Systematic Reviews of the effectiveness of interventions for addictions: questions and answers

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SUMMARY

- Why all this

- What are systematic reviews and which questions they try to answer

- Future challenges and perspectives

Trends of mortality of young adult males in Italy
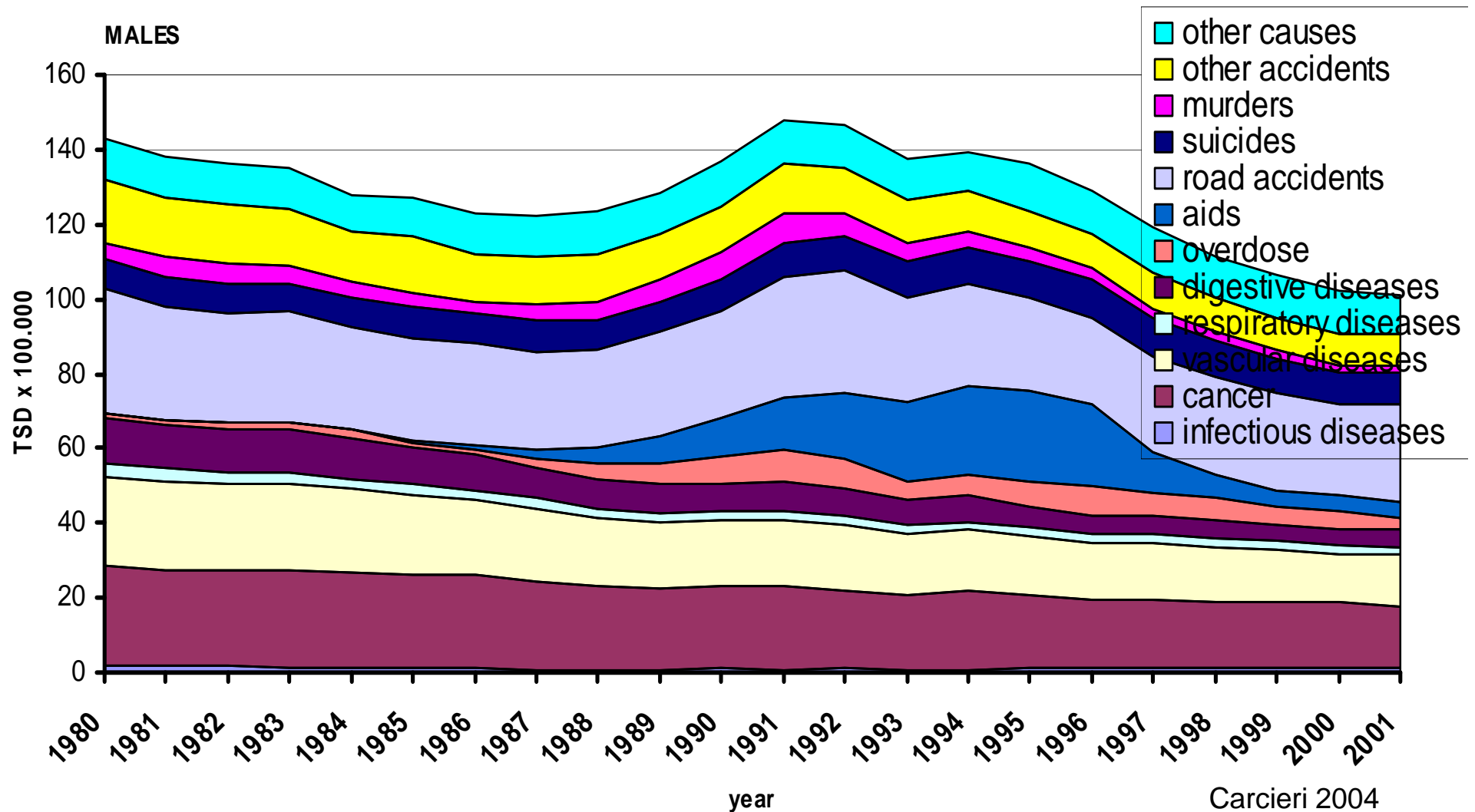
Mortality of Intravenous Drug Users in Rome: A Cohort Study

Carlo A. Perucci, MD, Marina Davoli, MD, Elisabetta Rapiti, MD, Damiano D. Abeni, MD, and Francesco Forastiere, MD

SMR 9.3

SMR 18.1

TABLE 2—Cause-specific Mortality among Male Intravenous Drug Users (19 662 person-years)

Cause of Death[a]	OBS	EXP	SMR[b]	95% CI[c]
All causes (000–999)	200	21.50	9.3	8.1–10.7

TABLE 3—Cause-specific Mortality among Female Intravenous Drug Users (4334 person-years)

Cause of Death[a]	OBS	EXP	SMR[b]	95% CI[c]
All causes (000–999)	39	2.16	18.1	12.9–24.7

