

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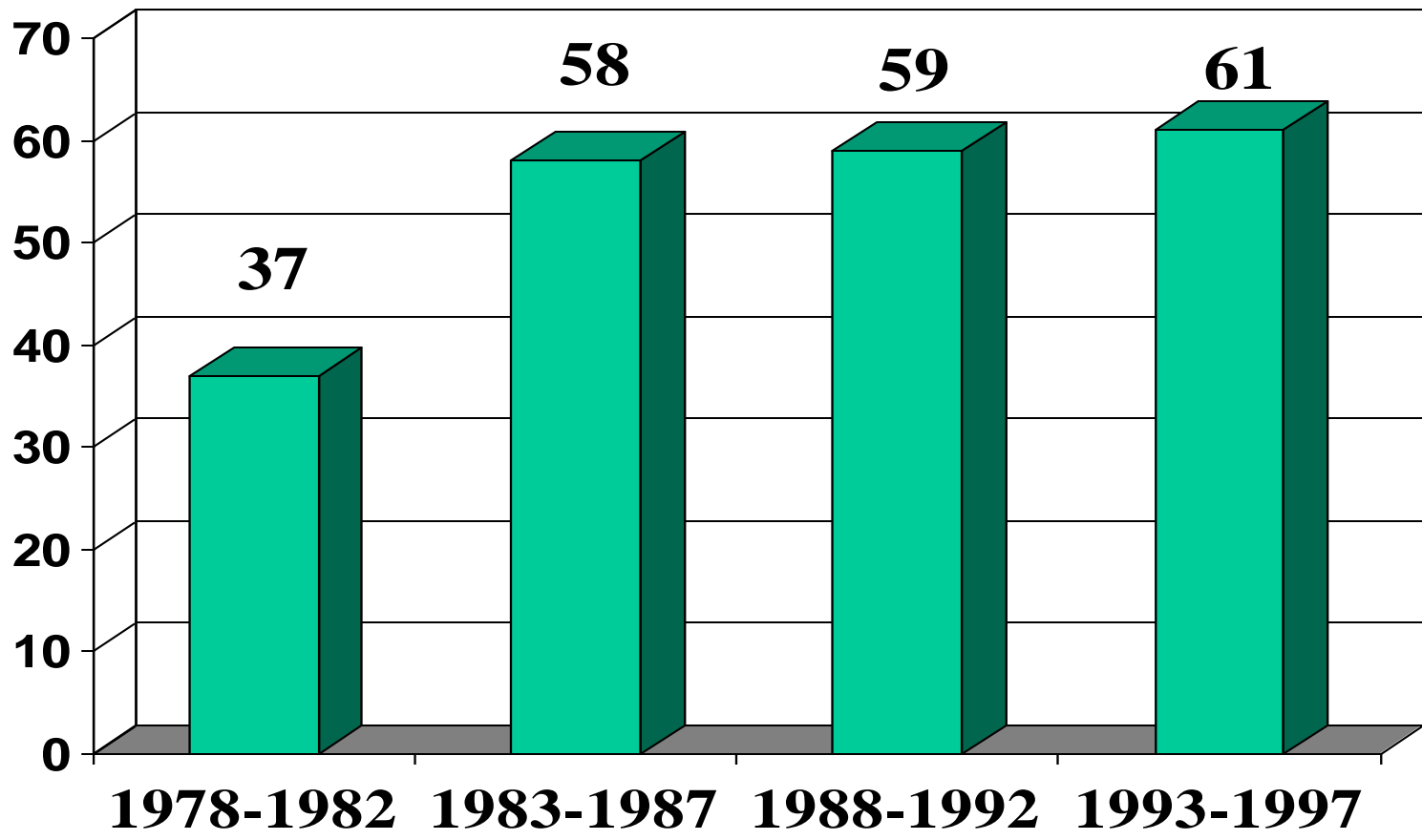
Supported by the European Science Foundation (ESF) under the EUROCORES Program European Clinical Trials (ECT), through contract No. ERASCT-2003-980409 of the European Commission, DG



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

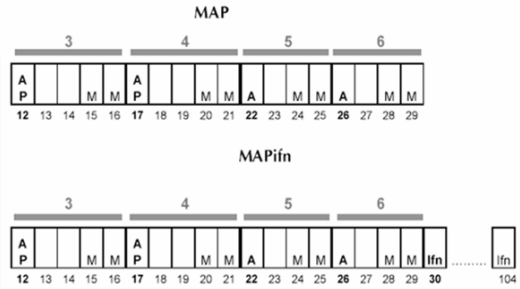
C.A. Stiller^{a,*}, S.S. Bielack^{b,c}, G. Jundt^d, E. Steliarova-Foucher^e

EUROPEAN JOURNAL OF CANCER 42 (2006) 2124-2135

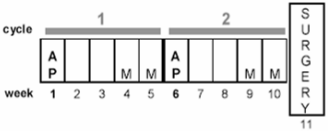


A = Doxorubicin 75mg/m²/course
 P = Cisplatin 120mg/m²/course
 M = Methotrexate 12g/m²/course
 E = Etoposide 500mg/m²/course
 I = Ifosfamide 14g/m²/course
 i = Ifosfamide 9g/m²/course
 lfn = Interferon-α 0.5-1.0µg/kg weekly

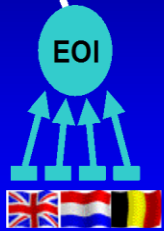
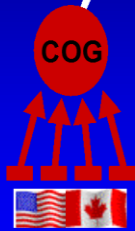
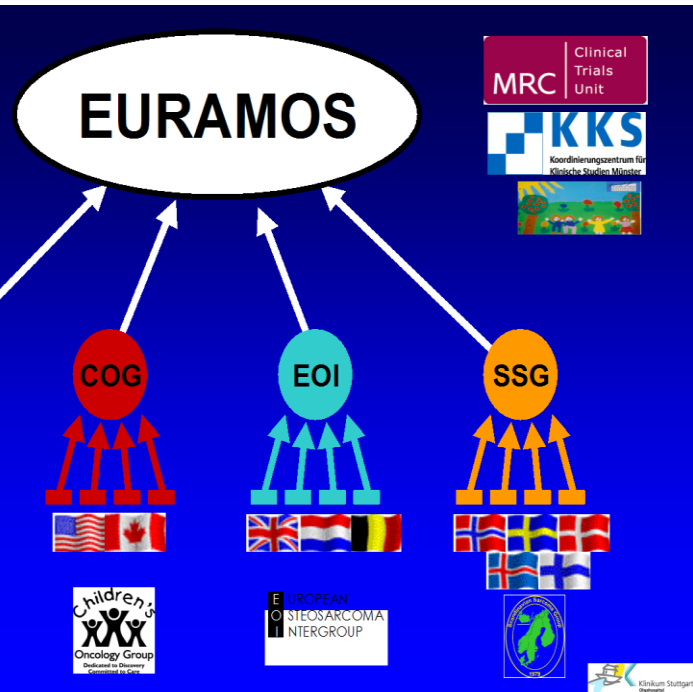
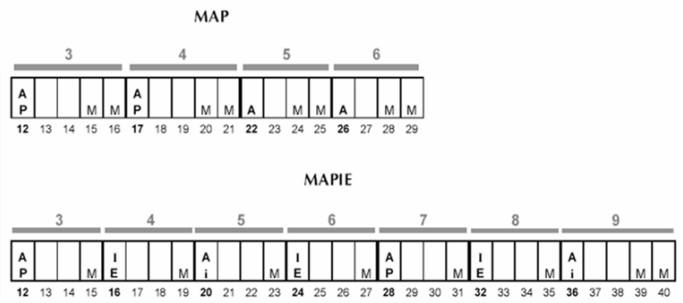
GOOD
RANDOMISE
RESPONSE



