

# Biologics in inflammatory disease

- a novel European network for pharmacovigilance  
and pharmacoepidemiology



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# Biologics in inflammatory diseases

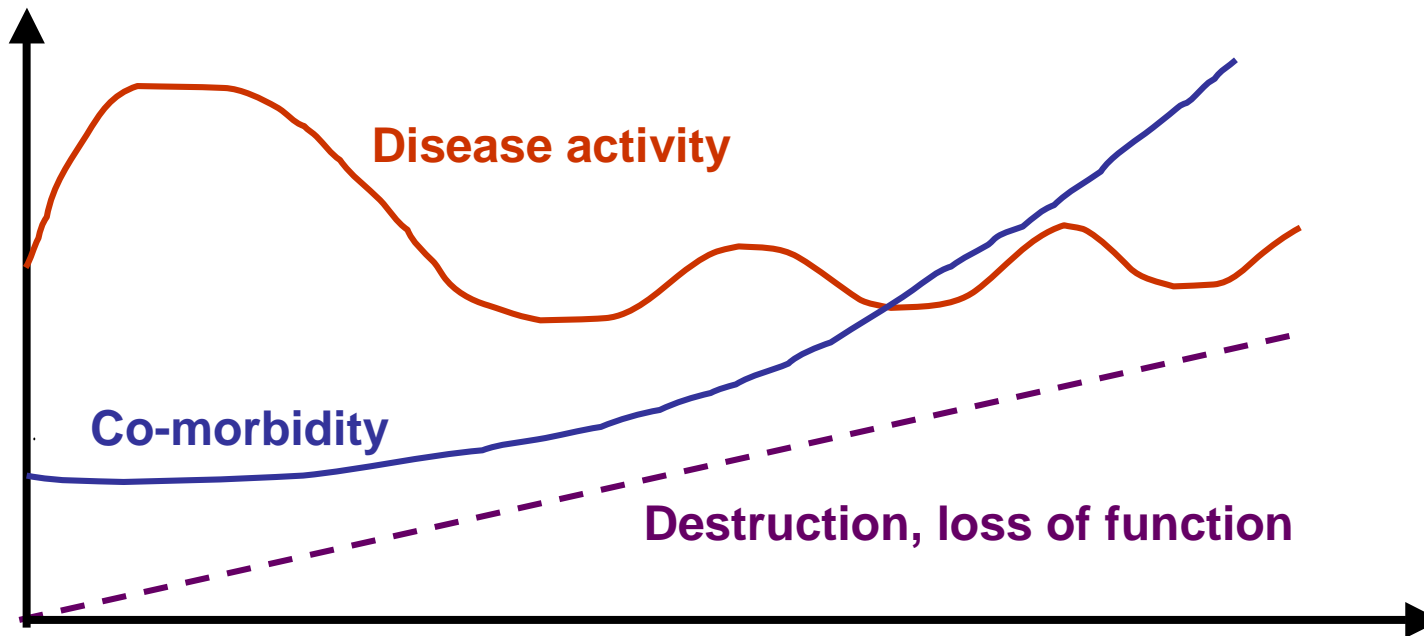
As a rheumatologist, you may choose between...

Anti TNF-alpha	Adalimumab
	Etanercept
	Infliximab
	Golimumab
Anti IL-1	Kineret
Anti B-cell (CD20)	Rituximab
Anti T-cell (CTLA4)	Abatacept
Anti IL-6	Tocilizumab

