

LA PREVENZIONE CARDIOVASCOLARE EFFICACE:  
LA DISTANZA FRA EVIDENZE SCIENTIFICHE E REALTÀ CLINICA.

UNA PROPOSTA PER IL SSN

Firenze, 12 settembre 2011

**Health technology assessment e aderenza alla terapia**

# **Il ruolo dei database amministrativi**

Giovanni Corrao





**Premessa** (di cosa stiamo parlando?)



**Esperienze** (cosa abbiamo imparato?)



**Nuove sfide** (cosa stiamo facendo?)

## Uso e impatto dei farmaci nella pratica clinica corrente Il modello osservazionale



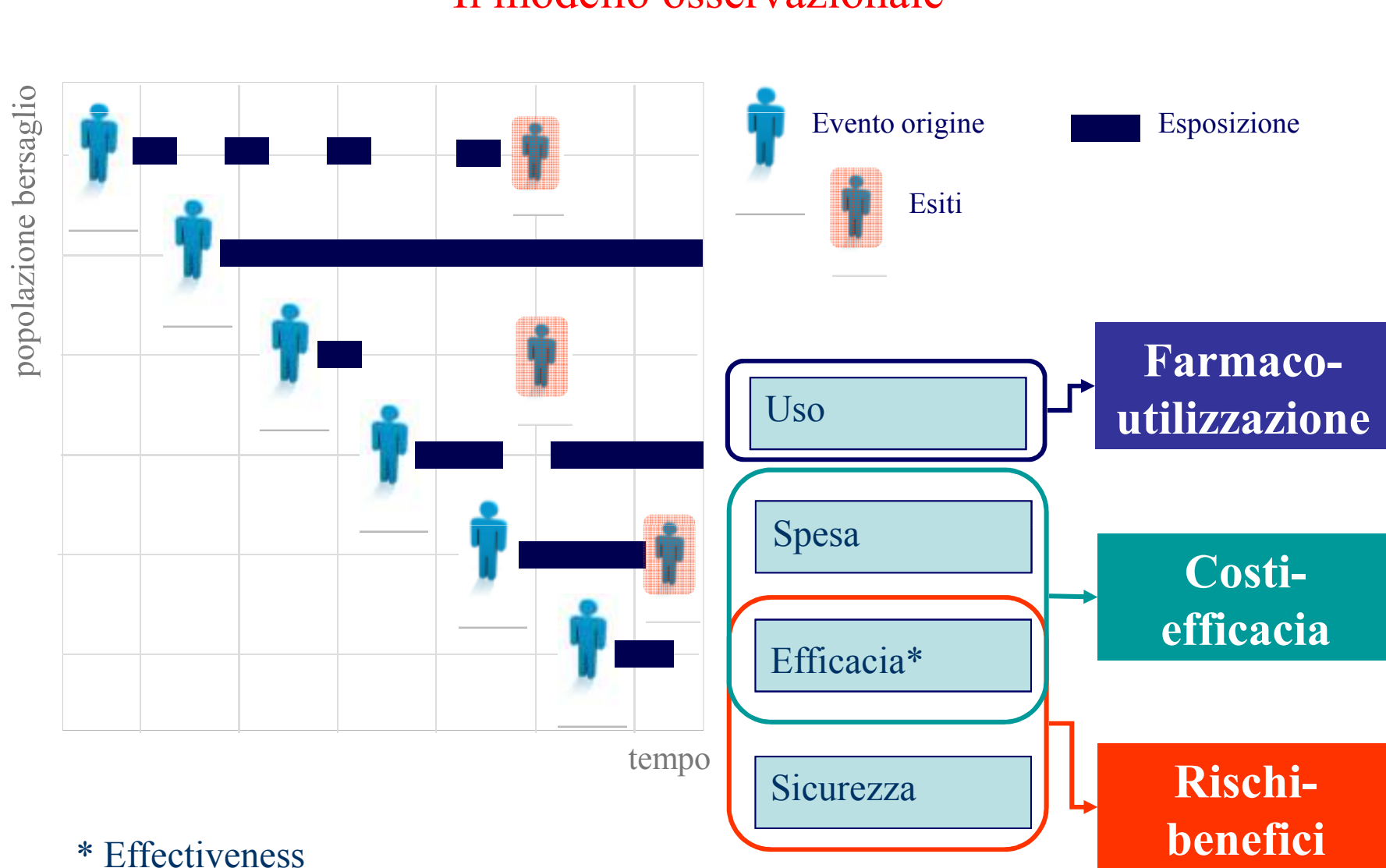
**Premessa**



Esperienze



Nuove sfide



## Healthcare utilization databases e Servizio Sanitario Nazionale (SSN)



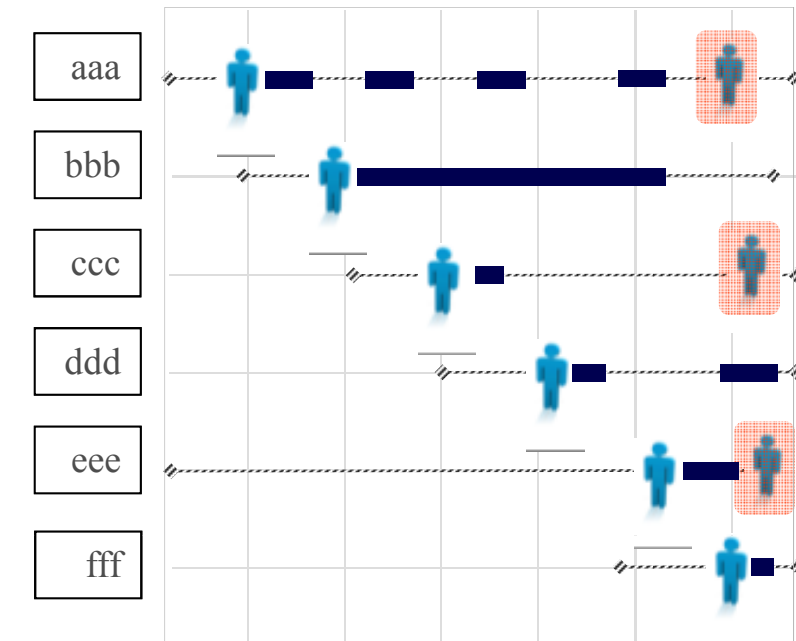
### Premessa



Esperienze



Nuove sfide



Codice identificativo

inizio fine

record linkage



Archivio prescrizioni



Archivio assistiti



Decessi



Ammissioni ospedaliere



Visite ambulatoriali

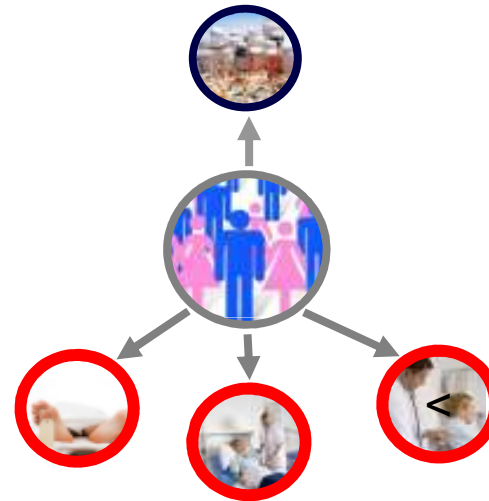
**FORZA**

**Healthcare  
utilization databases**

**DEBOLEZZA**

**Premessa**

- Dati disponibili
- Esperienze
- Popolazioni ampie e ben definite
- Nuove sfide
- Uso e impatto dei farmaci nella pratica clinica corrente



- Solo farmaci in classe A
- Prescrizione ≠ uso
- Incerta qualità dei dati
- Carenza di dati sul profilo clinico dei pazienti



## Generating signals and confirming evidence in pharmacoepidemiology: our experiences

### Antihypertensive therapy

- Corrao G, Mancia G, *et al.* Cardiovascular protection by initial and subsequent combination of antihypertensive drugs in daily life practice. *Hypertension* 2011;(in press)
- Mancia G, Corrao G, *et al.* Heterogeneity in antihypertensive treatment discontinuation between drugs belonging to the same class. *J Hypertens* 2011;29:1012-8
- Corrao G, Mancia G, *et al.* Better compliance to antihypertensive medications reduces cardiovascular risk. *J Hypertens* 2011;29:610-8
- Corrao G, Mancia G, *et al.* Reduced discontinuation of antihypertensive treatment by two-drug combination as first step. Evidence from daily life practice. *J Hypertens* 2010;28:1584-90
- Nicotra F, Wettermark B, Sturkenboom MC, *et al.* Management of antihypertensive drugs in three European countries. *J Hypertens* 2009;27:1917-22
- Corrao G, Mancia G, *et al.* Do socioeconomic disparities affect accessing and keeping antihypertensive drug therapy? Evidence from an Italian population-based study. *J Hum Hypertens* 2009;23:238-44
- Corrao G, Mancia G, *et al.* Discontinuation of and changes in drug therapy for hypertension among newly-treated patients: a population-based study in Italy. *J Hypertens* 2008;26:819-24

