The Psonet Collaboration

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CENTROSTUDI Gised

FROM

Ospedali Riuniti di Bergamo

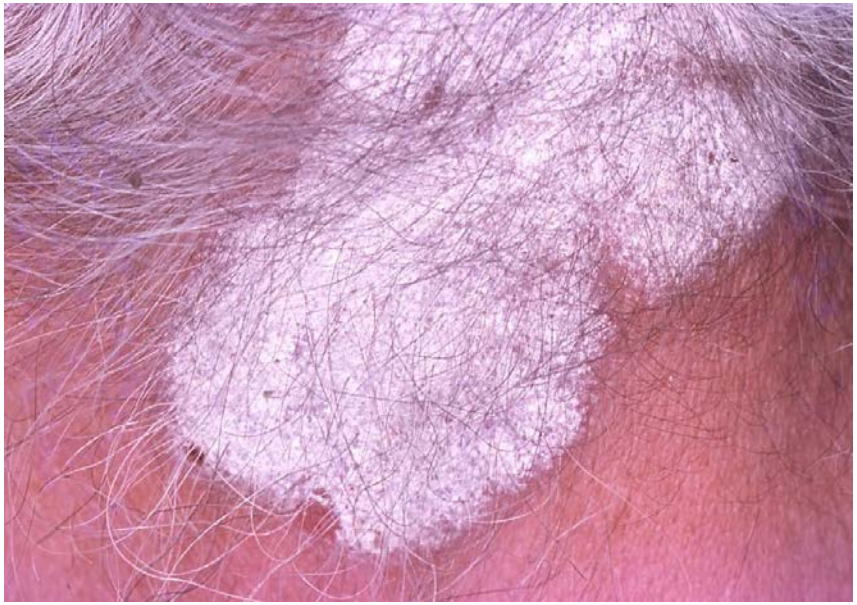
Conflict of interests disclosure

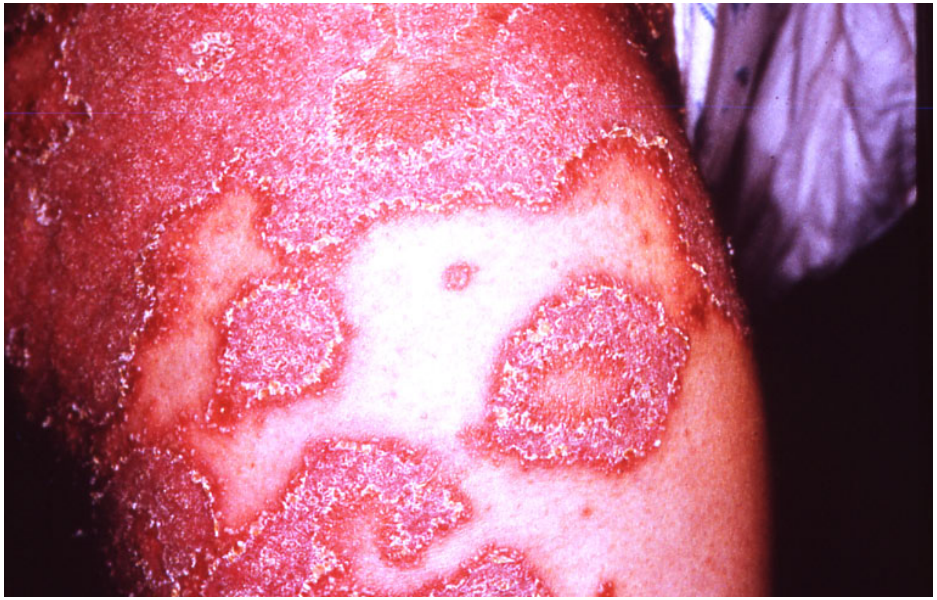
Contracting member of the EMA PSOLAR Registry Steering Committee (Janssen-CILAG)

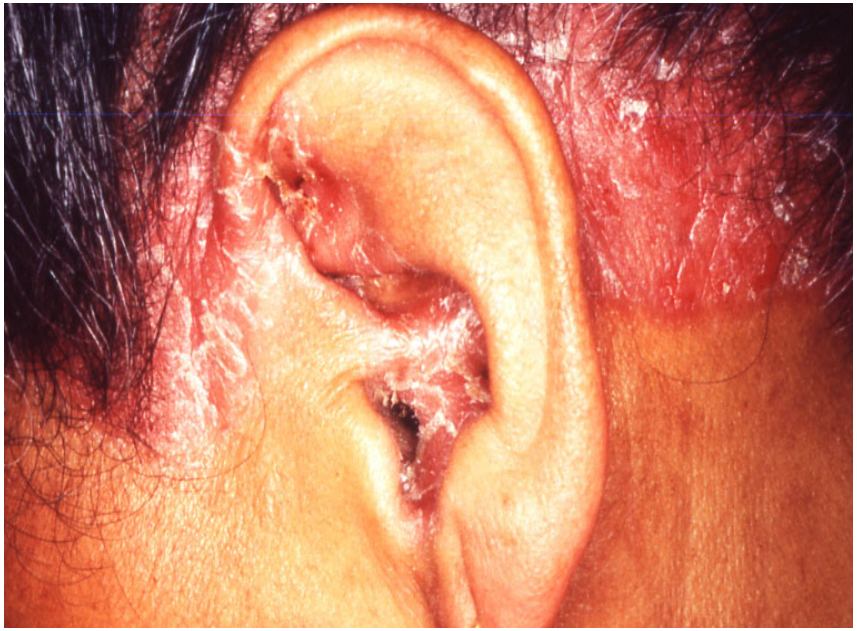
Member of the Psocare steering group (AIFA)

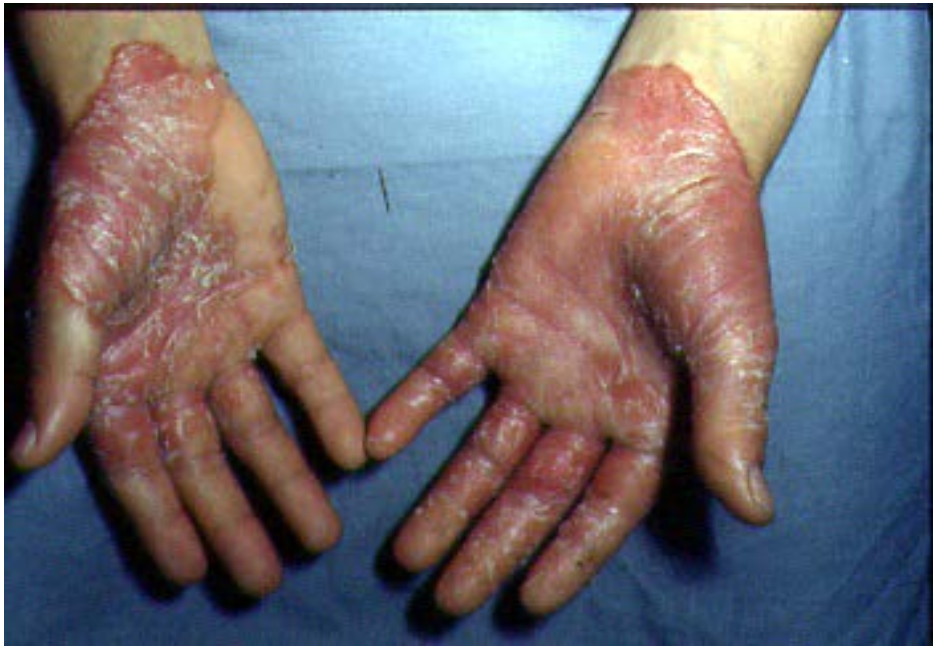
Consultation fees from IBSA, Helsinn, Pfitzer, Bayer Healthcare, Novartis, Menarini, Celgene