Evaluation of histological response

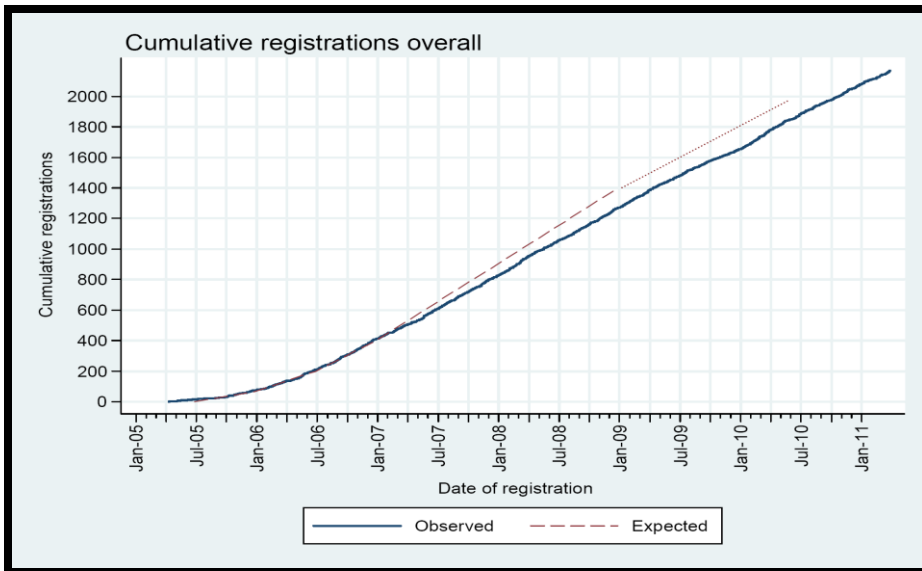


POOR
RANDOMISE
RESPONSE



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

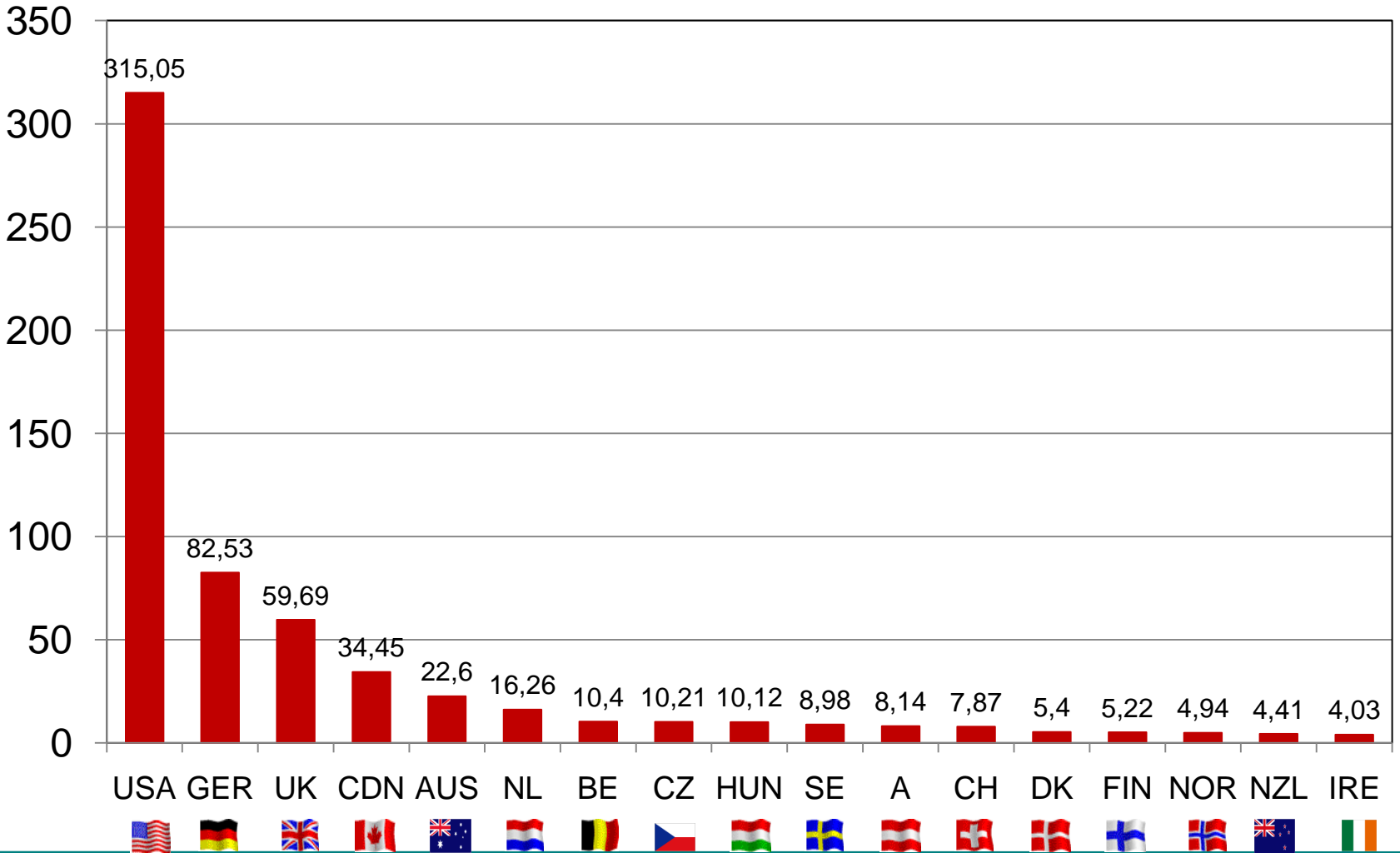
Total	2,169	100.00

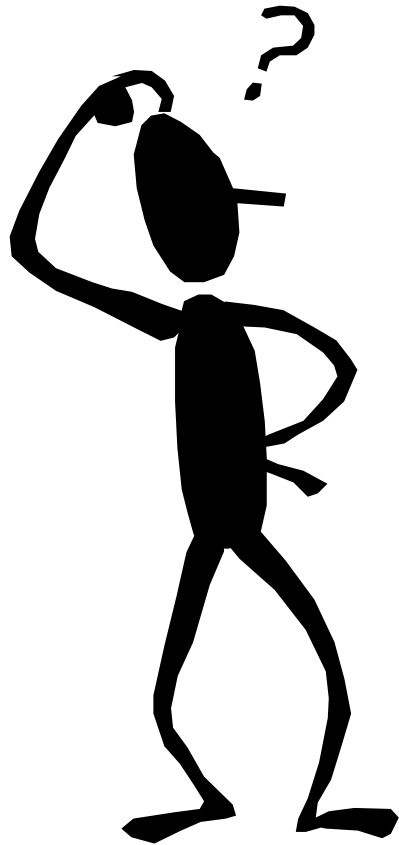
Thanks to EURAMOS-CDC,
MRC London



EURAMOS target population **606.57 million**

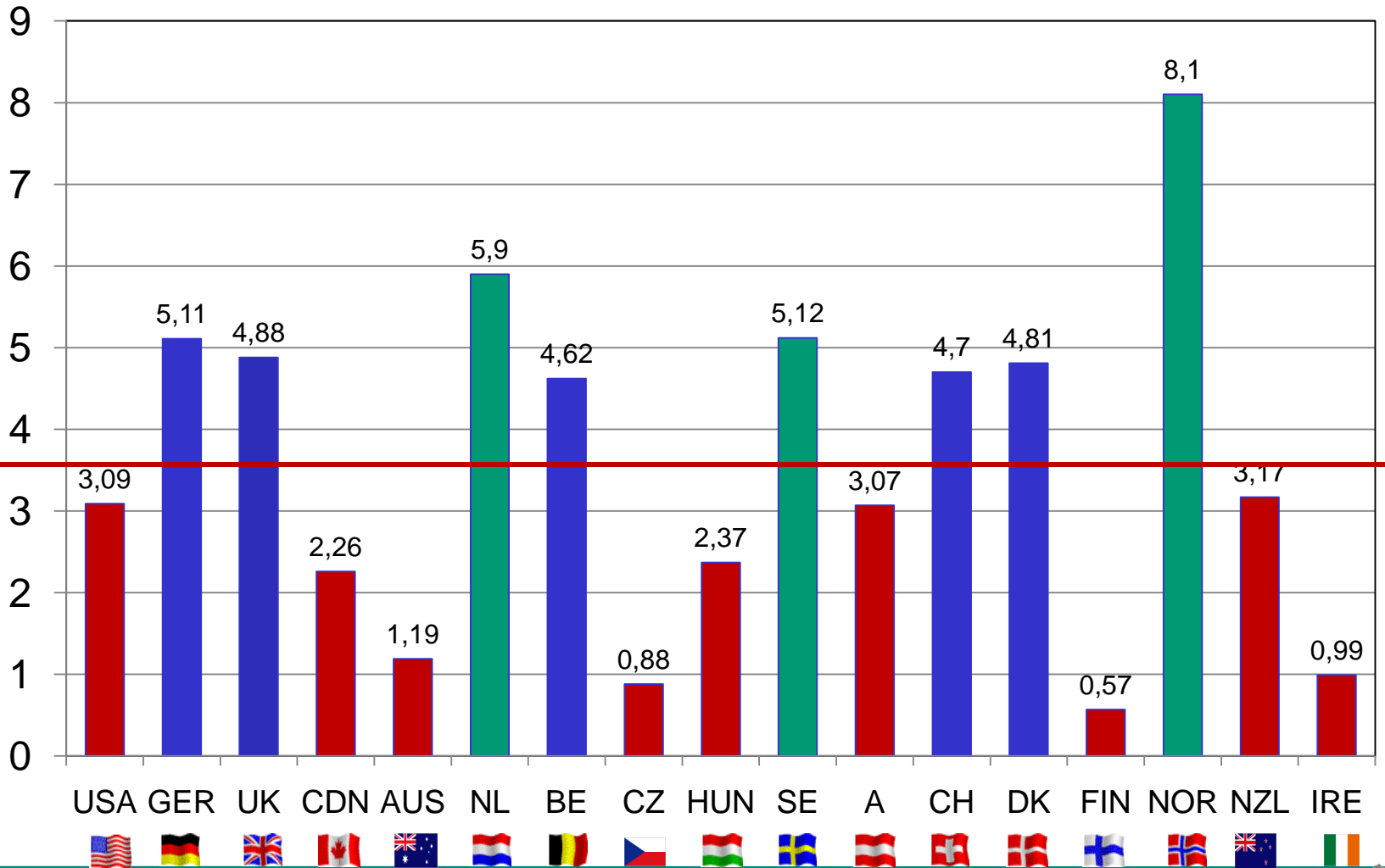
ca. 8.7% of world population





Do countries
achieve similar
population-adjusted
recruitment
rates?

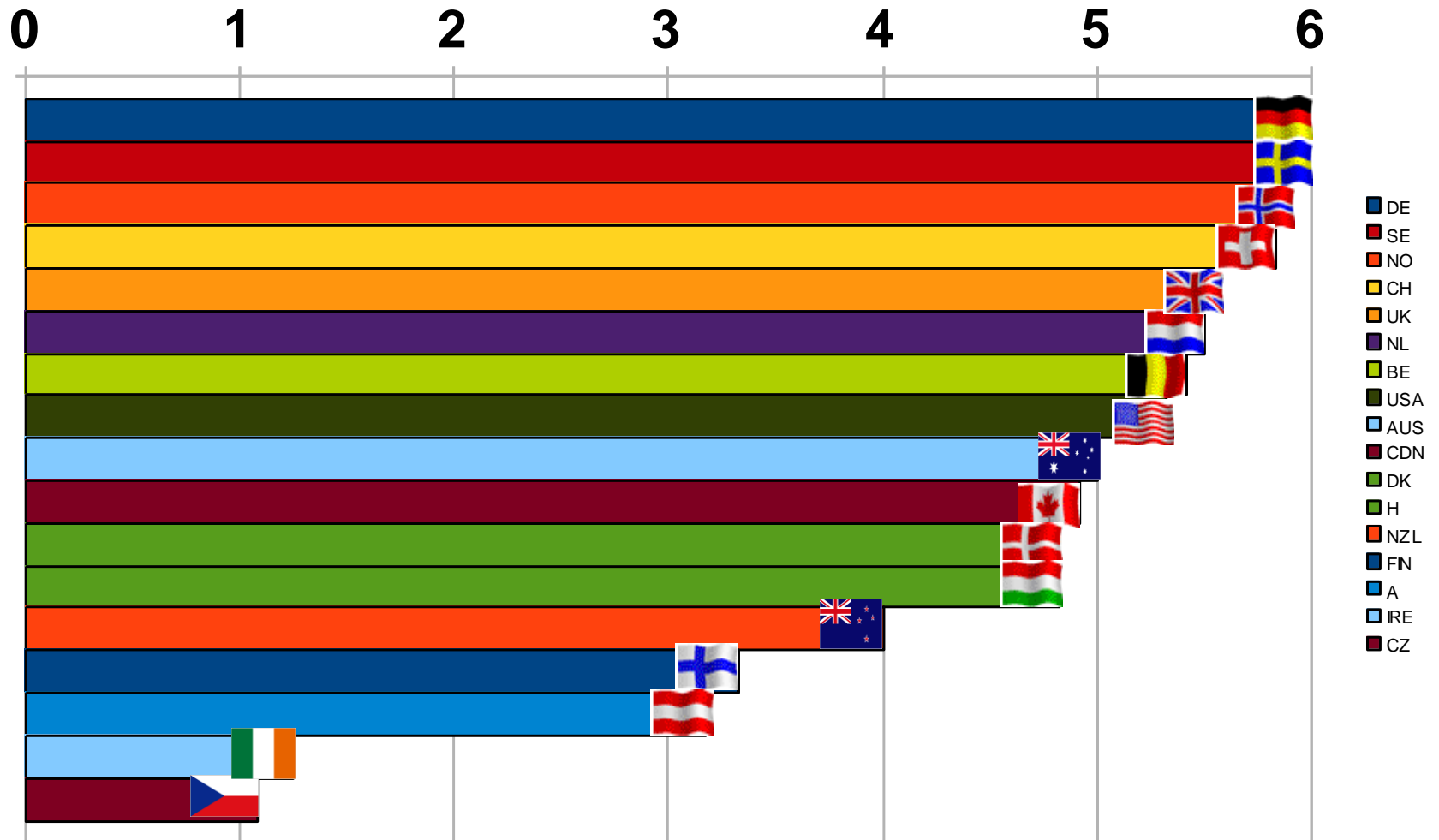
Recruitment / Country / Million population



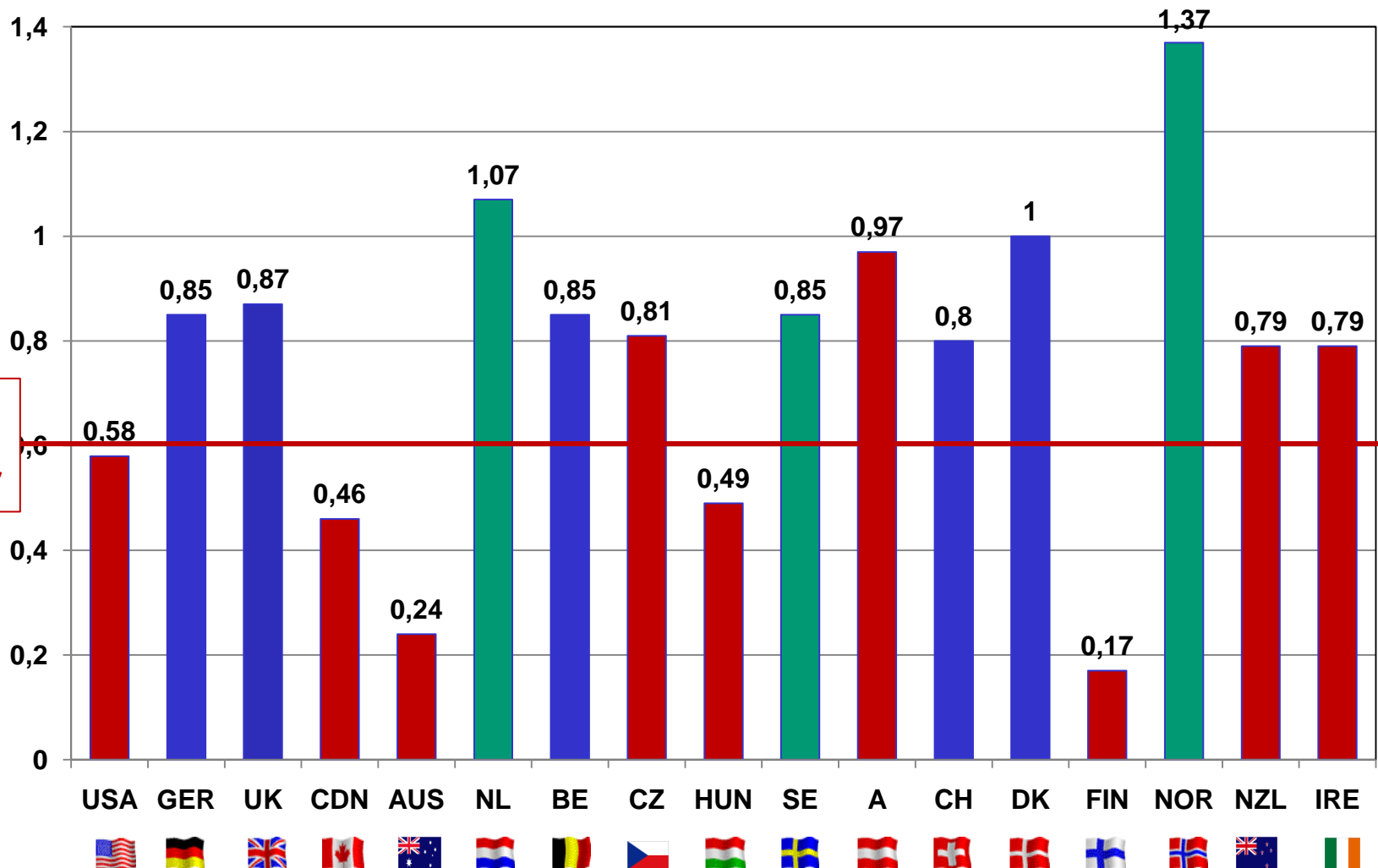
EURAMOS
mean
3.58



Years recruiting

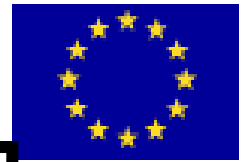


Recruitment / Country / Million population per year with trial open



**EURAMOS
mean
0.60/year**





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

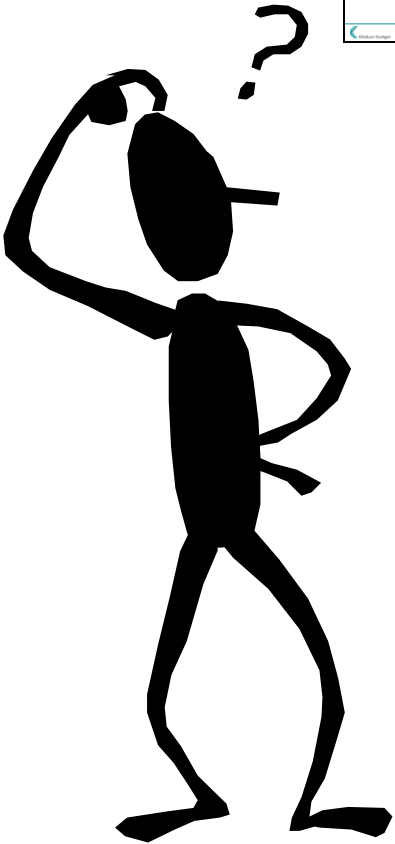
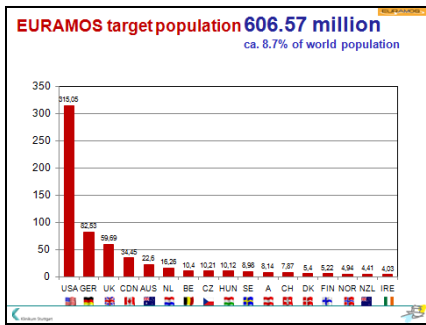
- **National Competent Authorities**
- **Ethics Committees**