Proportion of patients on methadone treatment in Italy. Ministry of Health 1991
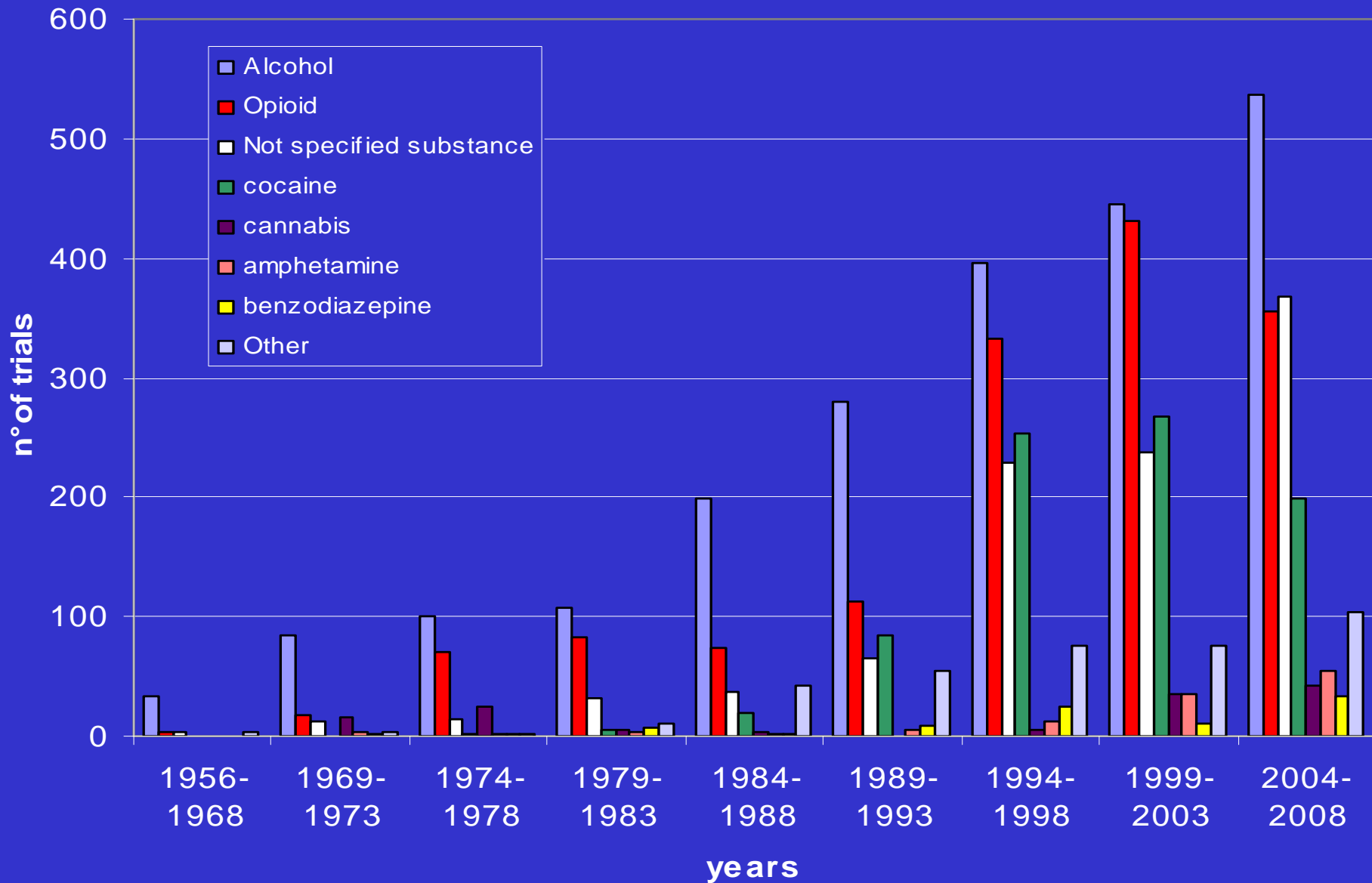
- **20%** of clients of public treatment centres in Italy in 1991 were on short term methadone treatment

- **10%** of clients of public treatment centres in Italy in 1991 were on protracted methadone treatment
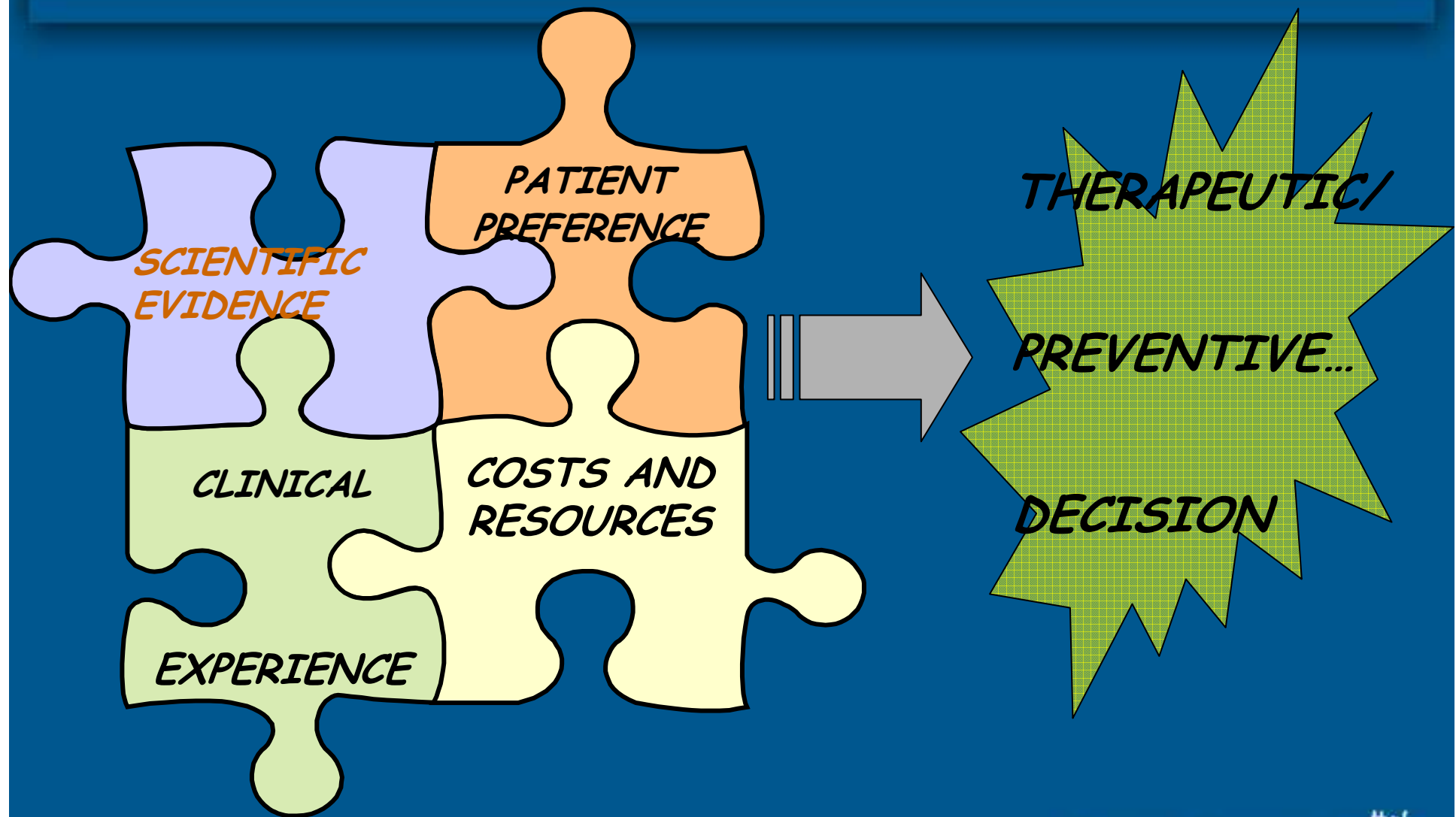
RCTs on interventions for drug addiction (n=6451)
Specialized Register Drugs and Alcohol Cochrane Group. CL 4.2008

The Cochrane Collaboration

An international network of people lunched in 1992 to conduct, update and disseminate systematic reviews of the effect of health care interventions.

