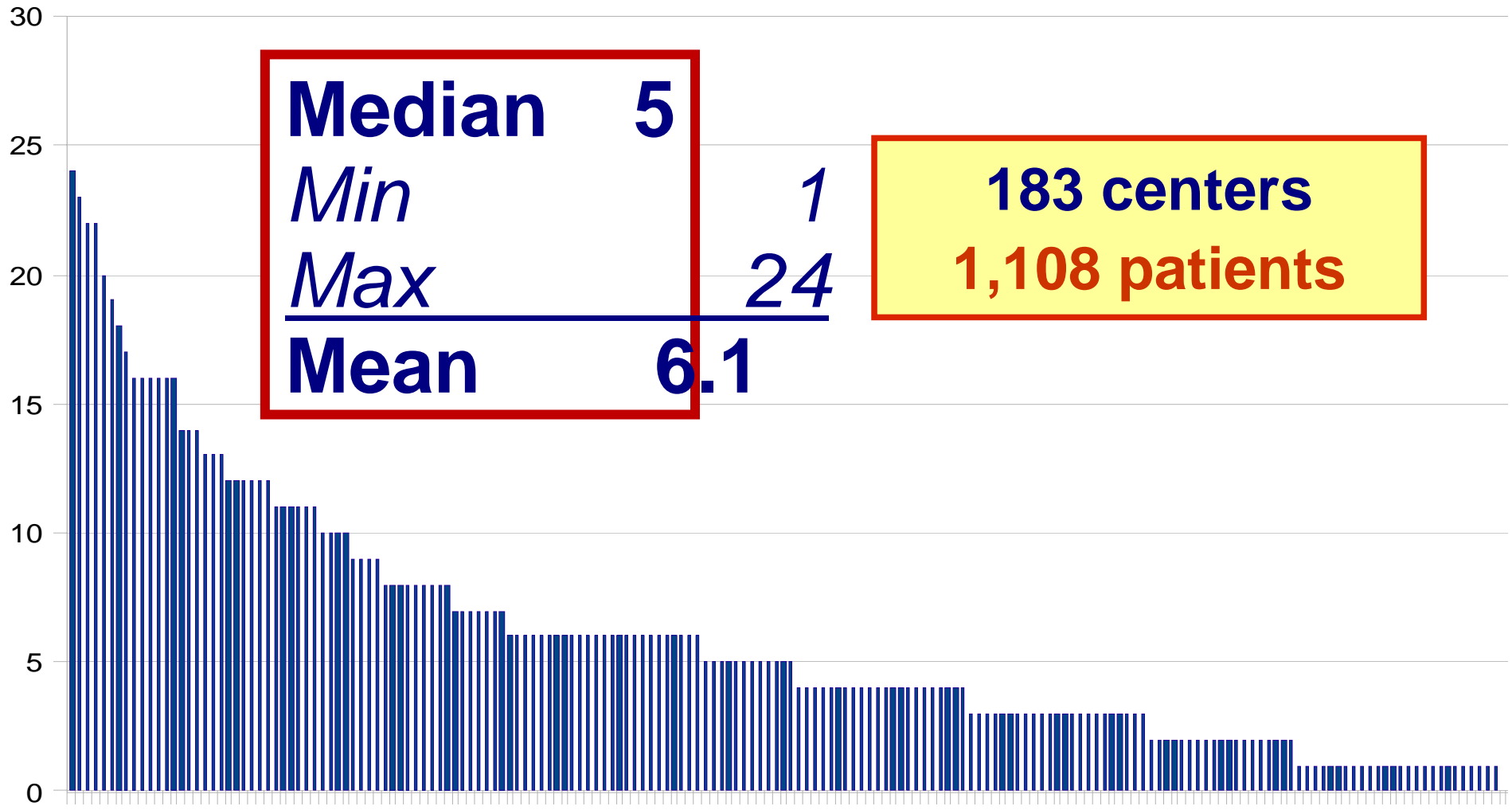
# EOI Patients per center



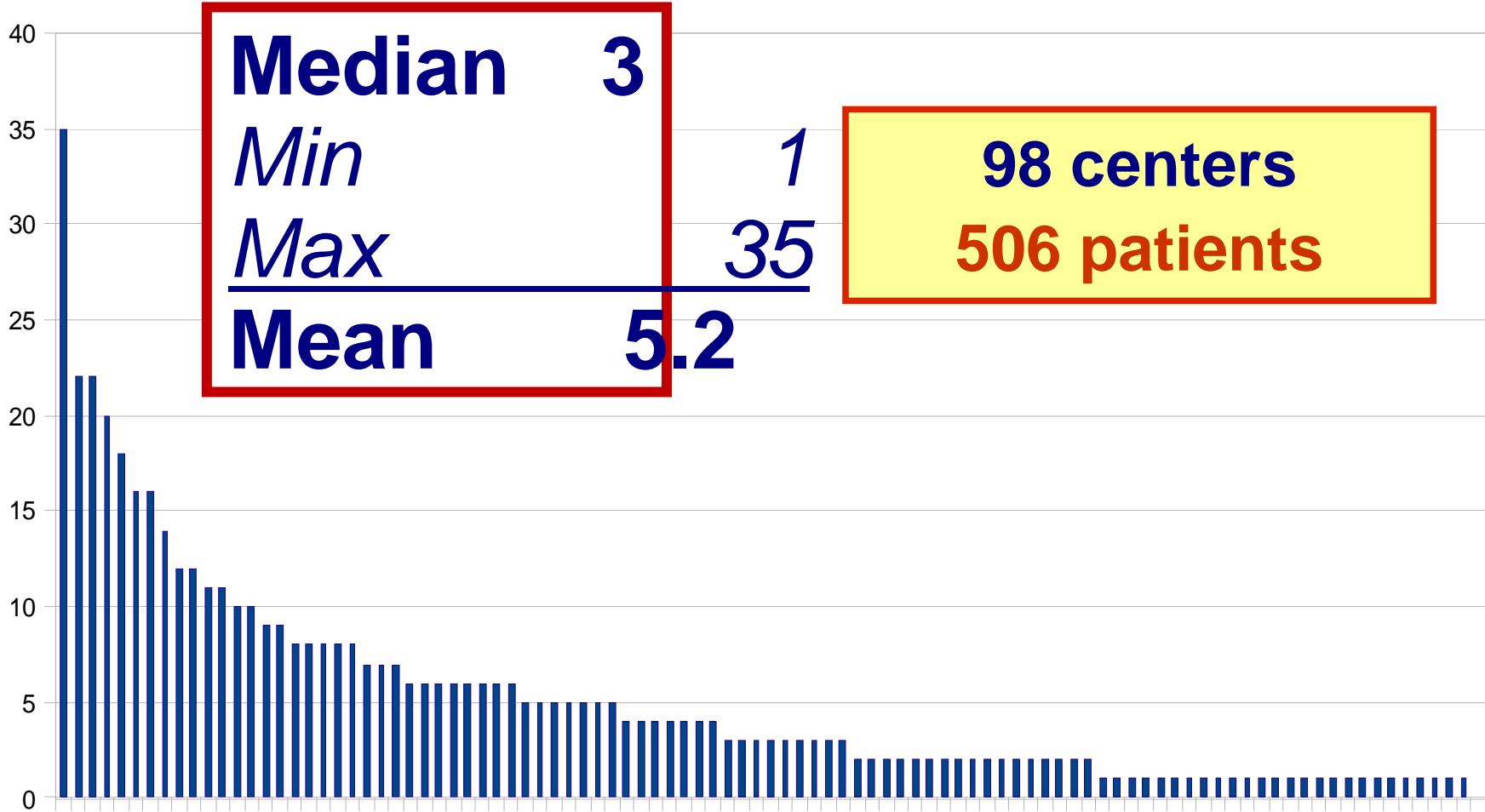