- **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

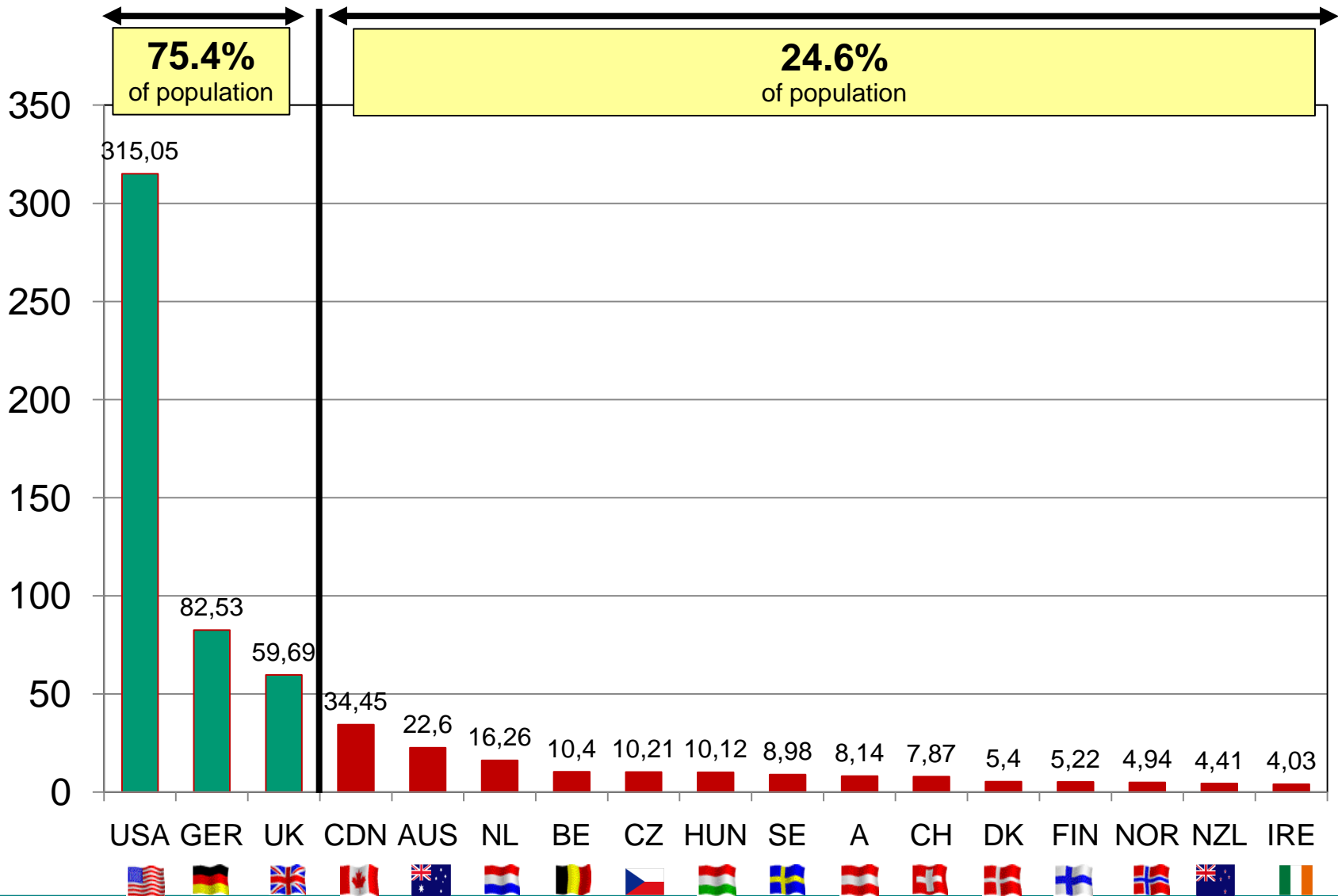


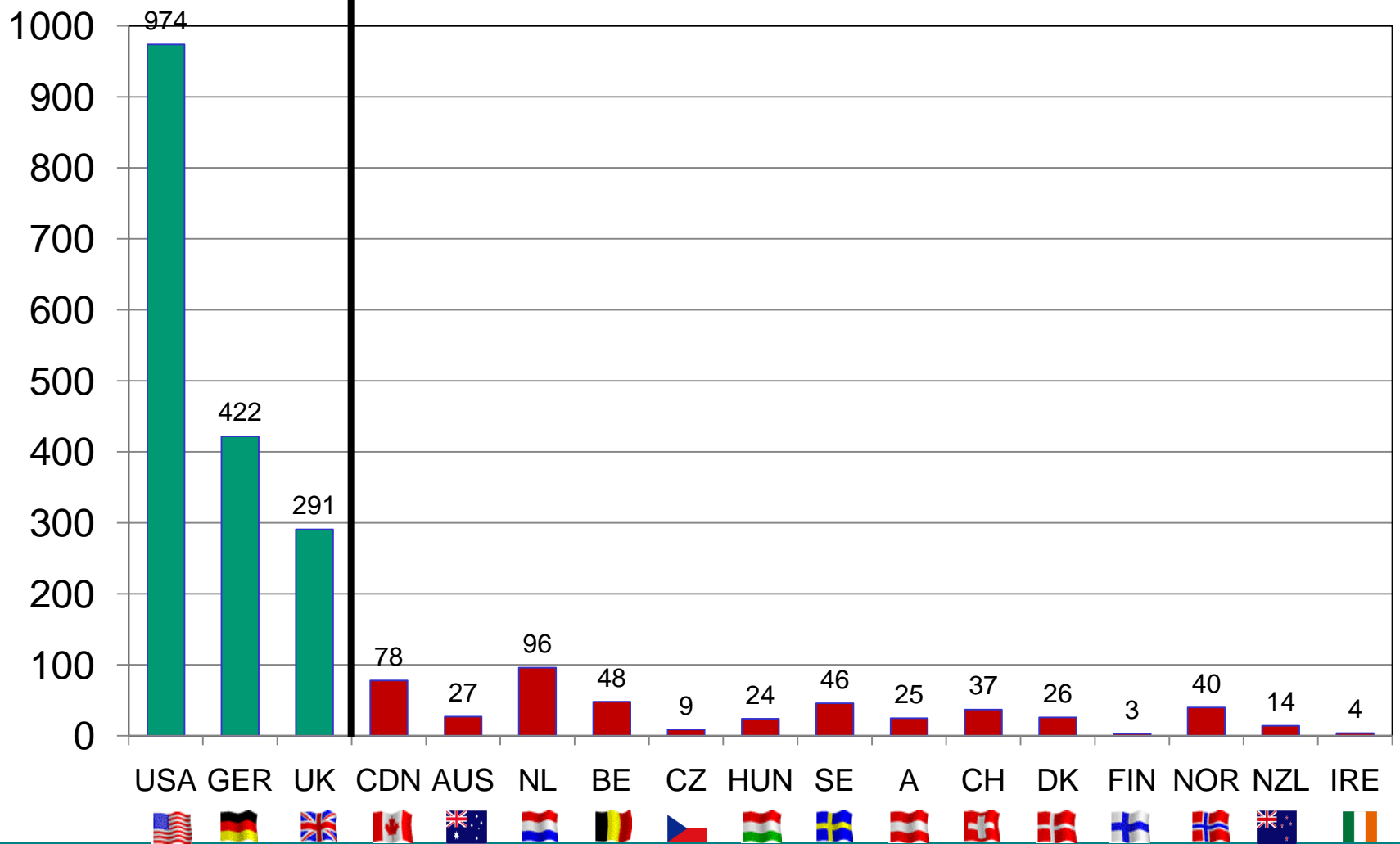
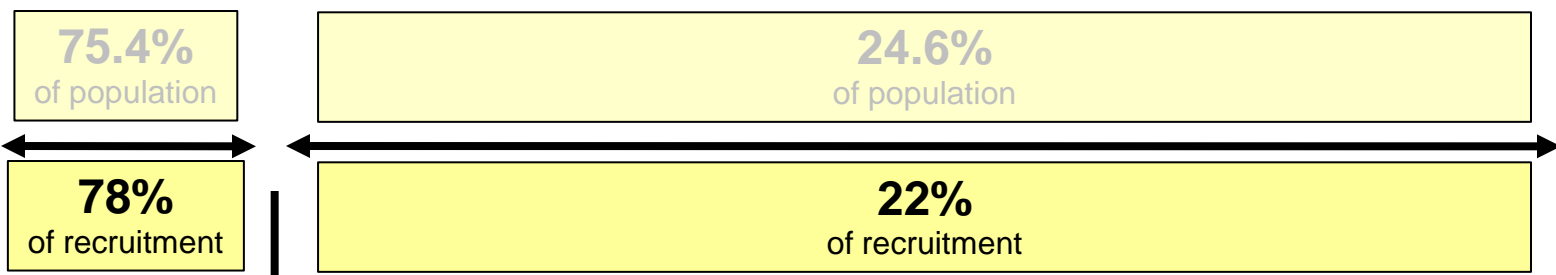
Would it be feasible
to limit
the number of centers
by performing the trial
in selected
large countries only?



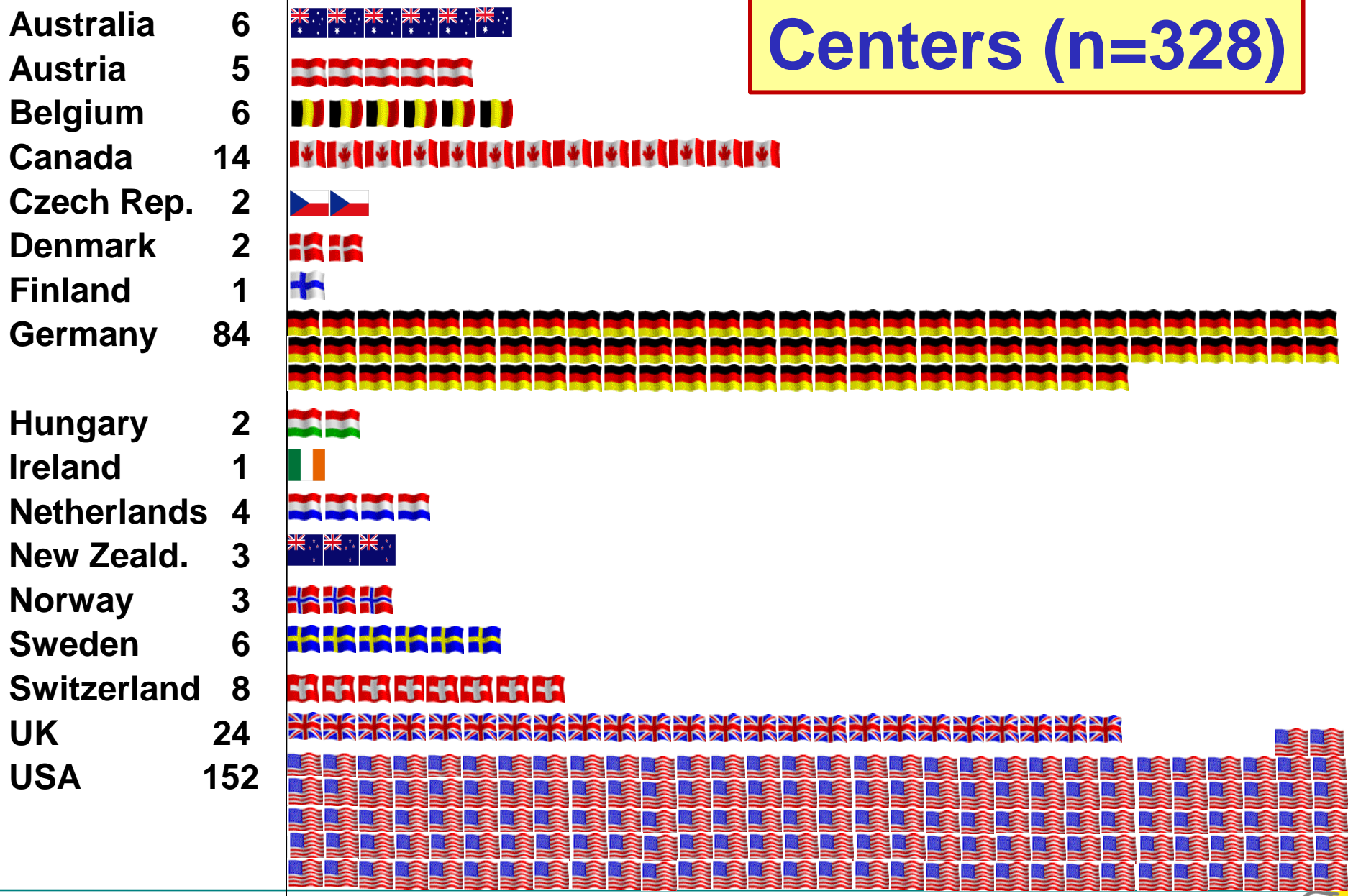
EURAMOS target population **606.57 million**

ca. 8.7% of world population





Centers (n=328)

