

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



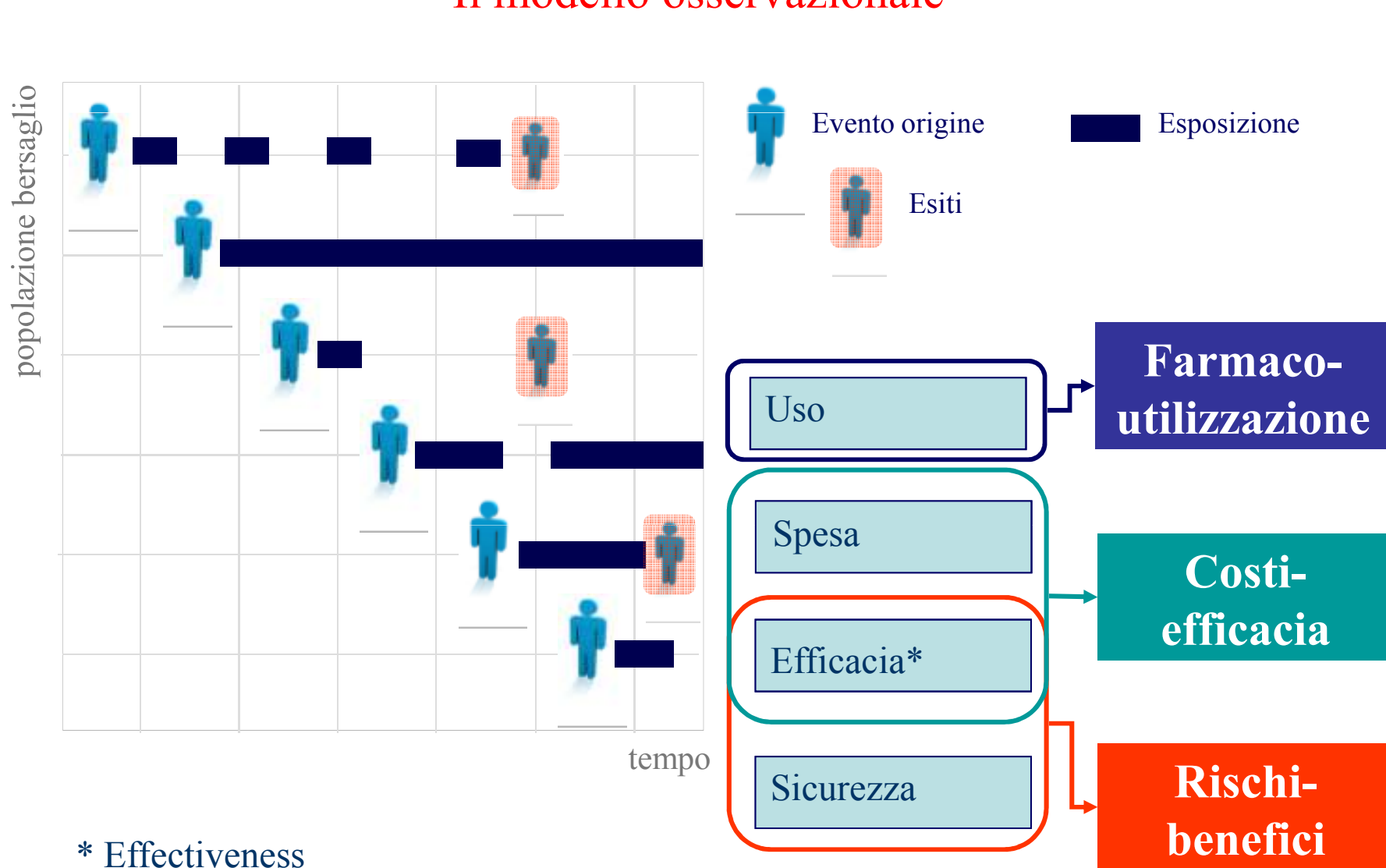
Premessa



Esperienze