### Lipid lowering therapy

- Corrao G, Catapano A, Mancia G *et al.* Cost-effectiveness of enhancing adherence to therapy with statins in the setting of primary cardiovascular prevention. Evidence from an empirical approach based on administrative databases. *Atherosclerosis* 2011 Apr 22 [Epub ahead of print]
- Corrao G, Catapano A, Mancia G *et al.* Results of a retrospective database analysis of adherence to statin therapy and risk of nonfatal ischemic heart disease in daily clinical practice in Italy. *Clin Ther* 2010;32:300-10

### Therapy for diabetes

- Corrao G, Romio SA, Zambon A, *et al.* Multiple outcomes associated with use of metformin and sulphonylurea in type 2 diabetes: a population-based cohort study in Italy. *Eur J Clin Pharmacol* 2011;67:289-99

### Therapy for osteoporosis

- Zambon A, Baio G, Mazzaglia G, *et al.* Discontinuity and failures of therapy with bisphosphonates: joint assessment of predictors with multi-state models. *Pharmacoepidemiol Drug Saf* 2008;17:260-9

### Hormonal replacement therapy

- Corrao G, Zambon A, Nicotra F, *et al.* Issues concerning the use of hormone replacement therapy and risk of fracture: a population-based, nested case-control study. *Br J Clin Pharmacol* 2008;65:123-9

- Corrao G, Zambon A, Conti V, *et al.* Menopause hormone replacement therapy and cancer risk: an Italian record linkage investigation. *Ann Oncol* 2008;19:150-5
- Corrao G, Zambon A, Nicotra F, *et al.* Persistence with oral and transdermal hormone replacement therapy and hospitalisation for cardiovascular outcomes. *Maturitas* 2007;57:315-24

### Miscellaneous on drug safety

- Imberti D, Bianchi C, Zambon A, Parodi A, Merlino L, Gallerani M, Corrao G. Venous thromboembolism after major orthopaedic surgery: a population-based cohort study. *Intern Emerg Med* 2011 Mar 26 [Epub ahead of print]
- Zambon A, Polo Friz H, Contiero P, Corrao G. Effect of macrolide and fluoroquinolone antibacterials on the risk of ventricular arrhythmia and cardiac arrest: an observational study in Italy using case-control, case-crossover and case-time-control designs. *Drug Saf* 2009;32:159-67
- Corrao G, Zambon A, Bertù L, *et al.* Evidence of tendinitis provoked by fluoroquinolone treatment: a case-control study. *Drug Saf* 2006;29:889-96
- Corrao G, Zambon A, Faini S, *et al.* Short-acting inhaled beta-2-agonists increased the mortality from chronic obstructive pulmonary disease in observational designs. *J Clin Epidemiol* 2005;58:92-7
- Corrao G, Zambon A, Bertù L, *et al.* Lipid lowering drugs prescription and the risk of peripheral neuropathy: an exploratory case-control study using automated databases. *J Epidemiol Community Health* 2004;58:1047-51