- **The problem**
- **Psonet**
- **Funding issues**
- **Organizational challanges**
- **Analytical challanges**



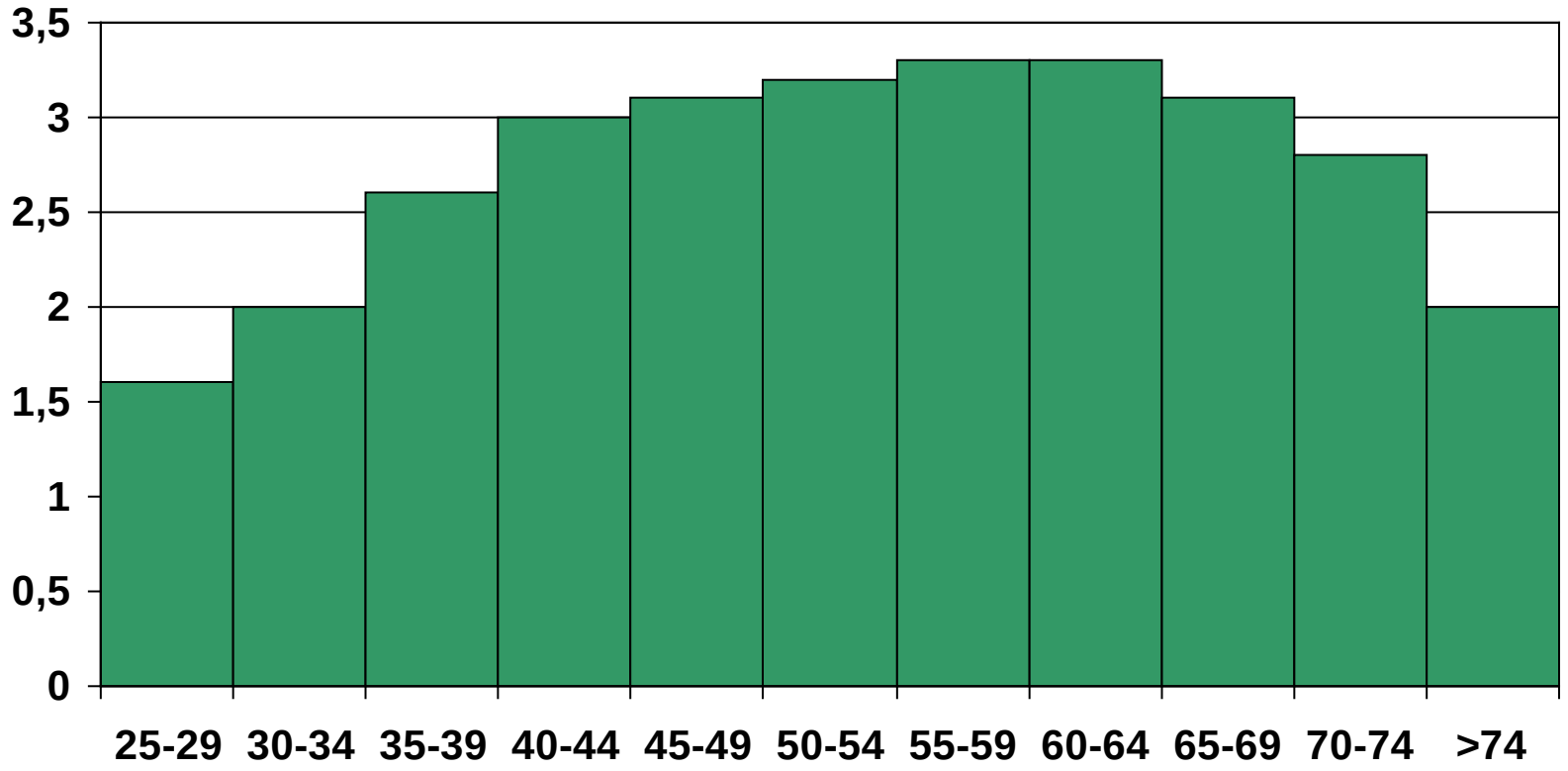


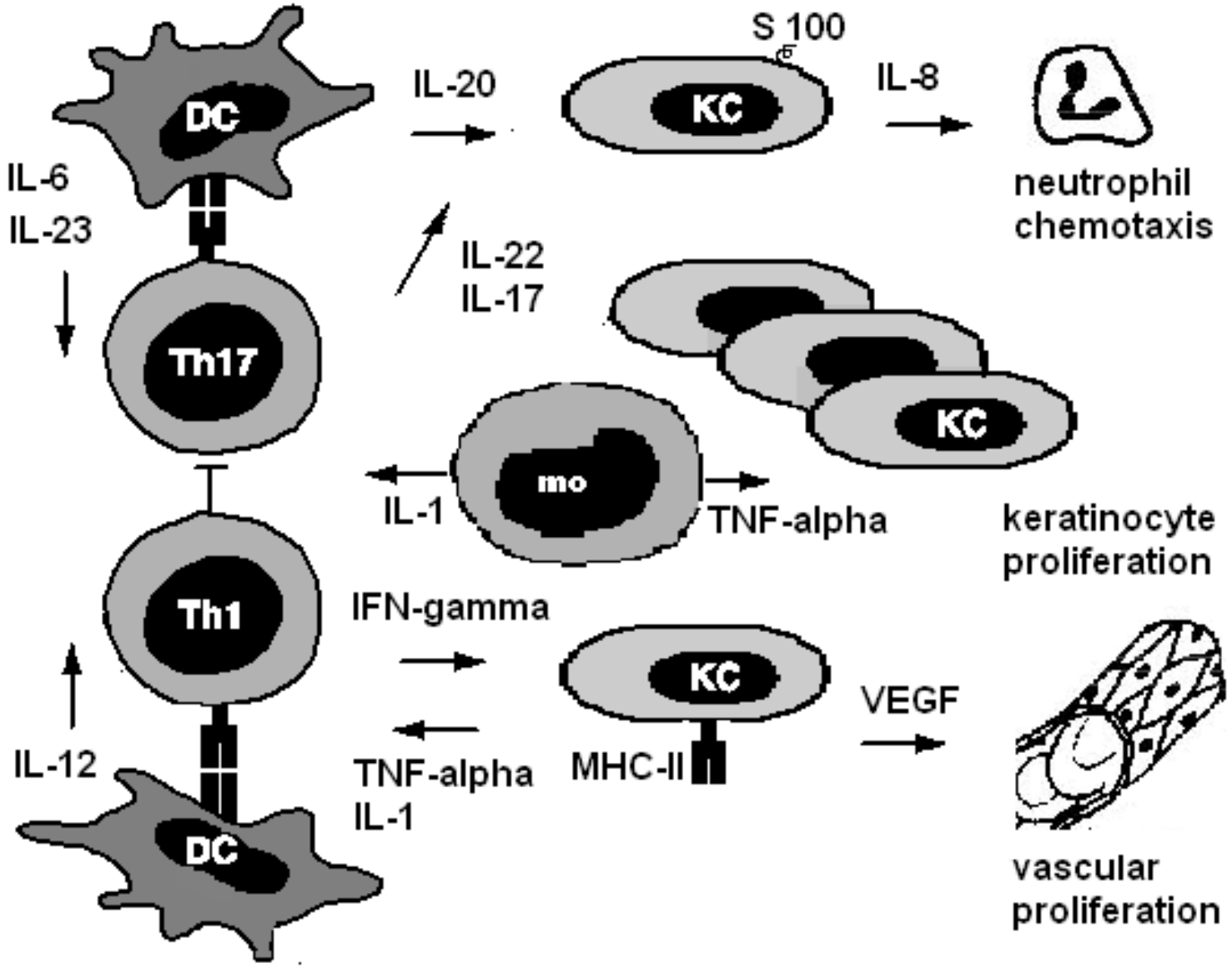




Lifetime prevalence of psoriasis according to age- PraKtis study 2004

praktis
la tua pelle in primo piano.

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keratinocyte
proliferation
Th1
IFN-gamma
KC
VEGF
IL-12
TNF-alpha
IL-1
MHC-II
DC
vascular
proliferation

Biological agents registered indications for psoriasis

Adults with moderate to severe plaque psoriasis, who are candidates for systemic therapy or phototherapy

Adults with moderate to severe plaque psoriasis for whom phototherapy or conventional systemic treatments have been inadequate or inappropriate

Safety issue	Anti TNF	Anti IL12/23
Severe infections and opportunistic infections	X	X
Malignancies	X	X
Reversible posterior leukoencephalopathy		X
Deterioration of congestive cardiac failure	X	X
Demyelinating disease	X	
Formation of autoantibodies	X	
Formation of antibodies against the drug	X	X

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European Network of Psoriasis Registries

To establish a network of independent European population registries, in order to perform coordinated post-marketing surveillance studies aimed at monitoring the effectiveness and safety of systemic agents, including biologicals and any new medications in the treatment of psoriasis

Country	Registry Name	Logo
