

Workshop

La *drug utilization* attraverso i database amministrativi

Milano, 27 novembre 2012

“APPROPRIATEZZA”

Elisabetta Poluzzi

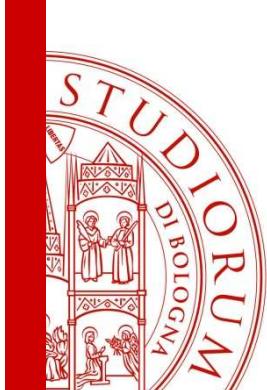
Emanuel Raschi

Carlo Piccinni

Fabrizio De Ponti

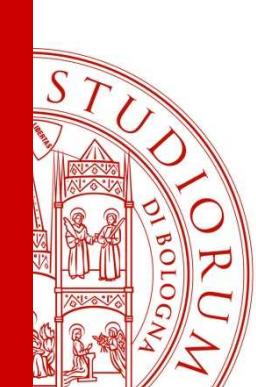
Dipartimento di Scienze Mediche e Chirurgiche

Alma Mater Studiorum - Università di Bologna



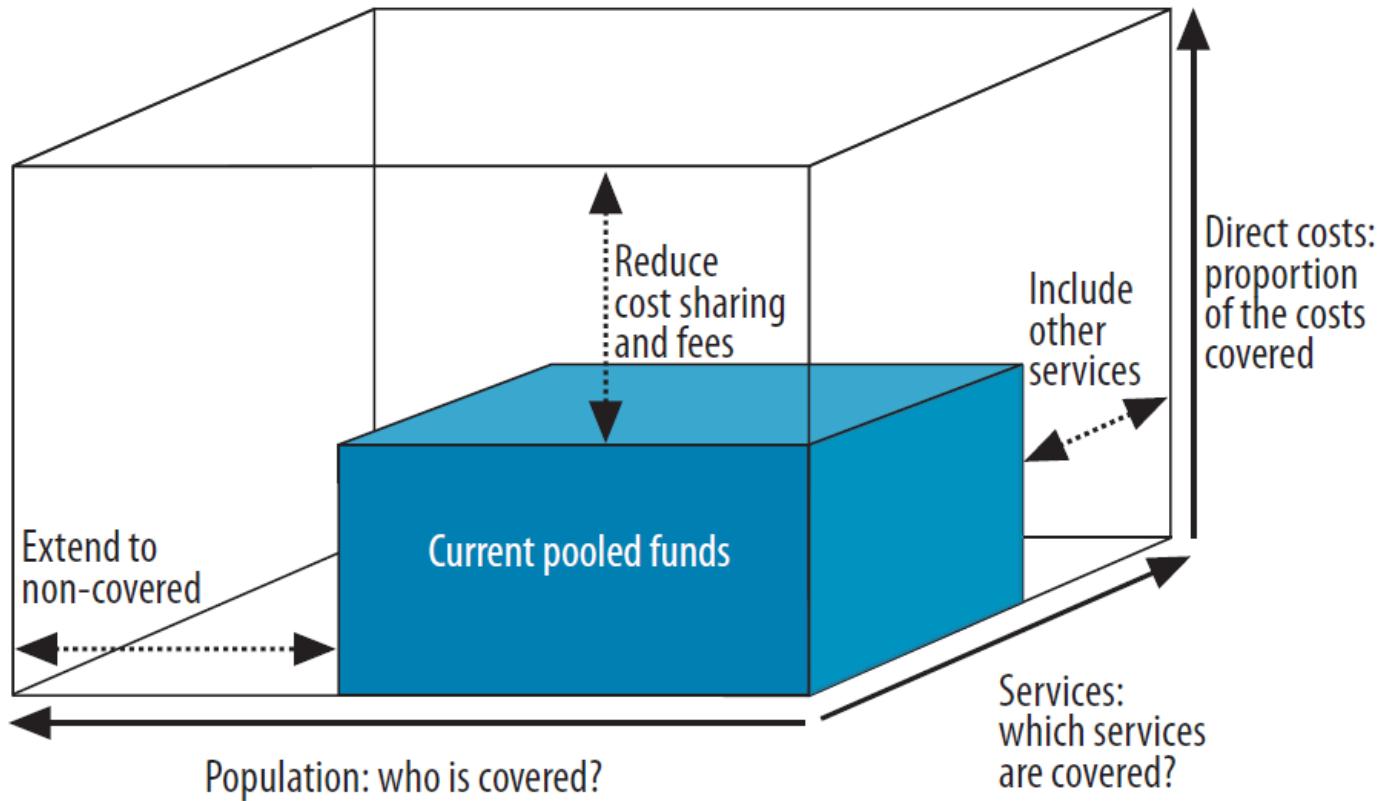
APPROPRIATEZZA: molteplici aspetti

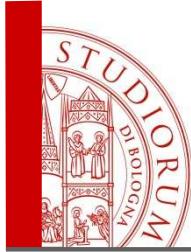
- 1) Efficacia della terapia: da RCT e linee-guida al paziente individuale**
- 2) Sicurezza dei farmaci: sospetto e diagnosi di ADR**
- 3) Aderenza alla prescrizione**
- 4) Contesto socio-economico: ospedale-territorio**



APPROPRIATEZZA: le tre dimensioni per raggiungere la copertura

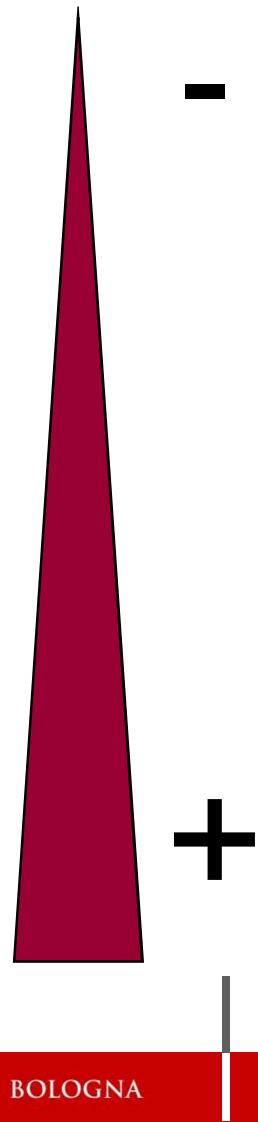
HEALTH SYSTEMS FINANCING
The path to universal coverage

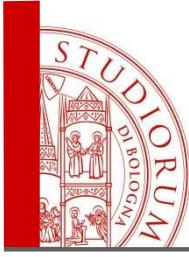




Esperienze in Emilia Romagna di utilizzo database clinici/amministrativi con finalità di ricerca

1. Analisi del **consumo** di dronedarone e altri antiaritmici
2. Studi di **aderenza** alla terapia degli antidepressivi
3. Studi sui **profili prescrittivi e socio-demografici** (predittori) degli antipsicotici
4. Studi sui **registri** nella Sclerosi Multipla
5. Studi di **aderenza e outcome** sulle statine

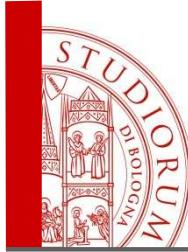




tipologie di dati

finalità

	Dati di consumo/ prescrizione/ vendita	+ prescrizione con identificativo paziente	+ diagnosi e dati socio- demografici da cartelle cliniche elettroniche	+ ospedalizzazione (diagnosi/esito)
Trend	X			
Aderenza		X		
Preditori			X	
Esiti				X



1. Analisi del consumo

Tipologia di dati: prescrizioni aggregate

I database in Emilia Romagna

- Assistenza Farmaceutica Ospedaliera – AFO** (dati aggregati)
- Assistenza Farmaceutica Territoriale – AFT** (ricette rosse)
- Farmaci a Erogazione Diretta - FED**



Commento editoriale

Tra linee guida e decisioni regolatorie: l'odissea del dronedarone

Fabrizio De Ponti¹, Alessandro Mugelli²

(già rispettivamente Segretario e Coordinatore della Sezione Clinica della Società Italiana di Farmacologia)

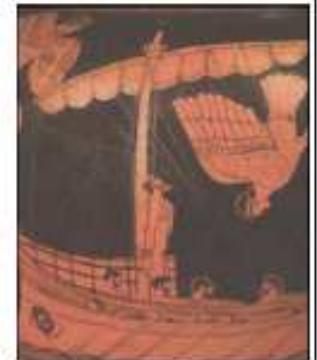
¹Dipartimento di Farmacologia, Università di Bologna

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G Ital Cardiol

L'odissea del dronedarone

7 grandi trial clinici in pazienti con fibrillazione atriale (FA) o flutter atriale



ANDROMEDA

vs. placebo

DAFNE

definire dosaggio

ERATO

vs. placebo

EURIDIS

vs. placebo

DYONISOS

vs. amiodarone

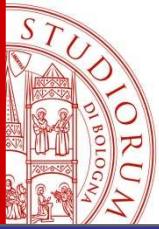
ATHENA

vs. placebo

ADONIS

vs. placebo

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Dronedarone: Primo o Secondo?

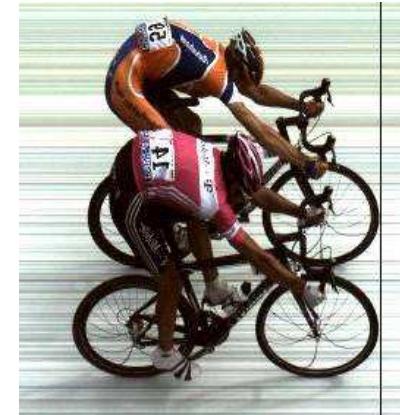
Linee Guida EUR¹ e USA²

Raccomandano il **dronedarone come 1° linea** di trattamento nel controllo della frequenza e del ritmo dei pazienti con FA non permanente.

Al contrario l'**amiodarone** dovrebbe essere usato **come 2° linea**, solo qualora gli altri agenti farmacologici abbiano fallito o siano controindicati.

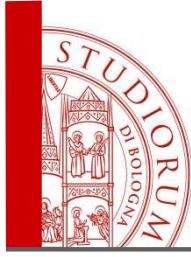
1. Camm AJ, et al. Eur Heart J 2010

2. Wann LS et al. Circulation 2011



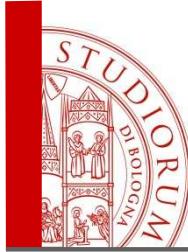
Enti Regolatori (FDA, EMA, AIFA)

Considerato la mancanza di evidenze robuste su efficacia e sicurezza, nonché le differenze esistenti in termini di costo, raccomandano l'uso del **dronedarone come 2° linea** nel controllo del ritmo in pazienti con controindicazioni all'amiodarone o nel controllo della frequenza nei pazienti che non tollerano betabloccanti, calcioantagonisti o amiodarone. Mentre, **amiodarone e beta-bloccanti** rimangono i trattamenti di **1° linea**.



Obiettivo

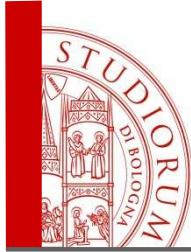
**Valutare se l'autorizzazione
del dronedarone ha avuto un
impatto sulle prescrizioni dei
farmaci antiaritmici in
generale e dell'amiodarone in
particolare**



Metodi

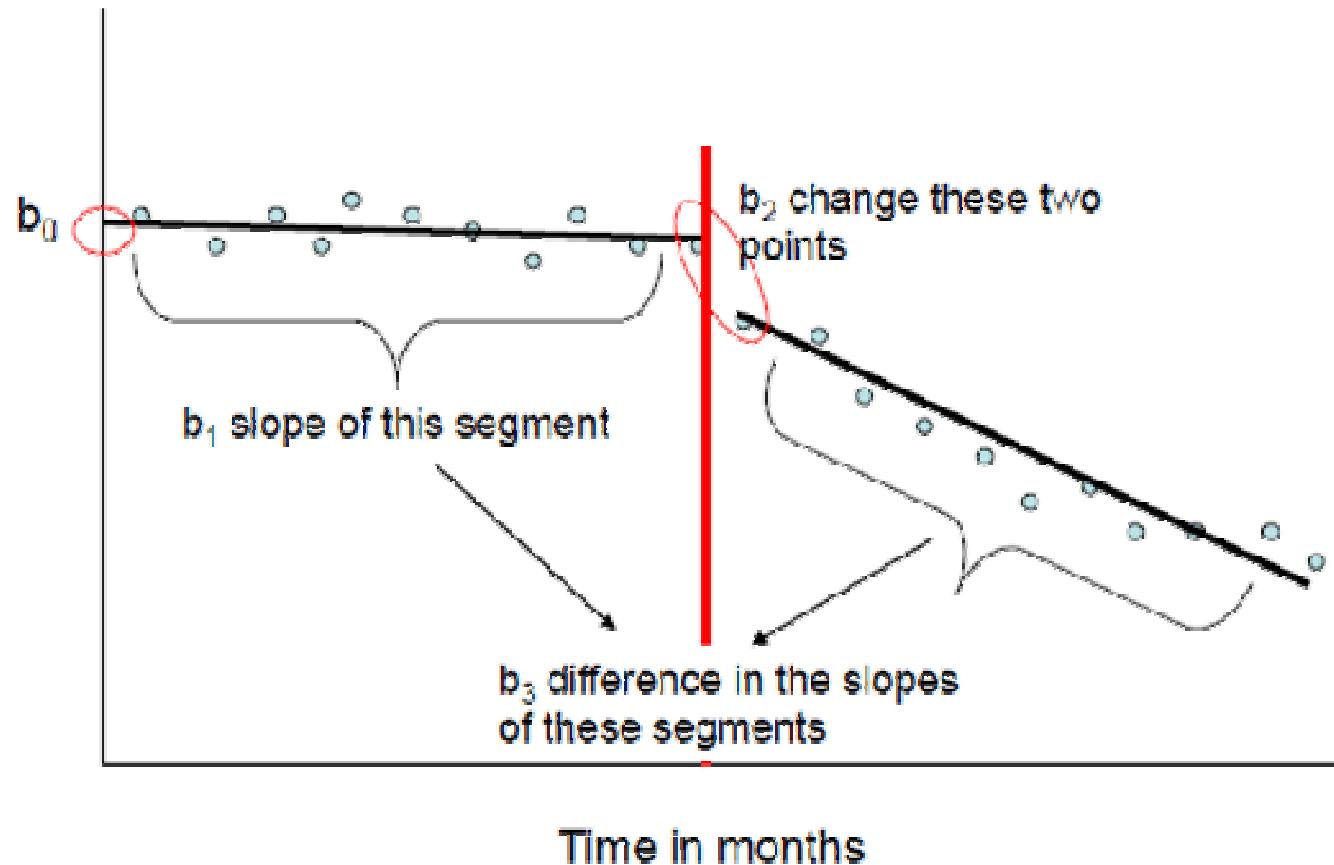


- Due scenari: **Emilia Romagna** (4,4 milioni)
Svezia (9,4 milioni)
- Raccolta delle prescrizioni ospedaliere (**AFO**) e territoriali (**AFT-FED**) degli antiaritmici di classe I e III (ATC: **C01B**), 12 mesi prima e dopo l'autorizzazione del dronedarone
- **DDD/ TID** : Defined Daily Dose/Thousand Inhabitants per Day
- Descrizione dei **trend prescrittivi**
- **Interrupted Time Series Analysis**