# SSG Patients per center



# COG Patients per center

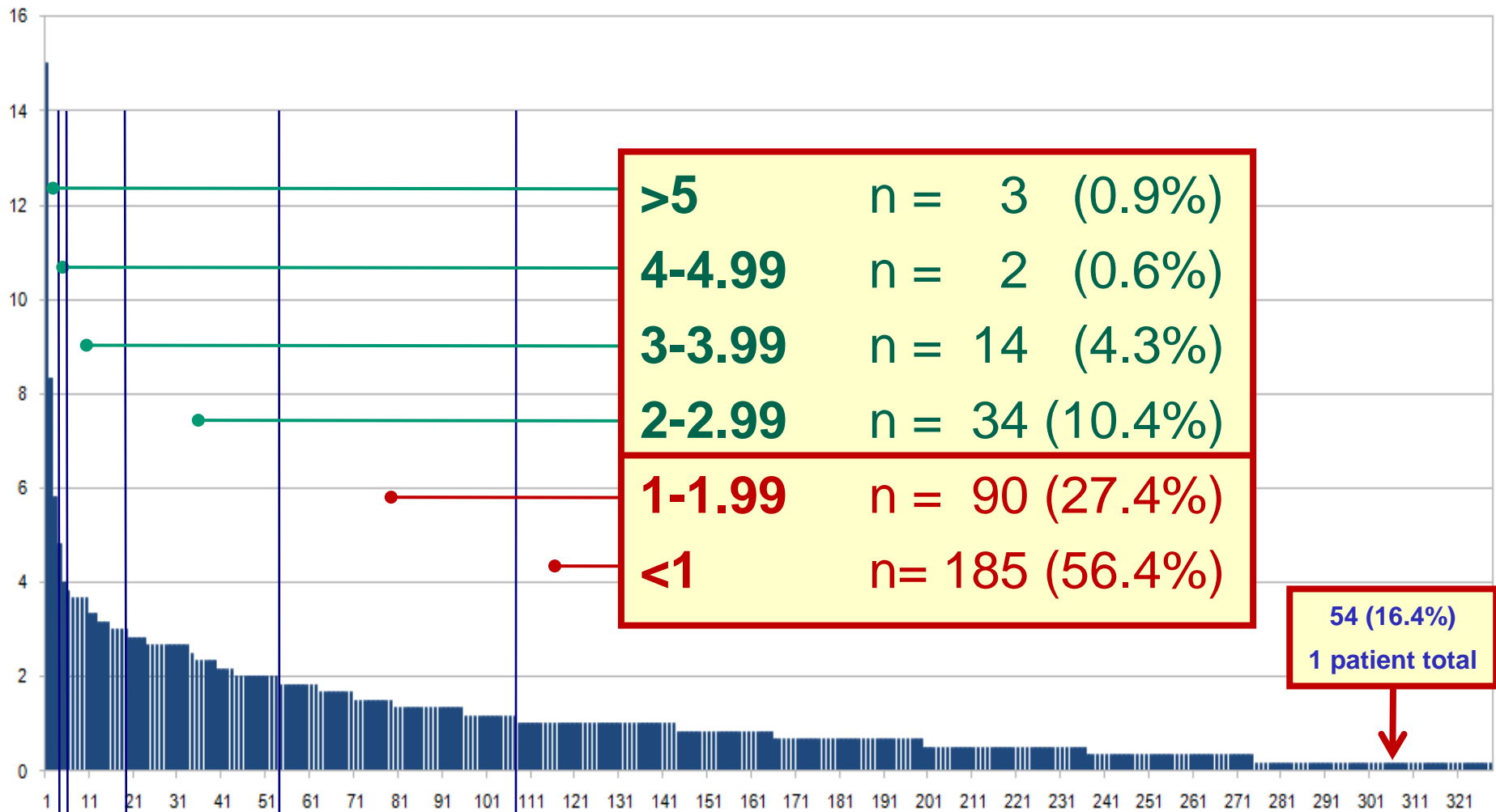