Australia	Australasian Psoriasis Registry	
Denmark	DermBio	
France	PsoBioTeq	
Germany	PsoBest	
Israel	Clalit Health Service	
Italy	Psocare, Psodit	
Spain	Biobadaderm	
Sweden	PsoReg	
Switzerland	Swiss Dermatology Network for Biologicals SDNB	
The Netherlands	AMC psoriasis registry	
United Kingdom	BADBIR	
Portugal	Not yet defined	
Romania	Not yet defined	
Tunisia	Not yet defined	
Lithuania	Not yet defined	

PSONET

EUROPEAN REGISTRY OF PSORIASIS

- How is Psonet supported?
- Which countries are involved?
- International Safety Review Board
- Drugs in development
- Links
- Events
- Glossary
- Contacts
- Forums
- Reserved area

Which countries are involved?

The initial proposal has been shared with people who are running registers of systemic treatment for psoriasis in different countries in Europe. A preliminary agreement to combine data was obtained from the following countries:

Click on the map to get more information on nation based registers

EDEN Papers

Dermatology

Dermatology
DOI: 10.1159/000183757

Received: May 12, 2008
Accepted: September 24, 2008
Published online: December 11, 2008

National Registries of Systemic Treatment for Psoriasis and the European 'Psonet' Initiative[1]

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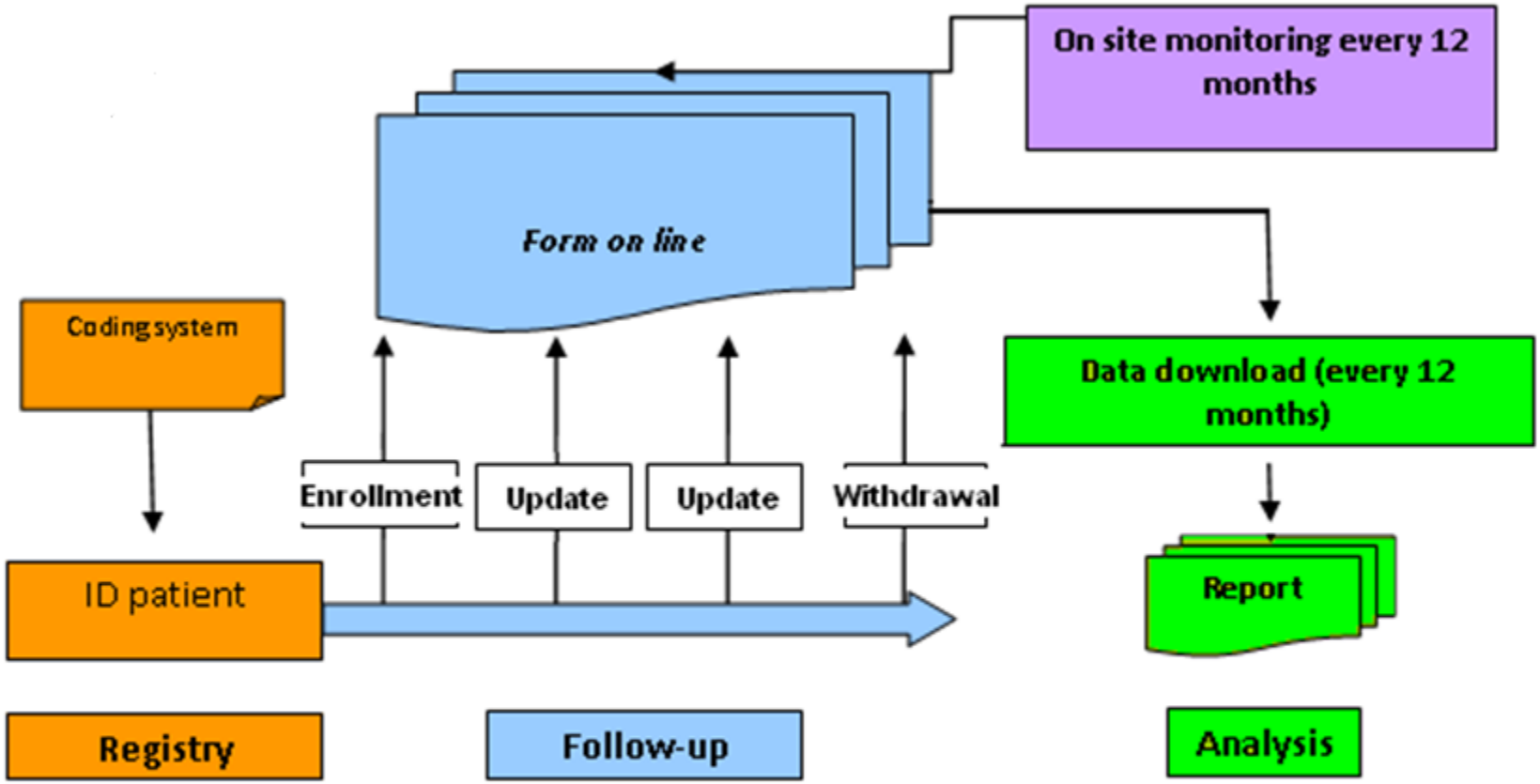
On site monitoring every 12 months
Form on line
Coding system
Data download (every 12 months)
Enrollment
Update
Update
Withdrawal
ID patient
Report
Registry
Follow-up
Analysis