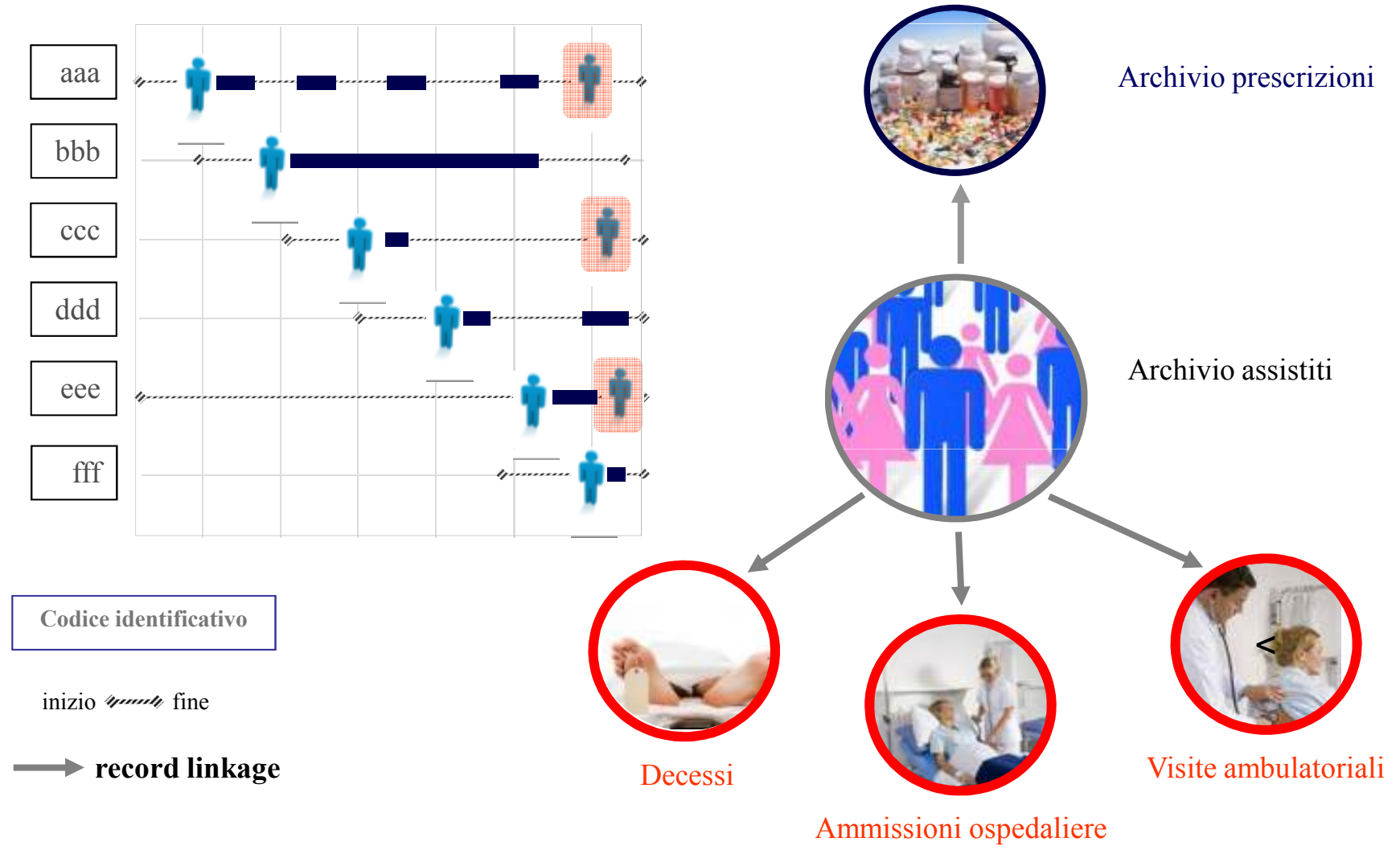
Nuove sfide



Healthcare utilization databases e Servizio Sanitario Nazionale (SSN)