# COSS Patients per center



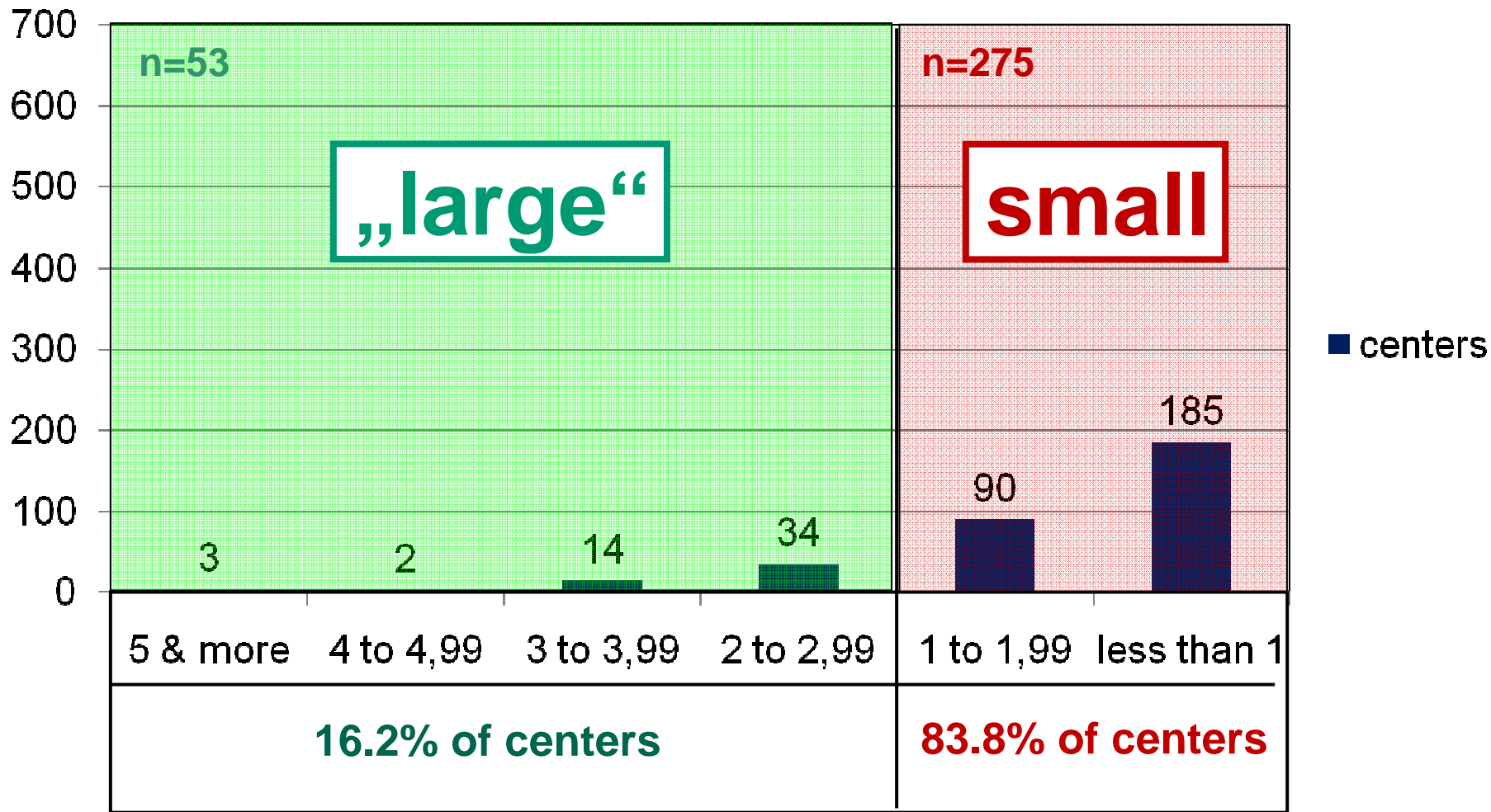
# EURAMOS

## Patients per center per year