### Miscellaneous on methods

- Coloma PM, Schuemie MJ, Trifirò G, *et al.* on behalf of the EU-ADR consortium. Combining electronic healthcare databases in Europe to allow for large-scale drug safety monitoring: the EU-ADR Project. *Pharmacoepidemiol Drug Saf* 2011;20:1-11
- Corrao G, Cesana GC, Merlino L. Studies of pharmacoepidemiology by linking electronic healthcare databases from the Italian Lombardia Region. *BioMedical Statistics and Clinical Epidemiology* 2008;2:117-25
- Fornari C, Madotto F, Demaria M, *et al.* [Record-linkage procedures in epidemiology: an Italian multicentre study]. *Epidemiol Prev* 2008;32(3 Suppl):79-88
- Simonato L, Baldi I, Balzi D, *et al.* [Objectives, tools and methods for an epidemiological use of electronic health archives in various areas of Italy]. *Epidemiol Prev* 2008;32(3 Suppl):5-14
- Bagnardi V, Botteri E, Corrao G. Empirical-Bayes adjustment improved conventional estimates in postmarketing drug-safety studies. *J Clin Epidemiol* 2006;59:1162-8
- Corrao G, Botteri E, Bertù L, *et al.* Exploring the effect of transient exposure on the risk of acute events by means of time-window designs: an application to fluoroquinolone antibacterials and arrhythmia. *Pharmacoepidemiol Drug Saf* 2006;15:31-7
- Corrao G, Botteri E, Bagnardi V, *et al.* Generating signals of drug-adverse effects from prescription databases and application to the risk of arrhythmia associated with antibacterials. *Pharmacoepidemiol Drug Saf* 2005;14:31-40

## Cosa abbiamo imparato?

- Farmacoutilizzazione (dimensione della scarsa aderenza)
- Impatto clinico (scarsa aderenza e rischio cardiovascolare)
- Costi-efficacia (degli interventi di miglioramento dell'aderenza)



Premessa



**Esperienze**



Nuove sfide

## Compliance entro un anno dall'inizio della terapia



	<b>ADERENZA</b>	<b>PERSISTENZA</b>
	Proporzione di giorni farmaco disponibile	Proporzione di pazienti liberi da episodi di discontinuità (più di 3 mesi senza terapia)

**Anti-ipertensivi** <sup>1</sup>

**50 %**

**55 %**

**Ipolipemizzanti** <sup>2</sup>

**40 %**

**50 %**

**Ipoglicemizzanti orali** <sup>3</sup>

**60 %**

**60 %**

**Bifosfonati** <sup>4</sup>

**30 %**

**30 %**

1 Corrao G, Zambon A, Parodi A, et al. I. Discontinuation of and changes in drug therapy for hypertension among newly treated patients: a population-based study in Italy. *J Hypertens* 2008;**26**:819-24

2 Corrao G, Conti V, Merlino L, et al. I. Adherence to statin therapy and risk of nonfatal ischemic heart disease in daily clinical practice. *Clin Ther* 2010;**32**:300-10

3 Corrao G, Romio S, Zambon A, et al. I. Multiple outcomes associated with use of metformin and sulphonylurea in type 2 diabetes: a population-based cohort study in Italy. *Eur J Clin Pharmacol* 2011;**67**:289-99

4 Zambon A, Baio G, Mazzaglia G, et al. Discontinuity and failures of therapy with bisphosphonates: joint assessment of predictors with multi-state models. *Pharmacoepidemiol DS* 2008;**17**:260-9