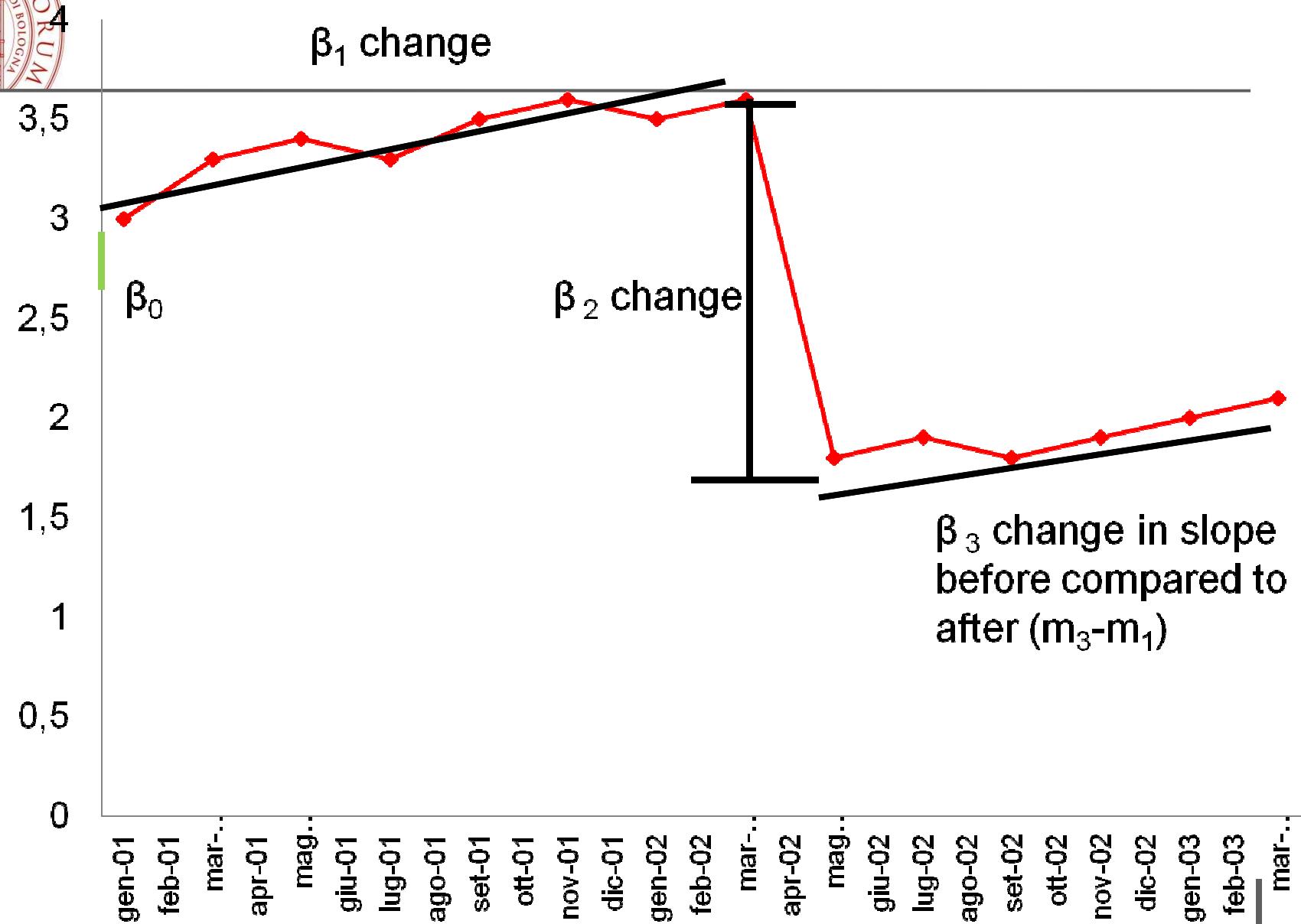
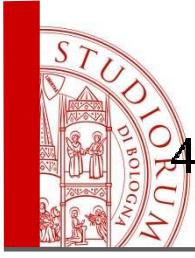


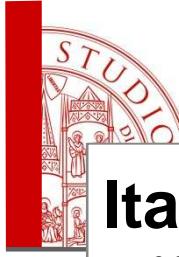
Interrupted Time Series Analysis

Consente di confrontare il trend prescrittivo pre/post- **intervento**, tenendo in considerazione le normali fluttuazioni stagionali (necessarie 12 osservazioni pre e 12 post- intervento)

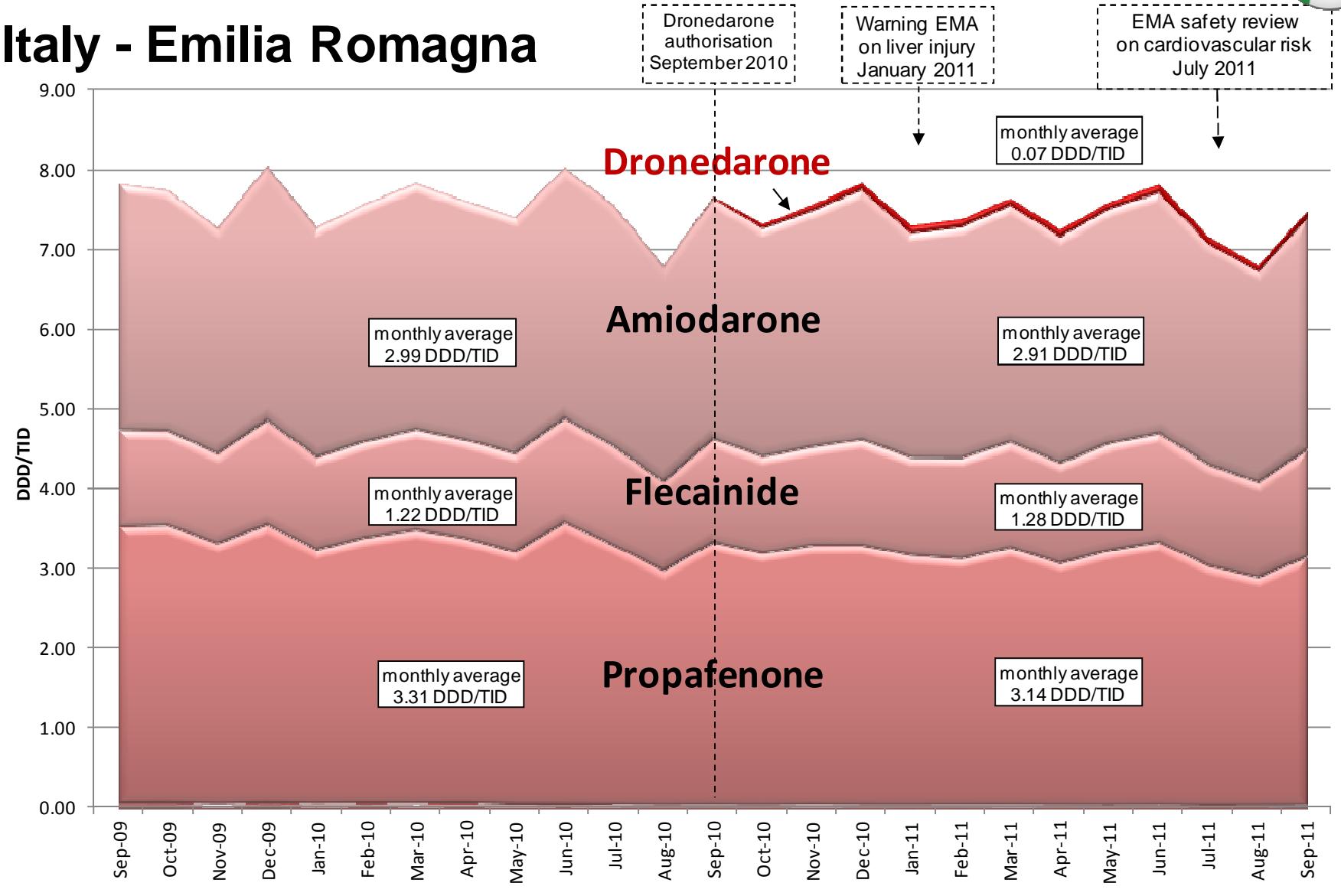


Wagner AK et al. *Journal of Clinical Pharmacy and Therapeutics* (2002)