There are 51 Review Groups in the Cochrane Collaboration

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CGR: "Drug and alcohol"

Scope

to produce and disseminate systematic reviews of all RCTs and CCTs that describe an active intervention (including prevention, treatment and rehabilitation) aimed at reducing the potential for harm or the actual harm

directly related to the use of different dependence producing substances

Cochrane Systematic reviews

- **Are the result of a complex process :**
  - **Formulate a proper question**
  - **Comprehensive data search**
  - **Objective selection and data extraction**
  - **Critical evaluation of primary studies**
  - **Synthesis**
  - **Update**

Formulate a proper question

- **Define :**
  - **Objectives**
  - **Criteria for considering studies**
    - **Type of studies**
    - **Type of participants**
    - **Type of interventions**
      - Experimental/control
  - **Outcomes**
    - **Primary/secondary**

Types of outcome measures
Primary outcomes

(1) **retention in treatment** **as measured by the number of participants still in treatment at the end of the study;**
(2) **use of opioids** **as measured by: a) urinalysis results positive for heroin metabolite (i.e., morphine), b) self reported heroin use;**
(3) **use of other substances** **of abuse as measured by: a) urinalysis results positive for cocaine, b) urinalysis results positive for benzodiazepines;**
(4) **criminal activity** **as measured by self report**
(5) **mortality**

Secondary outcomes
(6) **physical health;**
(7) **psychological health**
(8) **side effects of medication.**

- **Why a comprehensive search strategy?**
  - **It has been proved that negative studies are less likely to be:**

    - **published: (timely, completely, in well spread journals, in English)**
    - **Presented at conferences**
    - **Quoted in other articles**

Full publication of absracts submitted to CPDD according to study results

	N°trials presented N	N°trials published N (%)	Hazard Ratio	IC 95%
Positive	161	120 (74)	1.00	
Not reported	325	198 (61)	0.70	0.56-0.90
Null or negative	51	24 (47)	0.48	0.30-0.74
No results	44	17 (39)	0.38	0.23-0.64
TOTAL	581	359		

Vecchi S et al (data not published)

Systematic search: studies included 621/1704 considered

La maggior parte degli studi 569 (92%) sono stati reperiti nei database elettronici

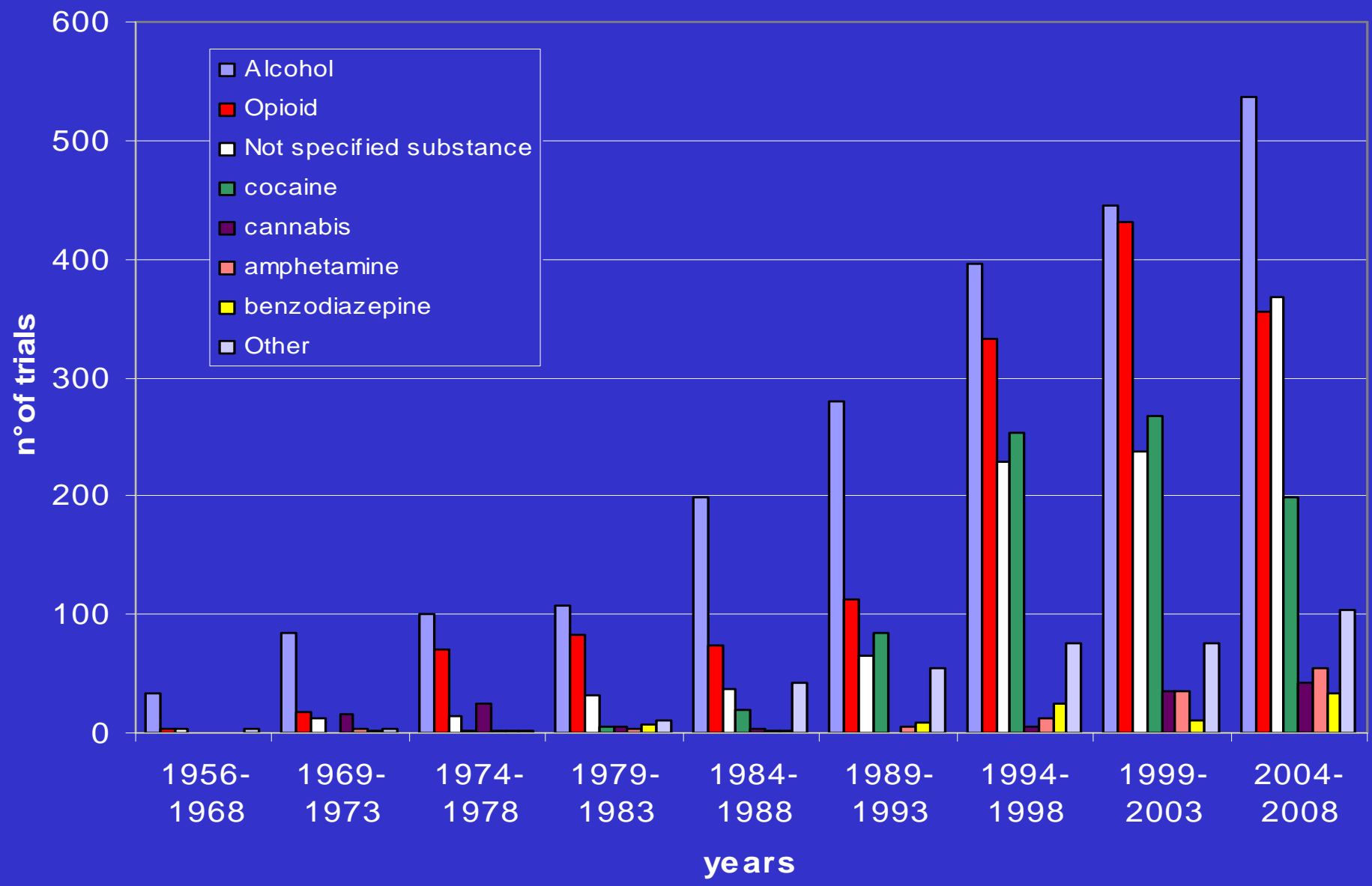| Studi reperiti nei database elettronici	MEDLINE and EMBASE	MEDLINE	MEDLINE, EMBASE e CINHAL	EMBASE	CINHAL e MEDLINE	CINHAL	CINHAL e EMBASE
569	360	84	75	34	8	4	4

Dei rimanenti 52 studi

Studies not found in electronic databases	Not indexed journals	Sections of book	Conference Proceedings	Thesis dissertation	Unpublished trials
52	32	7	6	6	2