Premessa

**Esperienze**

→ **Farmacoutilizzazione**

Impatto clinico

Costi-efficacia

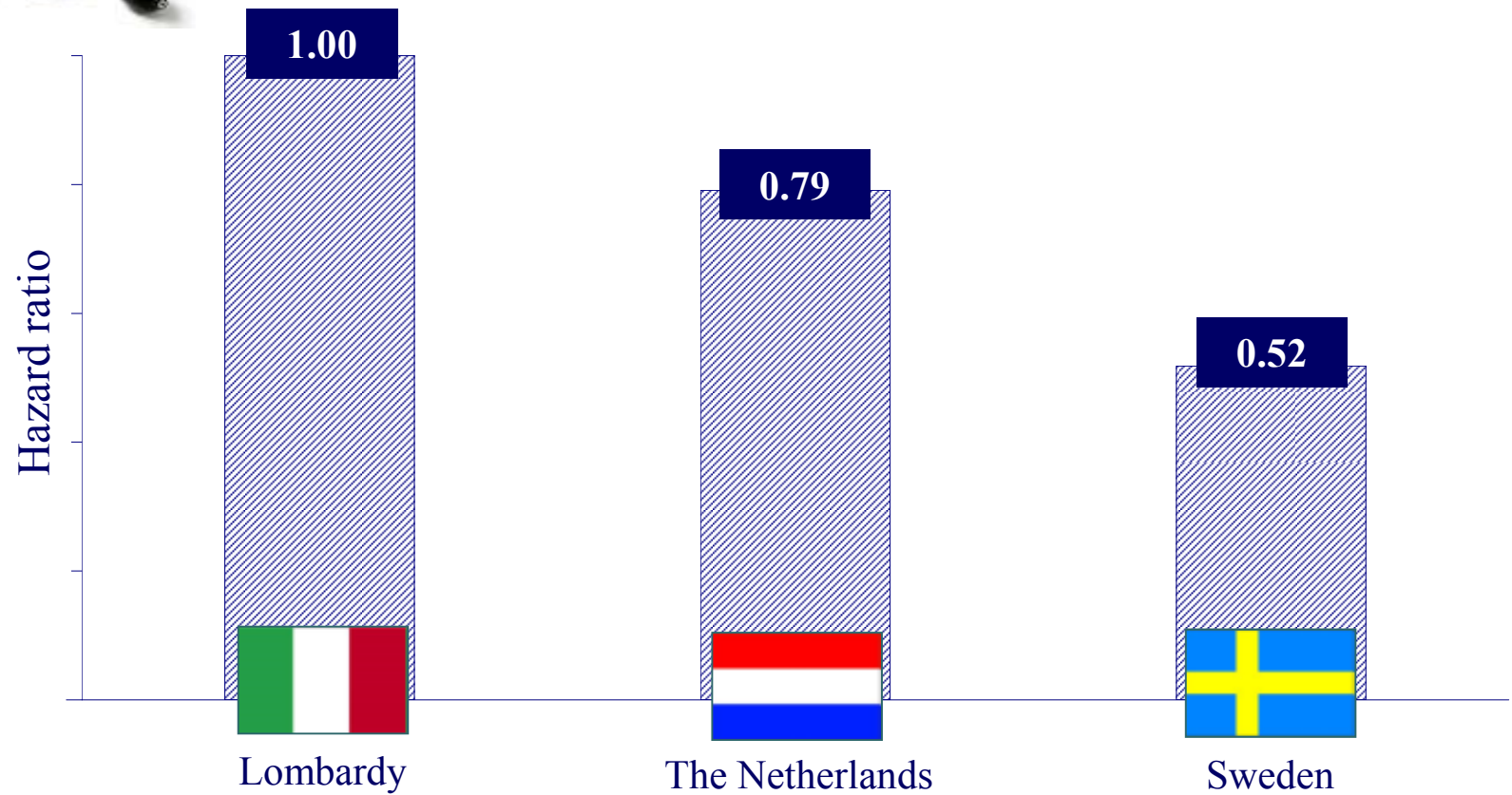
Nuove sfide



## Discontinuità a nove mesi dall'inizio della terapia



### Antihypertensive drugs



Premessa

**Esperienze**

→ **Farmacoutilizzazione**

Impatto clinico

Costi-efficacia

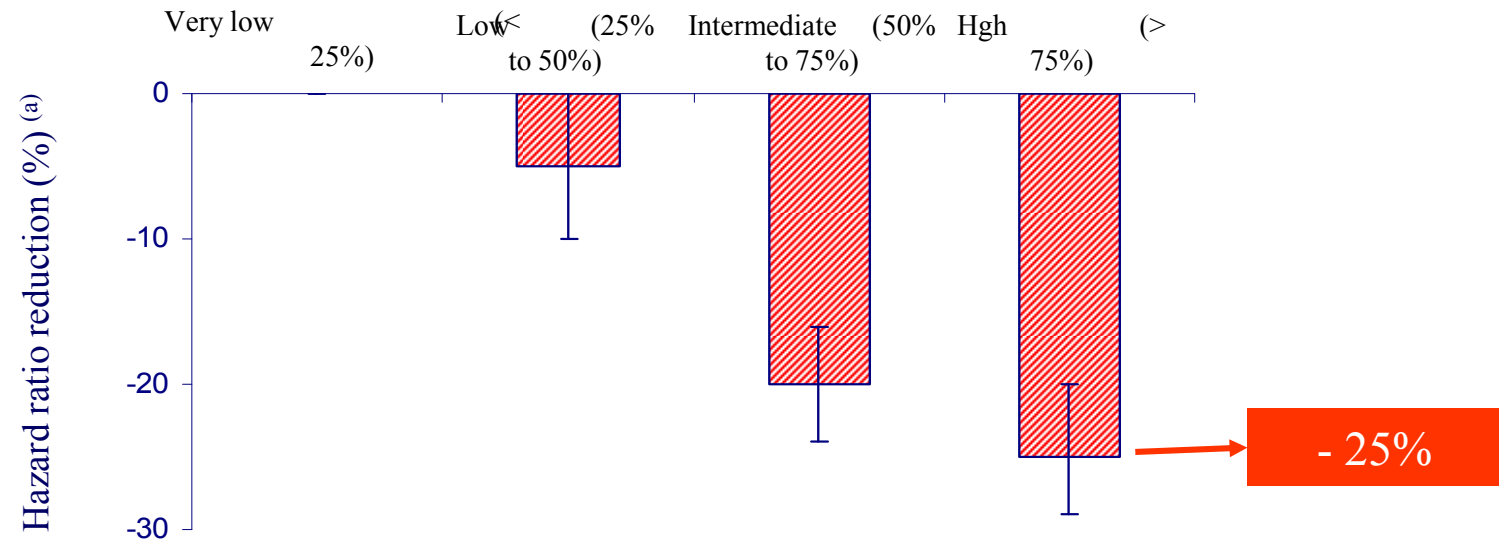
Nuove sfide

## Aderenza e riduzione del rischio di eventi cardiovascolari maggiori



### Antihypertensive drugs

#### Adherence



Estimates are adjusted for prescribed antihypertensive drug regimen at index date (one-drug only or combination of two or more drugs), number of antihypertensive classes dispensed during the follow-up, use of other drugs during follow-up, and categories of Charlson comorbidity index score

Corrao G, Parodi A, Nicotra F, et al. Better compliance to antihypertensive medications reduces cardiovascular risk. *J Hypertens* 2011;29:610-8