...and one out of four of your patients is treated

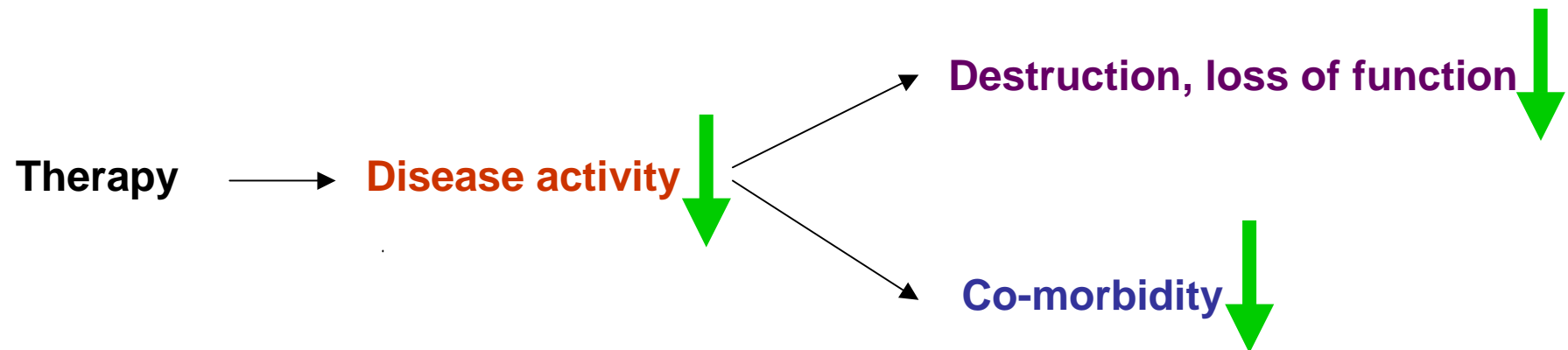
# Drug safety in chronic disease

## Time-course of *the chronic disease*



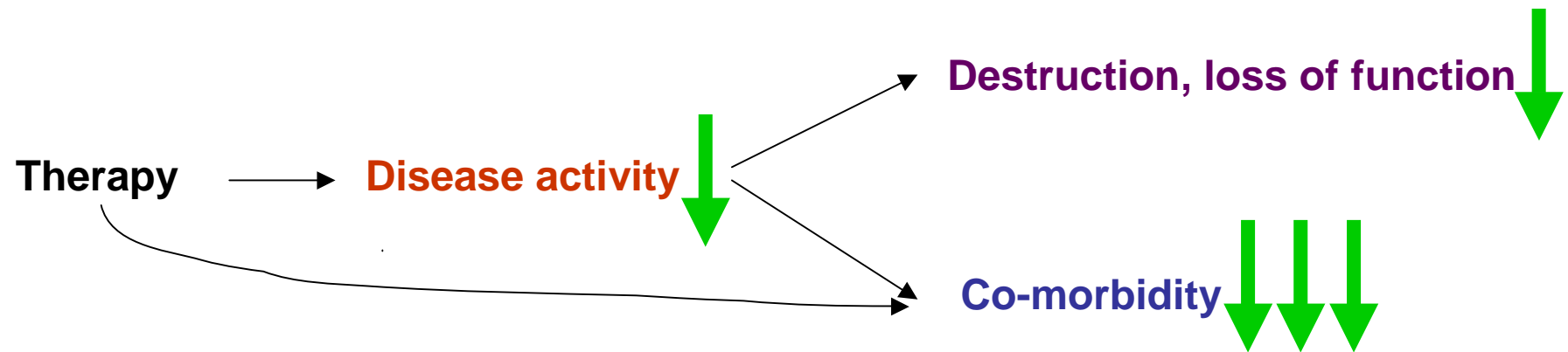
# Safety of biologics: challenges

## Co-morbidity as an *indirect treatment outcome*



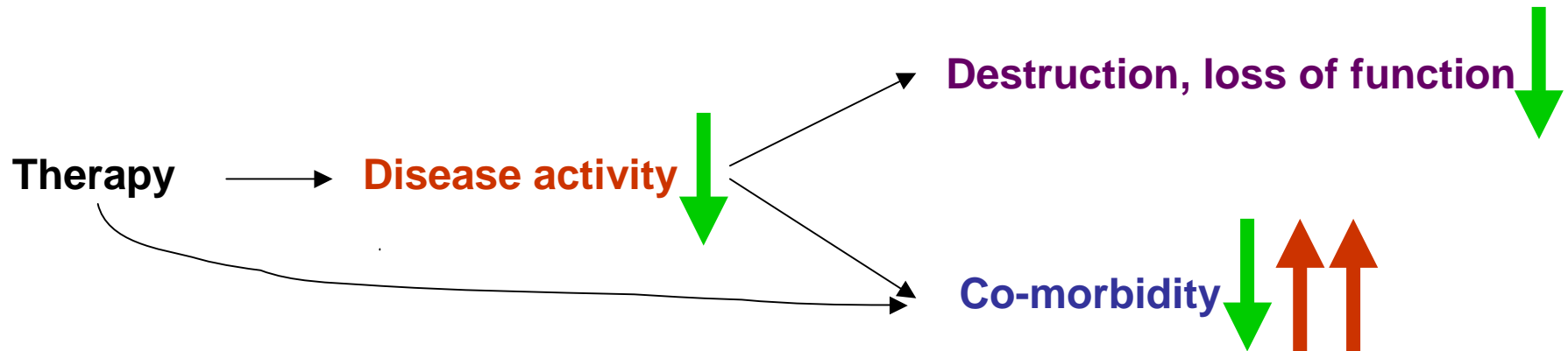
# Safety of biologics: challenges

## Co-morbidity as a *direct treatment outcome*



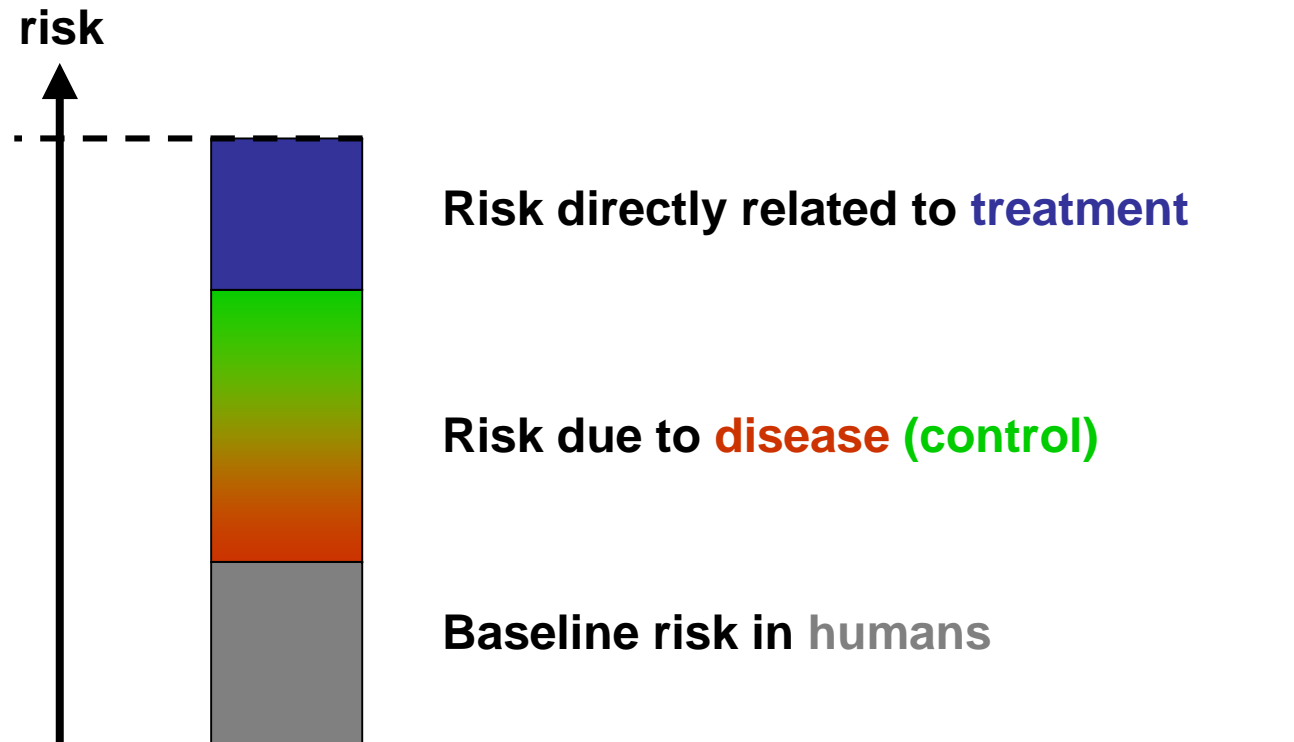
# Safety of biologics: challenges

## Co-morbidity as a *safety endpoint*



# Safety of biologics: challenges

## Attribution of an observed risk



# European Biologics Registers





# European Biologics Registers

name	started	coordination	type	inclusion	controls	current size	follow-up
<b>British Society for Rheumatology Biologics Register (BSRBR)</b>	2001	arc Epidemiology Unit Manchester	epidemiologic cohort study	new prescription of biologic; 4,000 per drug	control group collected at defined sites	>14,000 controls: > 3,000	baseline, 3,6,12,18,24,30, 36,48,60 months
<b>German Biologics Register RABBIT</b>	2001	Epidemiology Unit, German Rheumatism Research Centre	epidemiologic cohort study	new prescription of biologic; 1,000 per drug	internal control group: DMARD failures	>3,500 controls: 1,800	baseline, 3,6,12,18,24,30, 36,48,60,72,84,96, 108,120 months