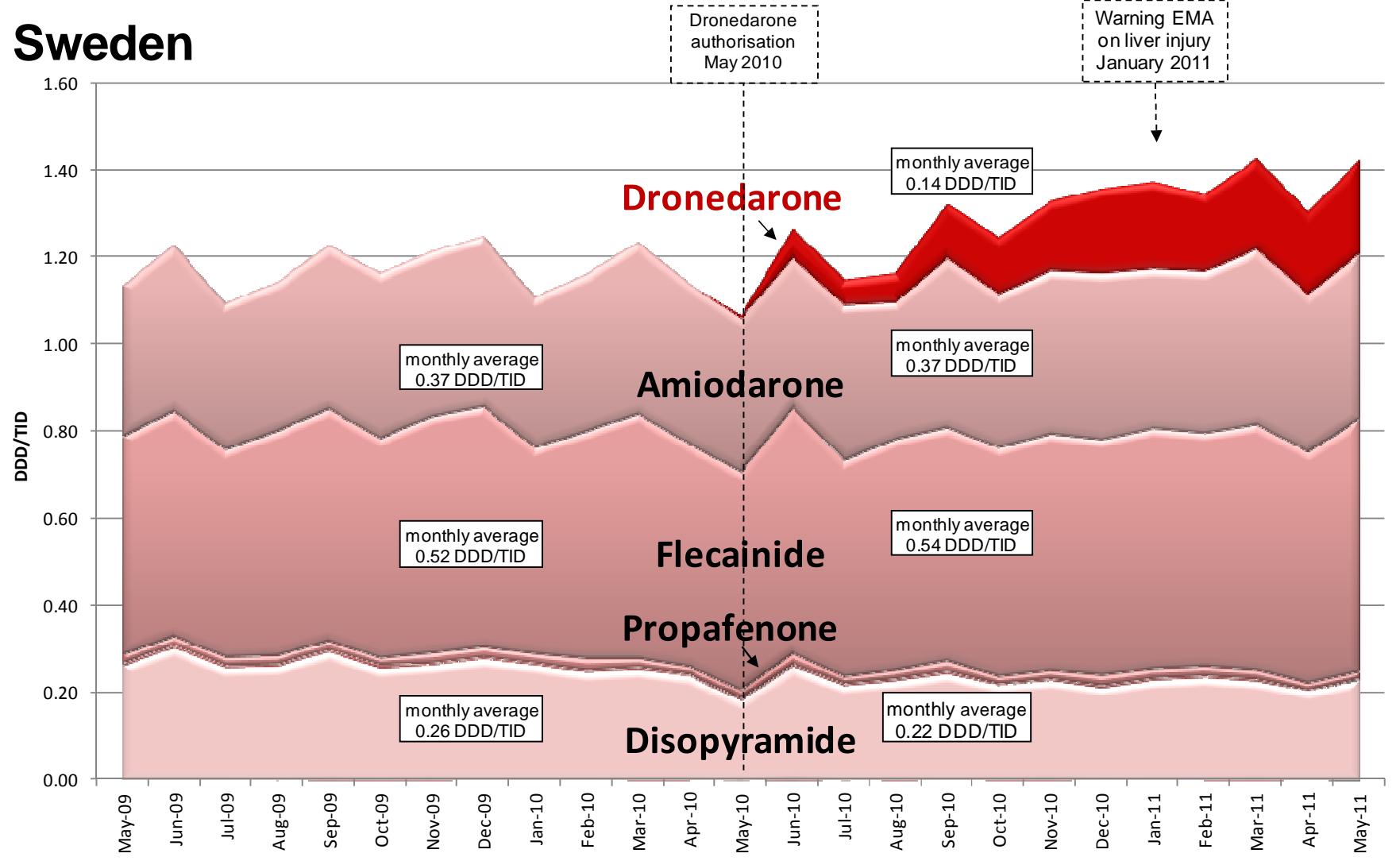


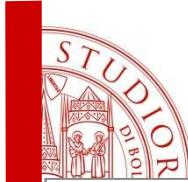
Italy - Emilia Romagna



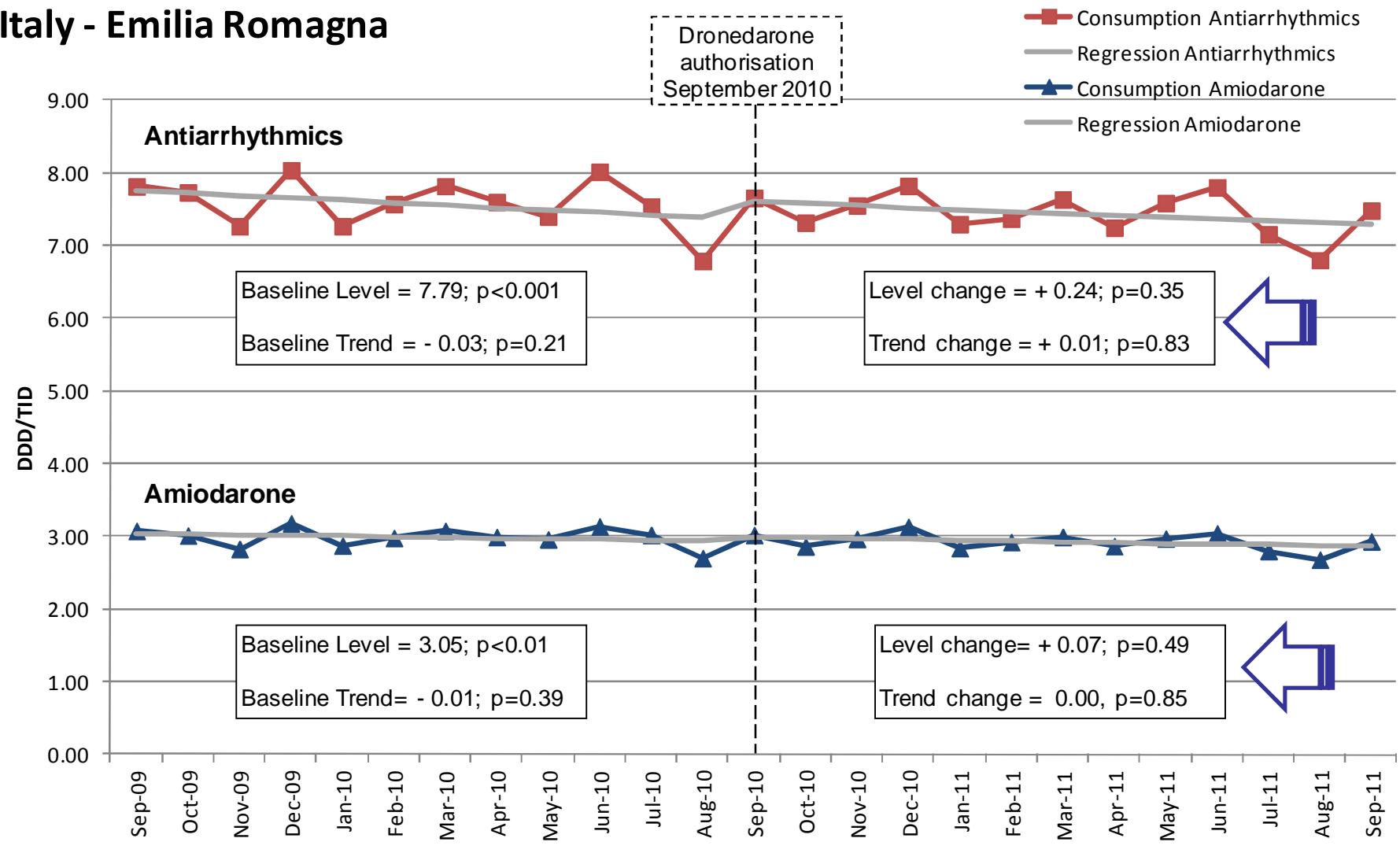


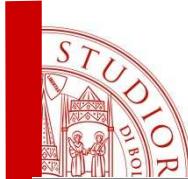
Sweden



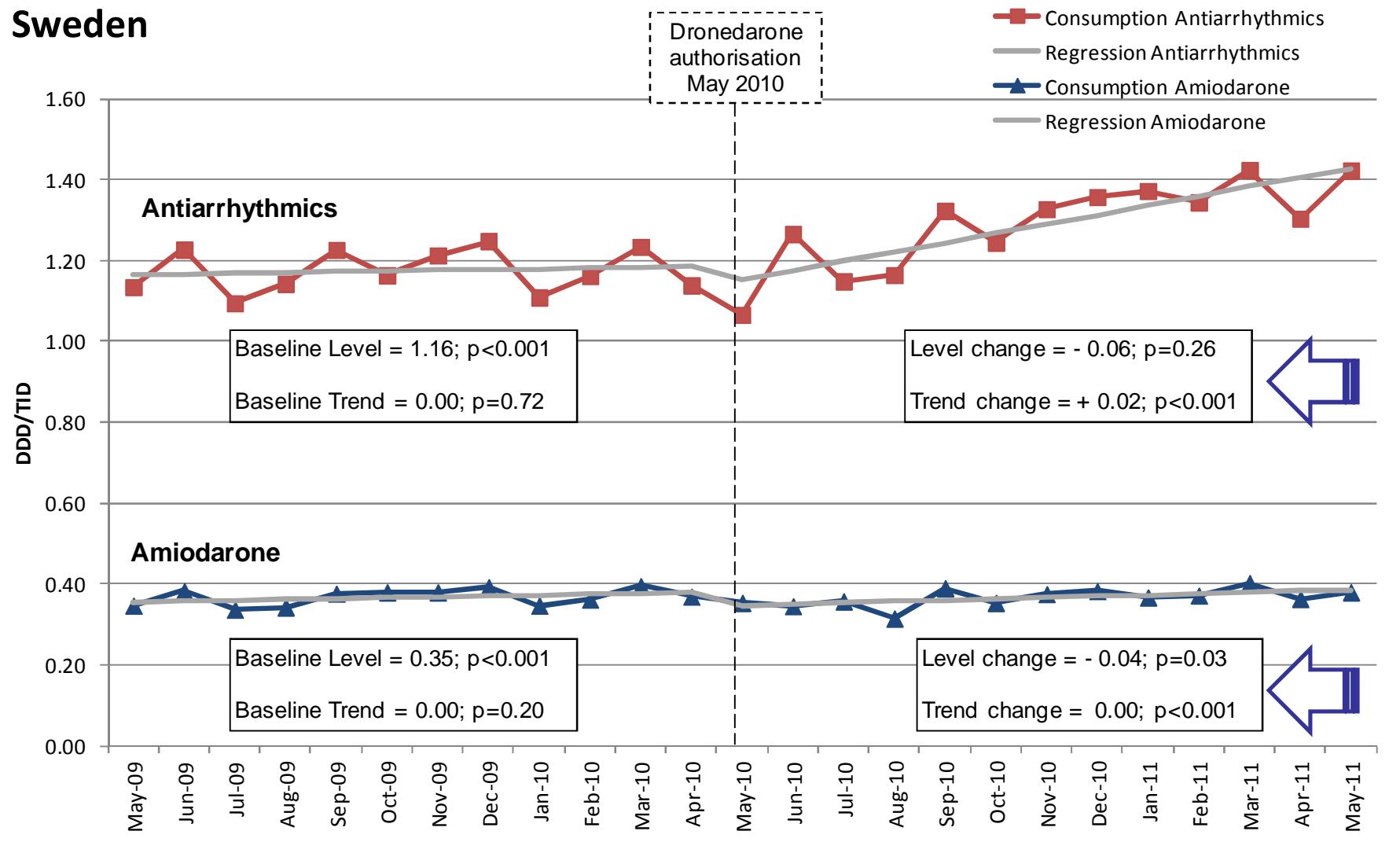


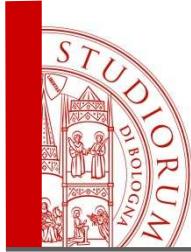
Italy - Emilia Romagna





Sweden



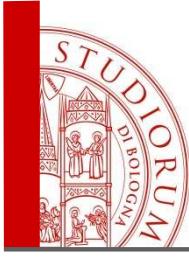


Conclusioni

In entrambe le realtà studiate il **dronedarone non ha sostituito l'amiodarone**

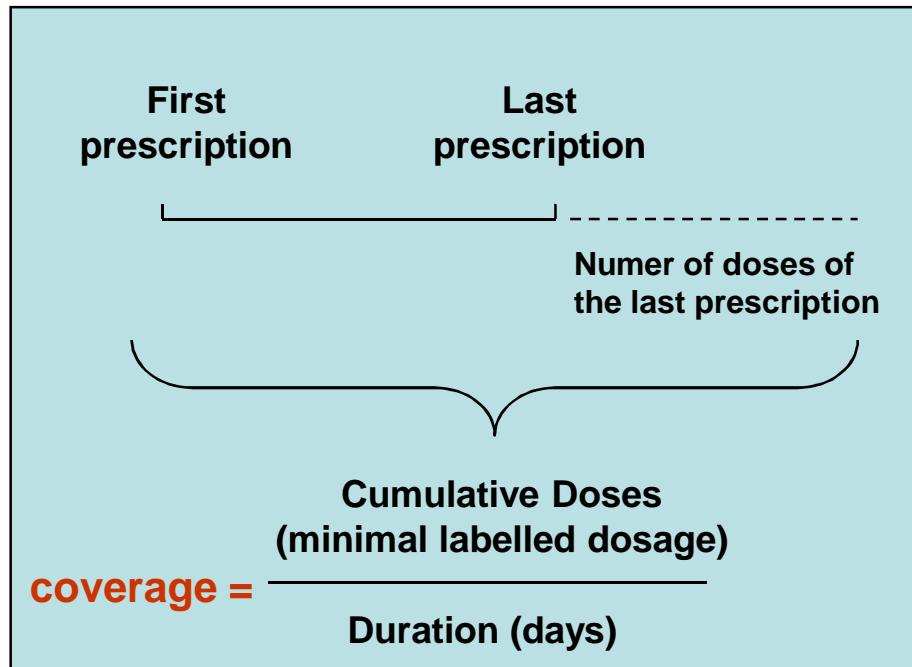
I clinici hanno seguito **le indicazioni degli enti regolatori**

Ogni farmaco appena autorizzato dovrebbe essere caratterizzato da uno status di **“sorvegliato speciale”**



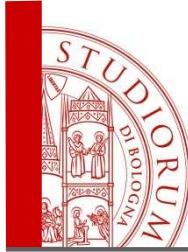
2. Studi di aderenza

Tipologia di dati: prescrizioni con identificativo paziente

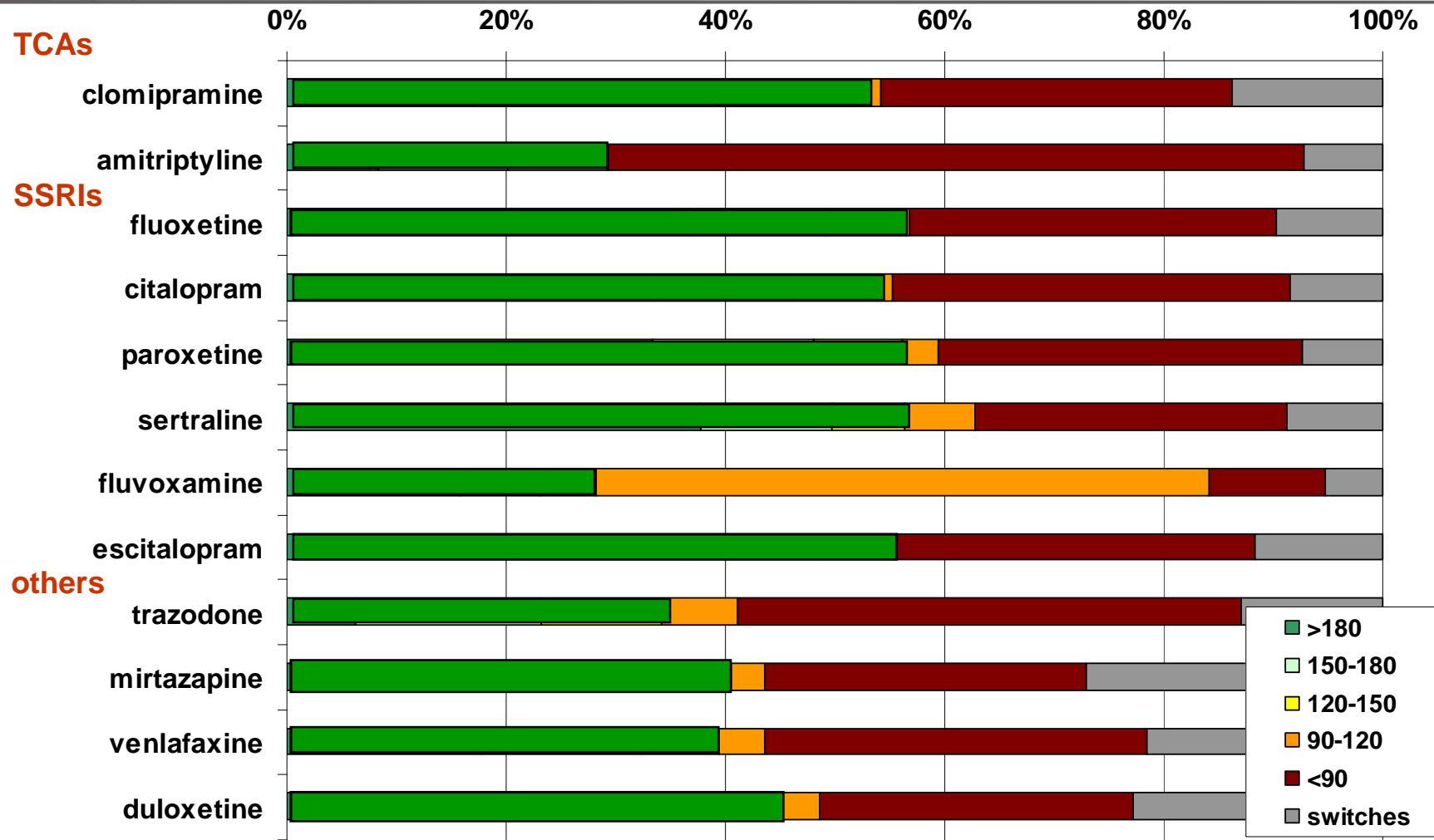


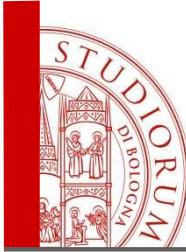
Adherent patients

Duration \geq 120 days.
Coverage \geq 80%.
No gaps in prescriptions >3 months.