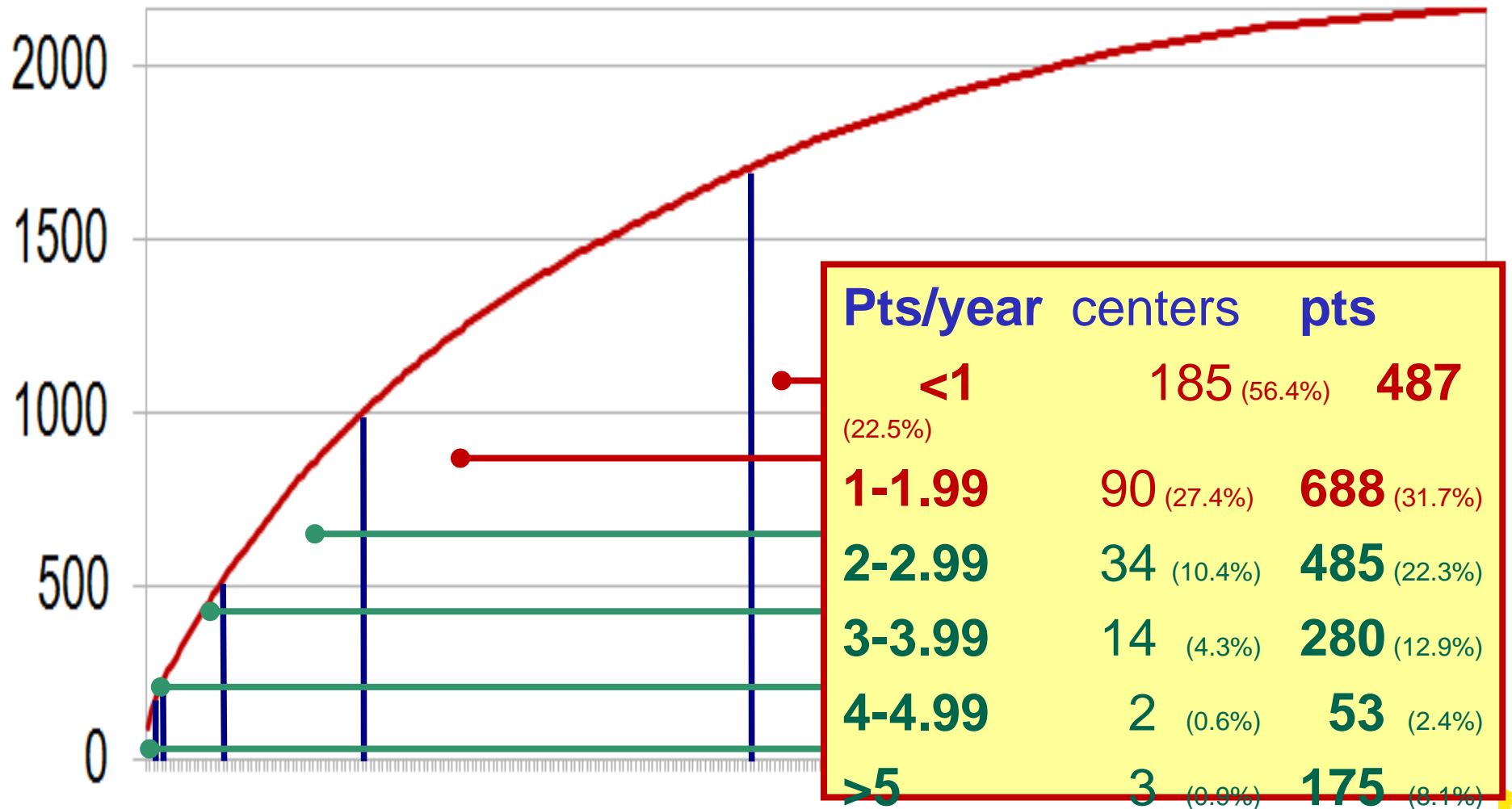


# Patients per center per year

(based on total 6 year EURAMOS recruitment period)