Premessa

**Esperienze**

Farmacoutilizzazione

→ **Impatto clinico**

Costi-efficacia

Nuove sfide

## Sono credibili le nostre stime?



Premessa



### Esperienze

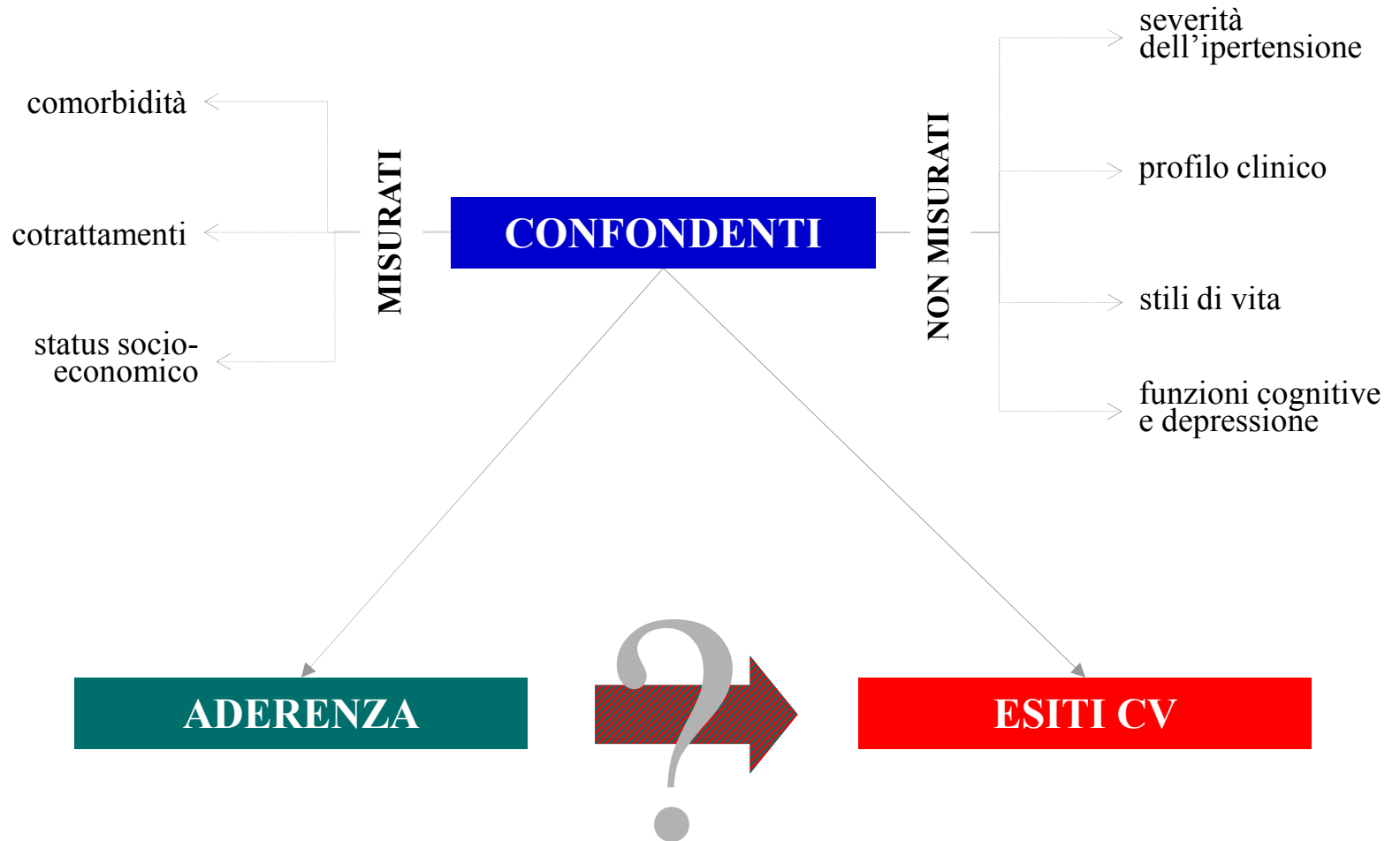
Farmacoutilizzazione

### ➔ Impatto clinico

Costi-efficacia



Nuove sfide



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Corrao G, Zambon A, Parodi A, et al. Do socioeconomic disparities affect accessing and keeping antihypertensive drug therapy? Evidence from an Italian population-based study. *J Hum Hypertens* 2009;**23**:238-44