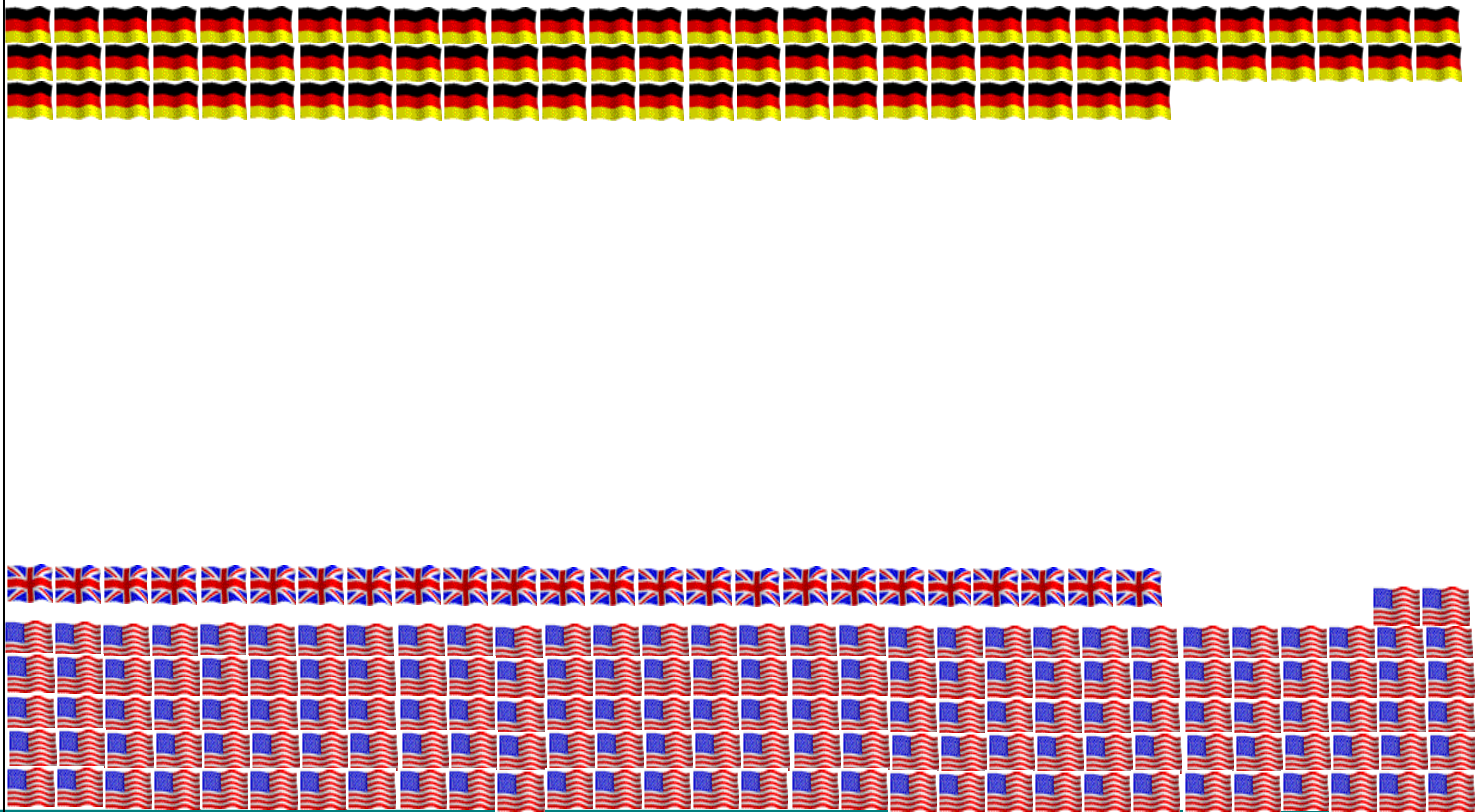


USA incl. Puerto Rico. 4 COG centers in 3 other countries



75.4% of population
79.3% of centers

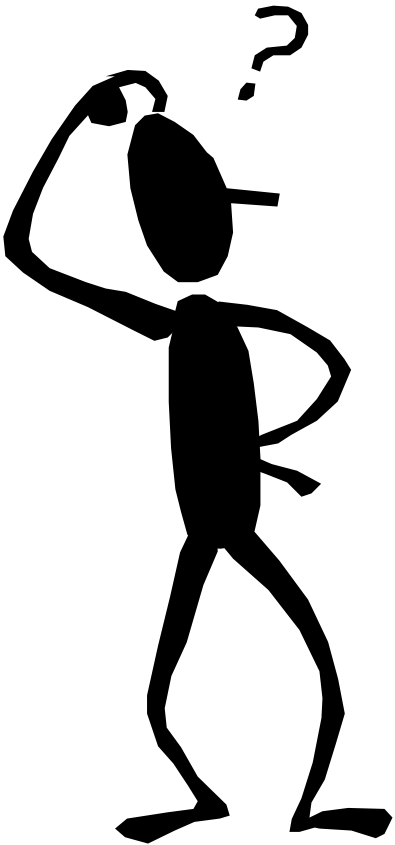
Australia	6
Austria	5
Belgium	6
Canada	14
Czech Rep.	2
Denmark	2
Finland	1
Germany	84
Hungary	2
Ireland	1
Netherlands	4
New Zeald.	3
Norway	3
Sweden	6
Switzerland	8
UK	24
USA	152



Limiting the trial to a few large countries

would reduce national regulatory and ethical submissions, but

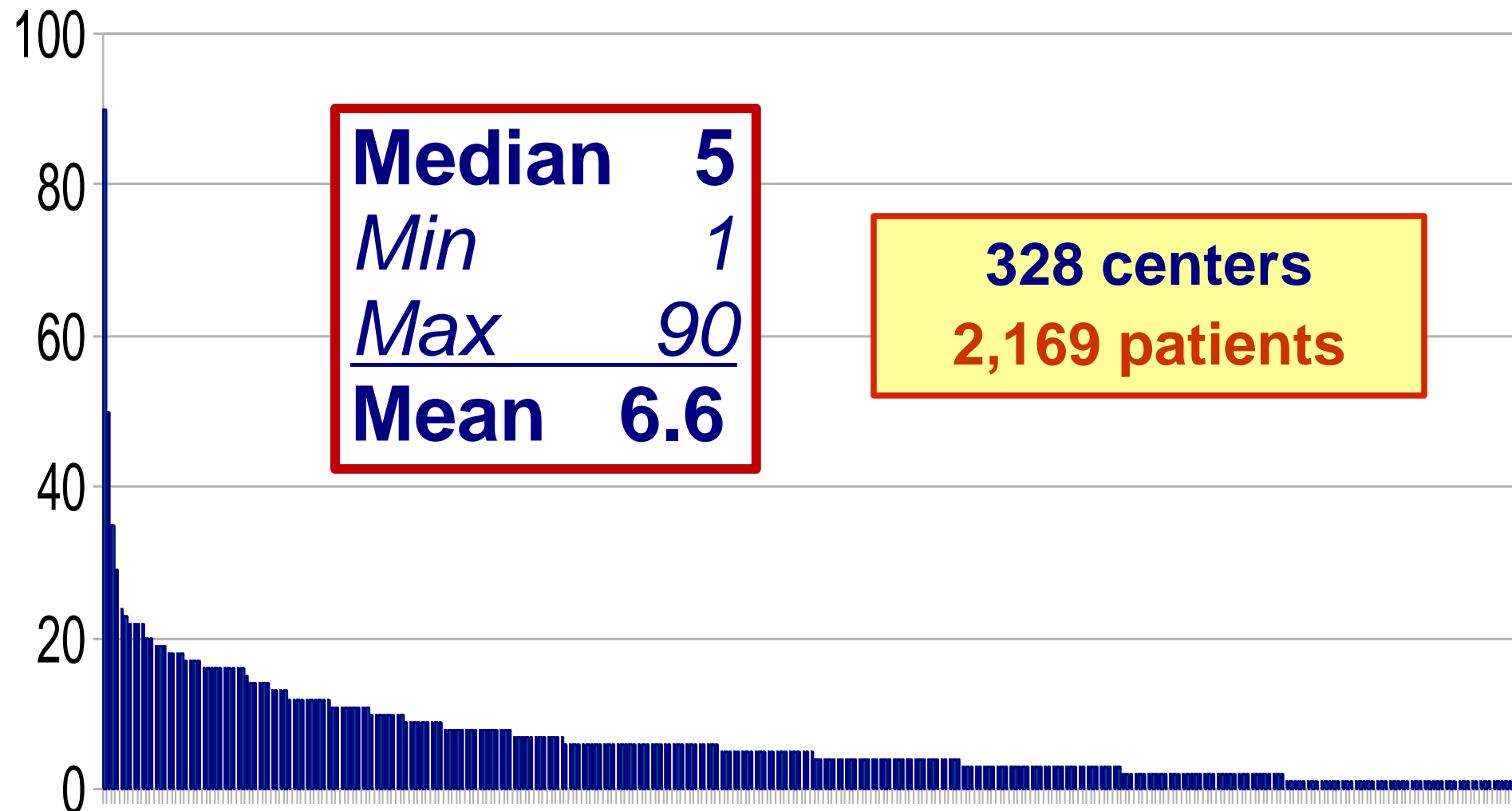
would not reduce the
number of centers
considerably



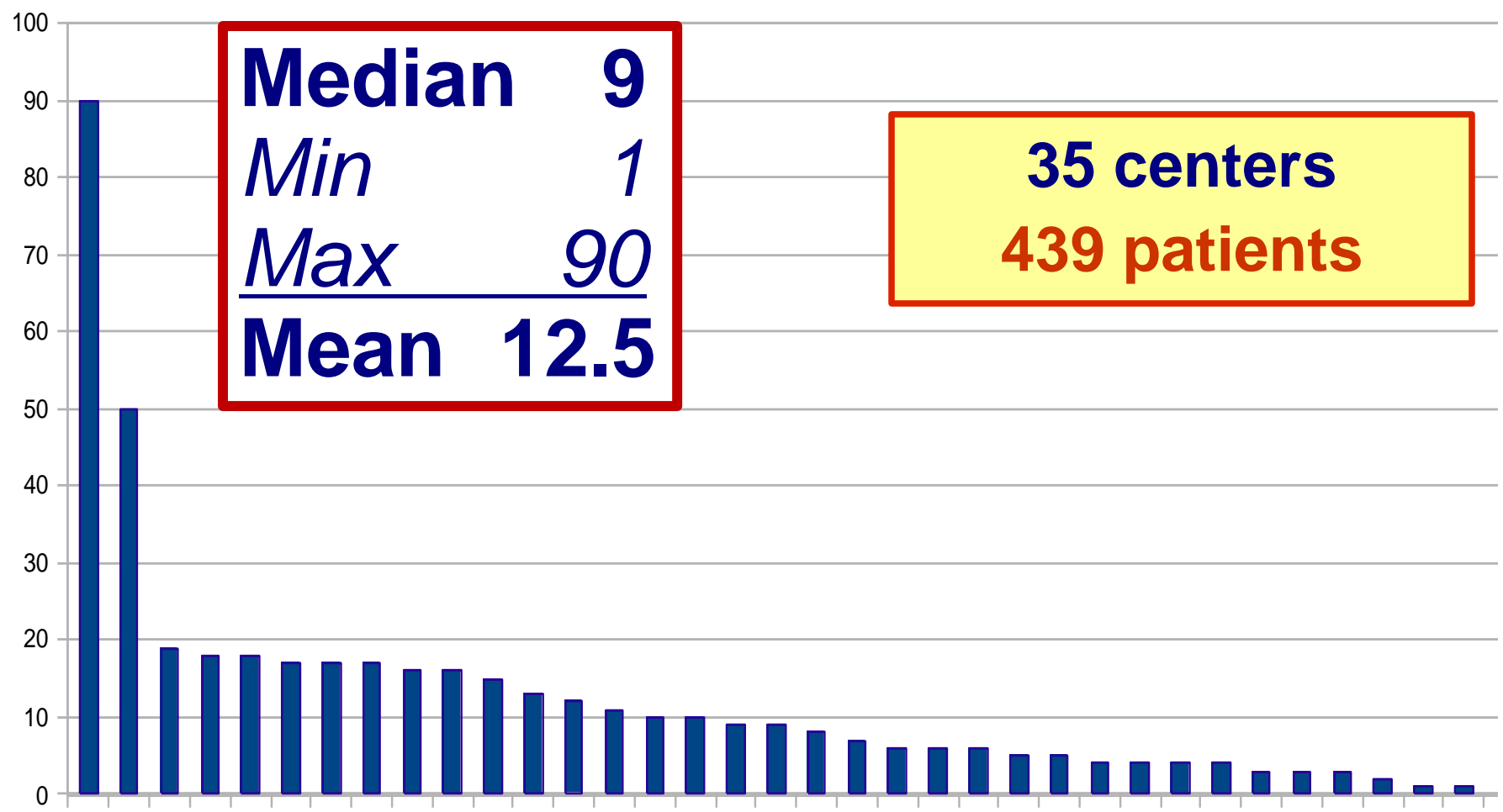
Would it be feasible
to perform such
trials in selected
large centers only?