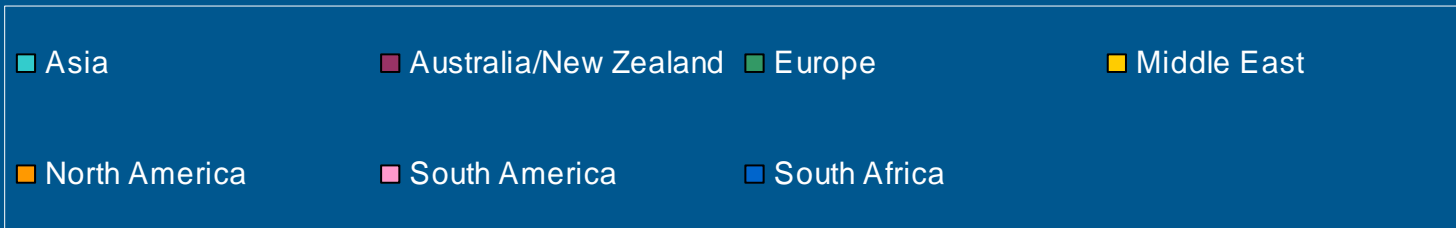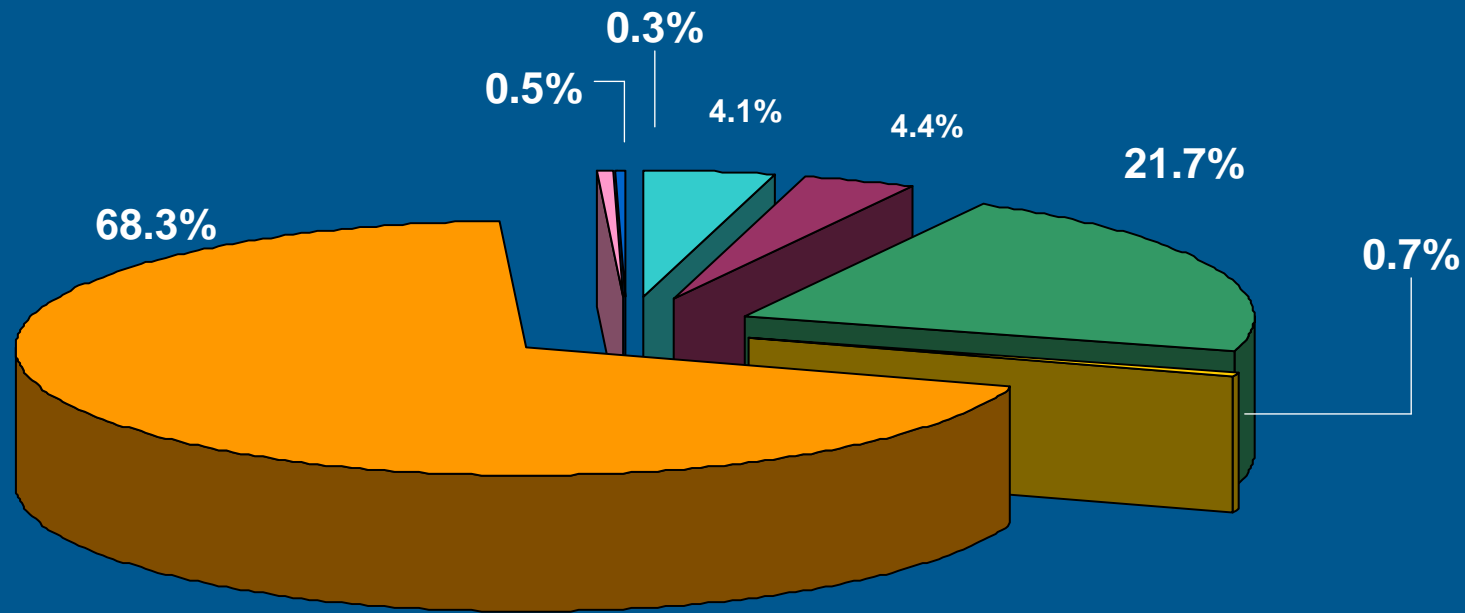**15% of trials not found on MEDLINE**

RCTs on interventions for drug addiction (n= 6451)

Specialized Register Drugs and Alcohol Cochrane Group. CL 4.2008

Country of origin of the studies included in the Specialized Register

Legend:
- Asia
- Australia/New Zealand
- Europe
- Middle East
- North America
- South America
- South Africa

Values shown: 68.3%, 0.5%, 0.3%, 4.1%, 4.4%, 21.7%, 0.7%

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- **Why critical appraisal of studies?**

  – **Many studies have shown an association between poor quality of the study and overestimation of effect**
  – **Good quality evidence is mixed with poor quality evidence**
  – **Can get biased estimates**
  – **Poor quality of primary studies = poor quality of systematic review**

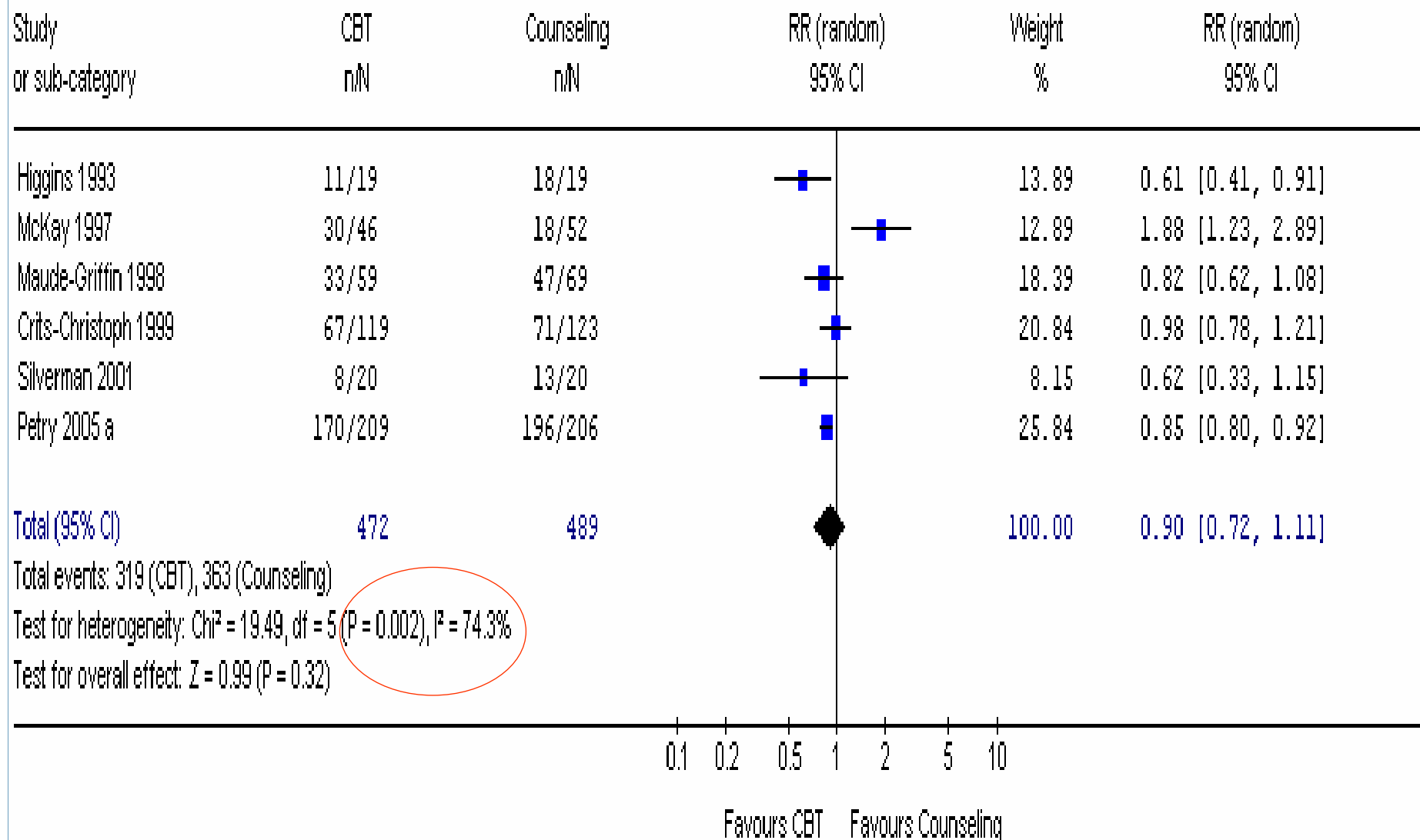- **Synthesis, principles of metanalysis**