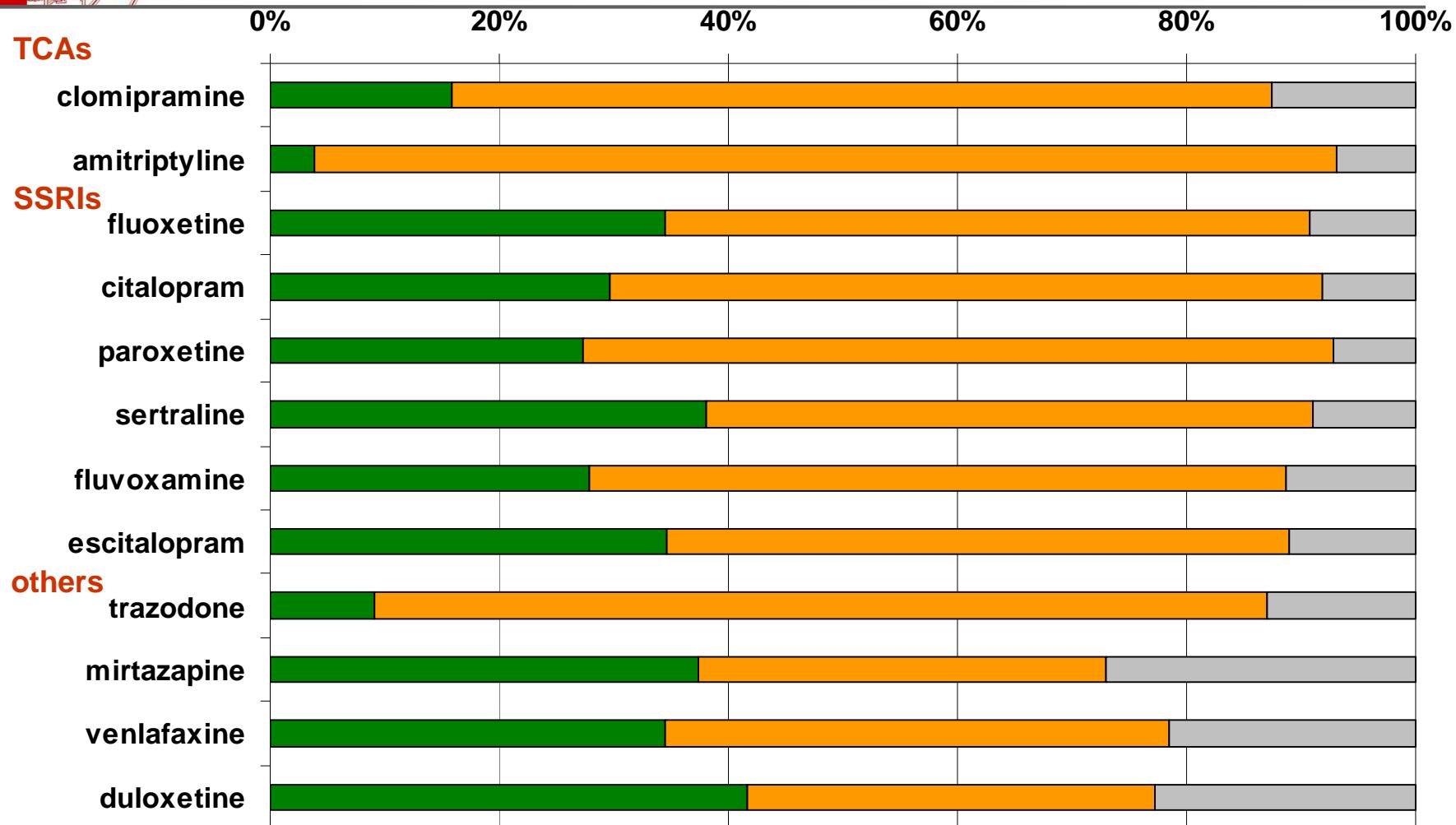


Duration of therapies (no matter the intensity of use)

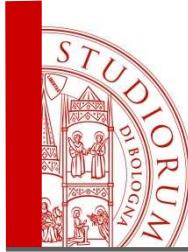




Adherence to antidepressant therapy (combination of duration and intensity)



Green bars = percentage of adherent patients



3. Studi sui profili prescrittivi

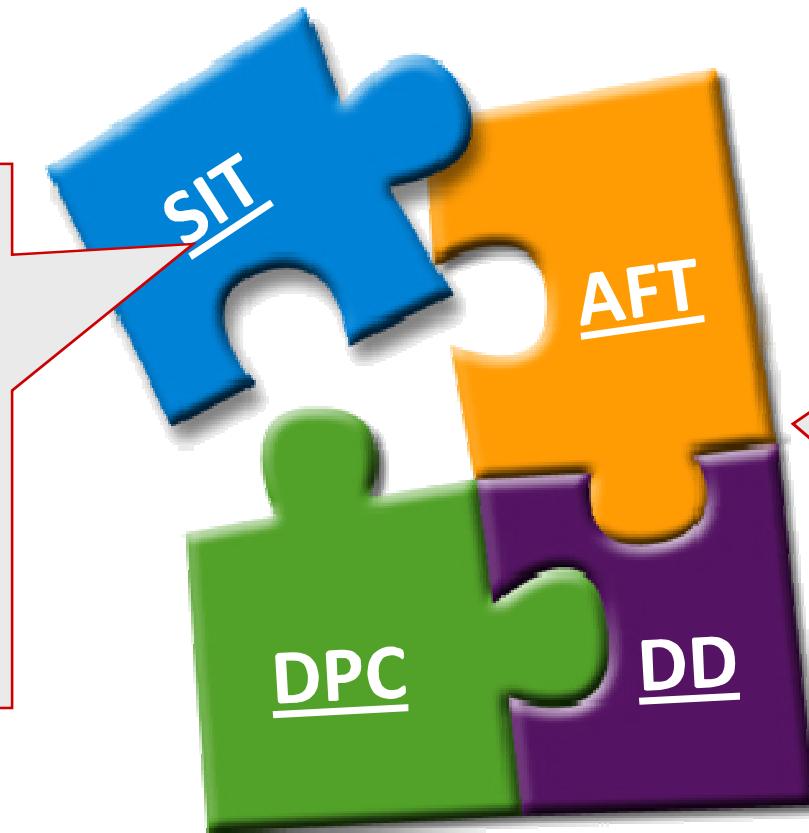
Tipologia di dati: prescrizioni con identificativo paziente + archivio clinico del Centri di Salute Mentale

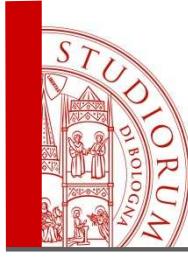
socio-demographic
and clinical
characteristics

From the Informative
system of the
Community Mental
Health Centres

prescription data

From different drug
administrative
databases





Study population

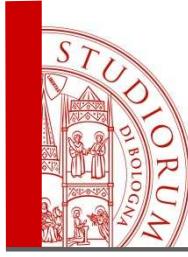


Patients:

- cared by the Community Mental Health Centres
- with at least one AP prescription (ATC: N05A - Antipsychotics, except for N05AN01-Lithium)
- period: January - June 2010

Psychiatric diagnosis were grouped into 4 groups:

- Schizophrenic-like disorders
- Major depressive disorders
- Personality disorders
- Bipolar disorders

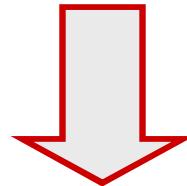


Analysis of prescription predictors



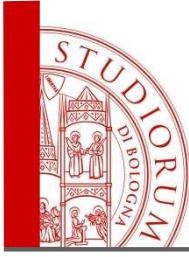
Drug prescriptions were grouped by:

- different preparation (depot or regular)
- different therapeutic strategy (polypharmacy or monotherapy)
- different AP class (atypical or typical)



To identify prescription predictors of AP among socio-demographic and clinical variables a **logistic regression model** was used.

A prescription predictor was defined when $p < 0.05$



Study Cohort

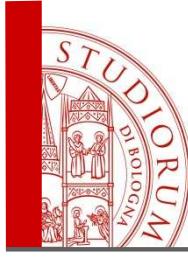


Study period: 01/01/2010 - 30/06/2010

Patients: 6,074

AP prescriptions: 42,121



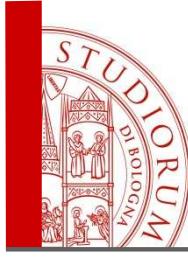


Socio-demographic and clinical characteristics



	N	%
Gender		
Female	3,149	51.8
Male	2,925	48.2
Age		
<35 years	740	12.2
35-64 years	3,912	64.4
>64 years	1,422	23.4
Nationality		
Italian	5,830	96.0
Non Italian	241	4.0
Unnown	3	0.0
Urbanicity		
Urban	2,512	41.4
Non urban	3,356	55.3
Non living in the carchment area	206	3.4
Education years		
<8 years	3,877	63.8
>8 years	2,044	33.7
Unknown	153	2.5
Occupation		
No	2,473	40.7
Yes	2,122	34.9
Unknown	1,479	24.3
Maital Status		
Married	2,877	47.4
Never Married	3,024	49.8
Unknown	173	2.8

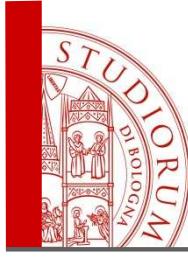
	N	%
Diagnosis		
Schizophrenic-like disorders	2,531	41.7
Major depressive disorders	1,150	18.9
Personality disorders	805	13.3
Bipolar disorders	667	11.0
Other	905	14.9
Unknown	16	0.3
Duration of CMHC treatment		
0-3 years	1,997	32.9
>3 years	4,077	67.1
CHM visits over the 6 months period		
0-12	3,446	56.7
>12	2,571	42.3
Unknown	57	0.9
Hospitalisation over the 6 months period		
No	5,464	90.0
Yes	610	10.0
Compulory admission over the 6 months period		
No	6,018	99.1
Yes	56	0.9