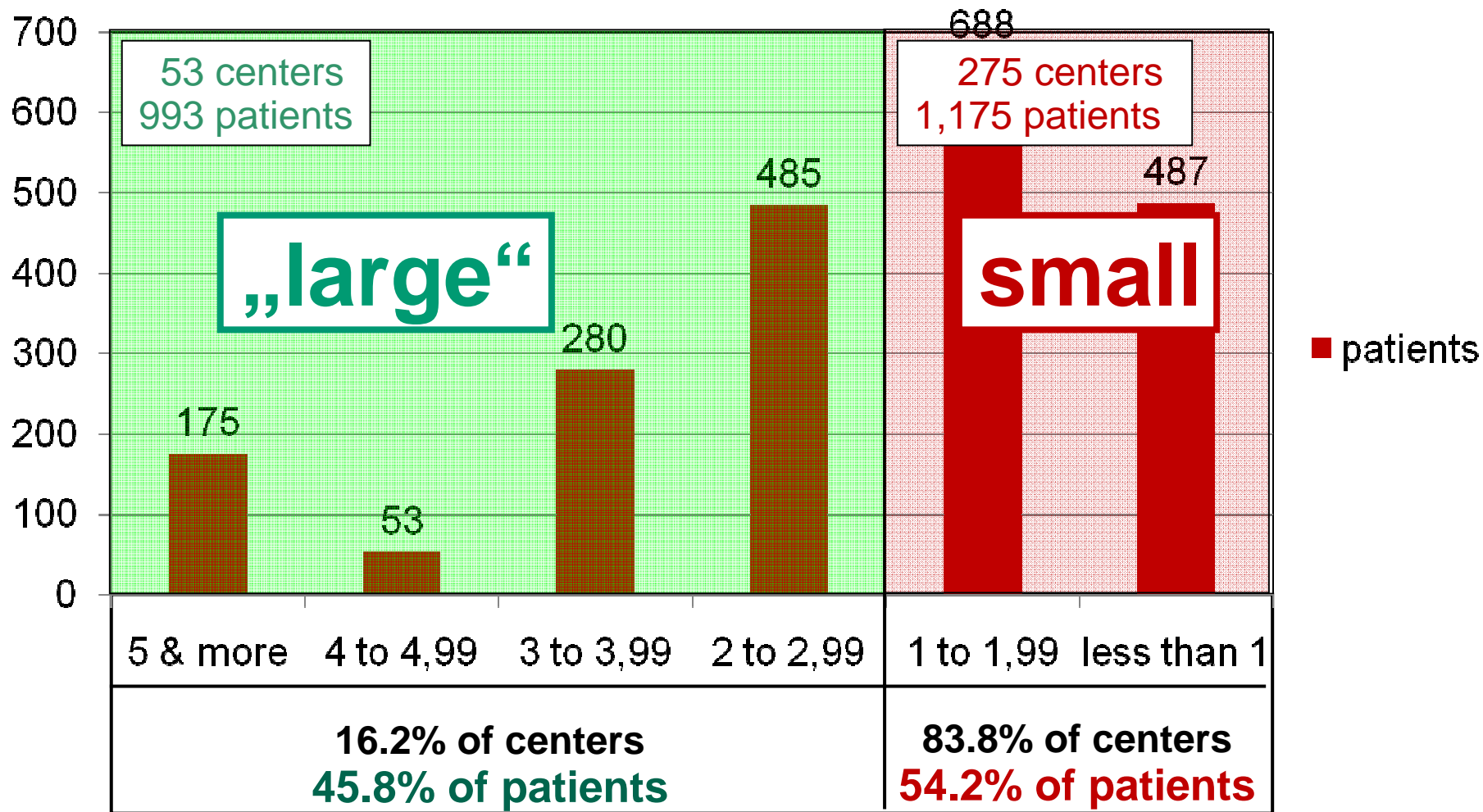


# EURAMOS Patients per center

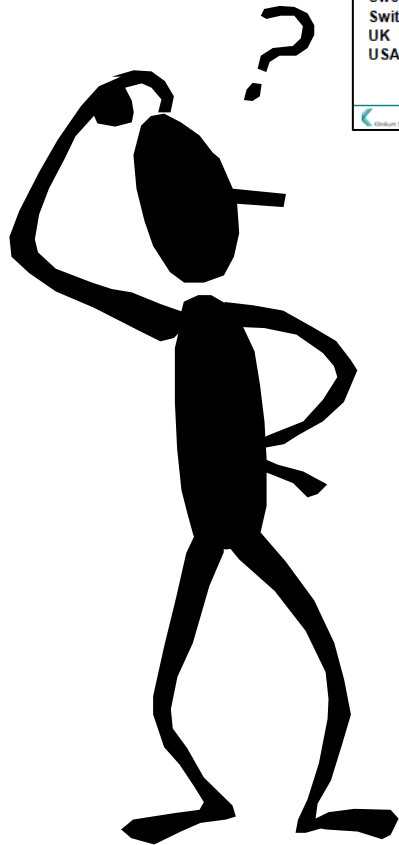
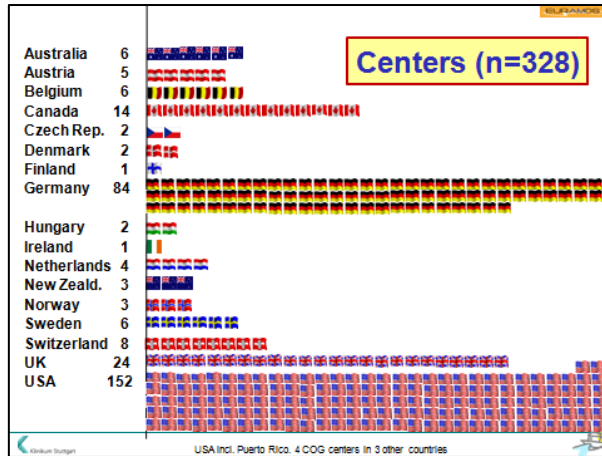


# Patients per center per year

(based on total 6 year EURAMOS recruitment period)