Entry criteria

The **study population** will consist of all the subjects with active psoriasis who receive at participating centres a new systemic agent for psoriasis

Minimum set of variables (basal time)

1. Patients' **socio-demographic characteristics** (age, gender), skin type*
2. **Personal habits:** smoking (yes/no/previous/unkwn), alcohol consumption (average n. drinks per week)*
3. **Anthropometric variables** (weight and height), waist circumference*
4. **Psoriasis characterization** date of first diagnosis, type of psoriasis, severity*, previous systemic treatments (yes/no/unkwn)
5. **Co-morbidities** ischemic heart disease, hypertension, dyslipidemia, diabetes, cerebrovascular disease, tuberculosis, HIV, chronic viral hepatitis, other infections requiring hospitalisation, cancer [type of cancer], kidney, liver disease
6. **Systemic treatment for psoriasis at entry** (drug and dosage)
7. **Gynecological information:** Pregnancy and its outcome*
8. **Systemic co-medication:** yes/no/unkwn for specific drug categories (immunosuppressive,lithium salt, calcium antagonists, ACE inhibitors, NSAIDs)

(*) Non mandatory information

Minimum set of variables (follow up)

1. **Updates on systemic treatments** for psoriasis during follow-up
2. **New diagnosis of conditions categorised as**: infections leading to hospitalization, cancer, any other new condition leading to hospitalisation or specialist consultation* (kind of condition categorised according to ICD-10 or other dictionaries)
3. **New systemic co-medications** taken for more than one month
4. **Any relevant suspected adverse event associated with treatment** (date of diagnosis, kind of event)
5. **Remissions and severe relapse** of disease during follow-up

Control groups

1. **Internal** vs **external** comparisons
2. Internal comparisons will involve analyses of event occurrence in groups defined by different dosages/duration of treatment and/or different drugs.
3. External comparisons can be made by considering incidence rates in selected population samples. For rare events such as cancer incidence, only marked increases of incidence (i.e., twice or more) with respect to the general population could be detected by our system.

Pooling of data from national registries

1. Individual patient data vs summary data
2. Definition of intervals for data extraction in a standardized form
3. Consistency checks of data and regular updates

International Safety Review Board

Diagnoses will be reviewed by an International Safety Review Board. According to the clinical diagnosis, additional information may be required with retrieval of information from medical records, family doctors or directly from the patient.

Registries for Evaluating Patient Outcomes: A User's Guide

Second Edition

Case Example 20: Linking registries at the international level

Description:	Psonet is an investigator-initiated, international scientific network of coordinated population-based registries; its aim is to monitor the long-term effectiveness and safety of systemic agents in the treatment of psoriasis.
Sponsor:	Supported by a grant from the Italian Drug Agency (AIFA) and coordinated by the Centro Studi GISED.
Year Started:	2005
Year Ended:	Ongoing
No. of Sites	9 different registries across Europe
No. of Patients:	20,000

Challenge

The number of options for systemic treatment of psoriasis has greatly increased in recent years. Because psoriasis is a chronic disease involving life-long treatment, data on long-term effectiveness and safety are needed for both old and new treatments. Several European countries have established patient registries

- The problem
- Psonet
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- Organizational challanges
- Analytical challanges

STUDY PROTOCOL TO BE SUBMITTED TO THE STUDY SESSION

Institute:

CENTRO STUDI GISED

1. Proposal Title

Establishment of a European surveillance network to assess the long term effectiveness and safety of biological agents, i.e., Tumor Necrosis Factor alpha (TNF-alpha) antagonists and T cell targeted molecules, in the treatment of psoriasis with particular attention to the risk of rare events

2006-2008

EADV

European Academy of Dermatology and Venereology

PSONET

EUROPEAN REGISTRY OF PSORIASIS

Support from EADV to Psonet for the year 2010-2011

Contact person from EADV: professor Louis Dubertret

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Hurdles and challenges identified for collaboration between multiple registries (1)

Hurdles	Challenges	Benefits/solutions
Governance / operational	Data ownership	Establishing a code of conduct
	Authorship	Adopt uniform guidelines for scientific publications
	Difficulties of international collaboration: expensive, need for translation of many documents to achieve transparency in methods, sources for support	Work in progress
	Ascertainment of the complexity of differences in registries is a huge effort	Meta-analysis of data preferred as it can define heterogeneity