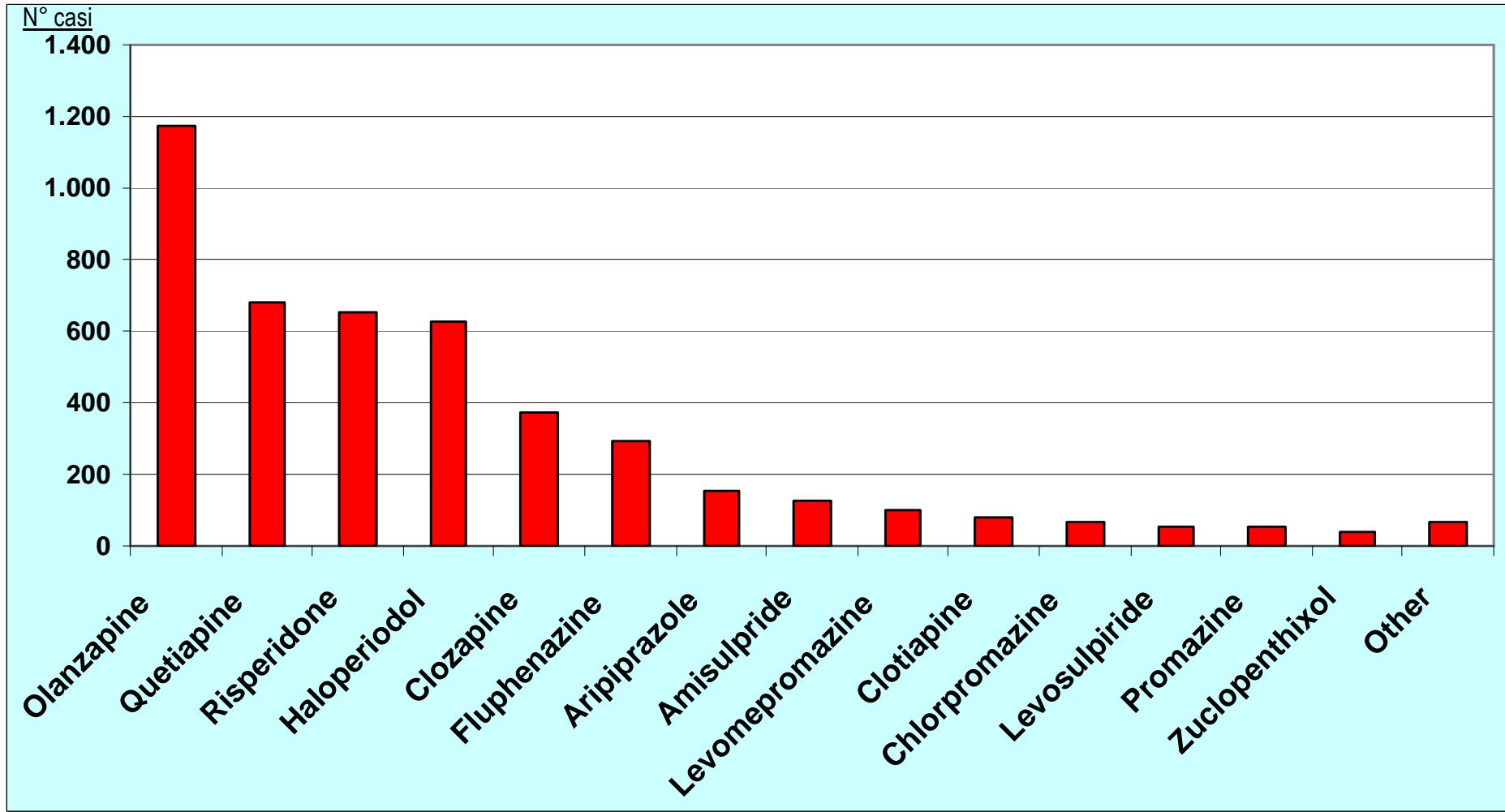
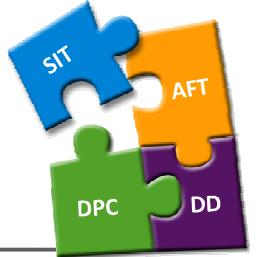
Characteristics of prescriptions

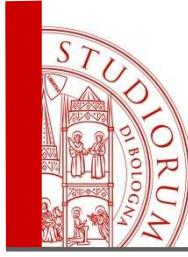


All diagnosis		
	N	%
	6,074	100
AP Preparation		
Regular	5,011	82.5
Depot	1,063	17.5
Class of AP		
Atypical	4,297	70.7
Typical	1,777	29.3
No. of different concomitant AP		
1	4,539	74.7
2 or more	1,535	25.3

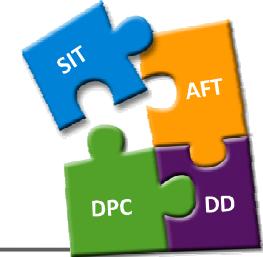


La scelta del principio attivo: gli AP più utilizzati in monoterapia

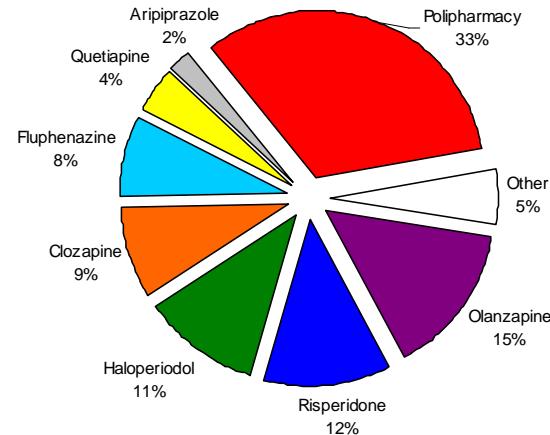




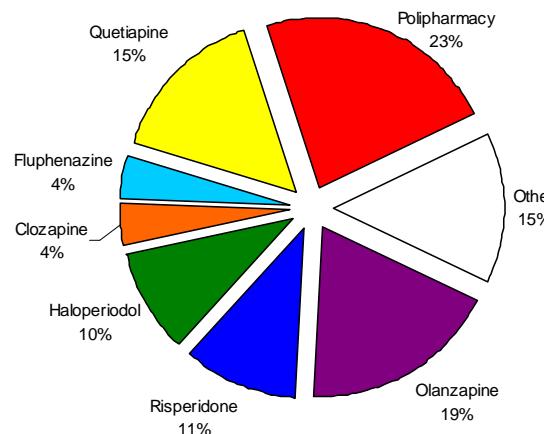
AP choice according to psychiatric diagnosis groups



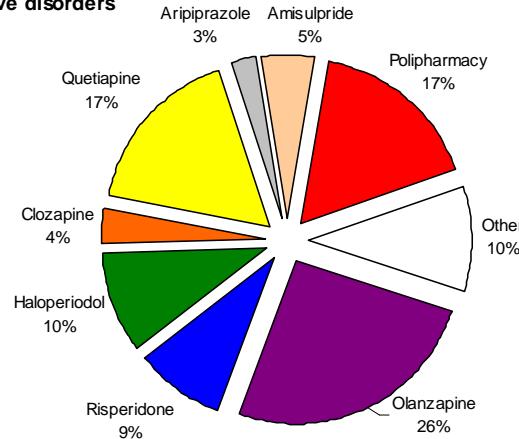
Schizophrenic-like disorders



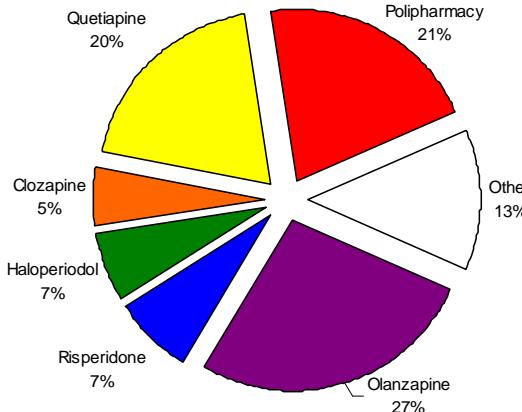
Personality disorders

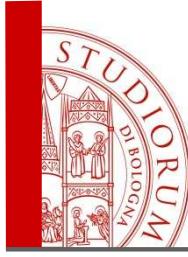


Major depressive disorders



Bipolar disorders

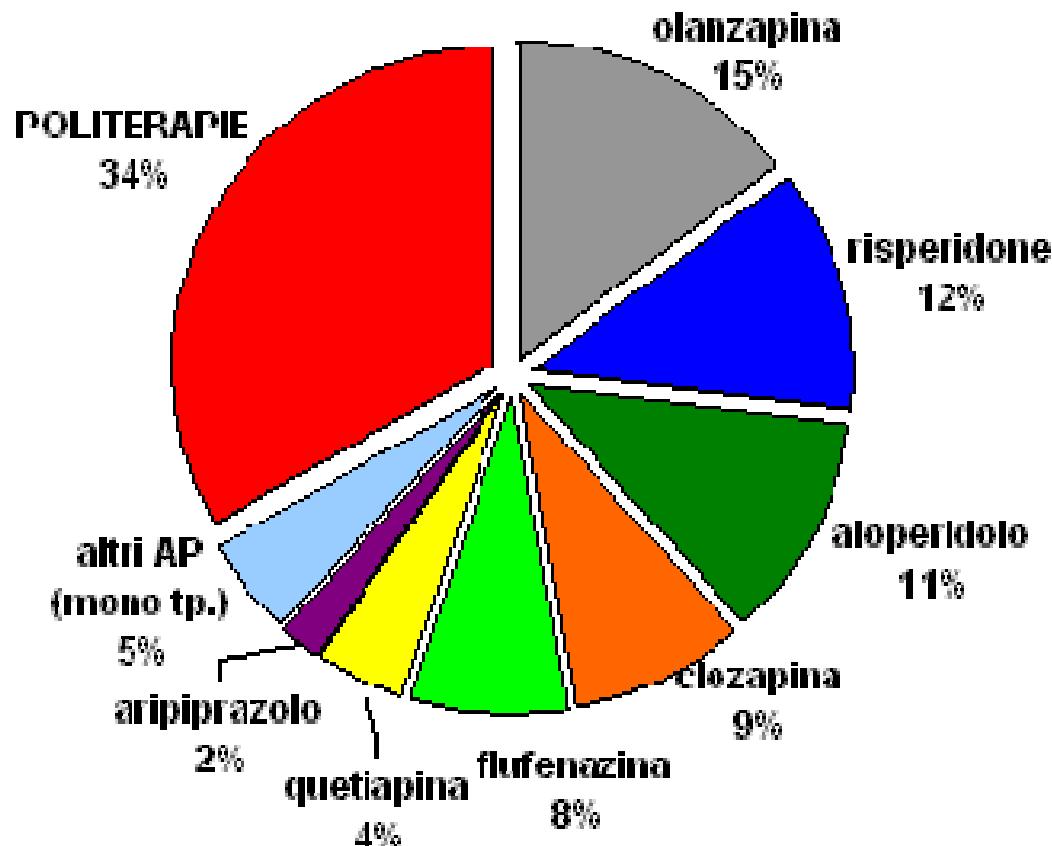


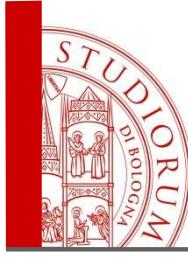


Scelta dell'AP per i pazienti con Psicosi Non Affettive



Psicosi Non Affettive (n=2531)

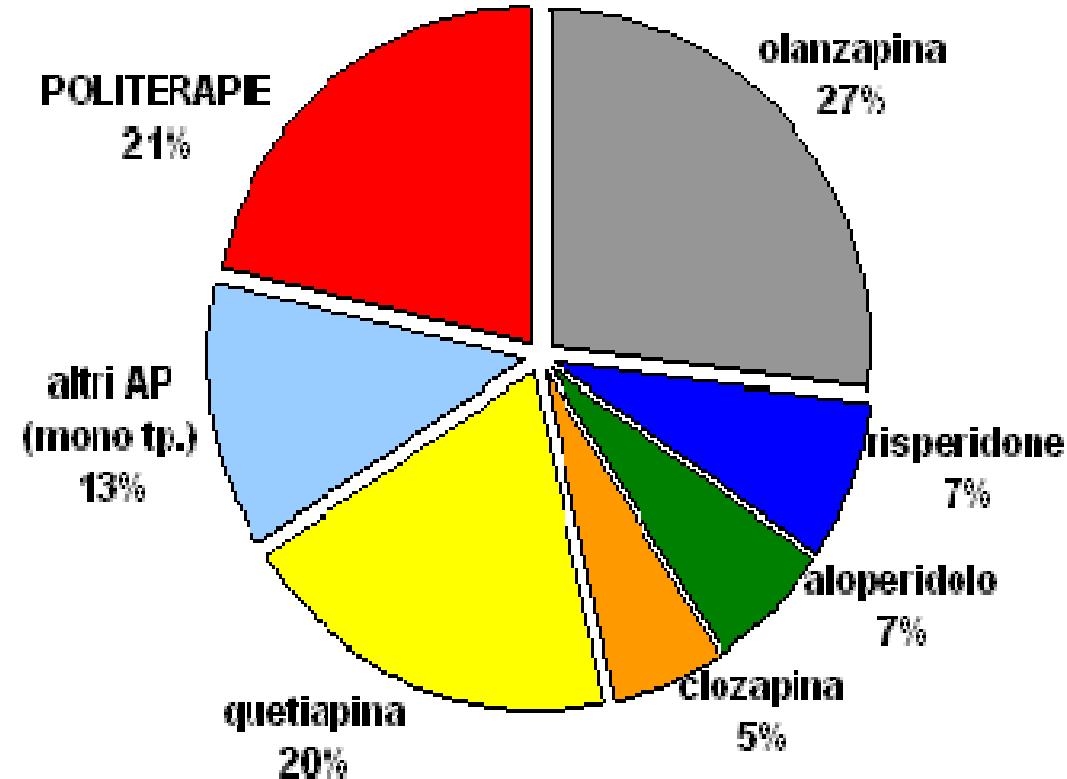


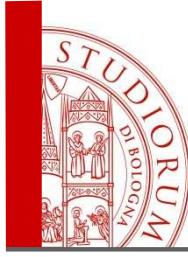


Scelta dell'AP per i pazienti con Disturbi Bipolari



Disturbi Bipolari (n=667)