Review
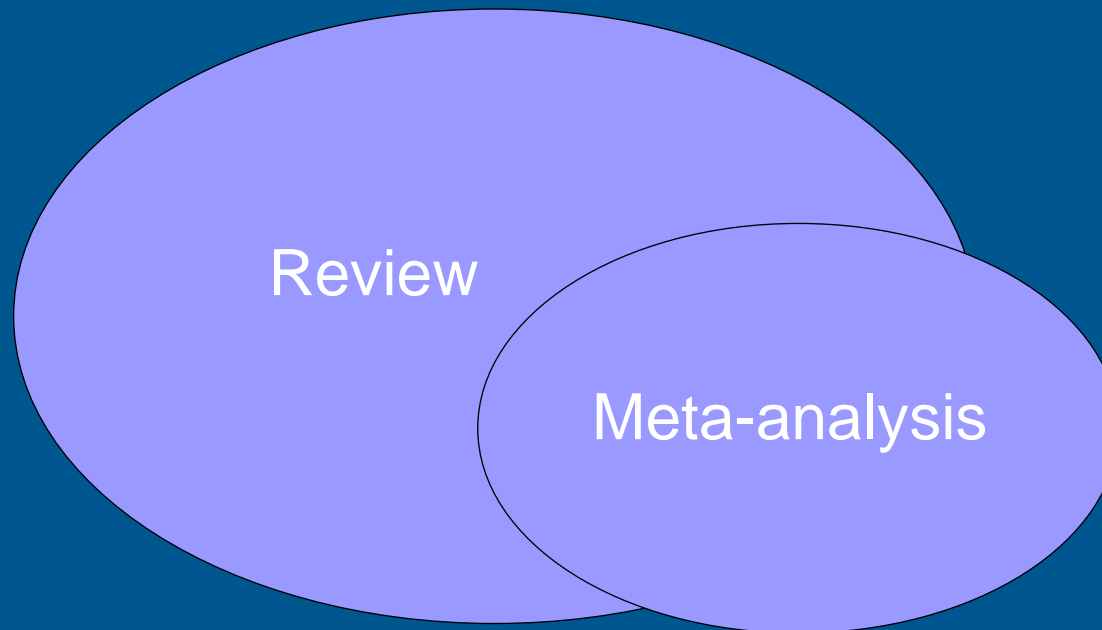
Meta-analysis

Meta-analysis is one part of the review, not always appropriate. There are reviews without metanalysis