From Ormerod et al, 2012, Dermatology accepted

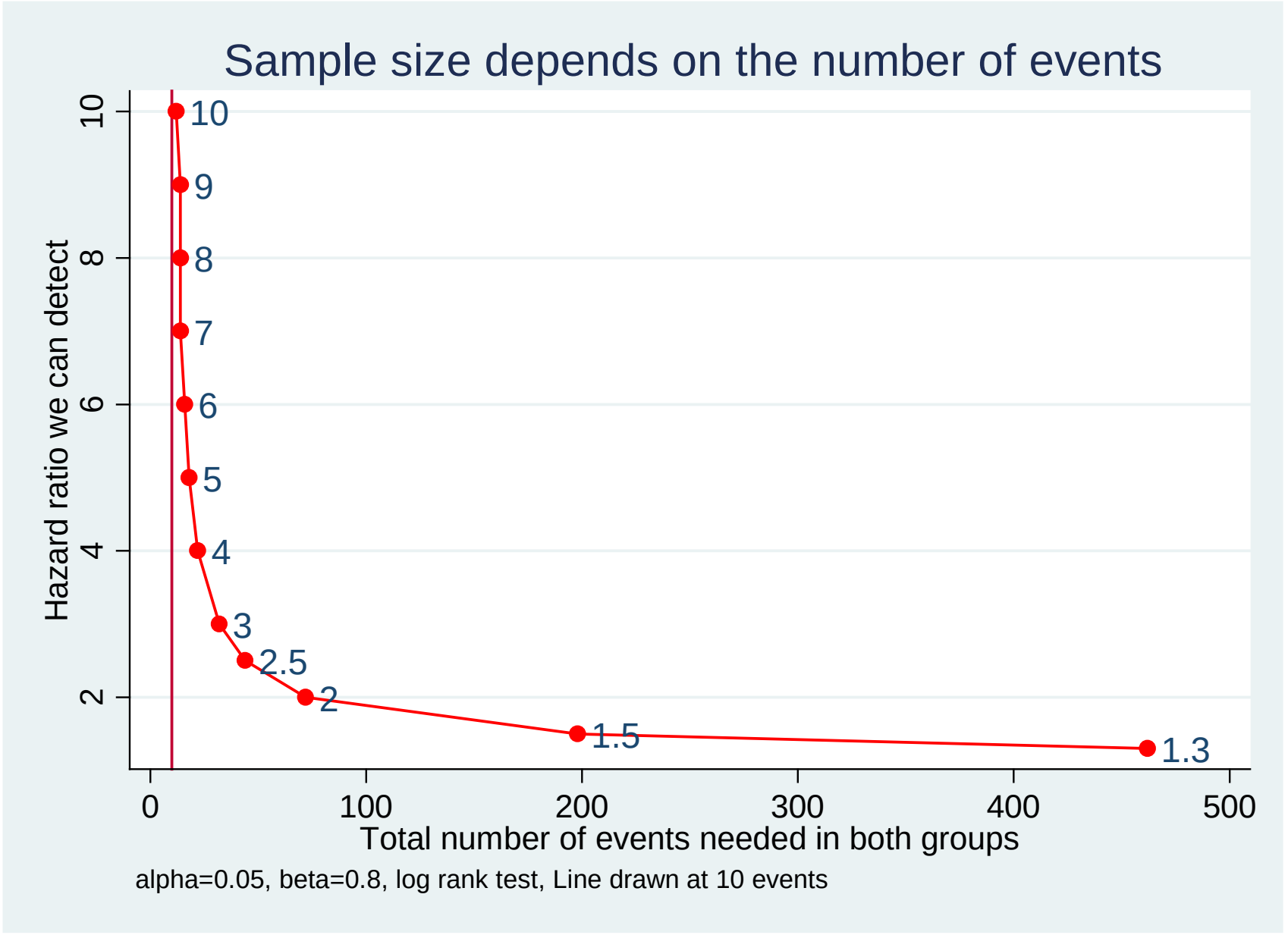
“CORe” requirements

- **Code of Conduct: Compliance with the rules of the Psonet Code of Conduct**
- **Operational Research Standards (ORS): Application of ORS (Checklist)**
- **Registry activity**

Hurdles and challenges identified for collaboration between multiple registries (2)

Hurdles	Challenges	Benefits/solutions
Structure / conduct	Database compatibility	Meta-analysis of data preferred as it can define heterogeneity
	Different size of registries	Meta-analysis of data preferred as smaller registries have similar weight
	Ascertainment / Coding of adverse events	Adopt MEDRA coding, define protocols for analysis
	Relevant treatment exposure window	Define protocols prior to analysis
	Different inclusion exclusion criteria	For control groups may be advantageous to have different types of control groups
	Different measures for risk factors / confounders	Define protocols prior to analysis Use of meta-analysis
	Different levels of quality control of data ascertainment	Use of hard outcomes and monitoring tools Consider replication /non-replication of findings across registries

From Ormerod et al, 2012, Dermatology accepted



from Ignacio Garcia Doval 2011

Typical registry by 2013

- 8.000py
- 8 cases of events with incidence rates around 1 cases/10^3 py
- 80 cases of events with incidence rates around 10 cases/10^3 py

from Ignacio Garcia Doval 2011

Easy rules for each registry

- **Under 10 cases: nothing to do in terms of describing relative risks**. Sharing should be compulsory on ethical grounds.
  - Registry means expenses, collaboration of patients and doctors,… Information that we obtain and might be useful to patients should be used.

- About **50 cases** are needed to be able to describe 2-3 times increased risk.

from Ignacio Garcia Doval 2011

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Some demographics of the Psonet registries
(Jan 2010)

	Australia	Denmark	Germany	Italy	Netherlnds	Israel	Spain	Sweden	UK
Starting year	2008	2007	2008	2005	2005	2007	2008	2007	2007
Patients on biologics	133	1200	540	8353	142	506	510	579	763
Age, mean	48.7	48.8	46.8	50.8	48.0	51.4	44	49.2	47
Baseline PASI, mean	29.0	13.6	15.3	17.8	16.1	NA	17	5.5	17.0
Percentage male	73	65.6	60.20	67	68	51	63	60	63

From Ormerod et al, 2012, Dermatology accepted

Different aspects of sampling the population covered by registries

Country	Number of centres participating in registry	Population of country millions	Estimate of the proportion of population sampled by registry	Estimated Percent of all psoriatic patients receiving biologics
Great Britain	62	66	50%	0.20%
Spain	13	46	<10%	U
Netherlands	1	16	0.5%	U
Israel	3500	7.7	100%	1.4%
Italy	164	70	about 80%	less than 1%
Denmark	5 Hospital, 10 private	6	>90%	0.20%
Sweden	50	9	80%	1.6%
Germany	530 hospital and private	81	10%	0.25%
Australia	10	22	0.5%	U
France	40	62	U	U