<b>Swedish Biologics Register ARTIS</b>	1999	Karolinska Institute, Stockholm	routine registration	new prescription of biologic	national register data	18,000 treatments	baseline, 3,6,12,18,24 months etc.
<b>Spanish BIOBADASER register</b>	2000	Research Unit of Spanish Society of Rheumatology	routine registration	new prescription of biologic	EMECAR cohort	>8,000 patients	registration at inception of adverse event
<b>Danish Rheumatologic database DANBIO</b>	2000	Hvidovre Hospital	routine registration in 26 rheumatologic departments	new prescriptions		> 3,500 RA	regular visits as long as patients is seen in department
<b>Norwegian DMARD register NOR-DMARD</b>	2000	Diakonhjemmet Hospital, Oslo	routine registration of all DMARDs and biologics	treatment start with DMARD or biologic agent	DMARDs	> 2000	Baseline, 3, 6, 12, 24, 36, etc. months
<b>Dutch Rheumatoid Arthritis Monitoring Register DREAM</b>	2003	Radboud University Nijmegen Medical Centre	epidemiologic cohort study	start of treatment with biologic agent	early RA cohort	>1,000	Baseline, 3,6,9,12,18,24,30, 36 etc. months
<b>Swiss Clinical Quality Management Database</b>	1996	University of Geneva	routine registration	start of treatment with biologic agent	DMARD patients	>2,000 patients	annually