Premessa

Esperienze
 Nuove sfide



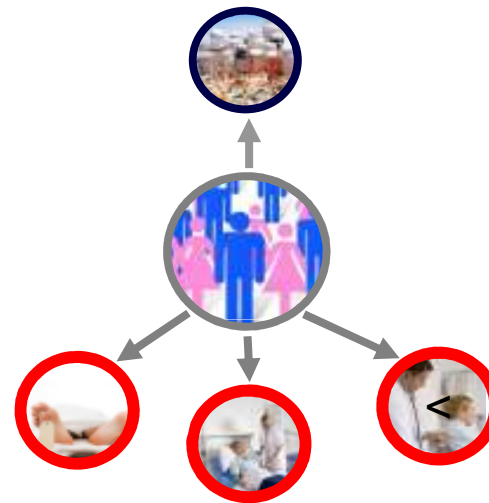
FORZA

**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



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

Anti-ipertensivi ¹

50 %

55 %

Ipolipemizzanti ²

40 %

50 %

Ipoglicemizzanti orali ³

60 %

60 %

Bifosfonati ⁴

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

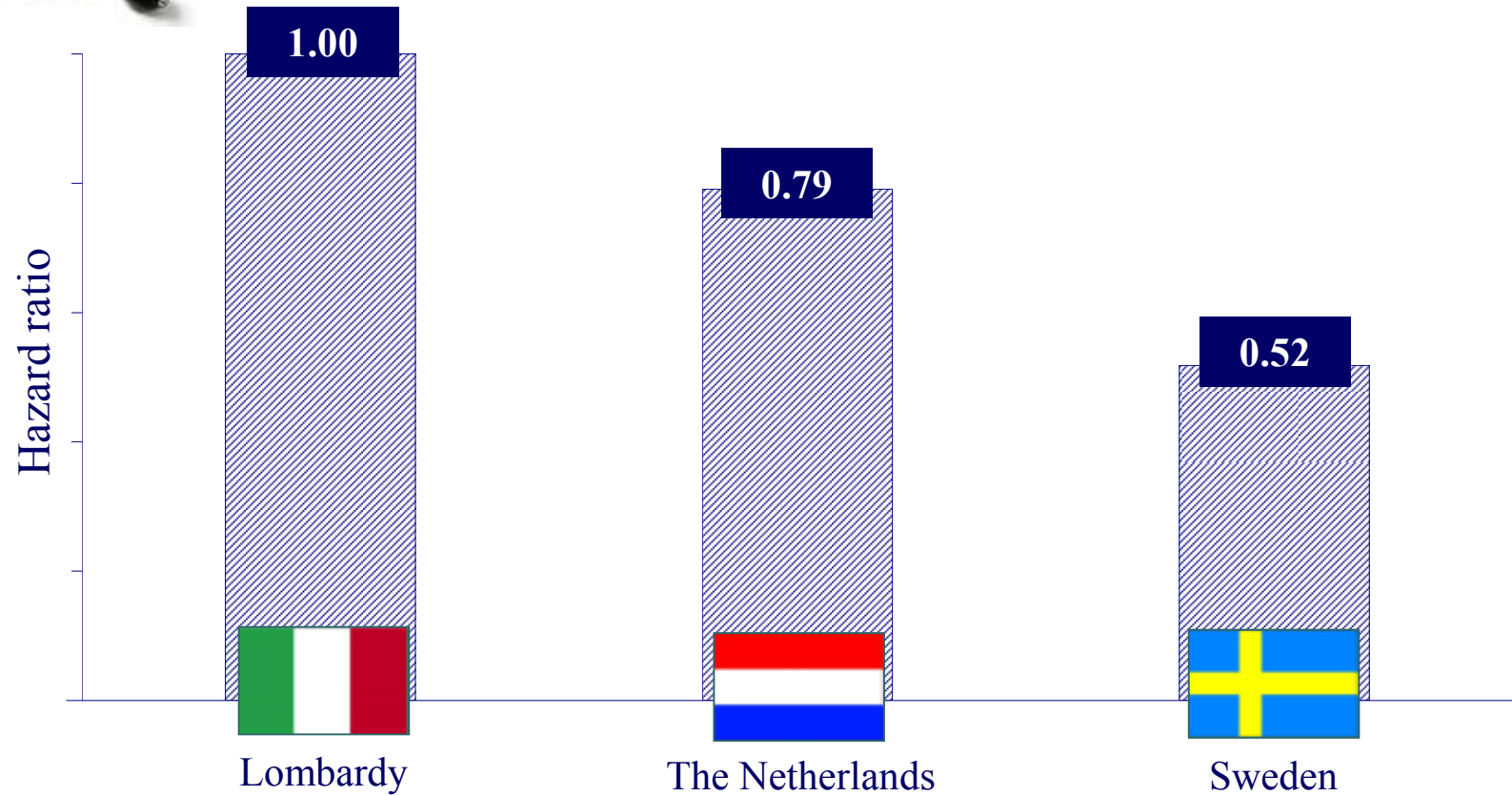
Costi-efficacia

Nuove sfide