U=Unknown Y=Yes N=No

From Ormerod et al, 2012, Dermatology accepted

Baseline description

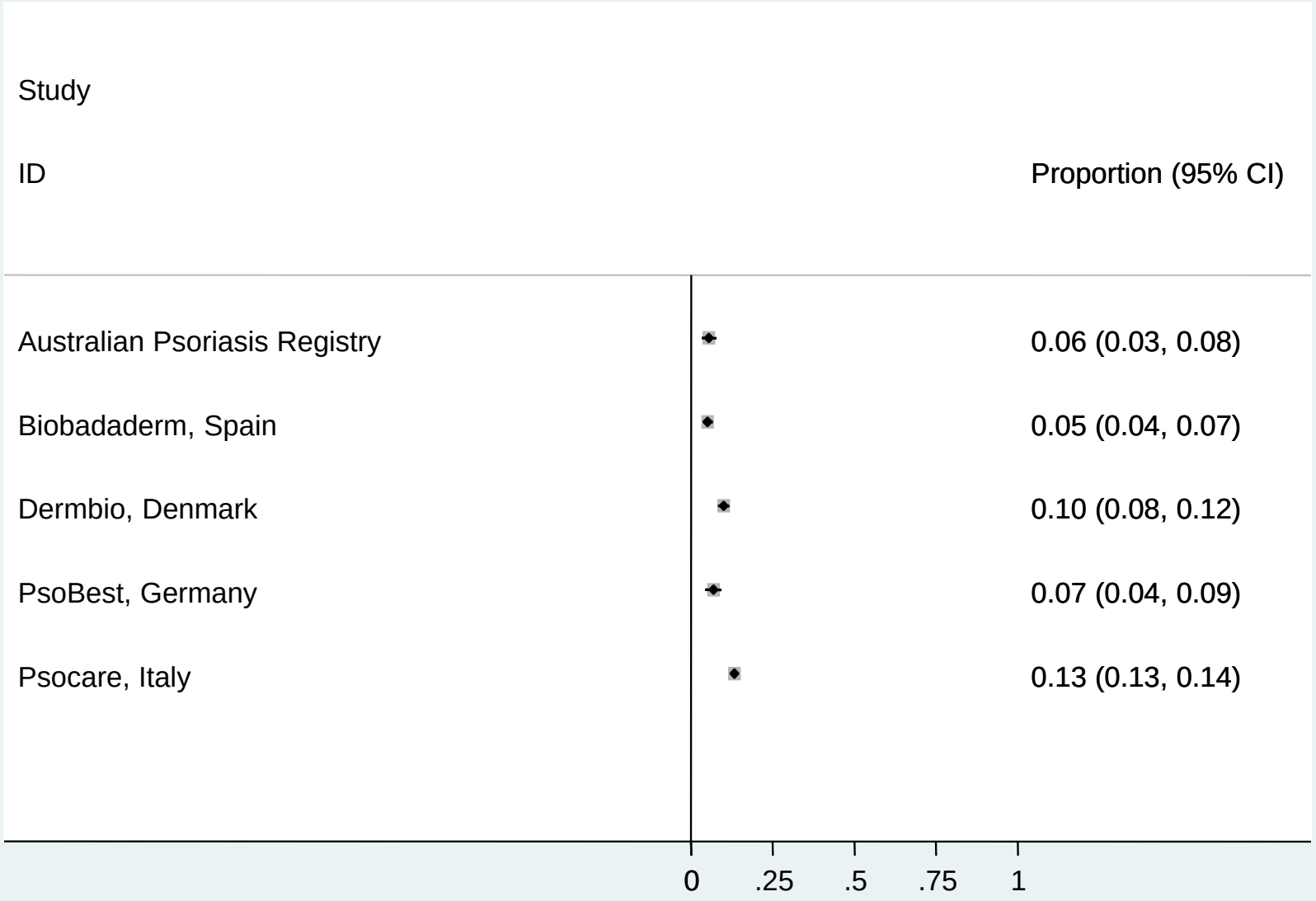
1. Baseline description of each registry