EURAMOS

Patients per center



EOI Patients per center

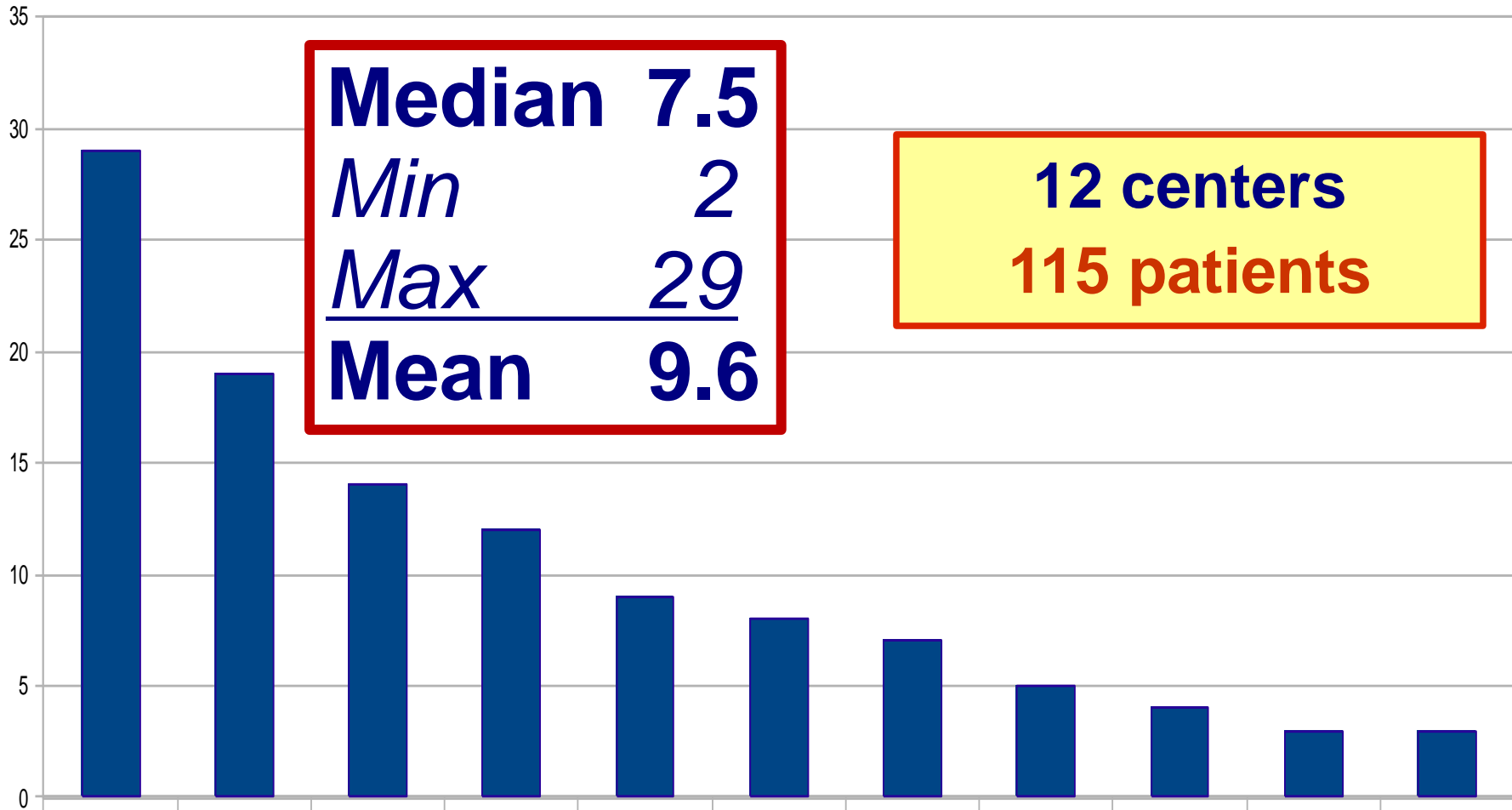


Median 9
Min 1
Max 90
Mean 12.5

35 centers
439 patients



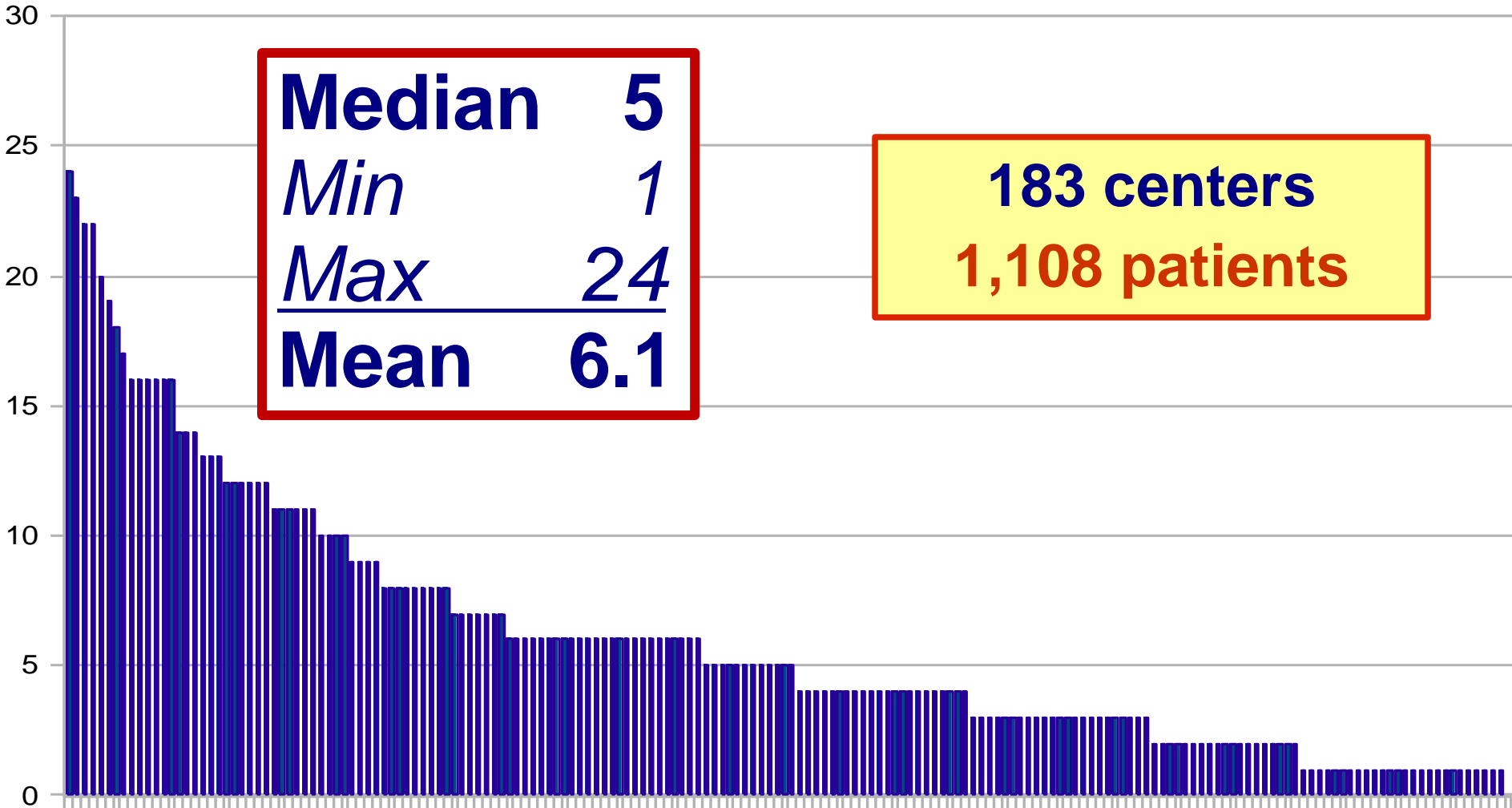
SSG Patients per center



COG Patients per center

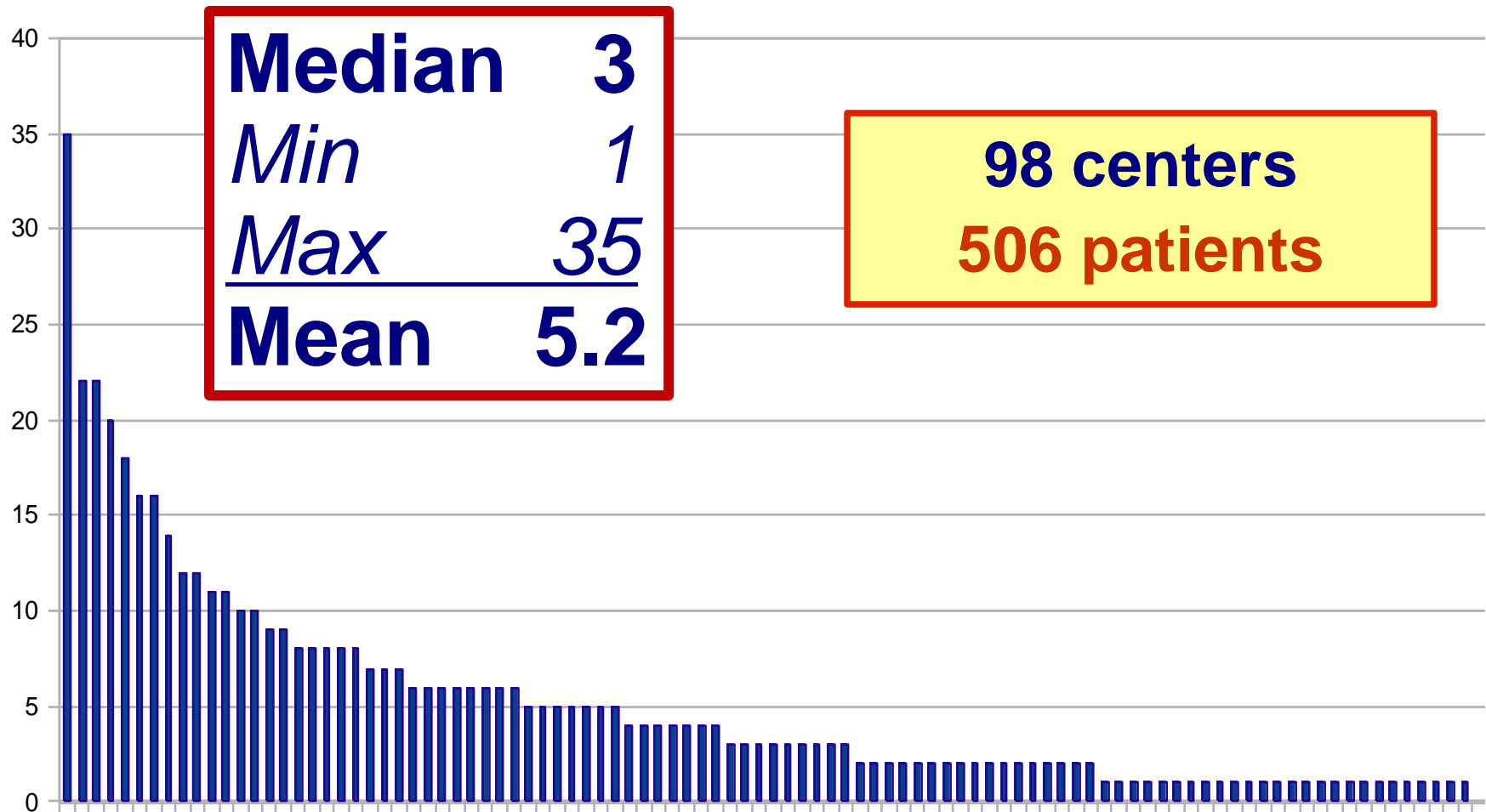
Median	5
<i>Min</i>	<i>1</i>
<u><i>Max</i></u>	<u><i>24</i></u>
Mean	6.1