**More than half of all patients**  
are recruited by  
*(very)* **low volume contributors**

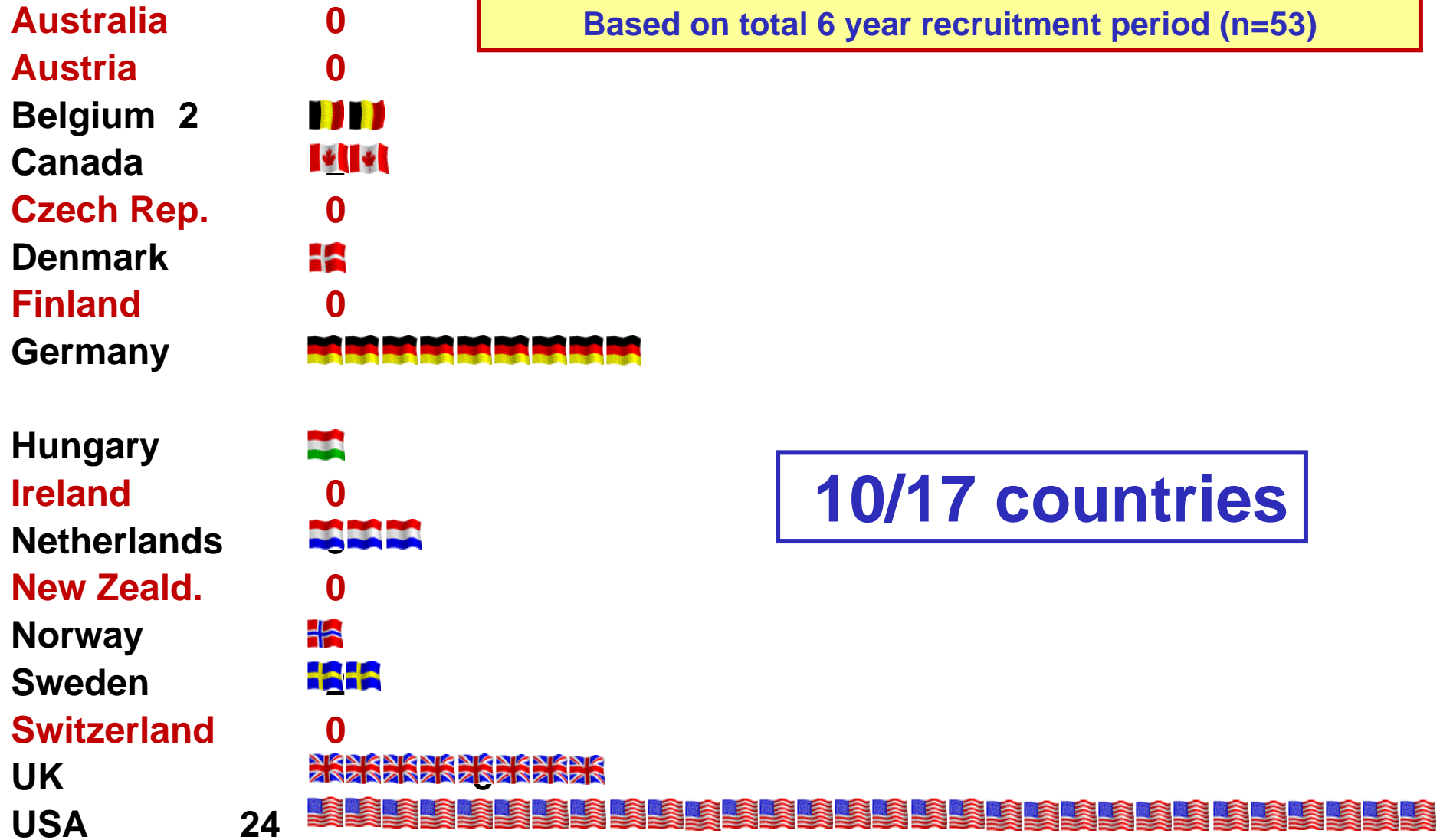


Are the  
high volume recruiters  
concentrated in a  