Review: Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders
Comparison: 01 All Cognitive Behavioural Therapy (CBT) versus all Drug Counseling
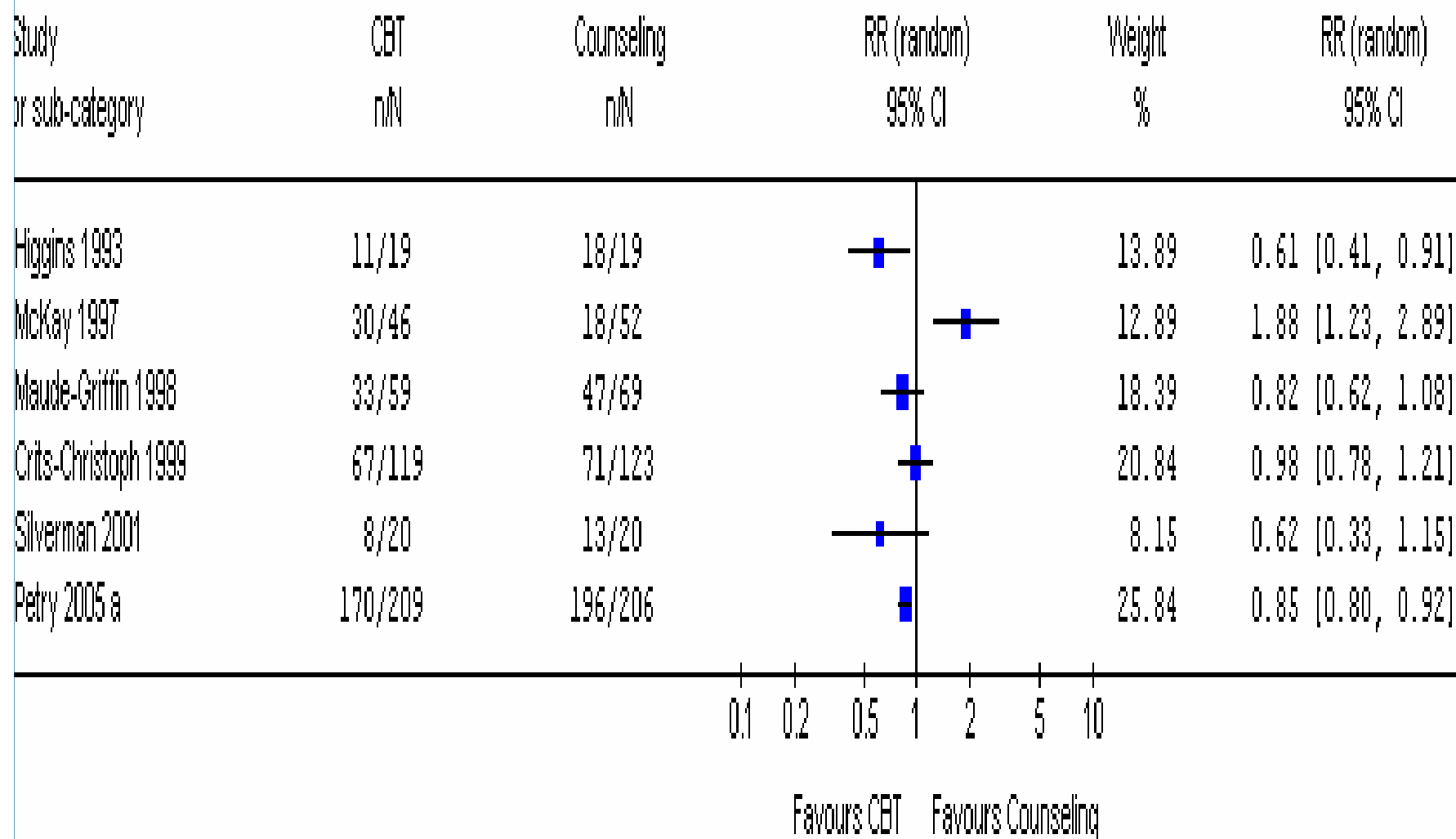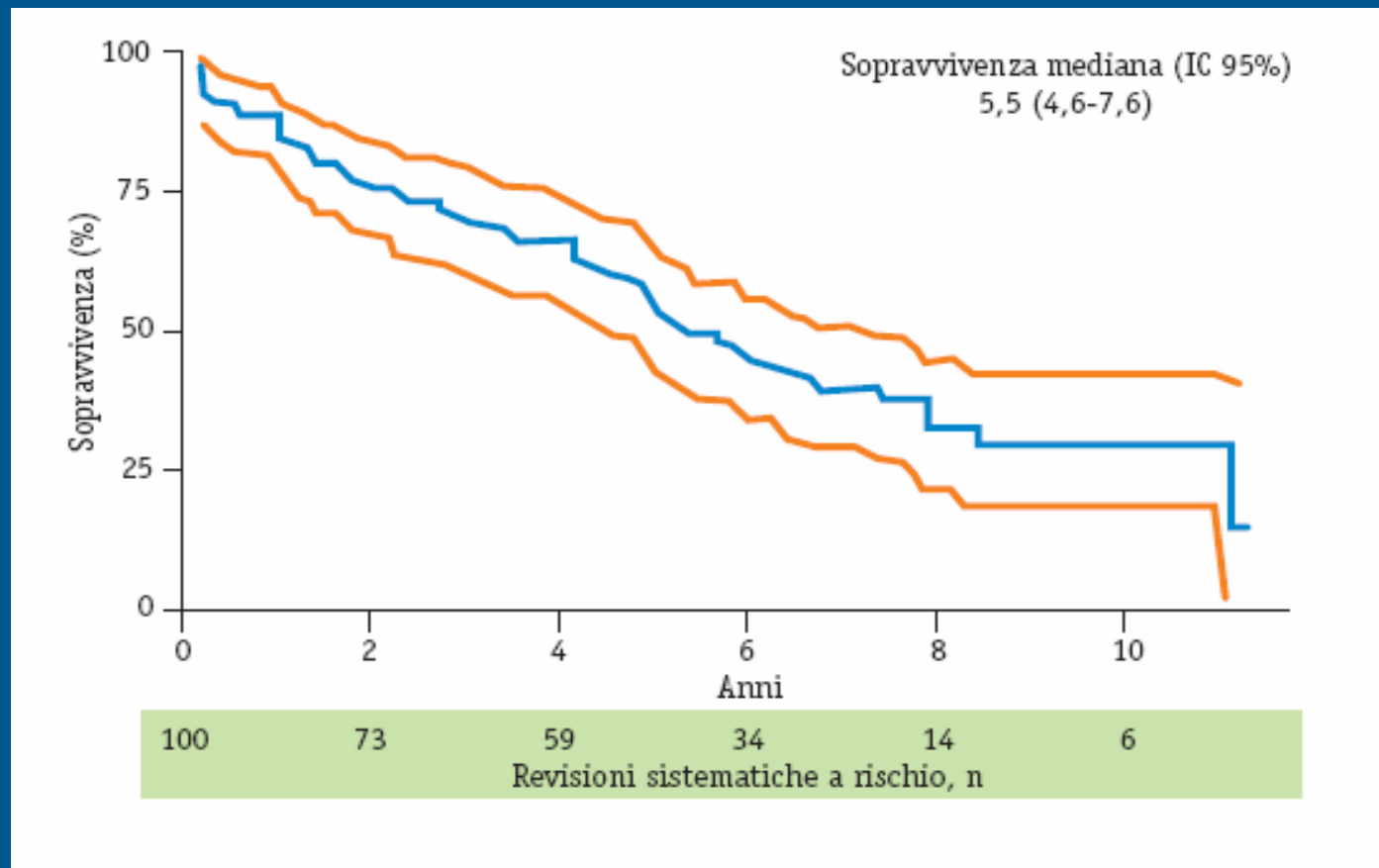Outcome: 02 Use of cocaine at endpoint

Study or sub-category	CBT n/N	Counseling n/N	RR (random) 95% CI	Weight %	RR (random) 95% CI
Higgins 1993	11/19	18/19		13.89	0.61 [0.41, 0.91]
McKay 1997	30/46	18/52		12.89	1.88 [1.23, 2.89]
Maude-Griffin 1998	33/59	47/69		18.39	0.82 [0.62, 1.08]
Crits-Christoph 1999	67/119	71/123		20.84	0.98 [0.78, 1.21]
Silverman 2001	8/20	13/20		8.15	0.62 [0.33, 1.15]
Petry 2005 a	170/209	196/206		25.84	0.85 [0.80, 0.92]
Total (95% CI)	472	489		100.00	0.90 [0.72, 1.11]

Total events: 319 (CBT), 363 (Counseling)
Test for heterogeneity: Chi² = 19.49, df = 5 (P = 0.002), I² = 74.3%
Test for overall effect: Z = 0.99 (P = 0.32)

0.1 0.2 0.5 1 2 5 10

Favours CBT   Favours Counseling

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0.1   0.2   0.5   1   2   5   10