183 centers
1,108 patients



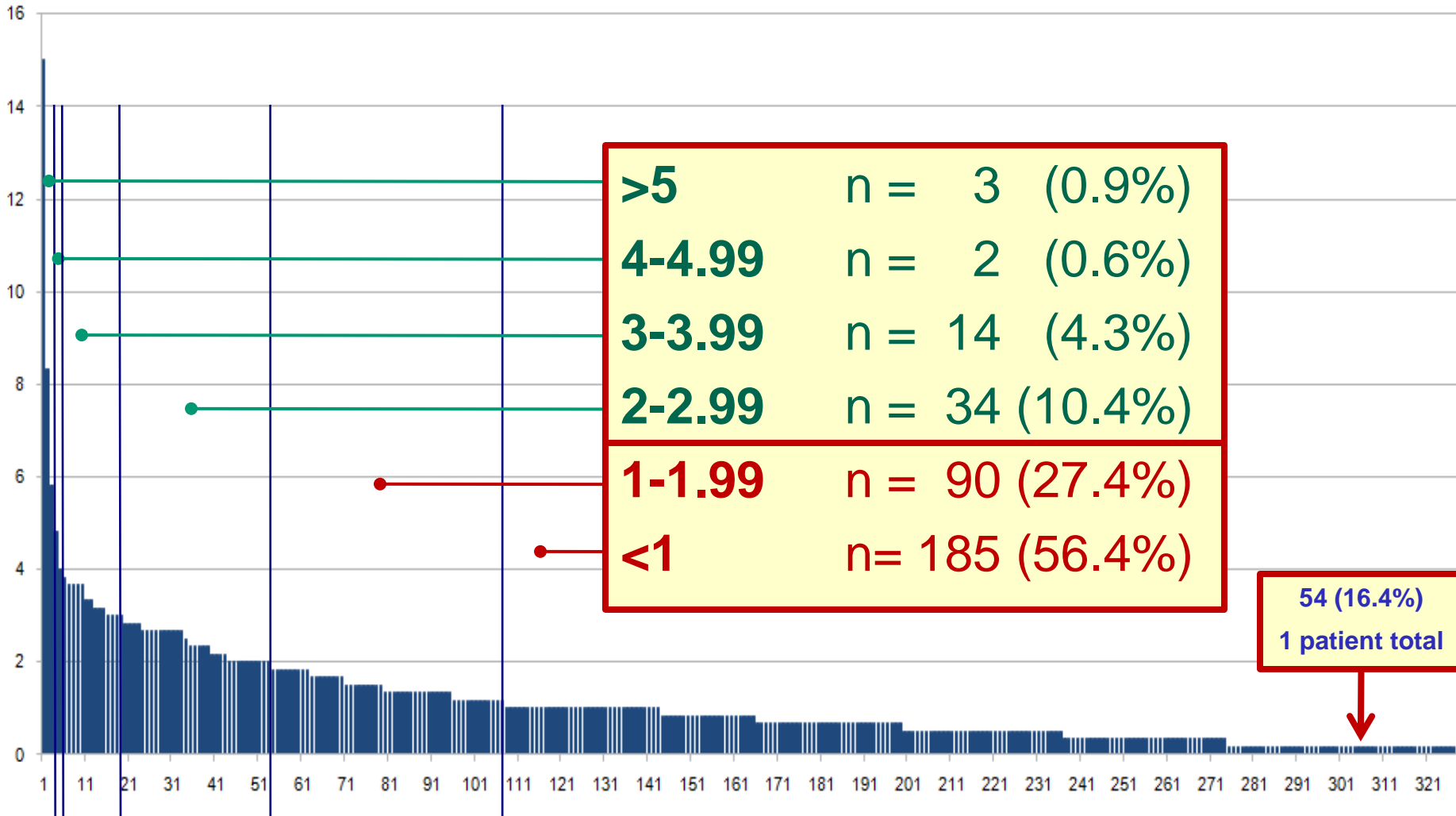
COSS

Patients per center



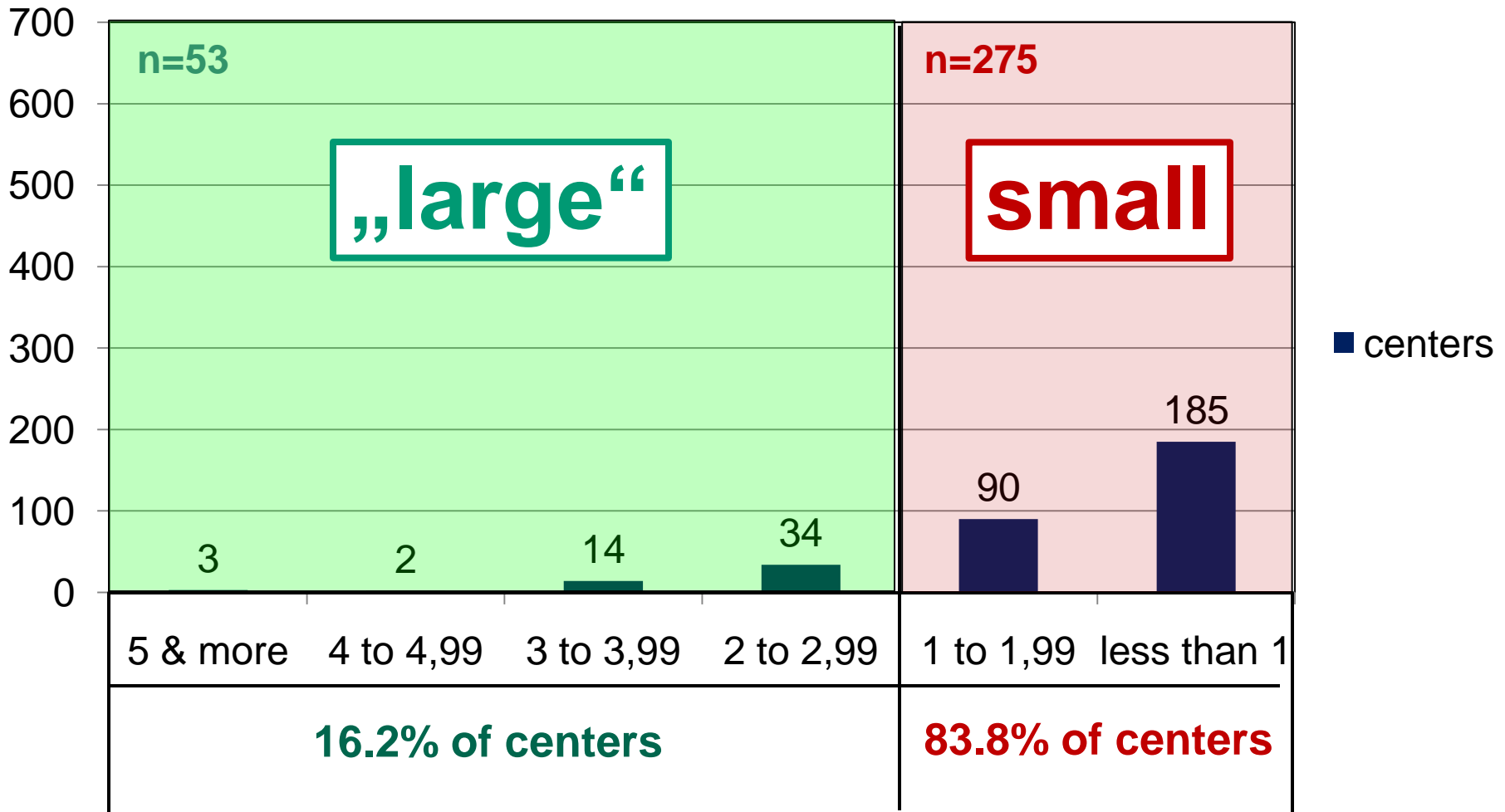
EURAMOS

Patients per center per year

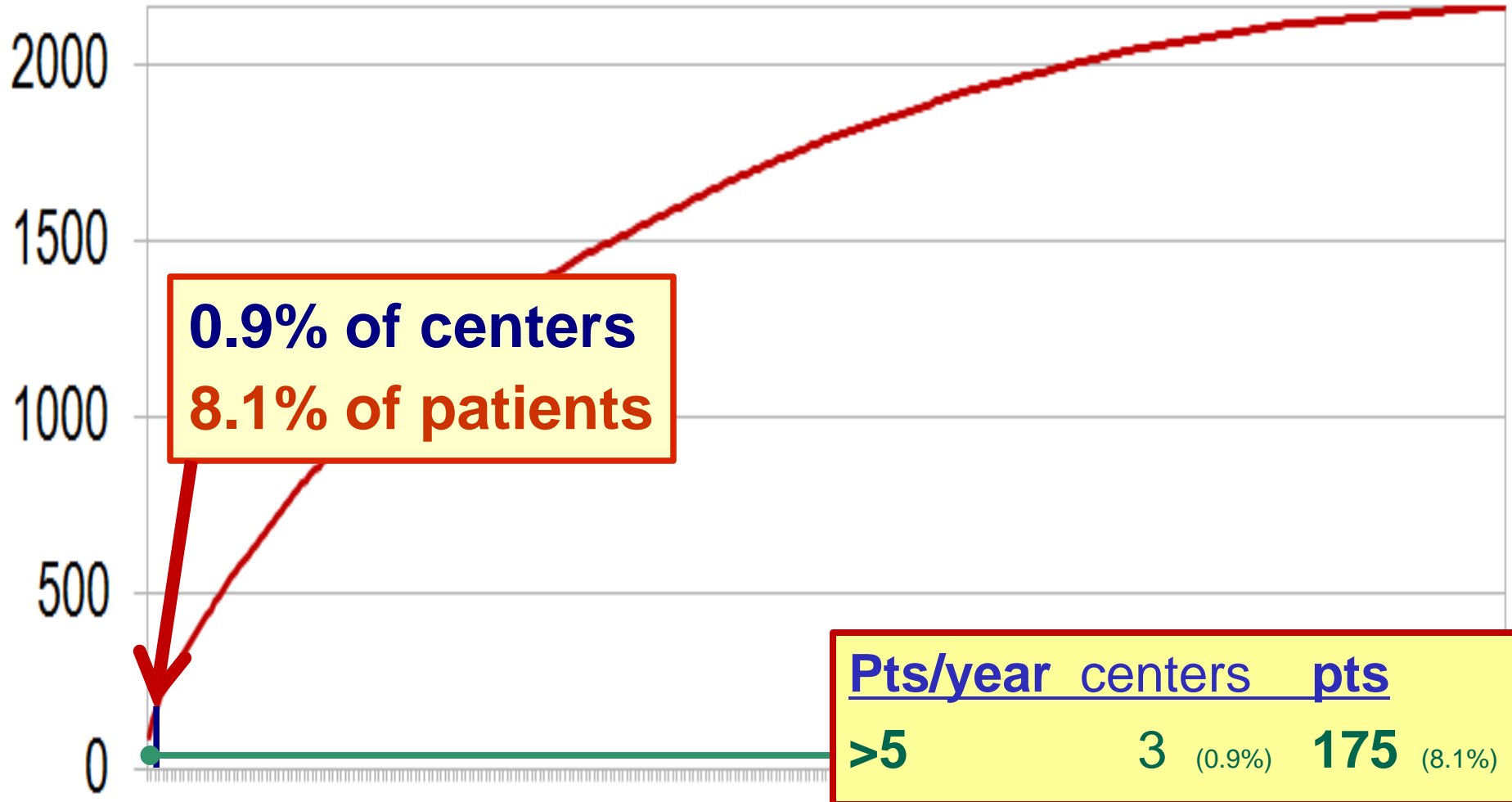


Patients per center per year

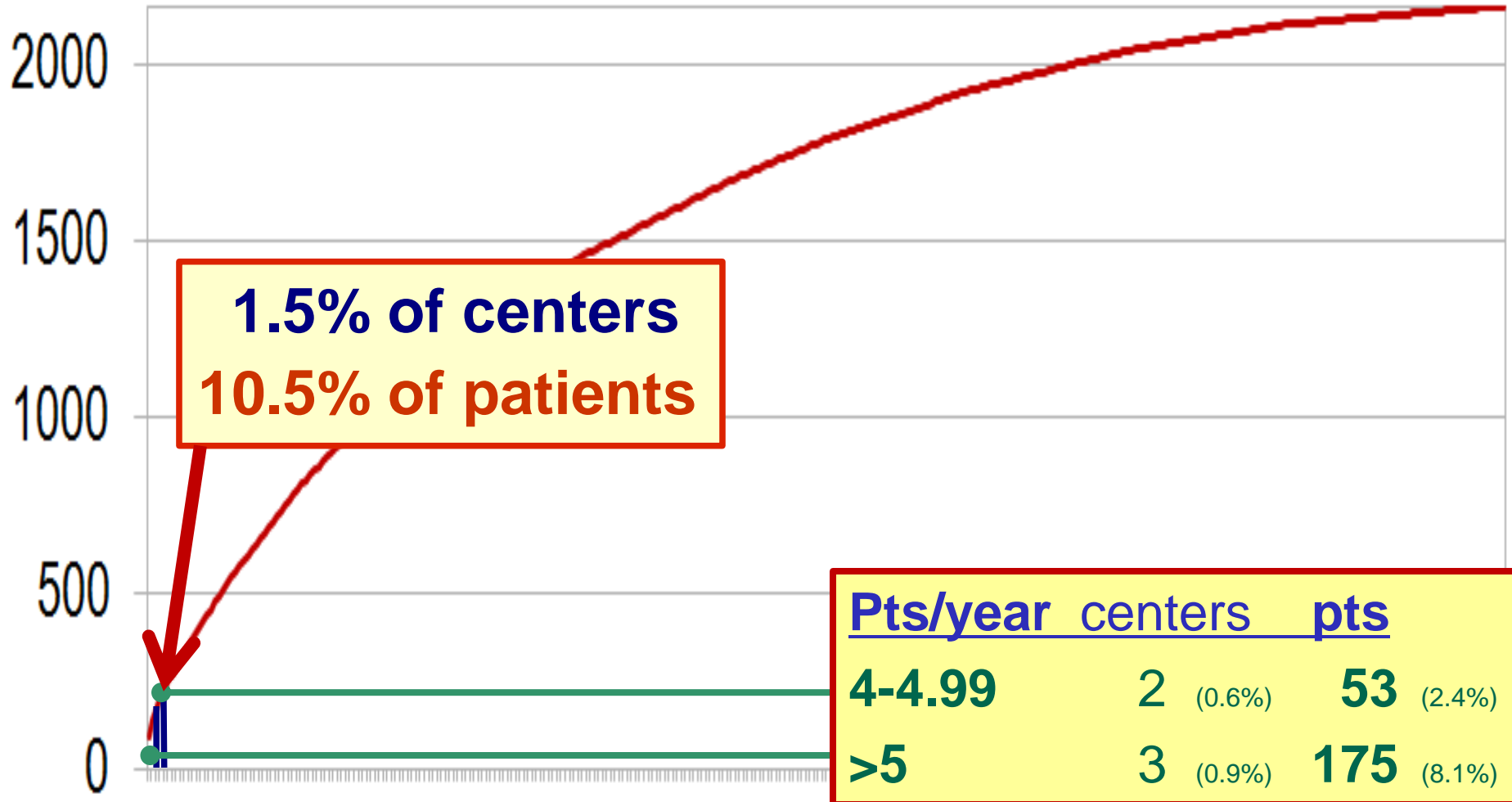
(based on total 6 year EURAMOS recruitment period)