Discontinuità a nove mesi dall'inizio della terapia



Antihypertensive drugs



Premessa

Esperienze

→ **Farmacoutilizzazione**

Impatto clinico

Costi-efficacia

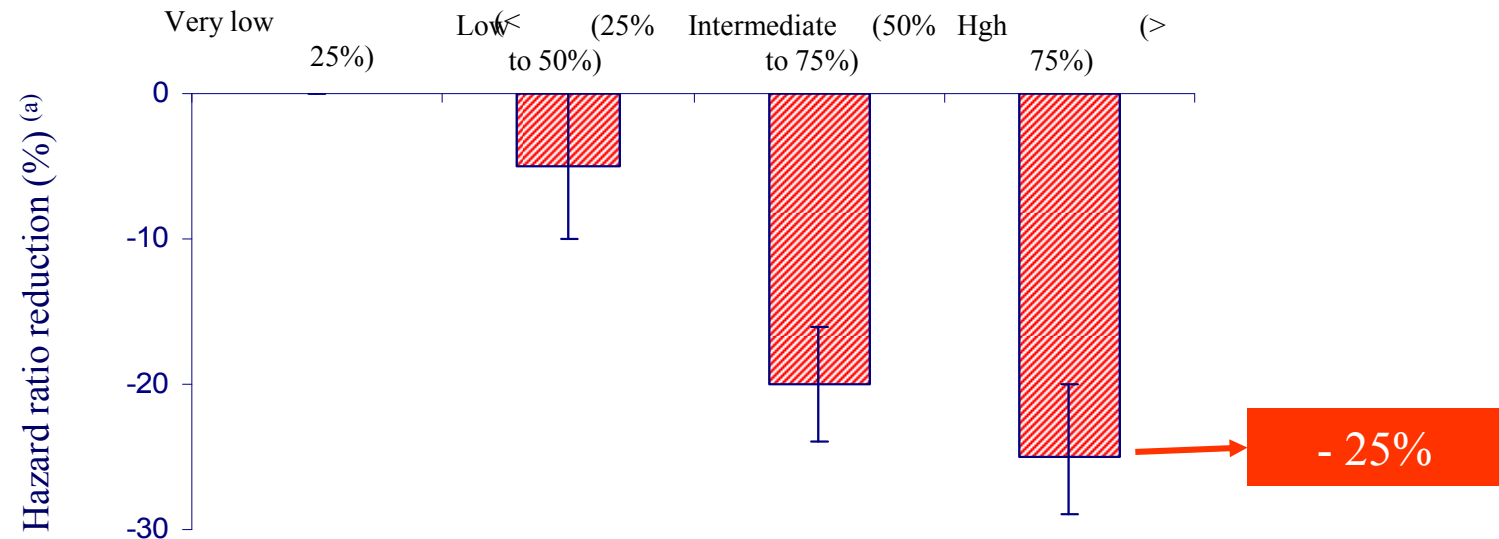
Nuove sfide

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

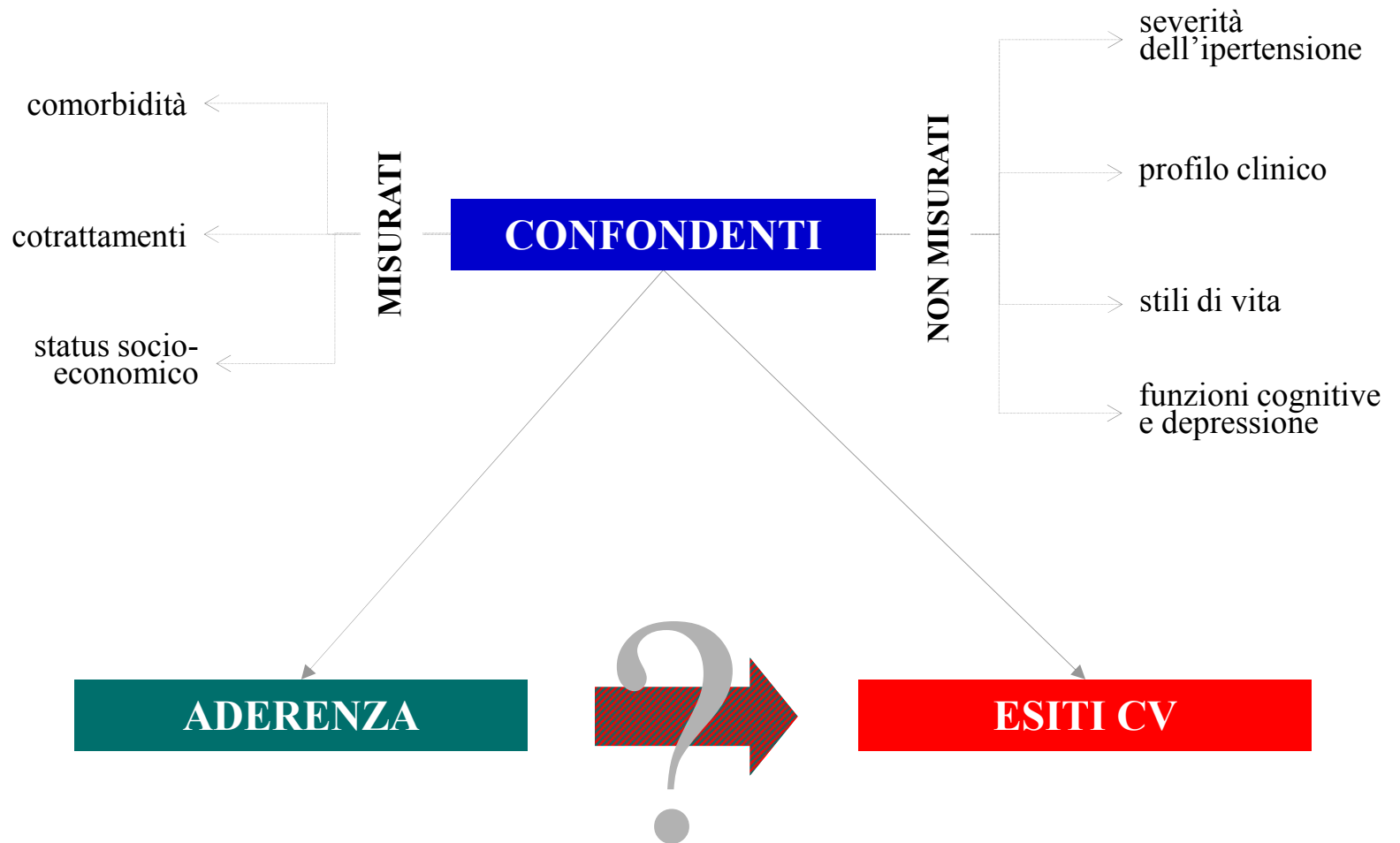
Farmacoutilizzazione

➔ Impatto clinico

Costi-efficacia



Nuove sfide



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