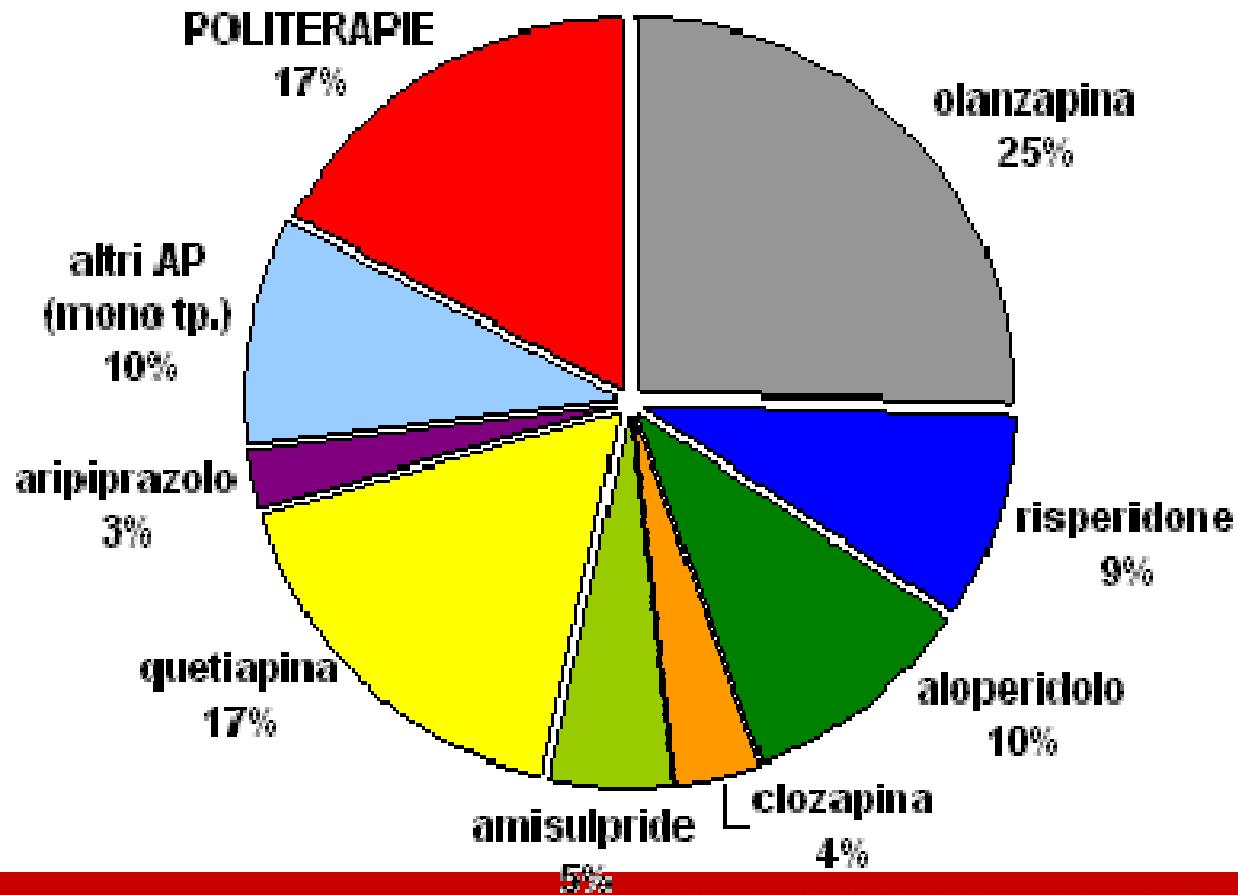


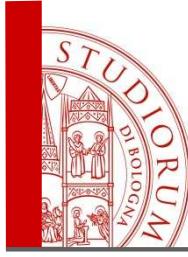


Scelta dell'AP per i pazienti con Disturbi Depressivi Maggiori



Disturbi Depressivi Maggiori (n=1150)

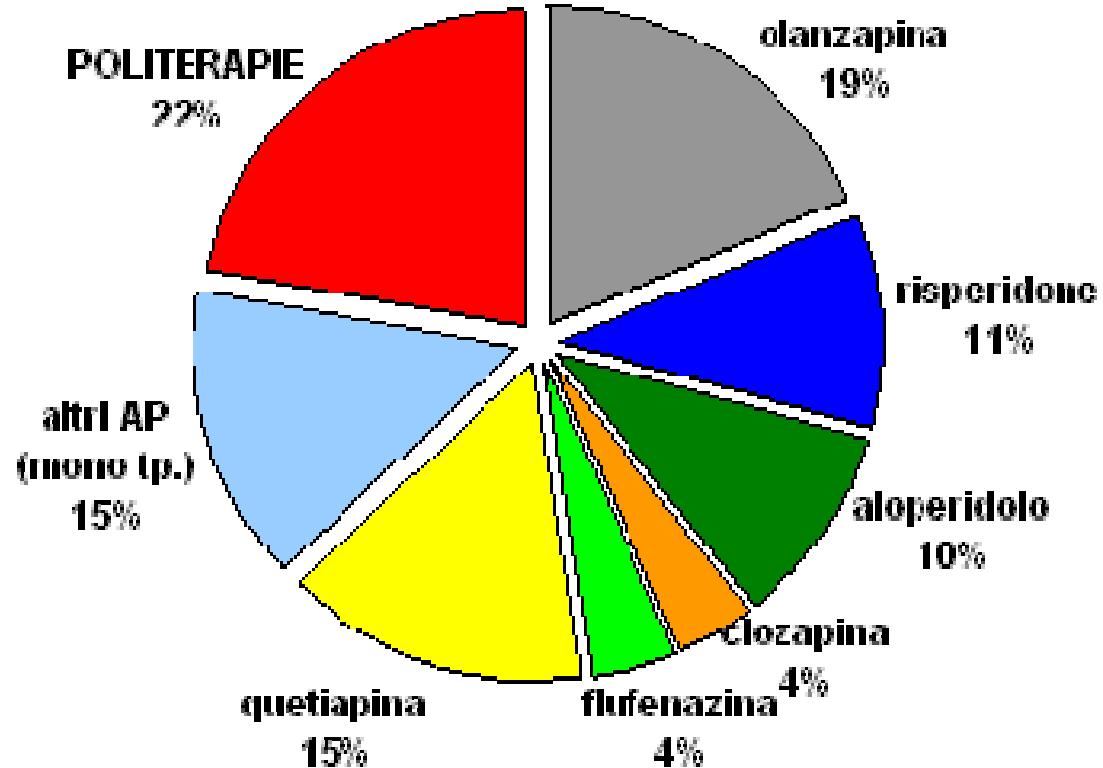




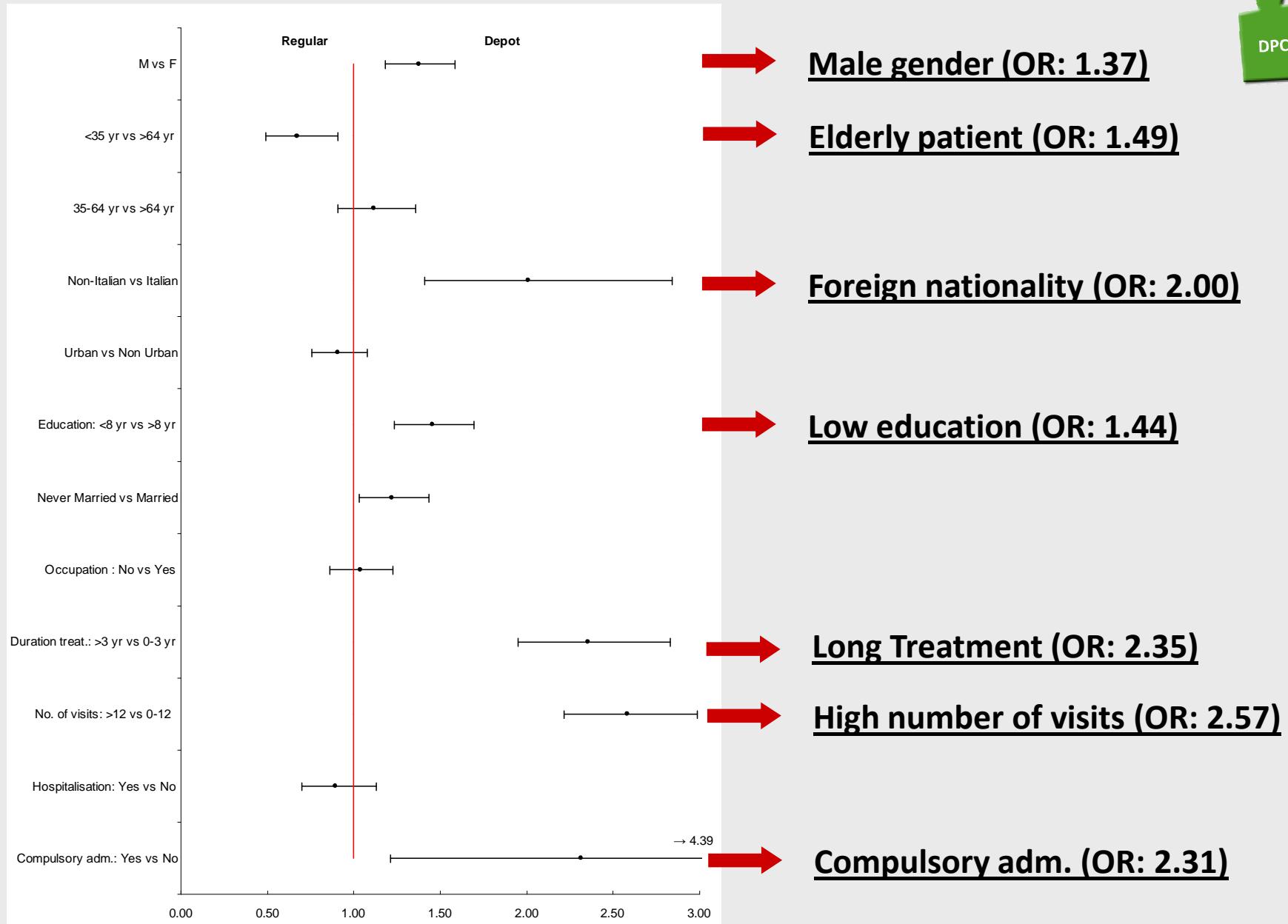
Scelta dell'AP per i pazienti con Disturbi di Personalità



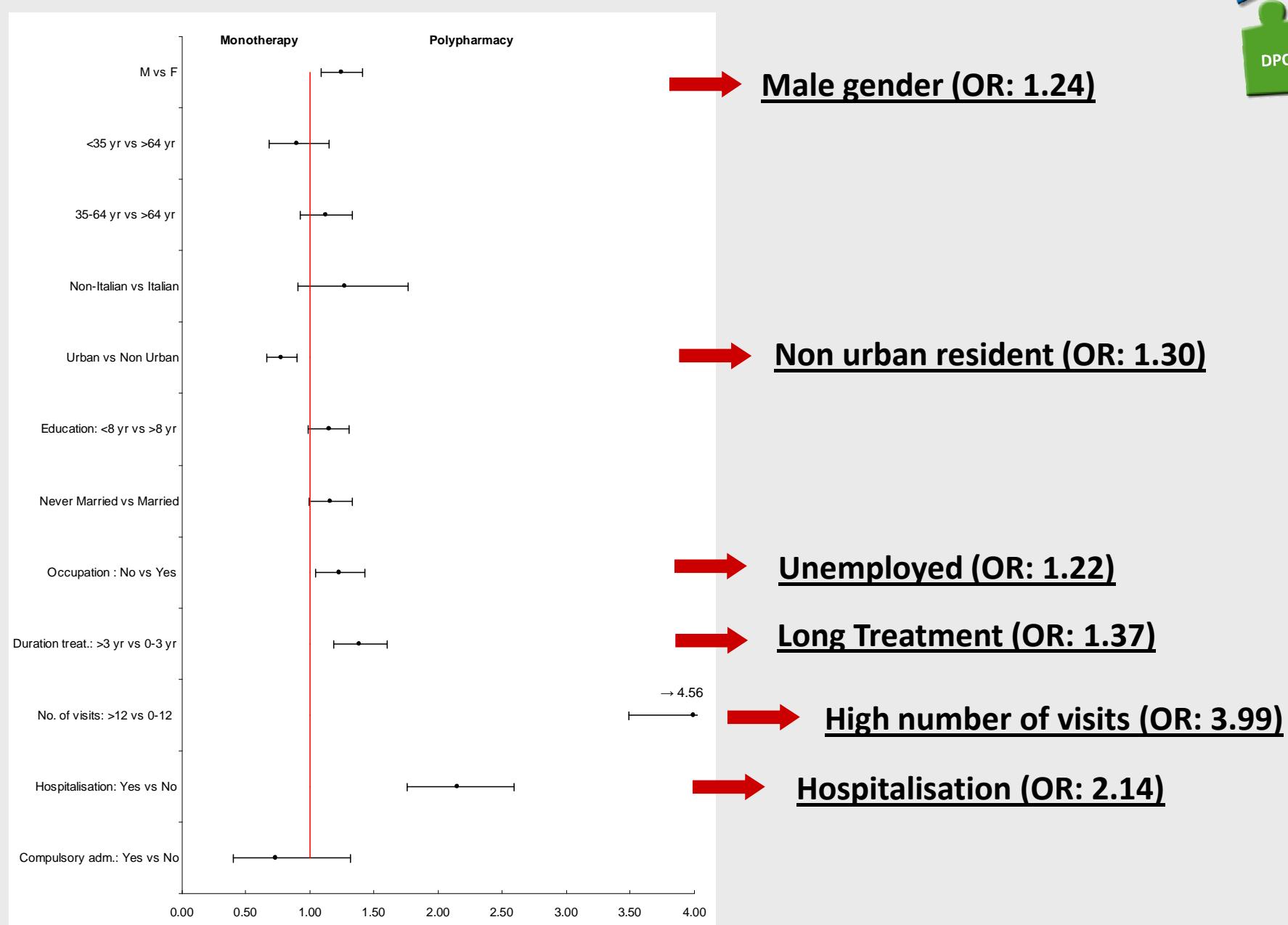
Disturbi Personalità (n=805)