## Come affrontare il problema della vulnerabilità al confondimento?



Premessa



**Esperienze**

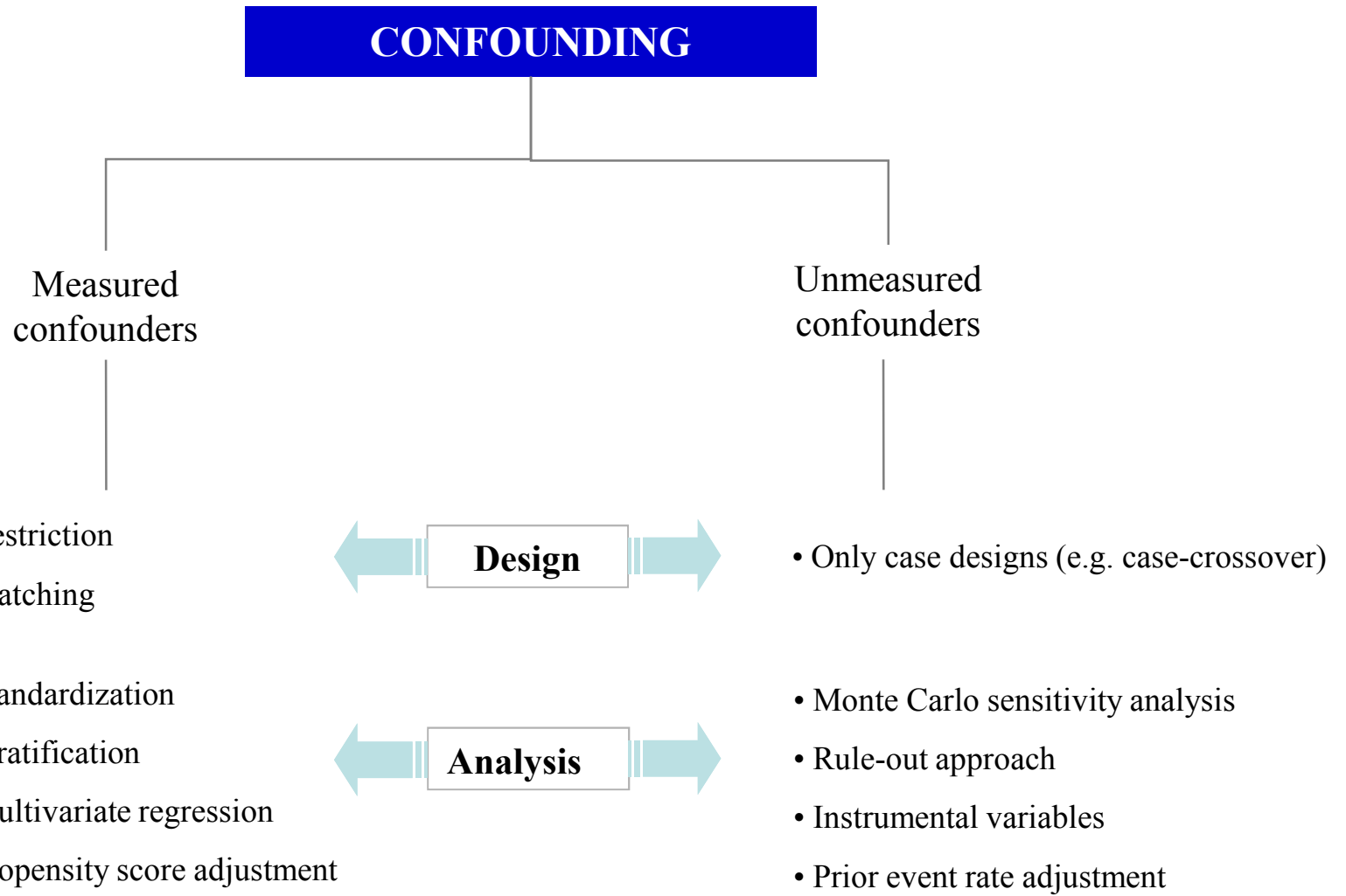
Farmacoutilizzazione

➔ **Impatto clinico**

Costi-efficacia



Nuove sfide

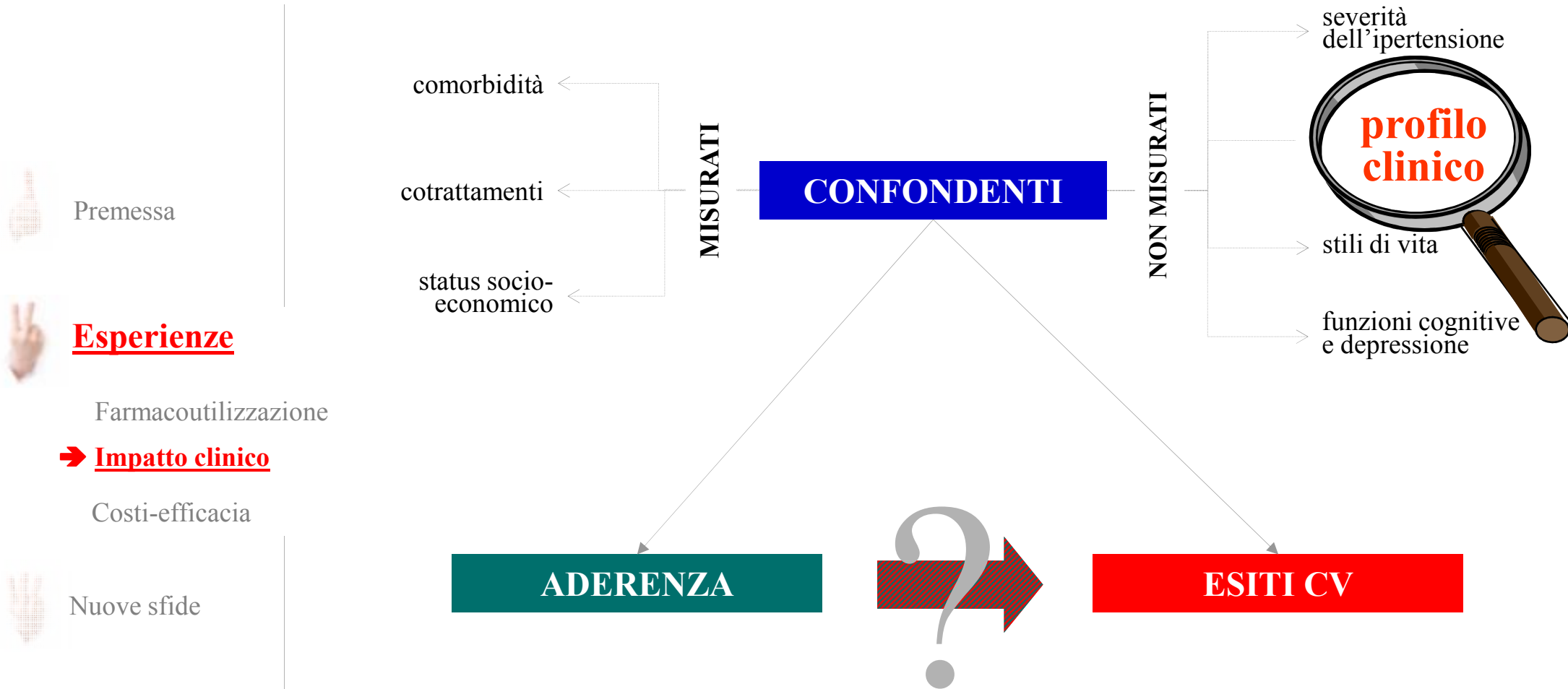


Schneeweiss S. Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. *Pharmacoepidemiol DS* 2006;15:291-303 (modified)