Corrao G, Zamboni 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

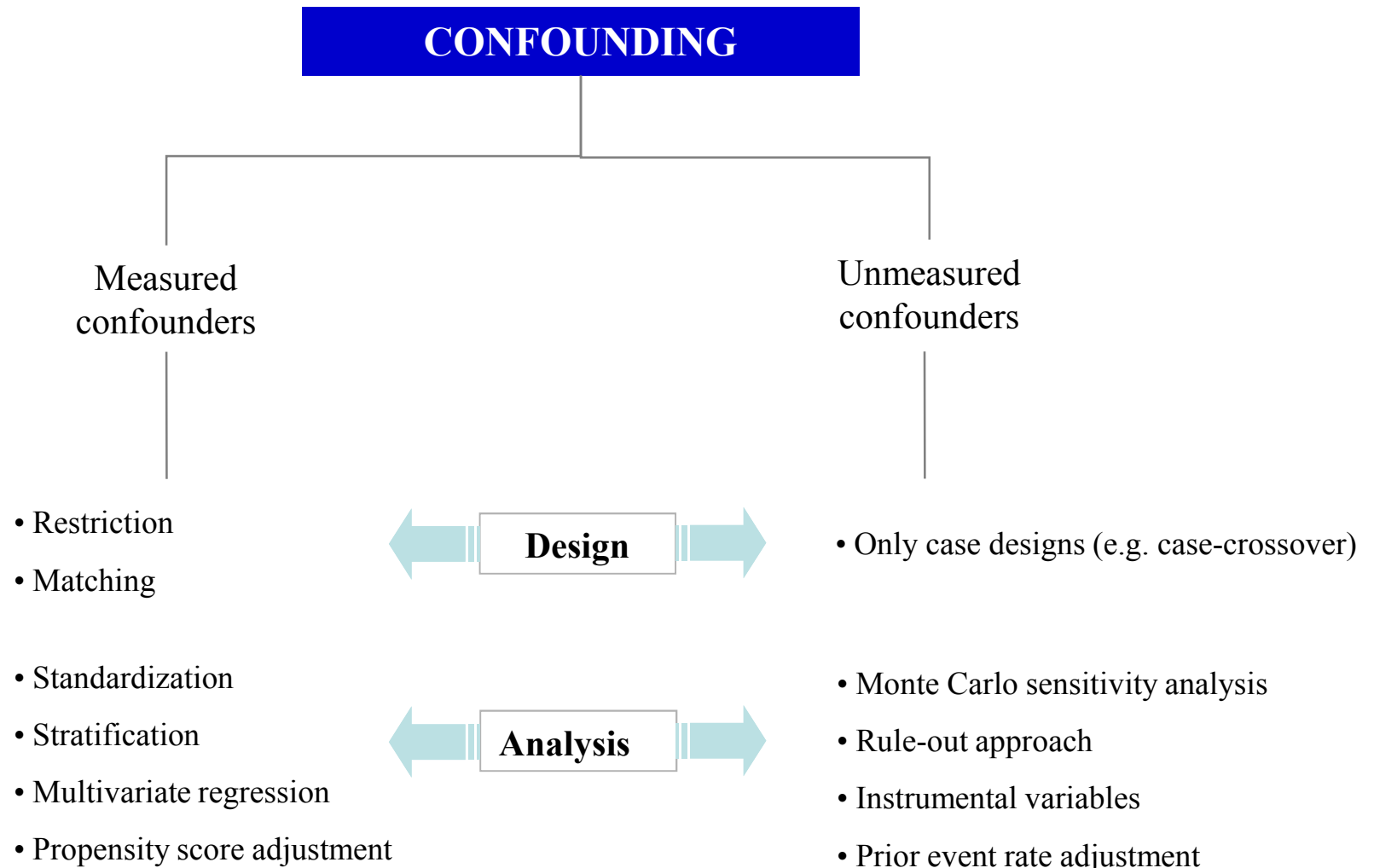
Farmacoutilizzazione

→ Impatto clinico

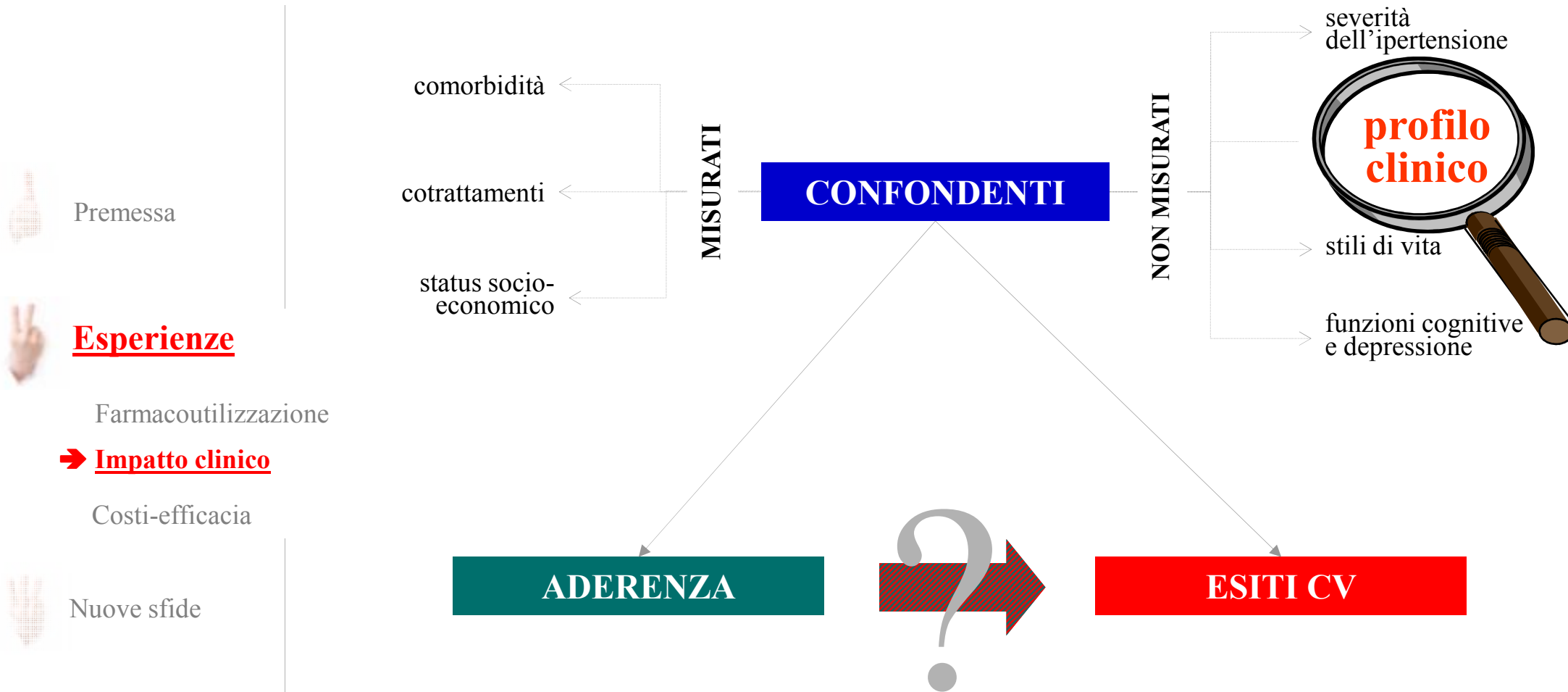
Costi-efficacia



Nuove sfide



Sono credibili le nostre stime?



Premessa

Esperienze

Farmacoutilizzazione


➔ **Impatto clinico**

Costi-efficacia

Nuove sfide

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

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



2009, 120:1598-605

Circulation American Heart Association. Learn and Live.

Adherence to Antihypertensive Medications and Cardiovascular Morbidity Among Newly Diagnosed Hypertensive Patients

Giampiero Mazzaglia, Ettore Ambrosioni, Marianna Alacqua, Alessandro Filippi, Emiliano Sessa, Vincenzo Immordino, Claudio Borghi, Ovidio Brignoli, Achille P. Caputi, Claudio Cricelli and Lorenzo G. Mantovani

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)