2. Baseline description of patients on biologics

3. Comparison biologics-controls

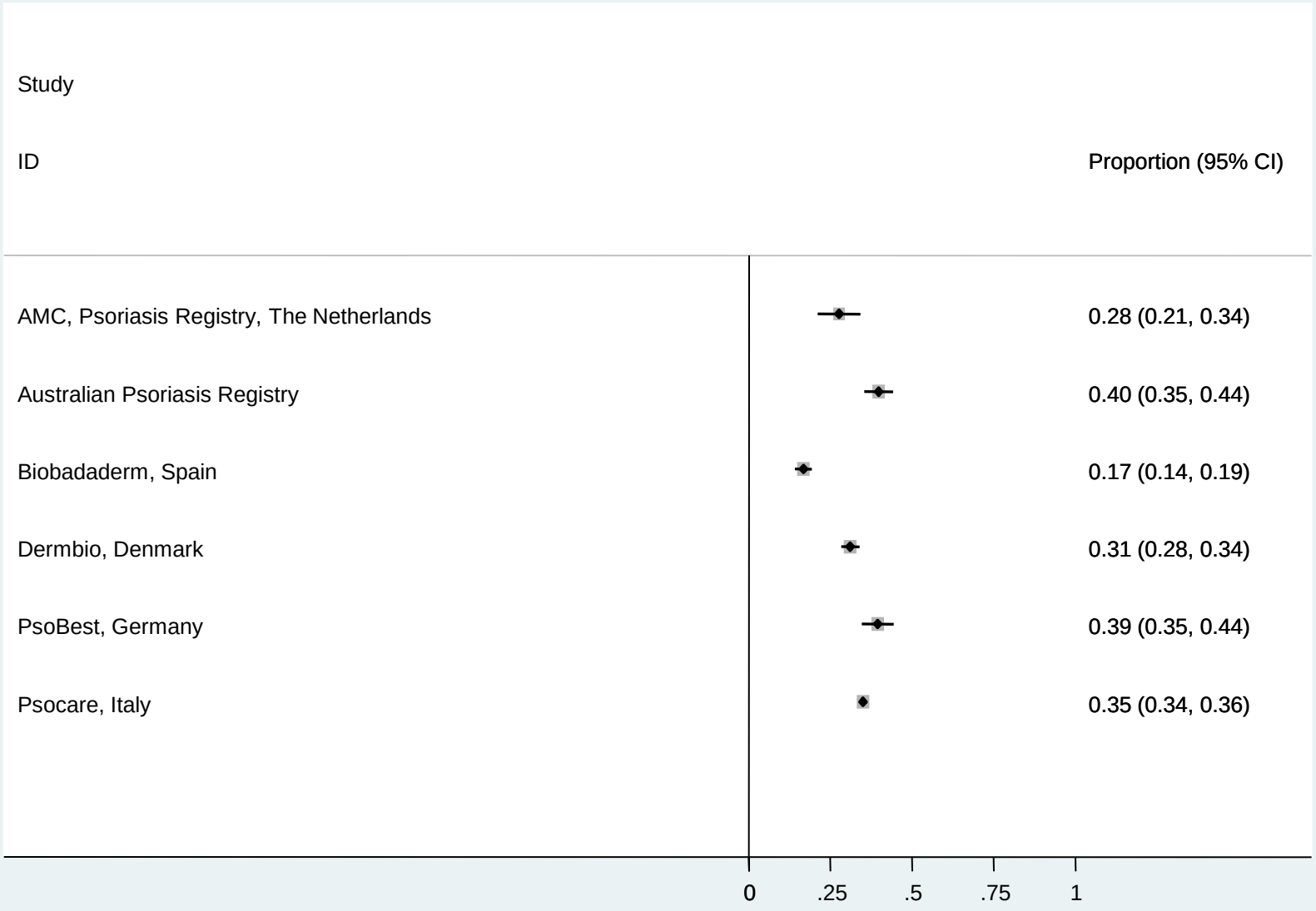
from Ignacio Garcia Doval 2012

Patients with psoriasis other than chronic plaque on biologics



from Ignacio Garcia Doval 2012

Patients with arthritis on biologics



from Ignacio Garcia Doval 2012

percentage of patients in which biologics were used as first line therapy:

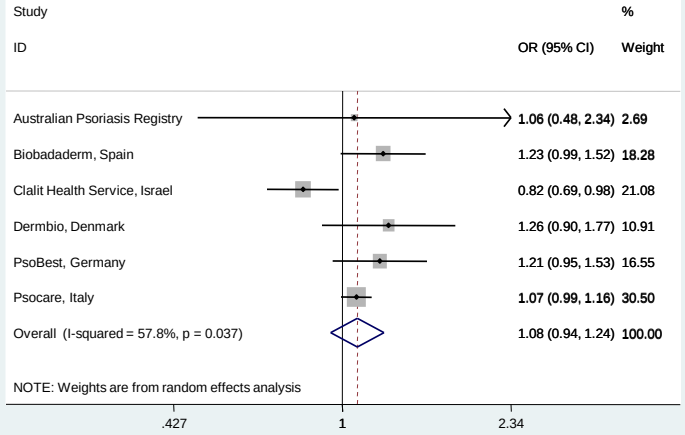
Study	% first line	[95% Conf.	Interval]
Australian Psoriasis	9.9	7.2	12.5
Biobadaderm, Spain	11.5	9.3	13.7
Clalit Health Servic	12.6	9.9	15.4
Dermbio, Denmark	48.2	45.2	51.2
PsoBest, Germany	5.3	3.0	7.5
Psocare, Italy	35.5	34.3	36.7
AMC, Psoriasis Regis	(Excluded)		

from Ignacio Garcia Doval 2012

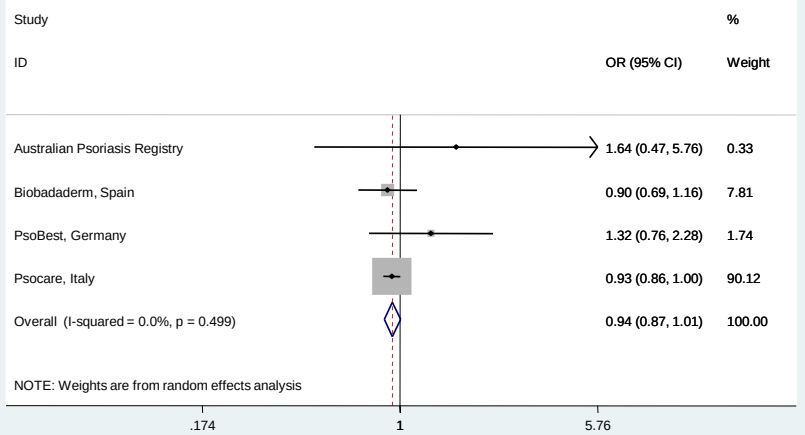
Differences between controls (conventional treatment) and biologics in each registry

- Confounding induced by unequal distribution can change risks in individual registries, leading to false differences.

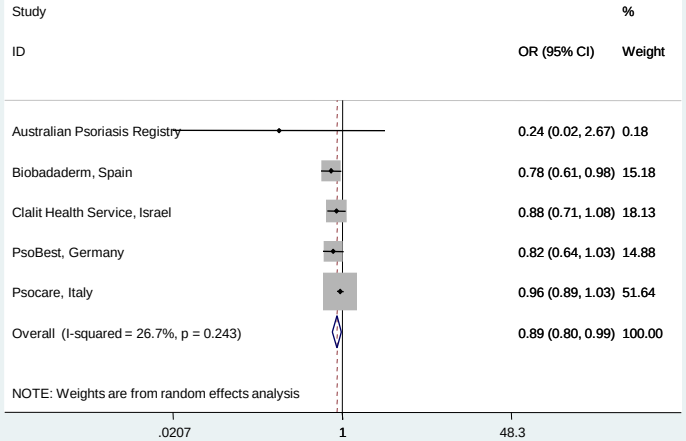
OR for being on biologics according to gender



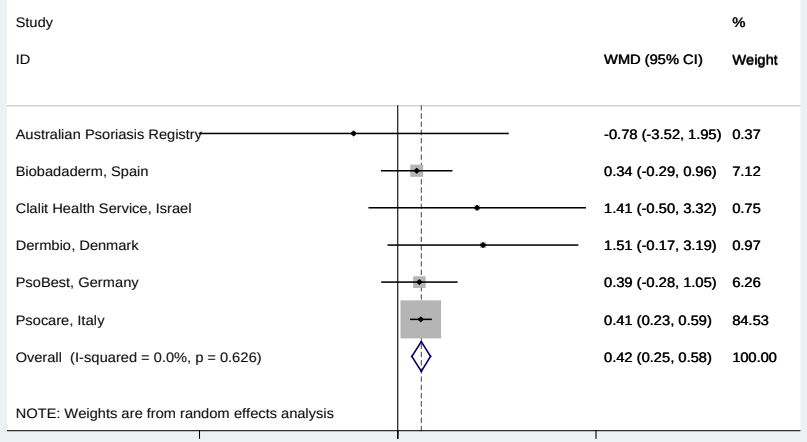
OR for being on biologics according to alcohol consumption