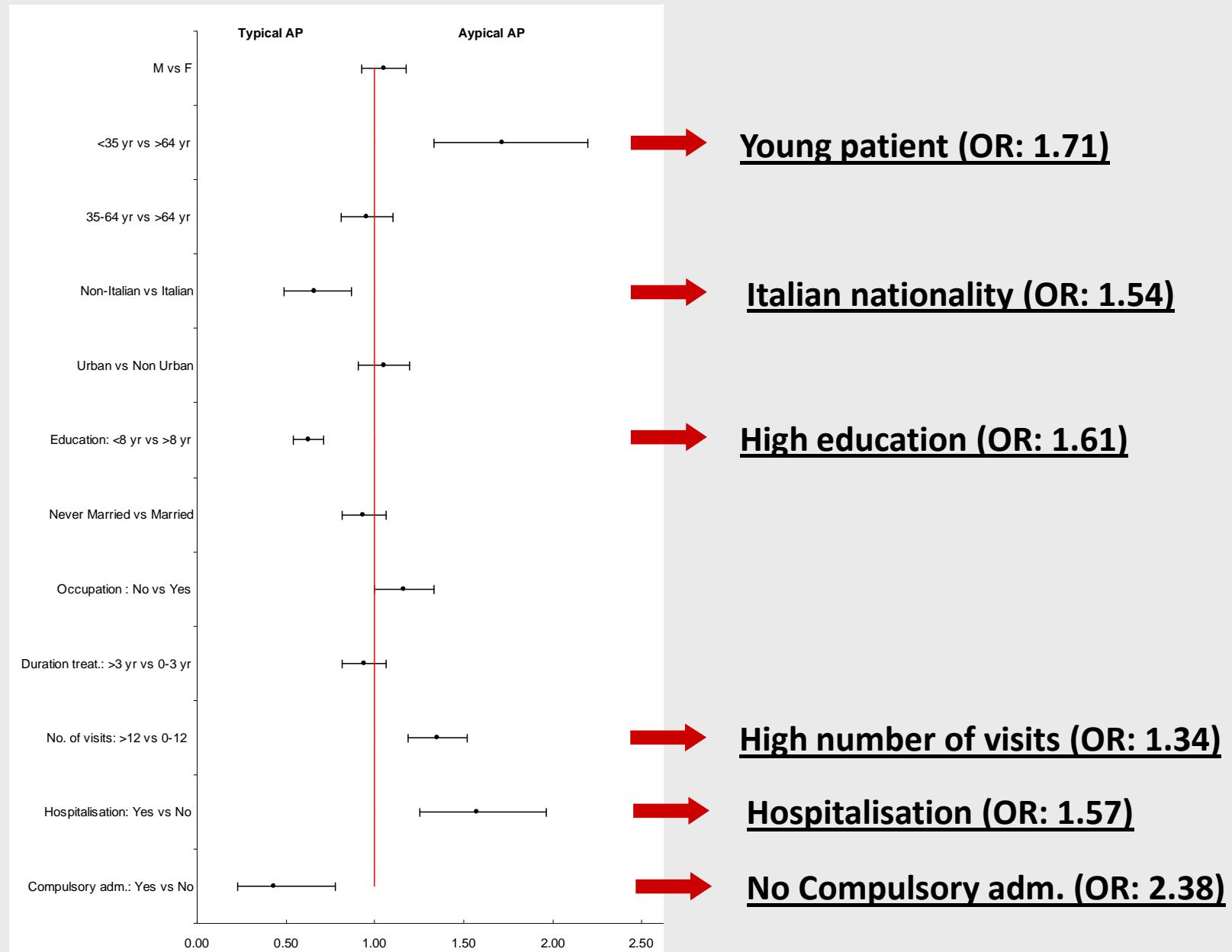
Predictors for Depot administration

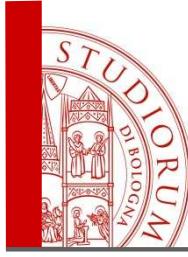


Predictors for Polypharmacy



Predictors for Atypical AP





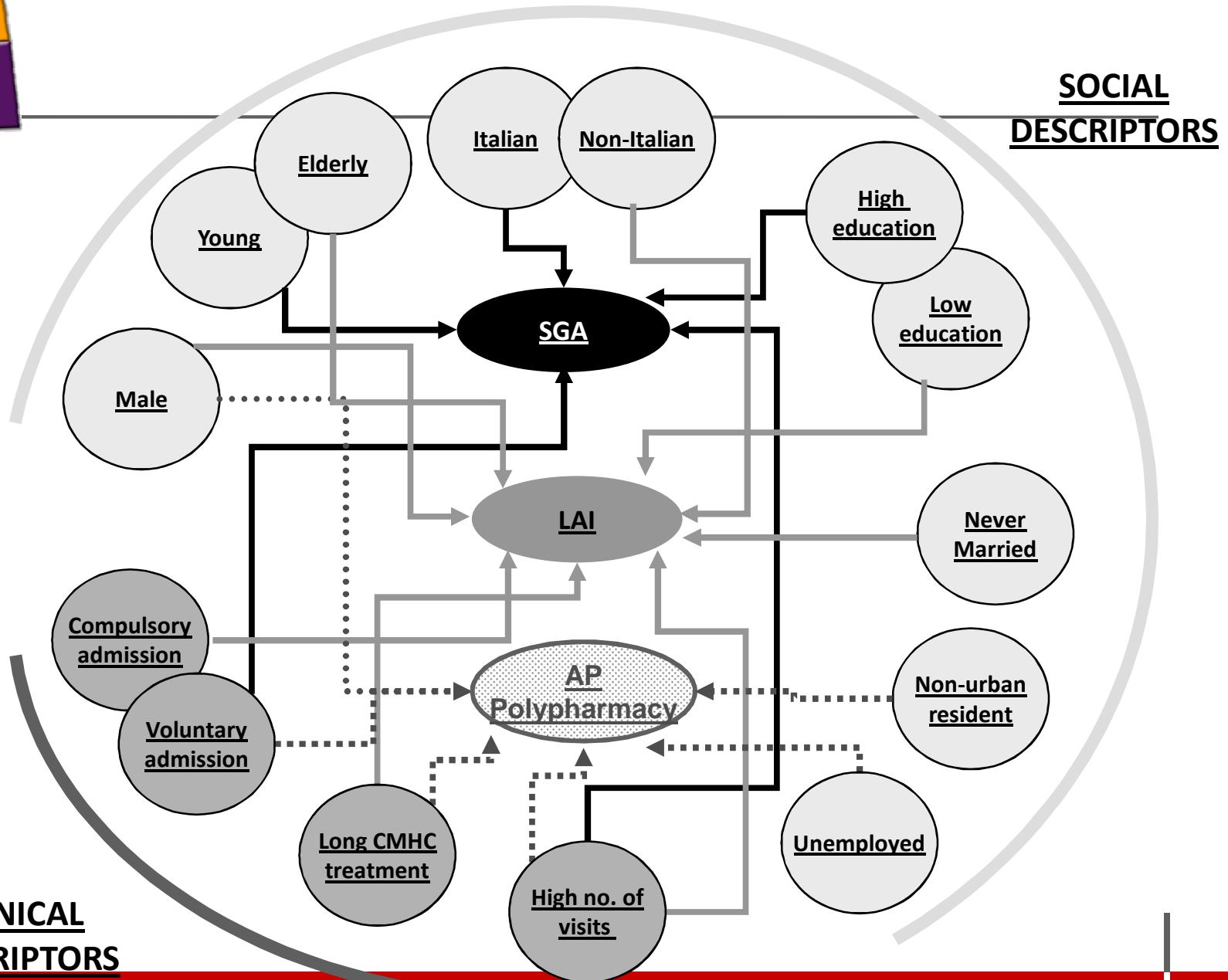
Summary of Results

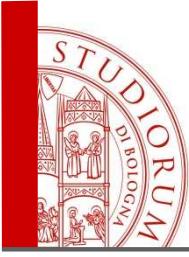


- Depot formulations and polypharmacy strategies were mainly used in patients with the most severe psychoses (long treatment) and frequent visits
- Depot prescribing was more frequent for male, elderly, foreign and low-education subjects
- Polypharmacy was chosen in male, non-urban resident and unemployed patients
- Atypical APs were preferred to Typical in young Italian patient with high education and who required several visits and hospitalisations

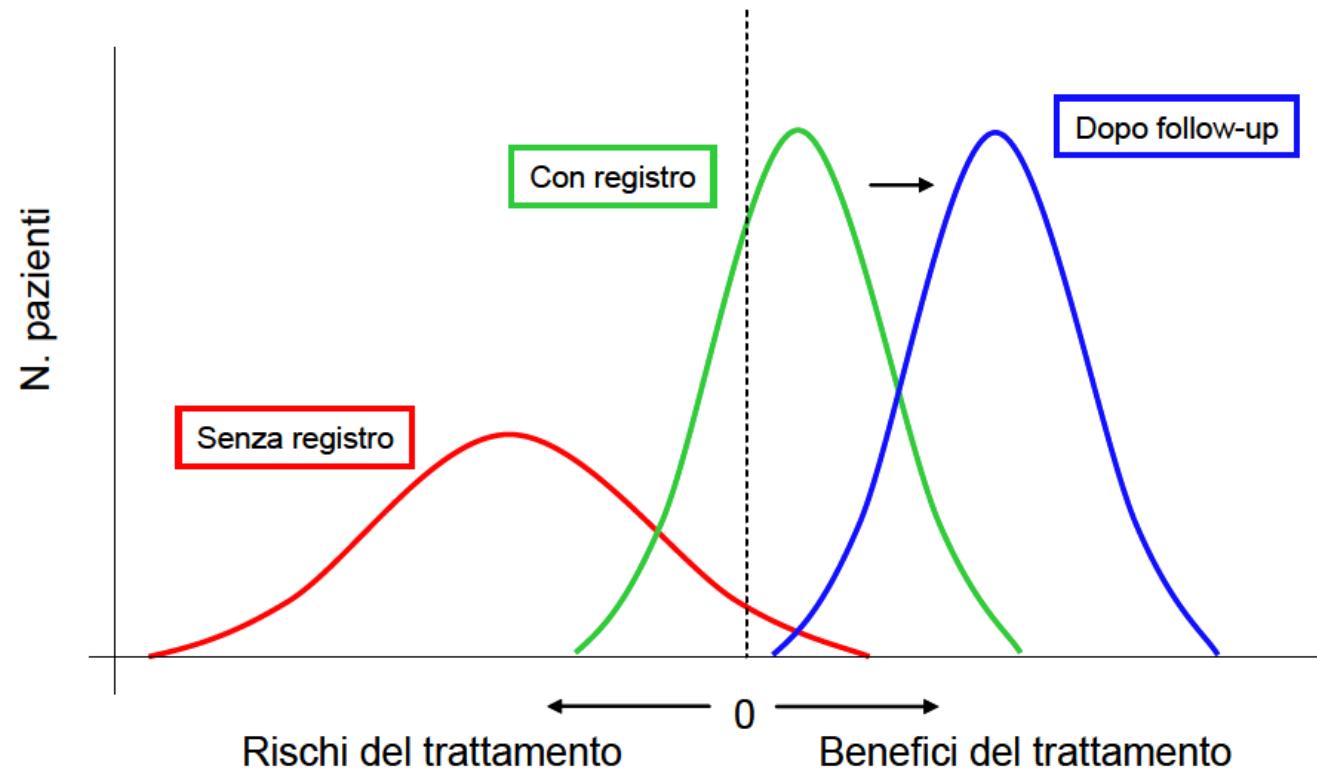


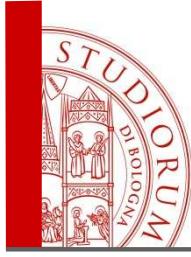
CLINICAL DESCRIPTORS





4. Studi sui registri

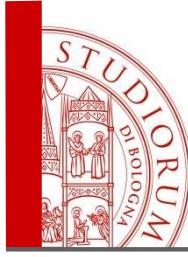




Il Registro SM – Emilia Romagna



**MONITORAGGIO REGIONALE
DEI TRATTAMENTI
IMMUNOMODULANTI E
IMMUNOSOPPRESSIVI
PER LA SCLEROSI MULTIPLA**

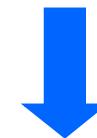


Obiettivo

Osservare le modalità di utilizzo e gli effetti (efficacia e tollerabilità)
dei diversi DMDs nella pratica clinica



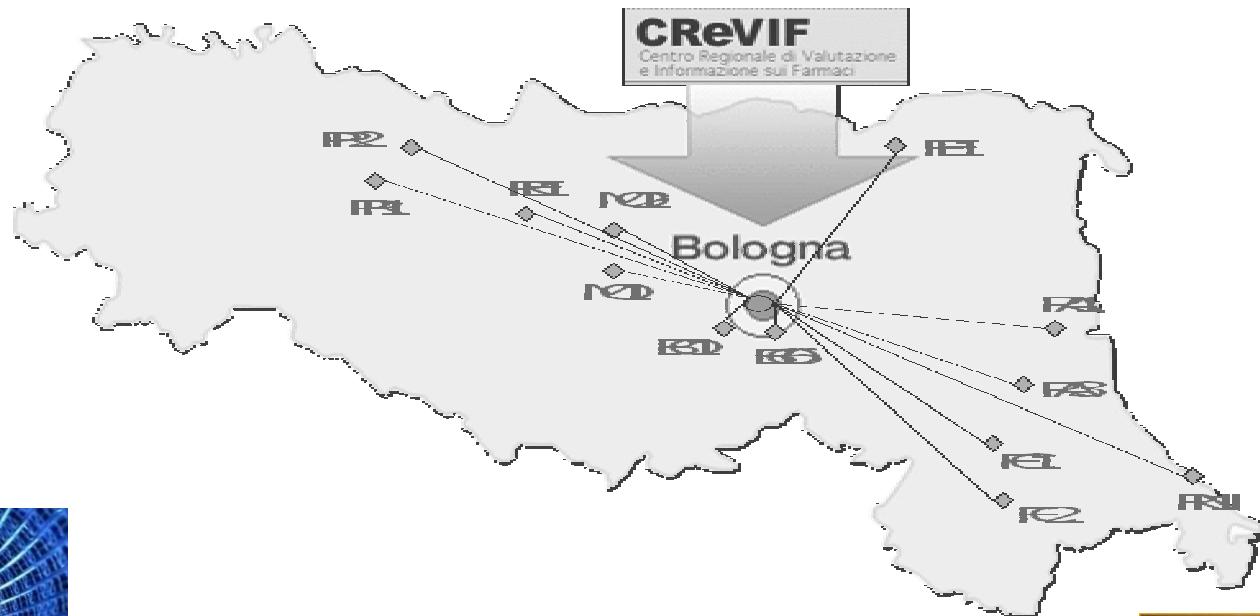
Individuare i determinanti di scelta operati dai clinici