Favours CBT   Favours Counseling

- **Why updating?**

Time since pubblication of SRs without need of updating

Shojania KG et al. Ann Intern Med 2007

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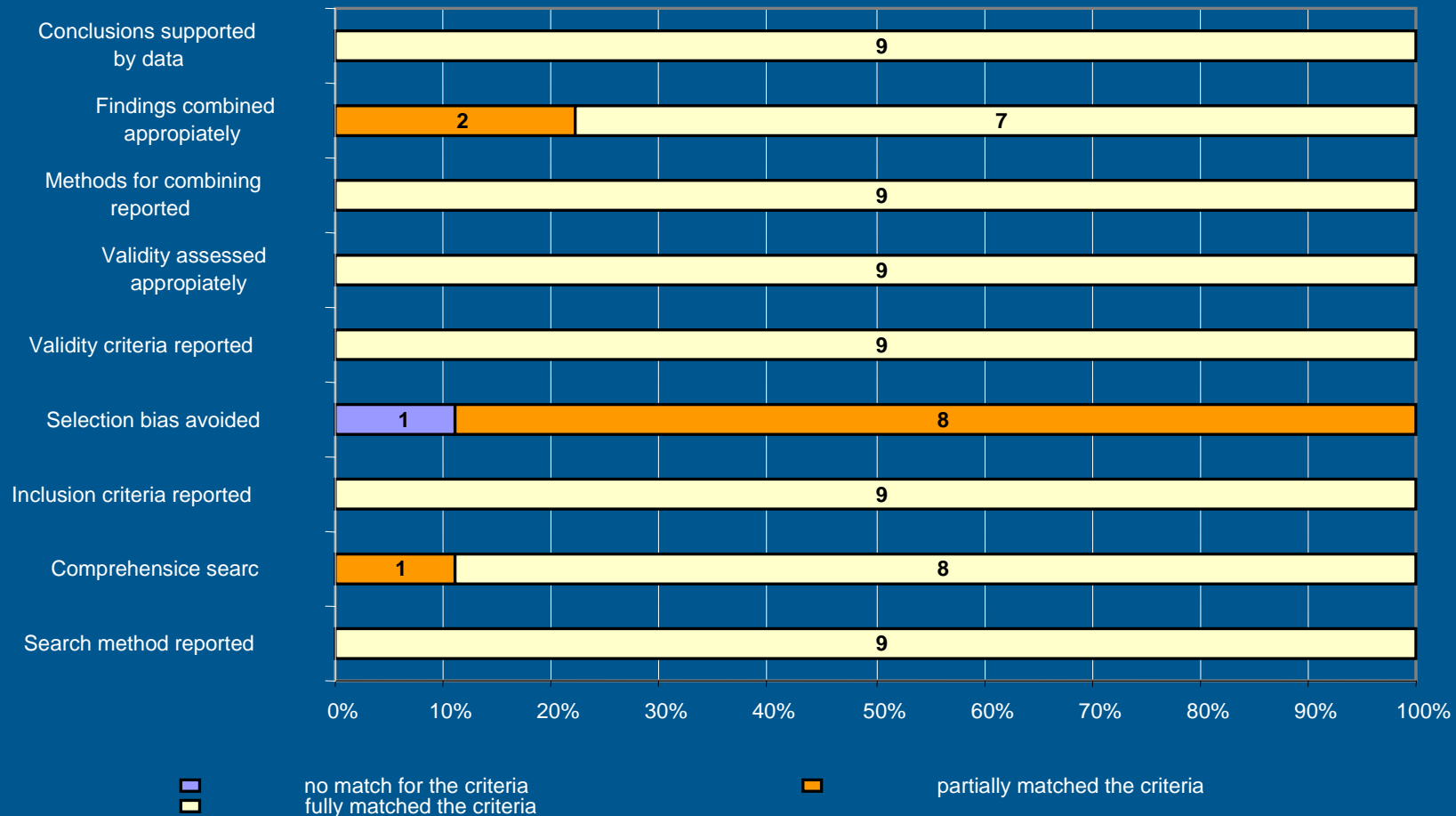# Update of Cochrane Drugs and Alcohol SRs

- 23 reviews to be updated

  - Range: 3 – 57 months
  - Mean: 23 months
  - Median: 15 months

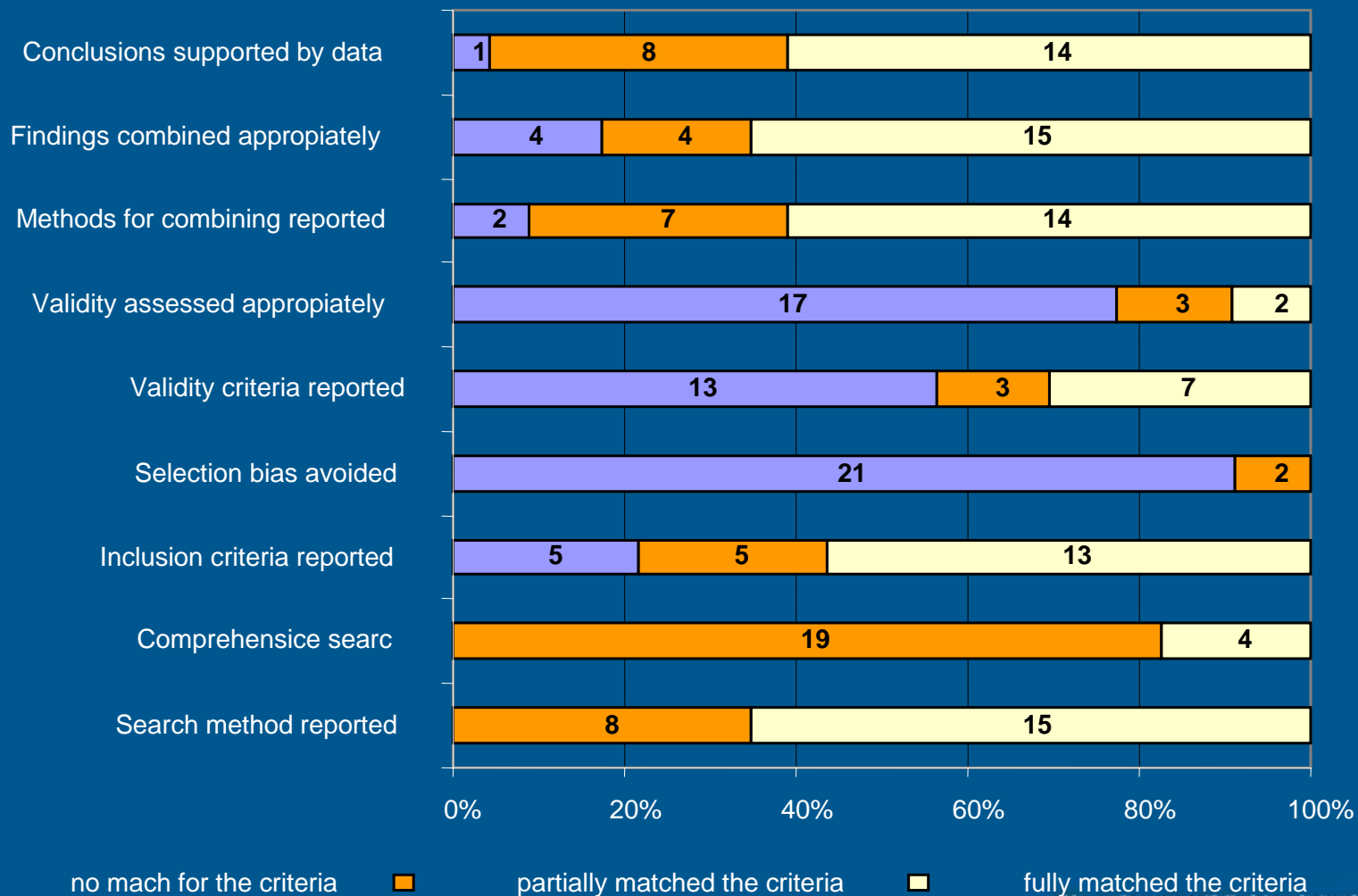Does all this rigorous and standardised process result in better quality?