few countries?



# Centers $\geq 2$ patients/year

Based on total 6 year recruitment period (n=53)

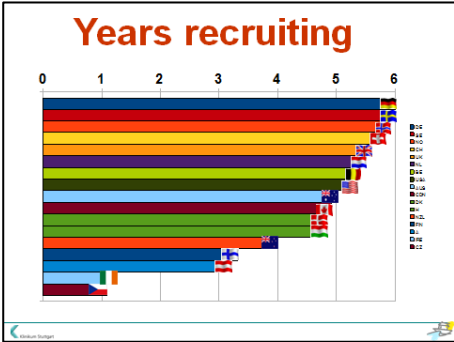
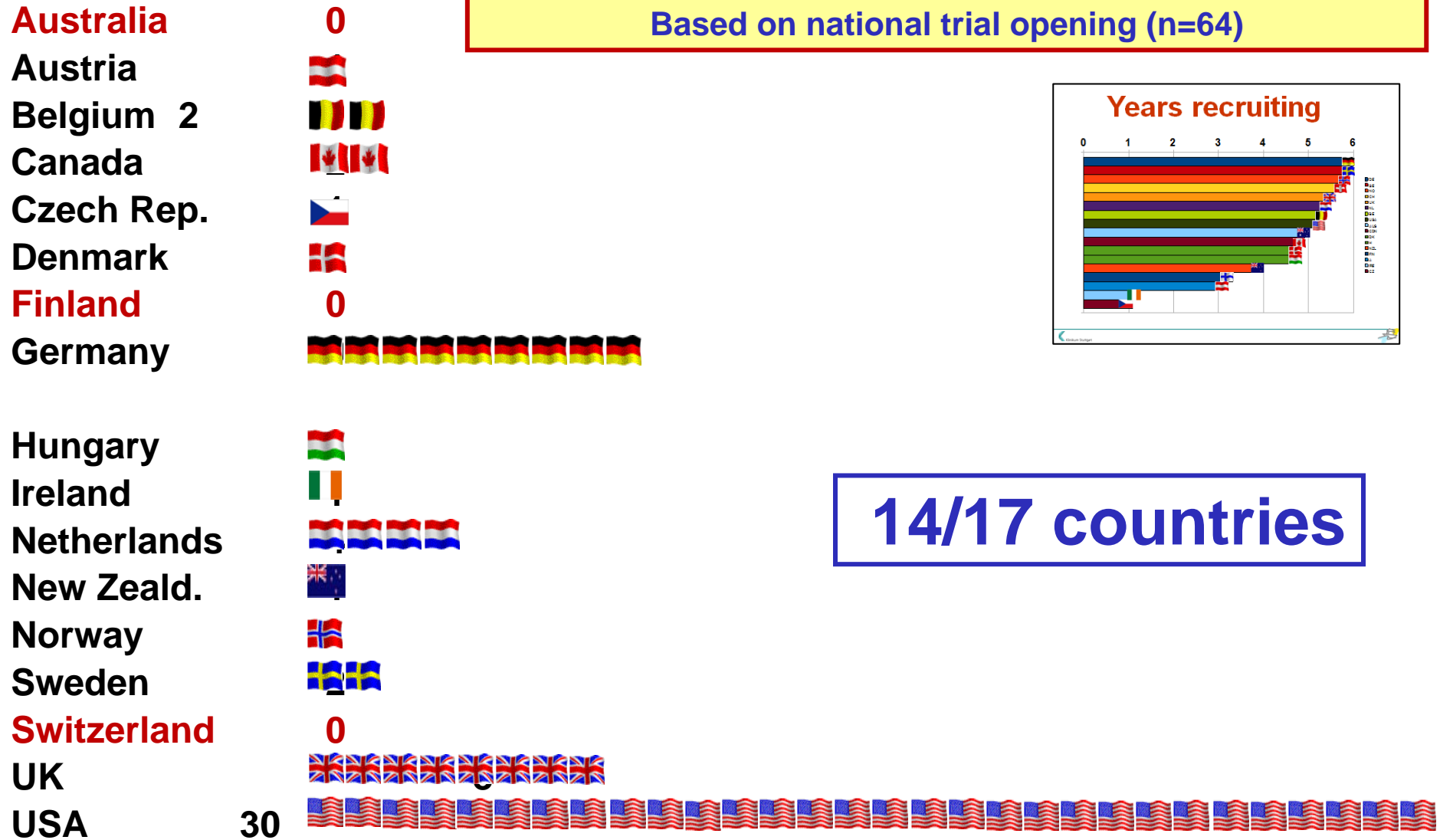