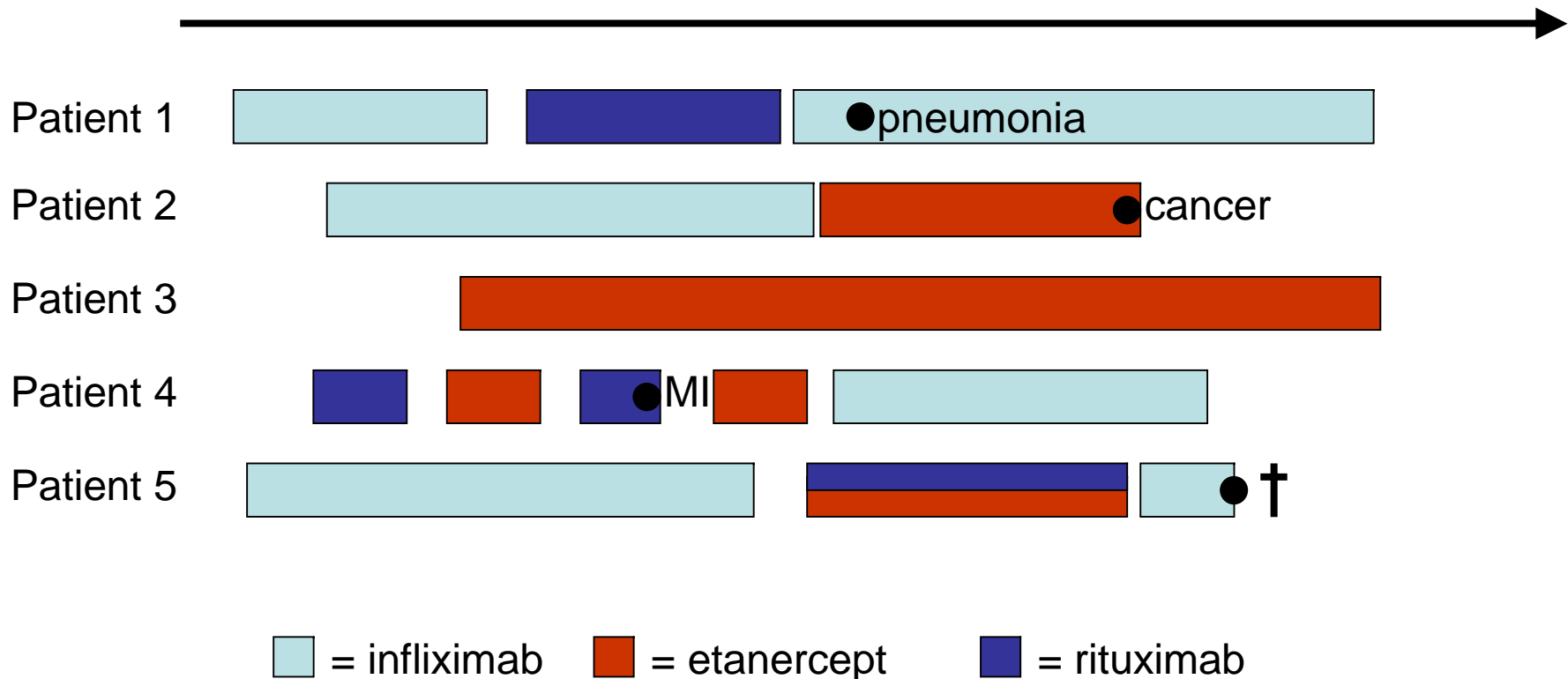
# European Biologics Registers

## Specific features

1. Initiated by the profession
2. Disease registers, not drug-specific

# Drug- or Disease-registers?

In reality, and as seen from a *disease-register*

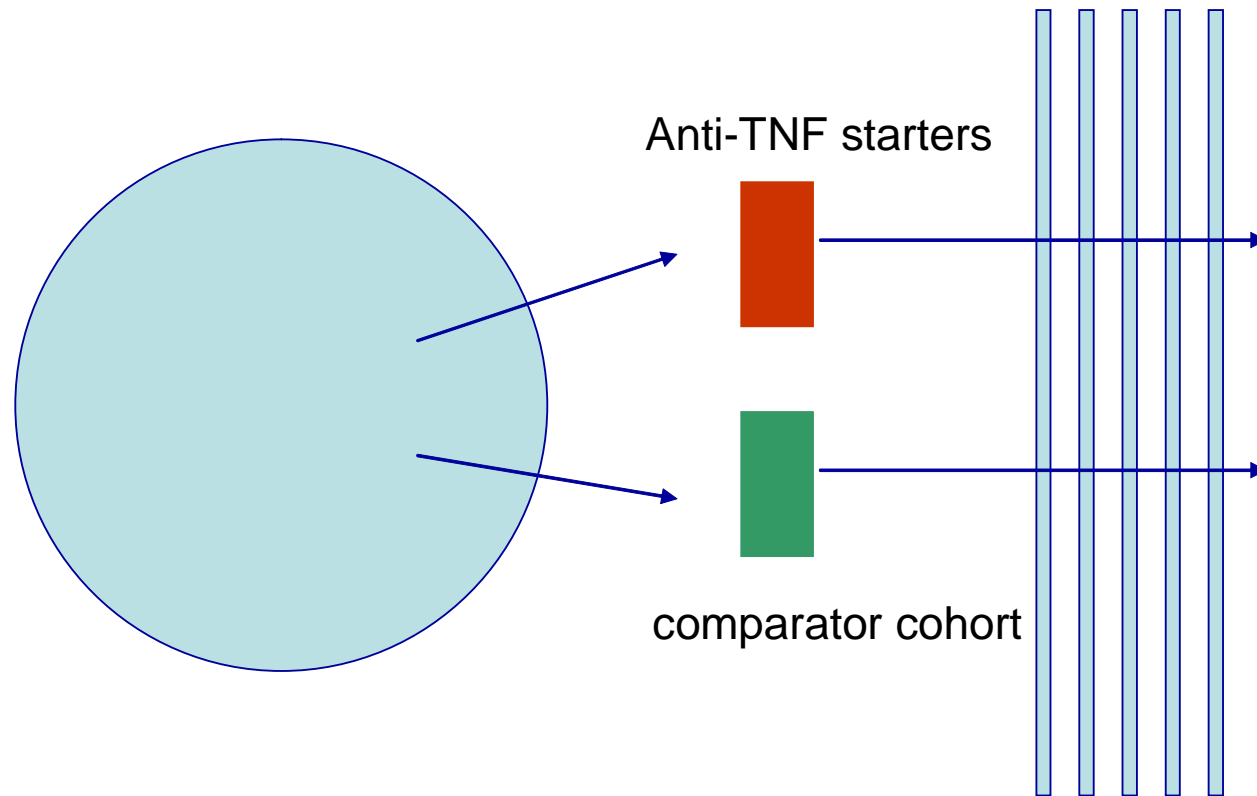


# European Biologics Registers

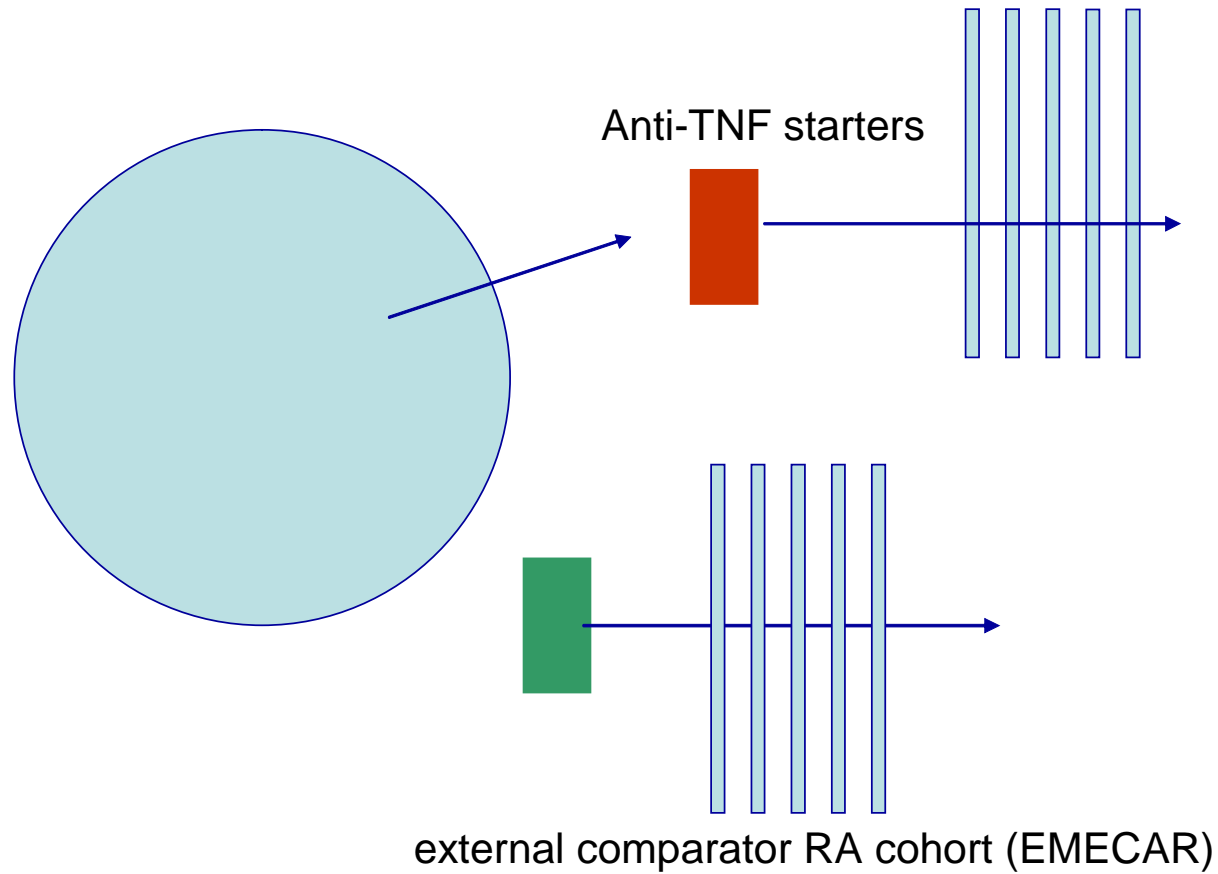
## Specific features

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# “project-based” biologics registers



# “project-based” biologics registers



# “integrated” biologics registers

## Swedish Rheumatology Registers

### Baseline data

### Follow-up data

► Basdata    ► Översikt    ► Händelser/Biv.

(KS5001) - Patienten har givit sitt informerade samtycke

Personnr/Kön: 760818-0126 Kvinna

Sjukdomsdebut(ÅÅMM): 88-06    Debutålder: 11-30    Efternamn/Förnamn: Pettersson Nina

Inklusionsdatum: 06-10-04    Duration mån.: 220    Patientansvarig läkare: JOHAN ASKLING

Distrikt: Solna    Nästa besök inbokat: 08-03-04

Diagnos: Polyartrit UNS    Annan diagnos ICD10:    vikt: 65 kg    längd: 179 cm

**RA-kriterier**

Morgonstelhet\* Ja (1)

Artrit i >=3 ledområden\* Ja (1)

Artrit i hand\* Nej (0)

Symmetrisk artrit\* Ja (1)

Reumatiska noduli Nej (0)

Reumatoid faktor pos. Nej (0)

Röntgenförändringar Nej (0)

\*sedan minst 6 veckor

**Patientkodning**

EIRA    Kod 1:

PARA    Kod 2:

TIRA    Kod 3:

Kod 4:

SWEFOT nr.     Tidig RA

Bio Patient

**Avslutning**

Datum/Orsak: 00-00-00

**BARFOT**

Ingår i BARFOT

ID nr:

**Övrigt**

Rökning: Värde inväntas (8)

Dominant hand: Värde inväntas (8)

Anti CCP: Värde inväntas (8)

► Läkemedelsuppföljn.    ► Tid. LARM o Kortison    ► Komorbiditet

Preparat	Ordinerat	Utsatt	Orsak	Totaldos
Enbrel	06-10-09	00-00-00		0

År	06	07
Månad	10	01
Dag	09	12
Besöksmånad	0	3
MK-grupp	1	3
Smärta	35	8
Arbetsförmåga	30	40
Funktion	1,13	0,00
Sjukdomskänsla	24	14
Svullna leder	4	0
Ömma leder	4	0
Sänka	14	10
CRP	1	2
Läkarbedömning	2	0
RTG(Eros./Prog./RF)		
DAS 28	3,86	1,81
Analgetika		
Antiinflam.		
Kortisondos		
LARM 1	MTX	MTX
LARM 1 dos	20	15
LARM 2		
LARM 2 dos		
LARM 3		
LARM 3 dos		
Uppföljd månad	0	3
Uppfölit preparat	ENB	ENB

# “integrated” biologics registers

## Other National Swedish Registers

### National health-related registers

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- Hospital Discharge Register
- Non-GP Outpatients Register
- Prescription Register
- Cancer Register
- Cause of Death Register
- Medical Birth Register
- TB register

### Demographics registers

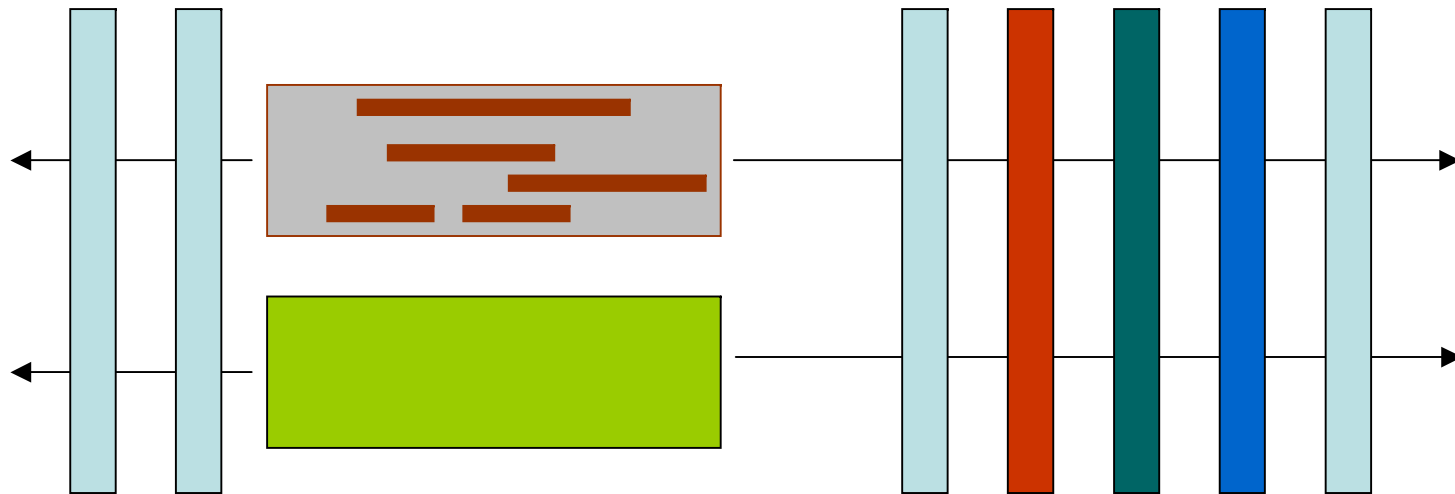
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- Population Register
- Emigrations Register
- Generation Register
- Census Surveys Data



# “integrated” biologics registers

- Biologics exposure
- Non-exposed subjects with the disease
- General population comparator