## Sono credibili le nostre stime?



Premessa

**Esperienze**

Farmacoutilizzazione

➔ **Impatto clinico**

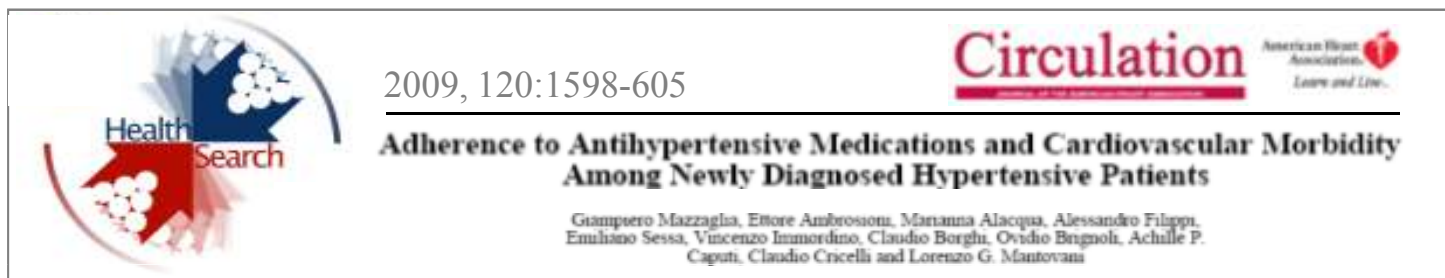
Costi-efficacia

Nuove sfide

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Corrao G, Zambon A, Parodi A, et al. Do socioeconomic disparities affect accessing and keeping antihypertensive drug therapy? Evidence from an Italian population-based study. *J Hum Hypertens* 2009;**23**:238-44





Premessa



**Esperienze**

Farmacoutilizzazione

**→ Impatto clinico**

Costi-efficacia



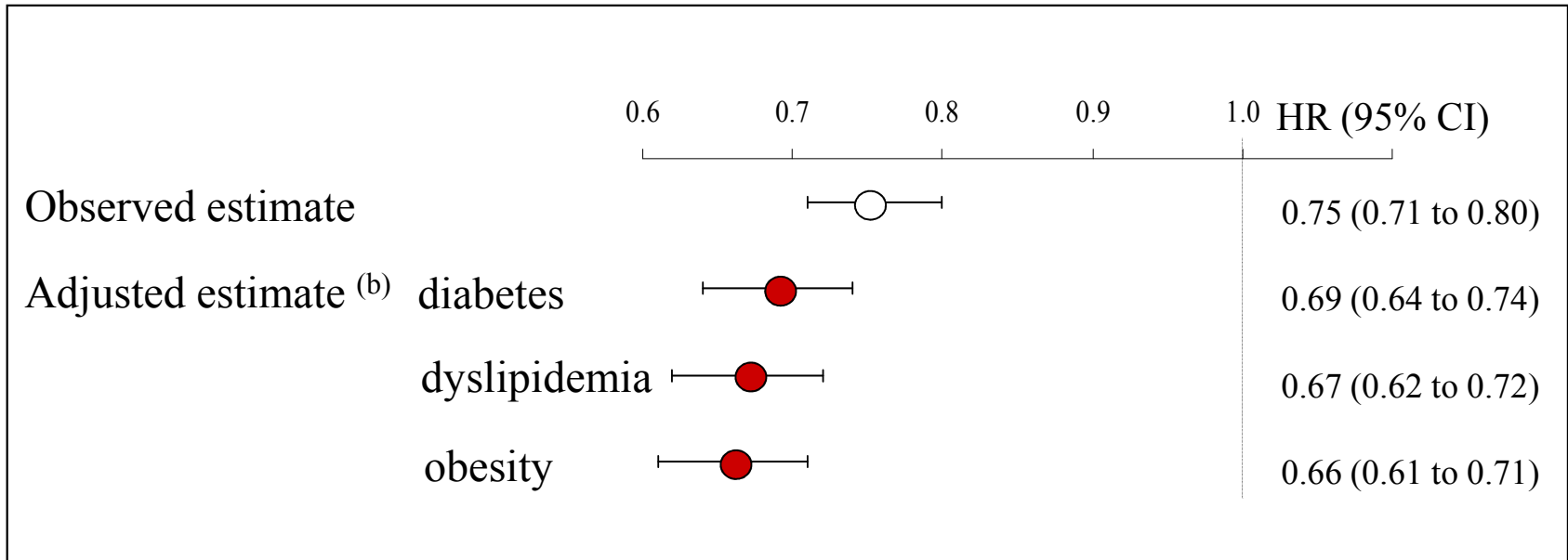
Nuove sfide

	Crude*		Adjusted†	
	High vs Low Adherence	P	High vs Low Adherence	P
Comorbidity at index diagnosis§				
Diabetes mellitus	1.65 (1.36–1.99)	<0.001	1.40 (1.15–1.71)	0.001
Arrhythmias	1.56 (1.18–2.06)	0.002	1.37 (1.03–1.82)	0.029
Peripheral vascular diseases	1.60 (1.22–2.09)	0.001	1.32 (1.00–1.75)	0.046
Dyslipidemia	1.68 (1.37–2.05)	<0.001	1.52 (1.24–1.87)	<0.001
Obesity§	1.61 (1.35–1.91)	<0.001	1.50 (1.26–1.78)	<0.001



Influenza di alcuni tratti clinici sull'effetto osservato dell'aderenza al trattamento anti-  
 ipertensivo sulla riduzione del rischio CV

**GGIUSTAMENTO ESTERNO SECONDO GREENLAND (a)**



(a) Greenland S. Sensitivity analysis, Monte-Carlo risk analysis and Bayesian uncertainty assessment. *Risk Anal* 2001;**21**:579-83

(b) Using data from the main Italian Network of General Practitioners (Health Search)

- 1 Premessa
- 2 **Esperienze**
- 3 Farmacoutilizzazione
- 4 **→ Impatto clinico**
- 5 Costi-efficacia
- 6 Nuove sfide