10/17 countries



# Centers $\geq 2$ patients/year

Based on national trial opening (n=64)

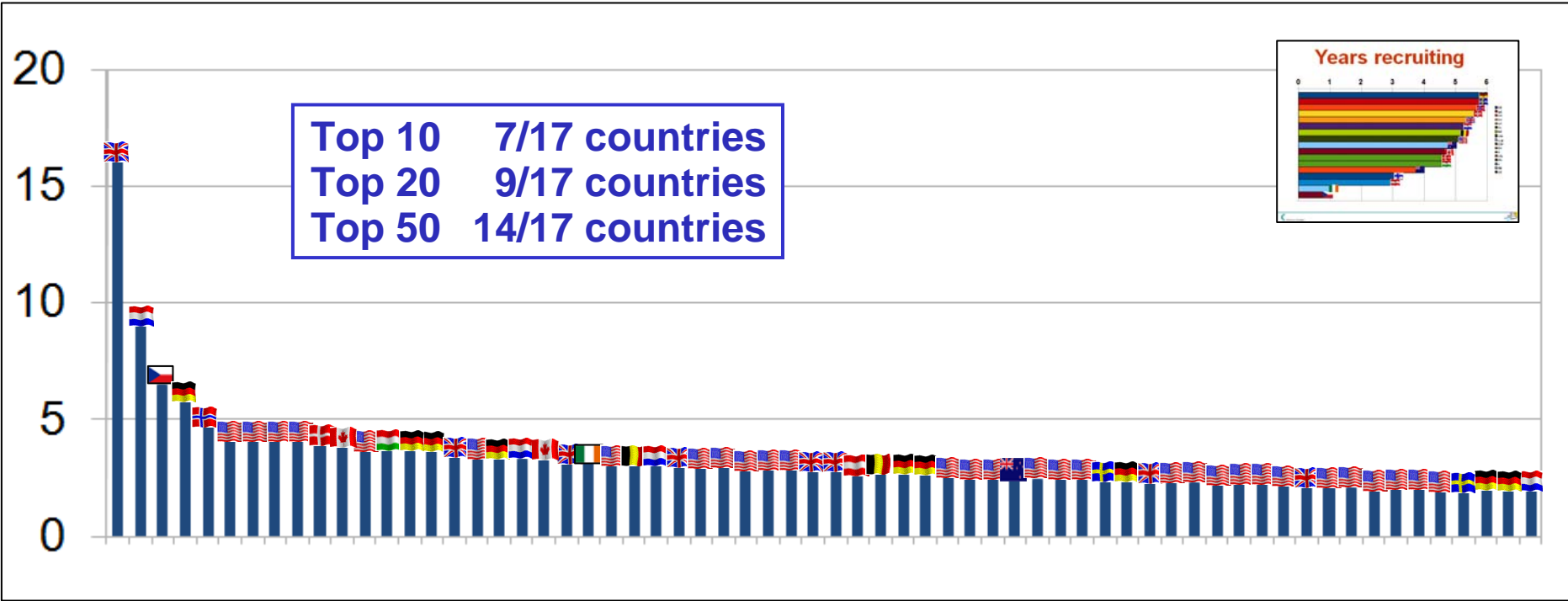


**14/17 countries**



# Centers $\geq 2$ patients/year

Based on national trial opening (n=64)



Unless major political changes occur:

**Considerable fragmentation of care**  
needs to be taken into account  
when planning, initiating,  
running, and regulating  
large scale clinical trials  
**in rare cancers.**



# EUROCORES Programme

European Collaborative Research

The EURAMOS investigators thank

**ESF**

and its Member Organisations

for their support



Supported by the European Science Foundation (ESF) under the EUROCORES Program European Clinical Trials (ECT), through contract No. ERASCT-2003-980409 of the European Commission, DG



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Danke für Ihre Aufmerksamkeit!