OR for being on biologics according to smoking



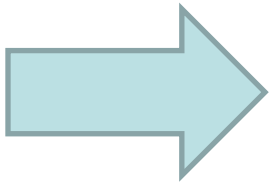
Mean difference between biologic and control in bmi



from Ignacio Garcia Doval 2012

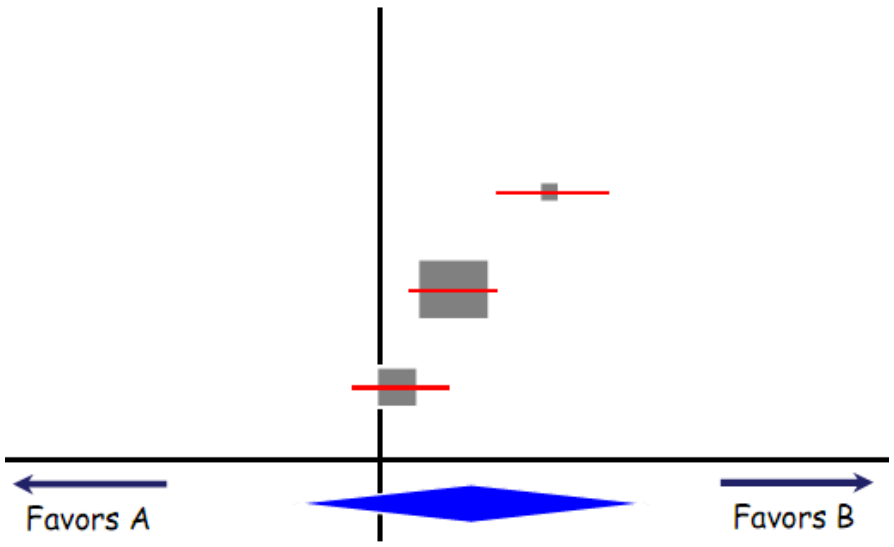
What we learnt about variations between registries

- Common confounders (age, severity) are distributed differently in registries.
- Proportion of exposed and controls vary largely among registries



- DO NOT simply agregate data from different registries! Adding up induces confounding:
- This is the perfect situation for creating Simpson´s paradox.
- To avoid it: each group should be compared with its own control group

from Ignacio Garcia Doval 2012



- Meta-analysis of **effect measures**
- Effect measures are calculated **using the same methods and after adjusting for the same confounders.**

Proposal
For each Psonet project

- Submission of a short protocol with:
  - Description of study population
  - Description of exposure (including method used to link drugs and adverse events)
  - Description of outcome
  - Description of confounders to use and method to control for confounding
  - **Definition of the measure to share**: Example: rate ratios with SE, after adjusting for age and initial severity.

Manchester template

European Rheumatology Biologic Registers

For all AEs except malignancy or death, the risk window begins with the start of the index biologic agent and continues until 90 days after the end of therapy, death or end of data collection, whichever comes first. SAEs, which occur beyond this risk window, will not count for purposes of incidence rate estimation.

For analyses of risk of death, the risk window begins with the start of the index biologic agent and continues until 90 days after the end of therapy, death or the cut-off date for the report.

For analyses of risk of malignancy, the risk window for any biologic therapy includes all person-time in the register (since starting that biologic therapy) and extends until the cut-off date for the report or date of death whichever occurs sooner, even in case of subsequent switching to another biologic agent. Where a malignancy is diagnosed after a second agent has begun, both agents will receive credit in the incidence rate estimations.

- Participation in the PSONET helps identify and solve common issues, enhancing the individual registries

- It provides larger sets of more powerful safety data in a diverse population

- Challenges to interpreting data include heterogeneity in sampling, variable penetration of biologics and compatibility of different datasets.

PARIS

PSORIASIS 2013

4th CONGRESS OF THE PSORIASIS INTERNATIONAL NETWORK

PALAIS DES CONGRÈS

4 - 7 JULY 2013

Organized by the Fondation René Touraine
An international foundation for dermatology

MAIN TOPICS

- PSORIASIS AND GLOBAL HEALTH
- THE BURDEN OF PSORIASIS
- EPIDEMIOLOGY OF PSORIASIS: RISK FACTORS AND CO-MORBIDITIES
- PHARMACOGENETICS AND PSORIASIS
- CONVENTIONAL SYSTEMIC TREATMENTS
- PHOTOTHERAPY
- NEW DRUGS IN THE PIPELINE
- MANAGING PSORIASIS IN COMPLICATED SCENARIOS
- HEALTH ECONOMICS OF PSORIASIS
- PSORIASIS AND CHILDREN
- PSORIATIC ARTHRITIS
- EVIDENCE BASED DERMATOLOGY AND PSORIASIS
- REGISTRIES AND INTERNATIONAL COLLABORATION

SCIENTIFIC COORDINATION

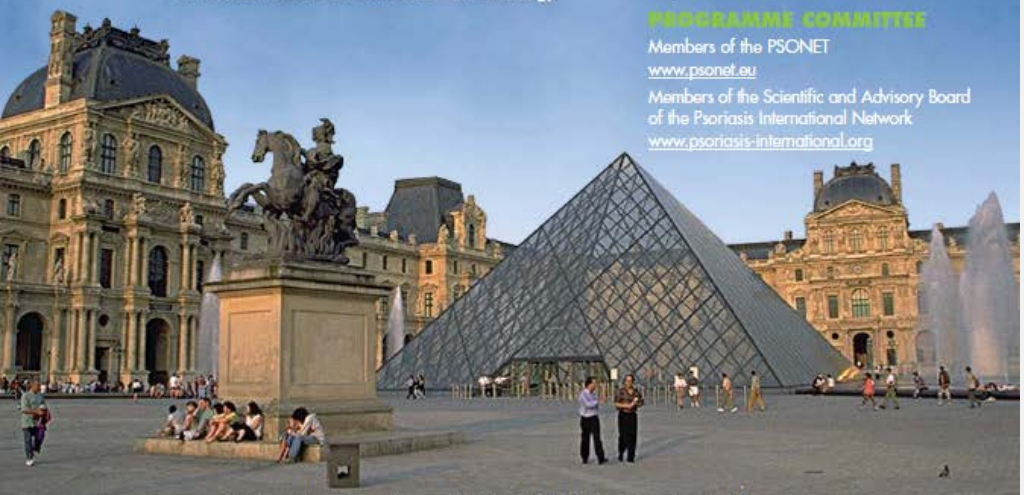
Luigi NALDI
on behalf of PSONET – European network of psoriasis registries
Eugenia CAGGESE, Congress Secretary

GENERAL COORDINATION

PIN Committee of the Fondation René Touraine
Carle PAUL, President
Luigi NALDI, President Elect

PROGRAMME COMMITTEE

Members of the PSONET
www.psonet.eu
Members of the Scientific and Advisory Board of the Psoriasis International Network
www.psoriasis-international.org



Under the auspices of the EADV Psoriasis Taskforce

▼ Registration & accommodation ▼

www.pso2013.com

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FONDATION RENÉ TOURAINE

PSORIASIS

PSORIASIS 2013

SAVE THE DATE!

4-7 July 2013

Palais des congrès
Paris – France

PSONET
EUROPEAN REGISTRY OF PSORIASIS

For more information please visit

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