## Sono credibili le nostre stime?



Premessa



**Esperienze**

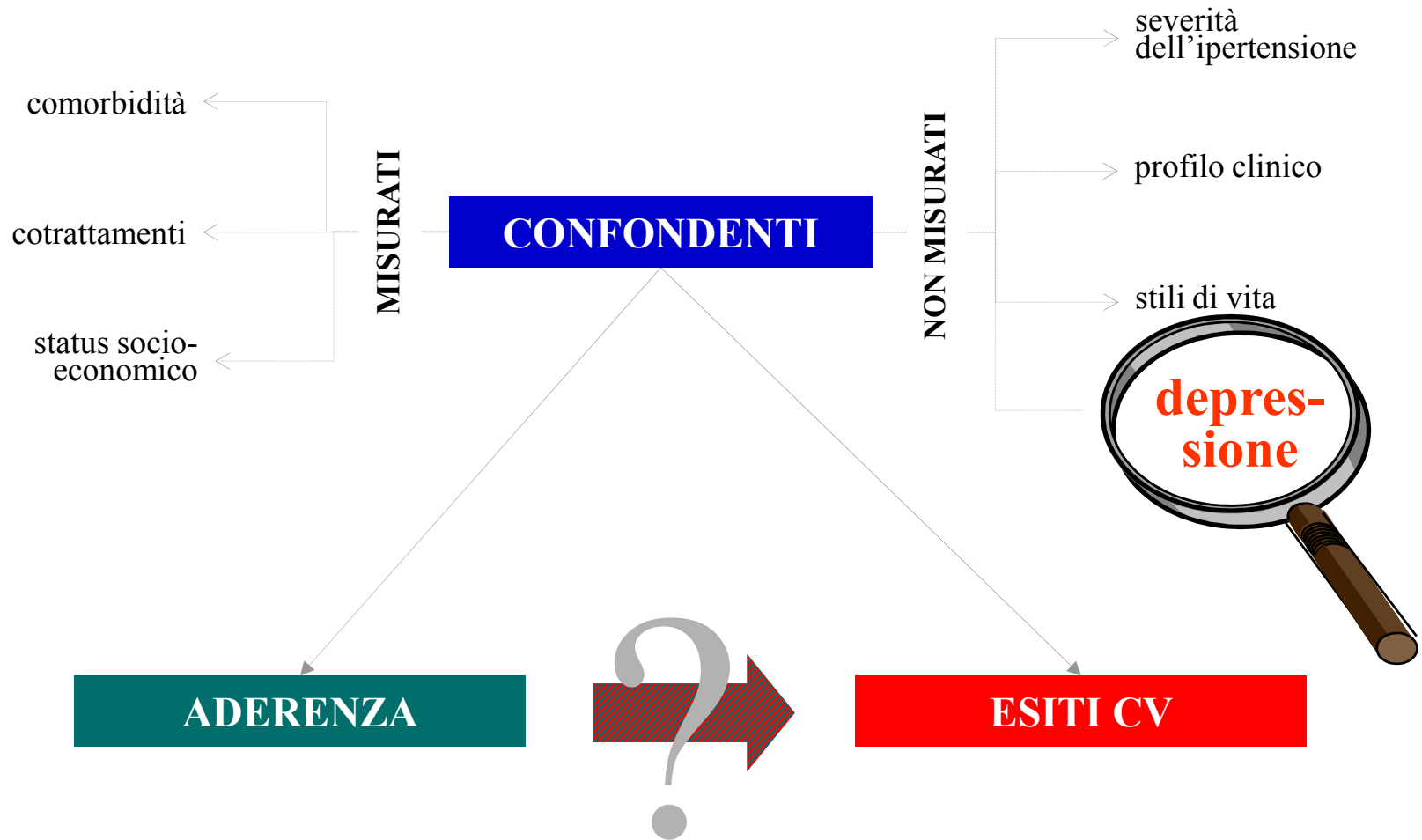
Farmacoutilizzazione

➔ **Impatto clinico**

Costi-efficacia



Nuove sfide



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## Cosa abbiamo imparato?

L'uso appropriato dei database amministrativi è utile per indagare su un ampio spettro di obiettivi:

Premessa

### **Farmacoutilizzazione**

La gestione farmacologica dei pazienti portatori di condizioni croniche è insoddisfacente nella pratica clinica corrente a causa della scarsa compliance alla terapia

Esperienze


### **Impatto clinico**

La scarsa aderenza spiega una quota rilevante degli eventi cardiovascolari che si verificano nella popolazione

Nuove sfide

### **Bilancio tra impatto clinico ed economico**

Gli interventi indirizzati a migliorare l'aderenza sembrano efficaci ed economicamente sostenibili

 Esiste un urgente **bisogno informativo** che integri le evidenze sperimentali con lo studio dell'impatto degli interventi nel mondo reale della pratica clinica

 Premessa

 Esperienze

 **Nuove sfide**

Il sistema sanitario sa quanto spende e per cosa spende, ma non è in grado documentare se la spesa sia appropriata (ovvero quanto sostenga prestazioni erogate al paziente giusto, nel momento giusto e per la giusta durata)

In queste condizioni è inevitabile che, piuttosto che il governo clinico, sia il governo finanziario a decidere quali innovazioni introdurre e quali negare ai pazienti




Premessa



Esperienze

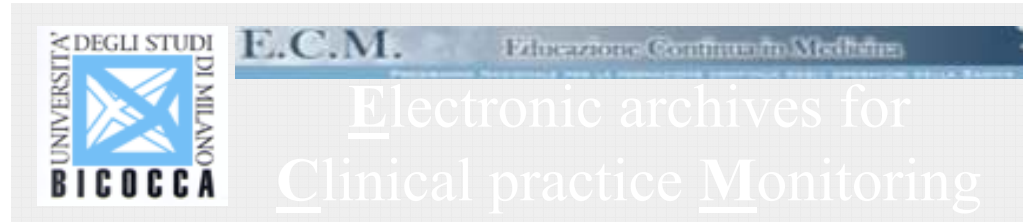




**Nuove sfide**

 Esiste un documentato e urgente **bisogno formativo** nel campo degli studi osservazionali basati sugli archivi elettronici

Ciò che manca non sono i dati, ma piuttosto professionisti caratterizzati da solide e integrate competenze informatiche, statistiche e clinico/epi-demiologiche





-  Premessa
-  Esperienze
-  **Nuove sfide**