Premessa



Esperienze

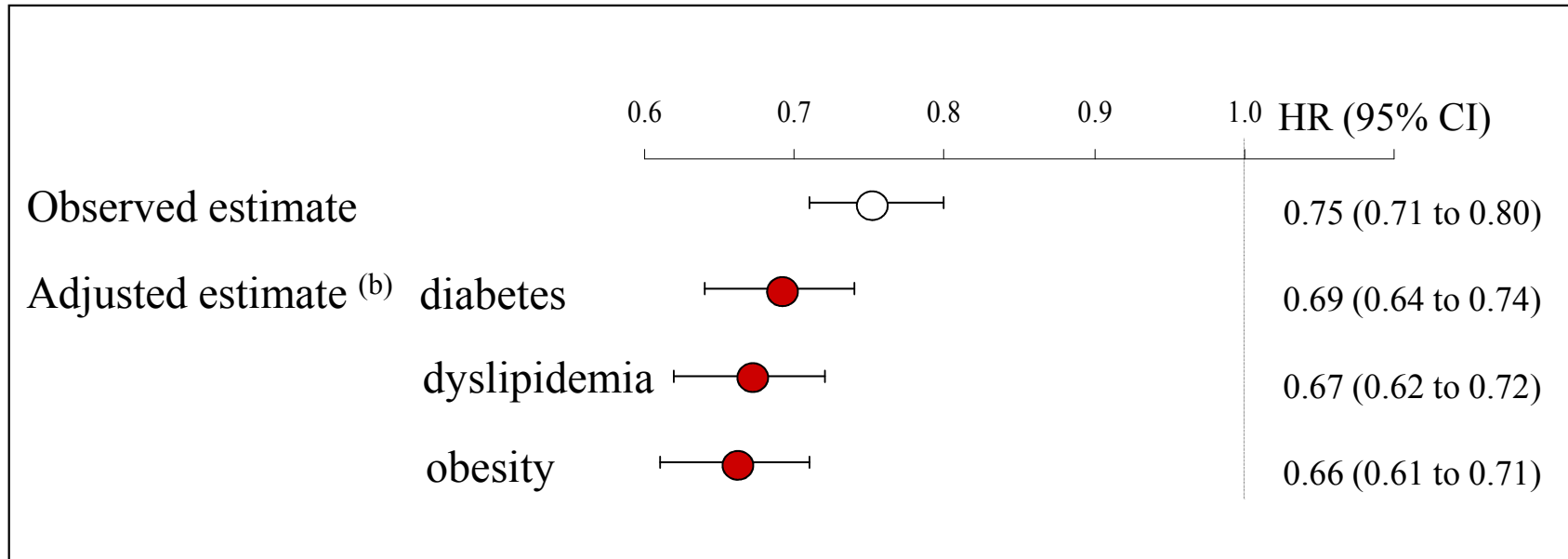
Farmacoutilizzazione

→ Impatto clinico

Costi-efficacia



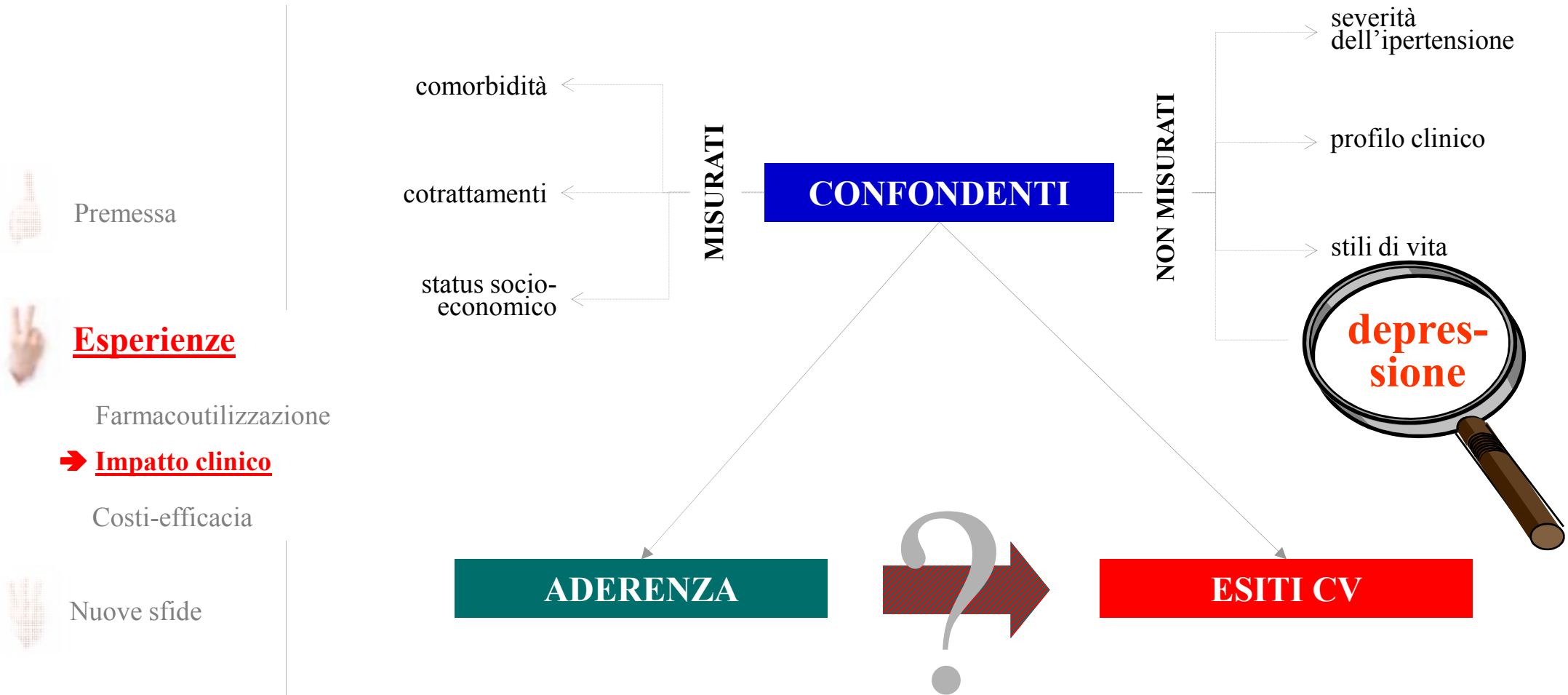
Nuove sfide



(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)

Sono credibili le nostre stime?



Premessa

Esperienze

Farmacoutilizzazione

➔ Impatto clinico

Costi-efficacia

Nuove sfide

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

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

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



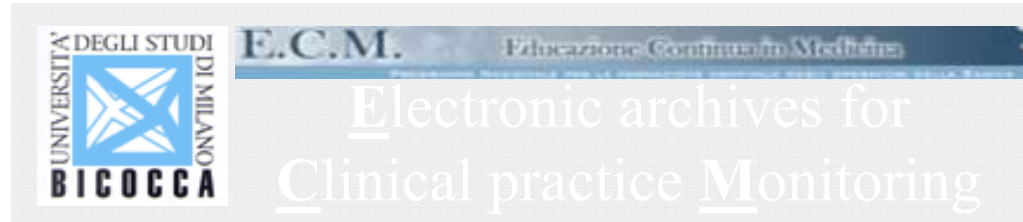
Esperienze



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**