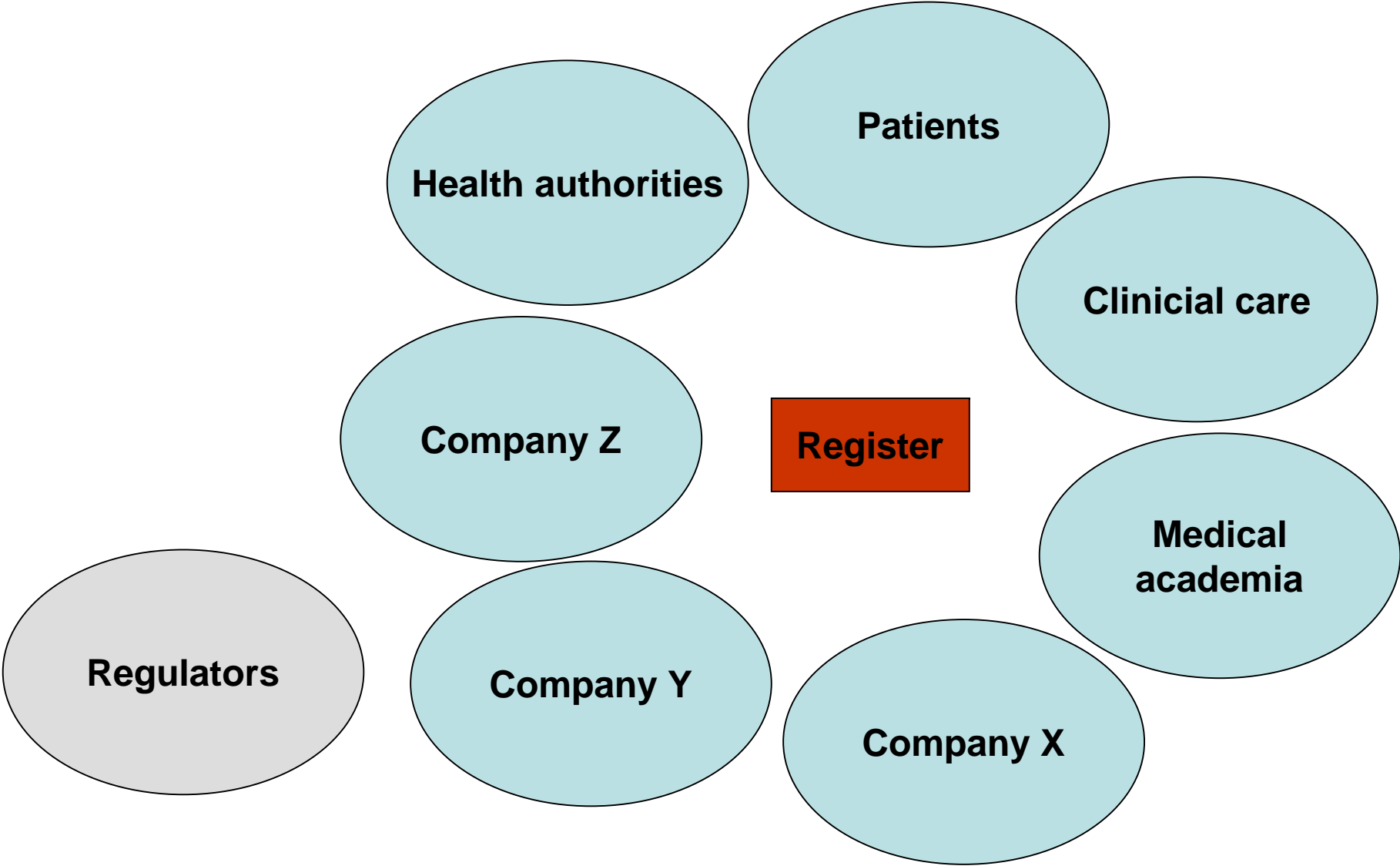


# European Biologics Registers

## Specific features

1. Initiated by the profession
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3. From treatment start, and onwards
4. Use of comparators
5. Supported by joint grants from all companies
6. Standardised reporting of data for PSURs
7. Inter-register collaboration

# Stake-holders in disease registers



# European Biologics Registers

## Specific features

1. Initiated by the profession
2. Disease registers, not drug-specific
3. Designed for "indefinite" follow-up
4. Use of comparators
5. Supported by joint grants from all companies
6. Standardised reporting of data for PSURs
- 7. Inter-register collaboration**

# Conclusions

# Further reading...

*European Biologics Registers – methodology, results, and perspectives.*

Zink A, Askling J, Dixon W, Klareskog L, Silman A, Symmons D. *Annals of Rheumatic Diseases*, Epub 2008