Armonizzare e ottimizzare la terapia della SM



Rete dei Centri SM Regionali (Emilia Romagna)



Condivisione dati tramite protocollo ftp protetto



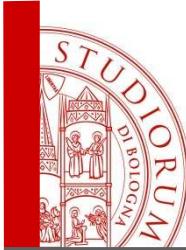
Incontri periodici con i neurologi



RISULTATI – V Report

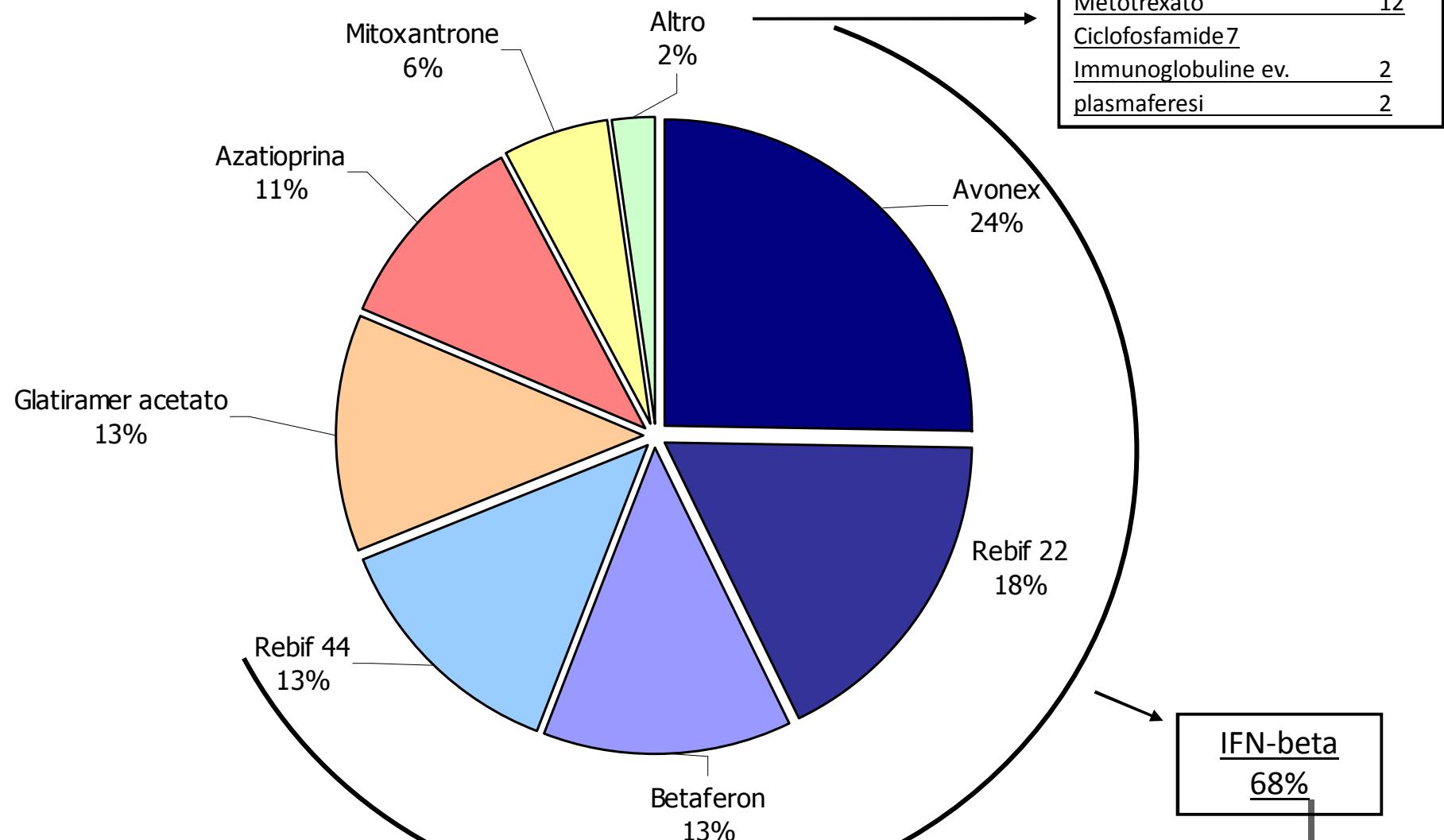
Caratteristiche dei pazienti

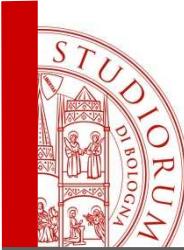
F:M	957:402	70:30
Classi di età al 2008	Presente di bande	750
minore di 30	109	8%
30-39	372	27%
40-49	442	33%
50-59	292	21%
60 e oltre	144	11%
Sottotipo di SM alla diagnosi	No lesioni	44
RR (Relapsing Remitting)	750	55%
SP (Secondary Progressive)	73	5%
PP (Primary Progressive)	27	2%
RP (Relapsing Progressive)	103	8%
dato mancante	406	30%
Classi EDSS alla diagnosi	dato mancante	267
minore di 1	93	7%
1-1,5	299	22%
2-2,5	206	15%
3-3,5	115	8%
4 e oltre	120	9%
dato mancante	526	39%



RISULTATI – V Report

Scelta del Trattamento





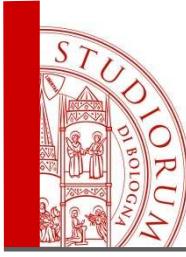
RISULTATI – V Report

Scelta del Farmaco in relazione ai parametri clinici

Farmaco	Sottotipo SM		Grado di disabilità		Esito MRI cerebrale	
	forme progr sul totale	OR [IC 95%]	EDSS ≥ 3 sul totale	OR [IC 95%]	lesioni attive sul totale	OR [IC 95%]
Avonex	9/243	Ref	30/230	Ref	65/193	Ref
Rebif 22	7/162	1,17 [0,39-3,53]	25/154	1,29 [0,70-2,38]	67/132	2,03 [1,26-3,28]*
Rebif 44	6/115	1,43 [0,44-4,53]	32/108	2,81 [1,54-5,15]*	47/96	1,89 [1,11-3,21]*
Betaferon	31/129	8,22 [3,59-19,37]*	51/126	4,53 [2,60-7,92]*	39/83	1,75 [1,00-3,05]*
Glatiramer acetato	7/134	1,43 [0,47-4,32]	29/129	1,93 [1,06-3,53]*	47/94	1,97 [1,16-3,36]*
Mitoxantrone	26/53	23,21 [9,19-60,15]*	26/52	6,67 [3,26-13,70]*	14/40	1,06 [0,49-2,29]
Azatioprina	32/62	27,73 [11,33-69,79]*	23/45	6,97 [3,28-14,90]*	16/50	0,93 [0,45-1,89]

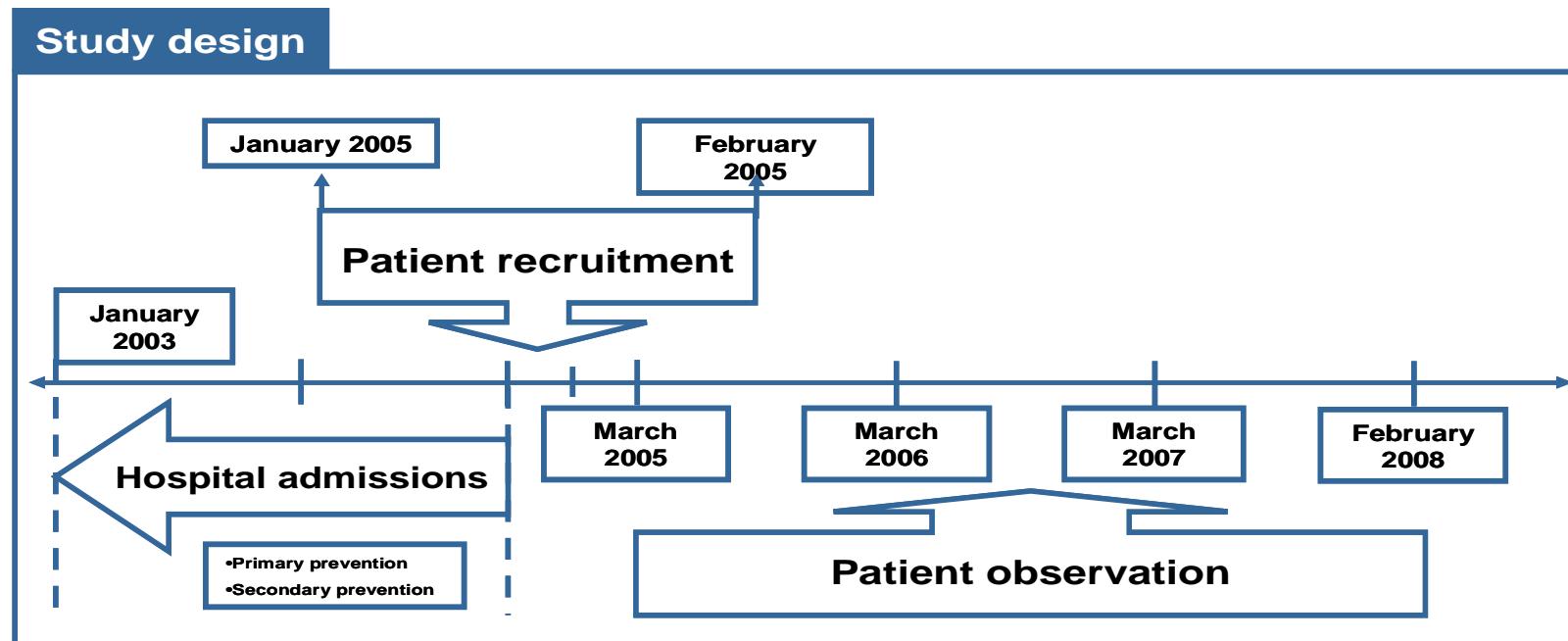
*dato statisticamente significativo

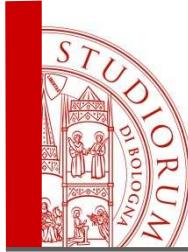
Non-Adjusted Odds Ratio: una misura della probabilità che un evento si verifichi rispetto alla probabilità che non si verifichi



5. Studi di outcome

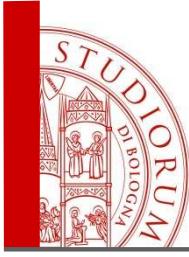
Tipologia di dati: prescrizione con identificativo paziente + ospedalizzazioni





Variables influencing occurrence of cardiovascular events

		Adjusted OR	CI Wald (95%)
Lack of Adherence^a	strongly non adherent	1.19	1.15-1.23
	slightly non adherent	1.25	1.21-1.30
	highly variable	1.69	1.62-1.77
Male gender^b		1.39	1.35-1.43
Age class^c	50-65	1.30	1.20-1.41
	65-80	2.04	1.88-2.20
	>80	2.78	2.56-3.03
Previous CV events^d		2.54	2.46-2.62
Diabetes^e		1.36	1.31-1.40
Angina, hypertension, heart failure^f		2.77	2.65-2.89
Thrombosis^g		1.87	1.81-1.93

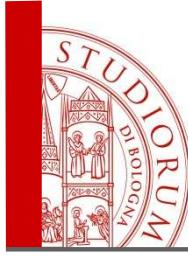


Conclusions

Only 24% of statin recipients adhered to treatment over a 3-year period.

Adherent patients had reduced lower odds of CV events irrespective of risk factors by an average of 30%, in comparison with non-adherent patients; paradoxically, among non-adherent patients, those strongly non-adherent had the lowest odds.

Rather than on strongly non-adherent patients, who probably include many subjects not requiring pharmacological treatment, efforts to improve adherence should focus on “slightly non adherent” and “highly variable” statin recipients (41%), who have the highest odds of CV events.



Take home messages

- La disponibilità di dati locali, regionali, nazionali e sovranazionali a fini clinici e amministrativi è sempre maggiore e di migliore qualità
- La ricerca dovrebbe continuare ad esplorare queste fonti, sviluppando metodi di analisi volti a valutare l'appropriatezza d'uso dei farmaci
- I metodi dovrebbero essere facilmente riproducibili per consentire un utilizzo routinario da parte dei *data owners* (ASL, regioni, AIFA, SIMG,).
- Metodi più complessi potrebbero essere utili per validare i precedenti (es. analisi di aderenza con contapillole elettronici).