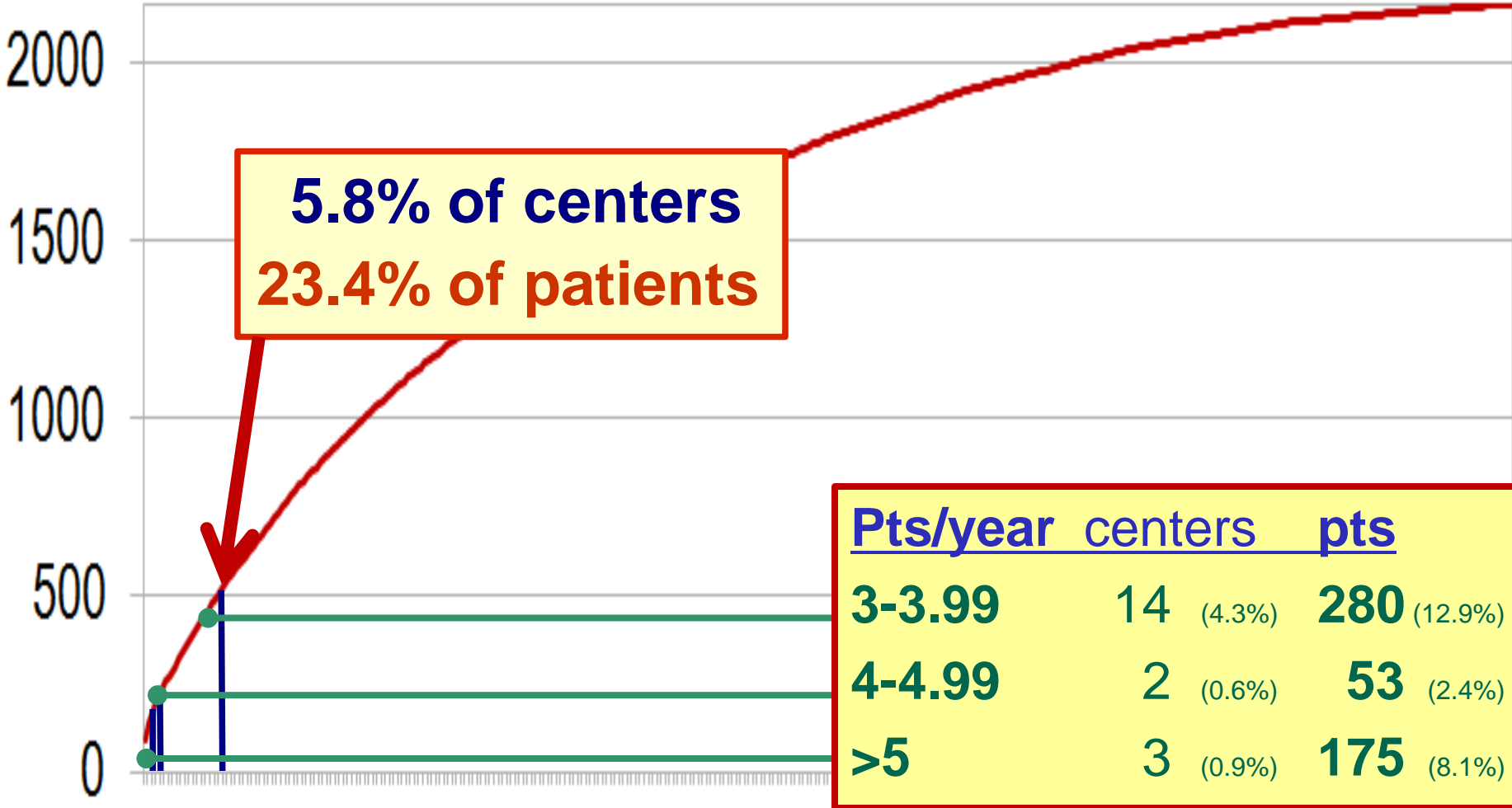
EURAMOS Patients per center



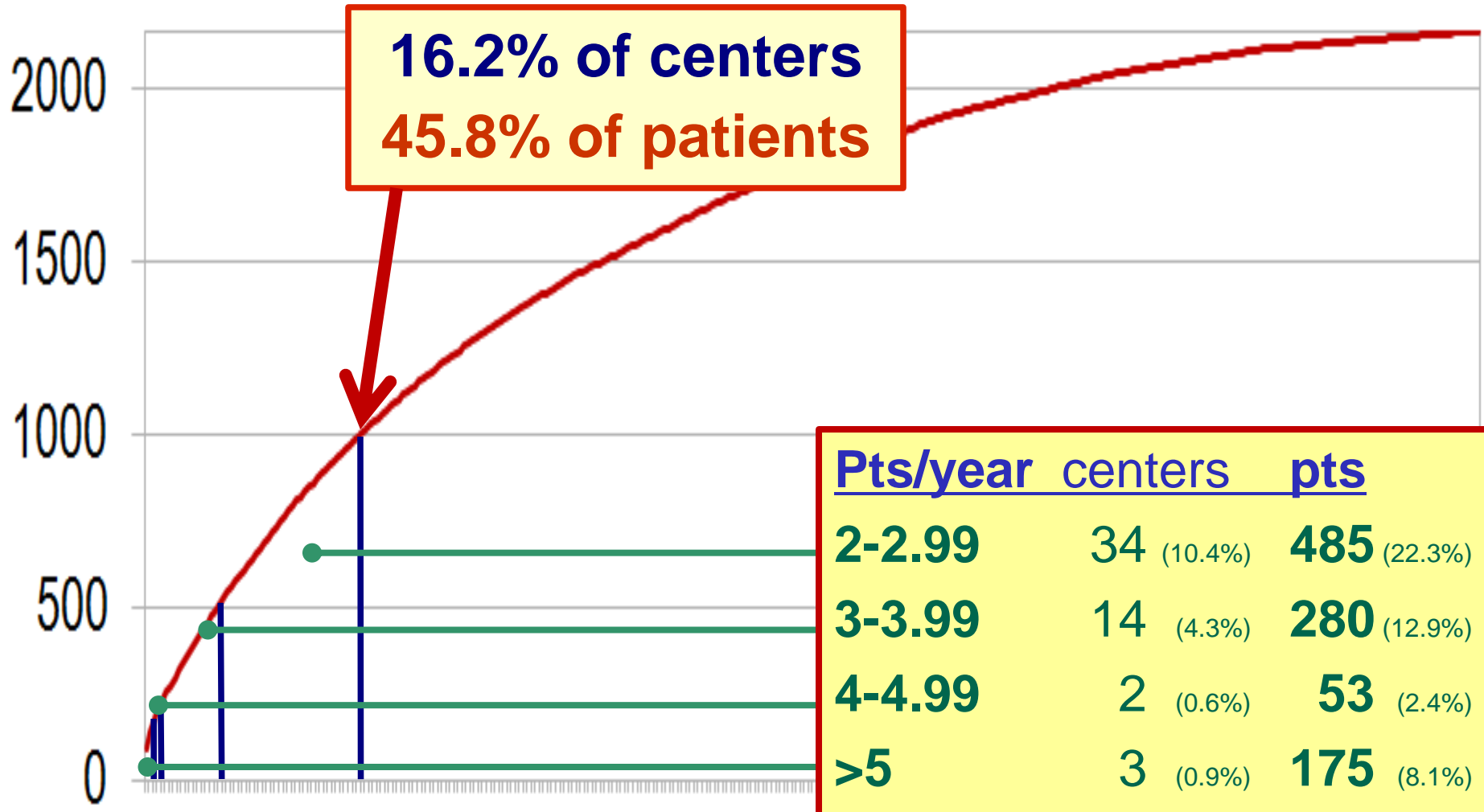
EURAMOS Patients per center



EURAMOS Patients per center



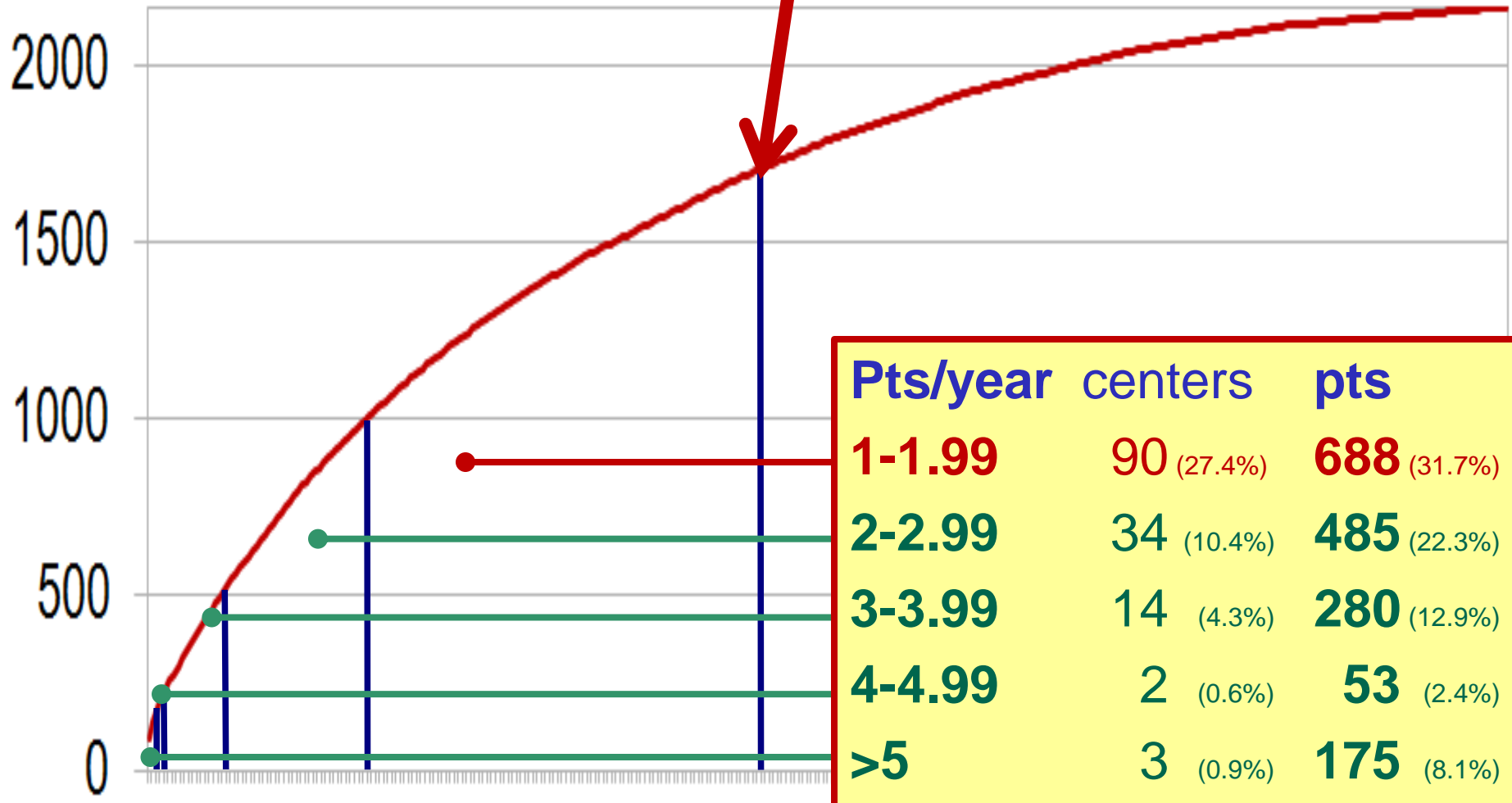
EURAMOS Patients per center



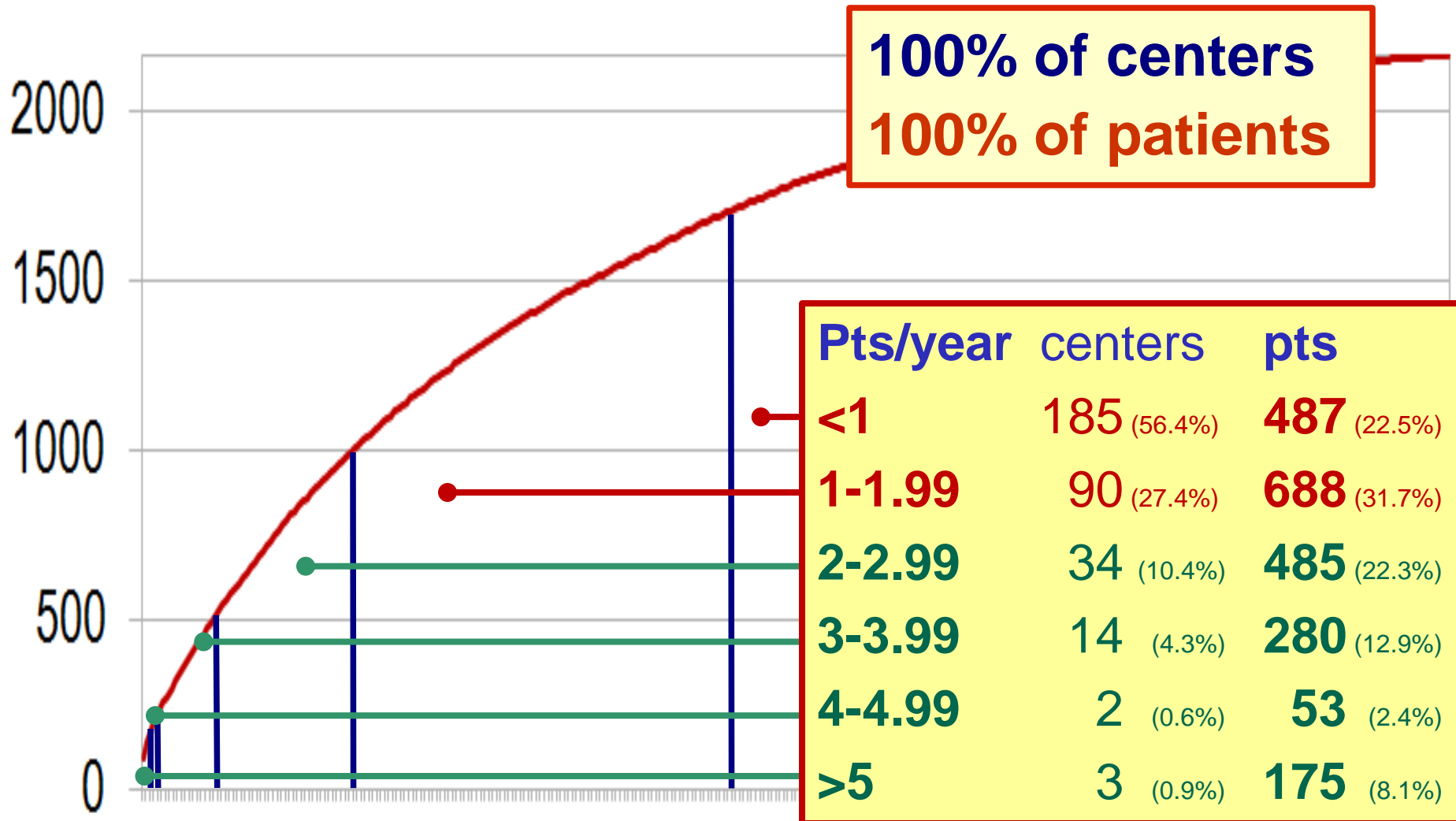
EURAMOS

43.6% of centers
77.5% of patients

center

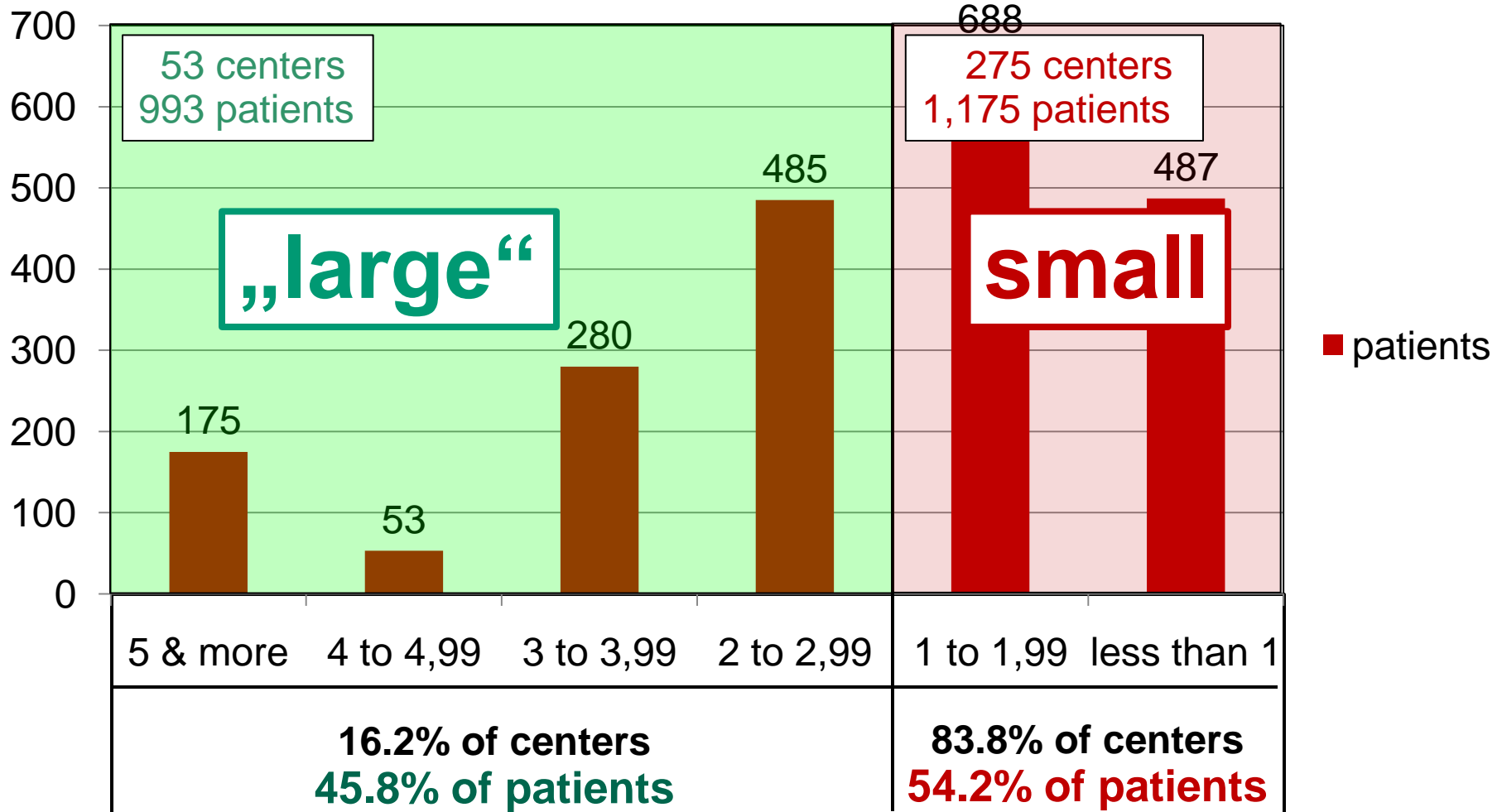


EURAMOS Patients per center

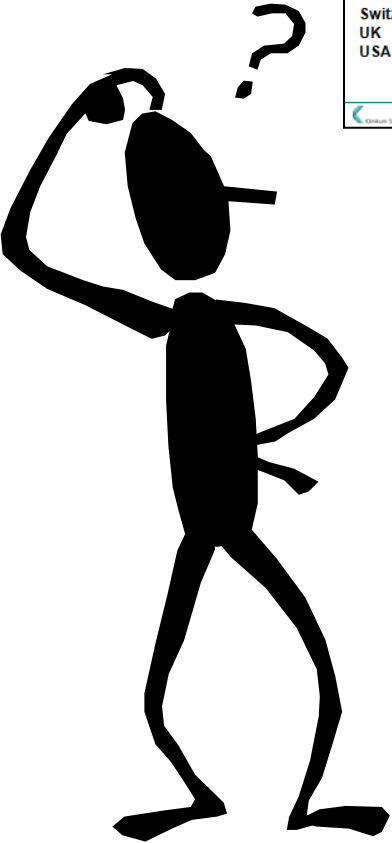
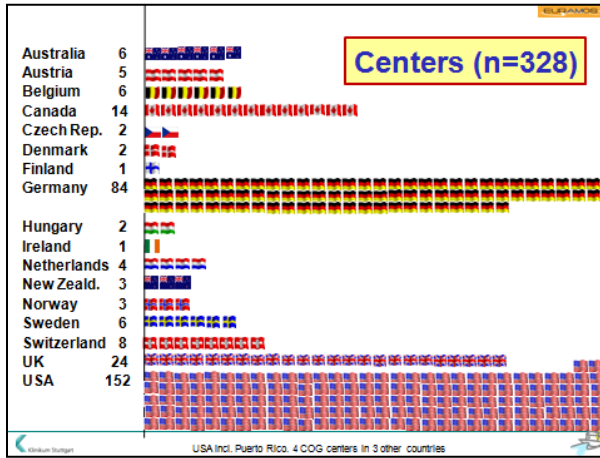


Patients per center per year

(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 ≥ 2 patients/year

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



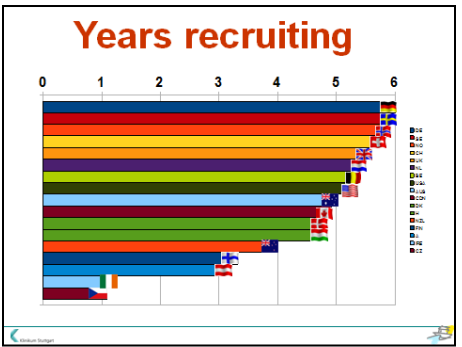
10/17 countries



Centers ≥ 2 patients/year

Based on national trial opening (n=64)

Australia	0	
Austria	1	
Belgium	2	
Canada	2	
Czech Rep.	1	
Denmark	1	
Finland	0	
Germany	9	
Hungary	1	
Ireland	1	
Netherlands	4	
New Zeald.	1	
Norway	1	
Sweden	2	
Switzerland	0	
UK	8	
USA	30	

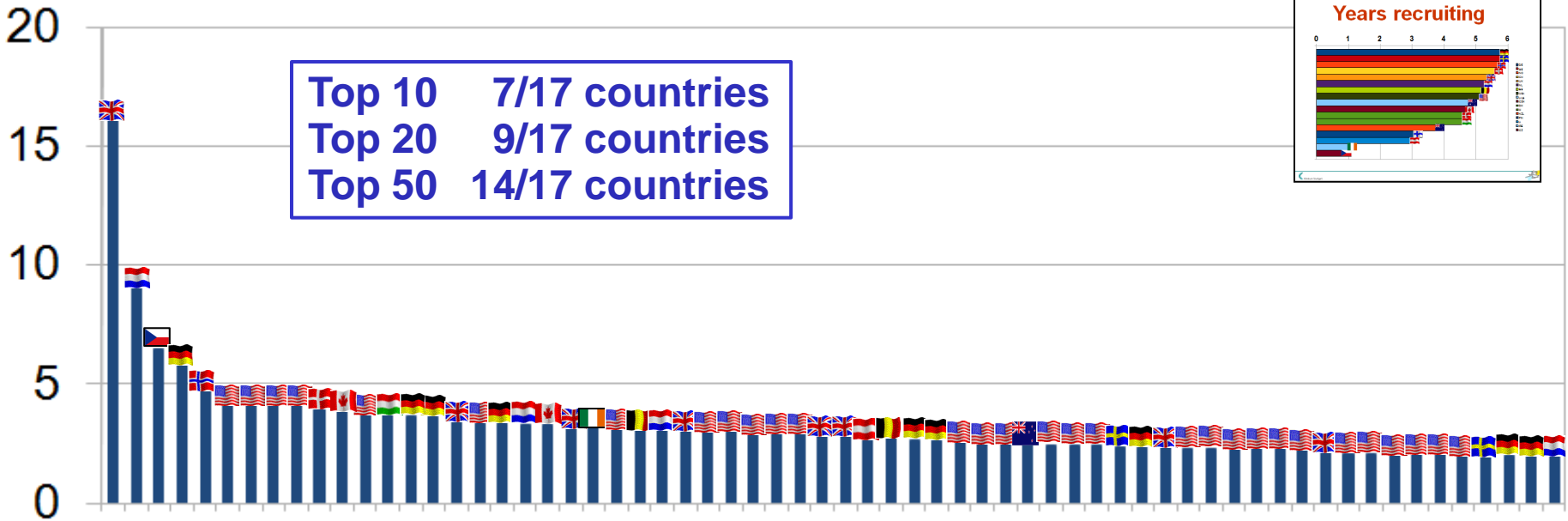


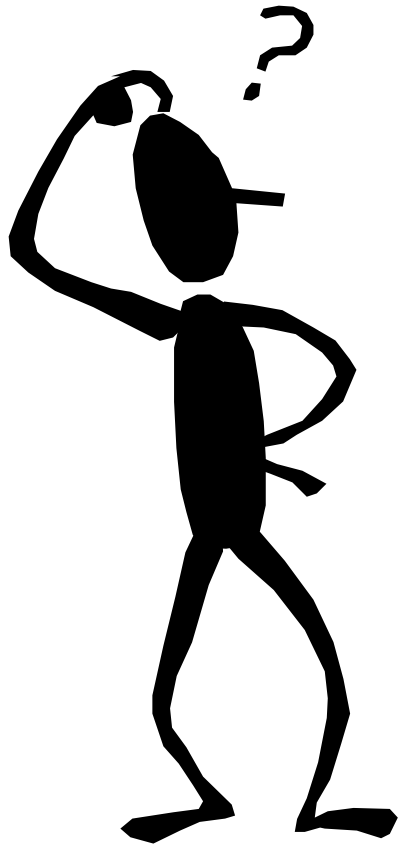
14/17 countries



Centers ≥ 2 patients/year

Based on national trial opening (n=64)





Is there
no way
to concentrate
patients?

Australia



Austria



Belgium



Canada



Czech Rep.



Denmark



Finland



Germany



Hungary



Ireland



Netherlands



New Zealand



Norway



Sweden



Switzerland



UK



USA



Resident Royals



Resident Royalty

No

11 countries, 287 centers

Median **4** pts/center

Min **1**

Max **50**

Mean **5.98**

+/- 5.88



Yes

6 countries, 41 centers

Median **8** pts/center

Min **1**

Max **90**

Mean **11.00**

+/- 14.10



Resident Royalty

No
11 countries, 287 centers

Yes
6 countries, 41 centers

$p < 0.00001$
(t-test)

Med	
Min	
Max	50
Mean	5.98
	+/- 5.88

Med	
Min	
Max	90
Mean	11.00
	+/- 14.10



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.

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!