Quality Assessment non Cochrane Reviews

Conclusions supported by data	1 / 8 / 14	
Findings combined appropiately	4 / 4 / 15	
Methods for combining reported	2 / 7 / 14	
Validity assessed appropiately	17 / 3 / 2	
Validity criteria reported	13 / 3 / 7	
Selection bias avoided	21 / 2	
Inclusion criteria reported	5 / 5 / 13	
Comprehensice searc	19 / 4	
Search method reported	8 / 15	

0%   20%   40%   60%   80%   100%

□ no mach for the criteria   ■ partially matched the criteria   □ fully matched the criteria

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Revisione bup e met, NICE, UK 2006

Reviews and protocols published by COCHRANE DRUGS and ALCOHOL GROUP
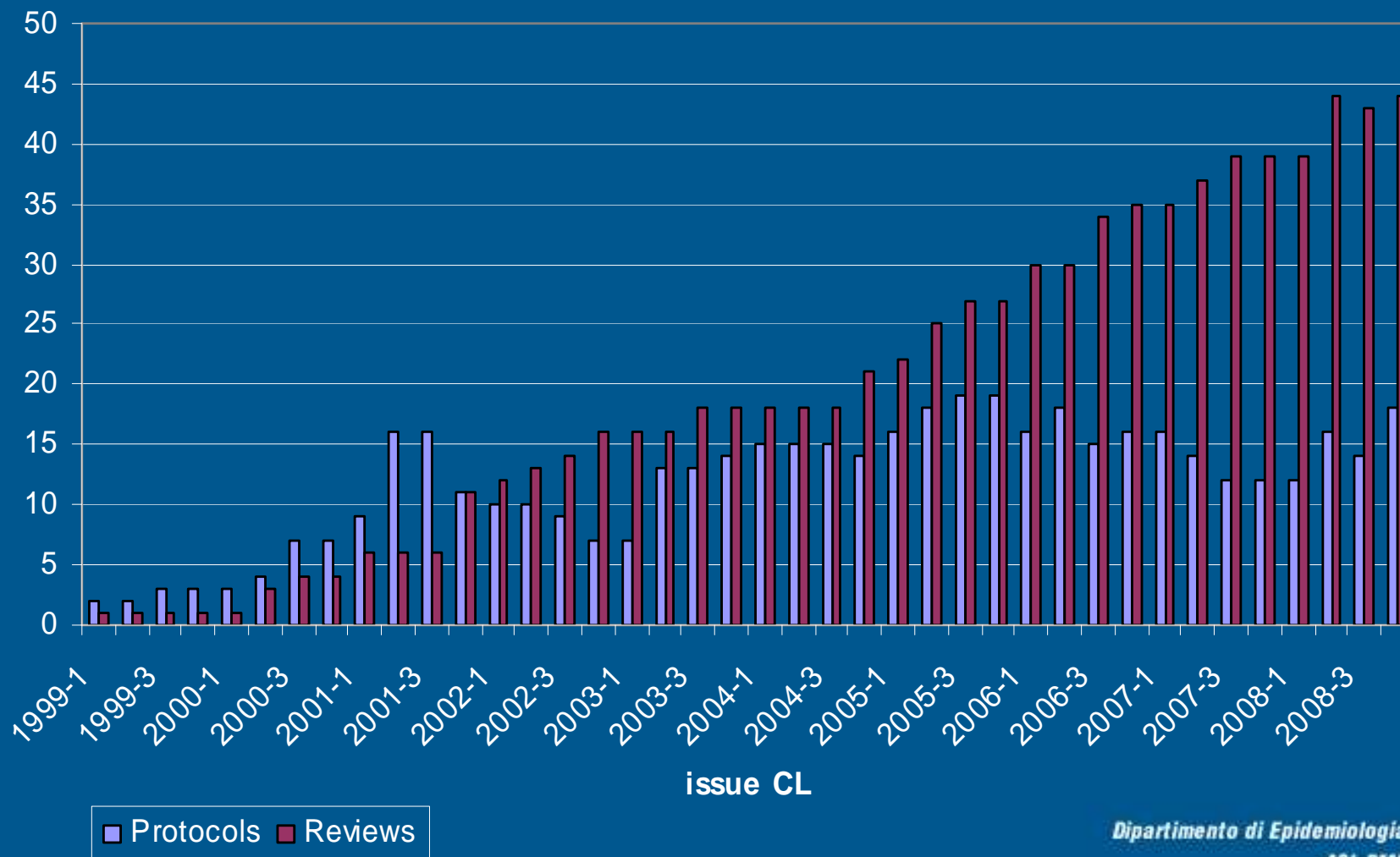
State of the art CLIB 4.2008

Sostanza	N° revisioni	N° Protocolli	N° Titoli	Totale
Oppiacei	18	4	4	26
Alcol	7	10	4	21
Psicostimolanti (cocaina ed amfetamine)	9	2		11
Altro	3		1	4
Più sostanze	4	2	5	11
Prevenzione	3			3
Totale	44	18	14	76

Effectiveness of all interventions
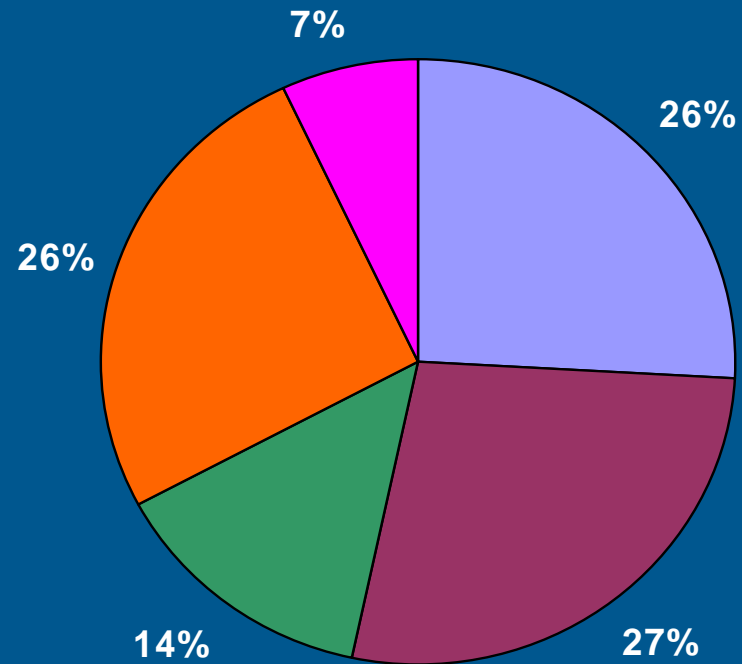
- beneficial or likely to be beneficial
- unknown effectiveness
- likely to be ineffective or harmful
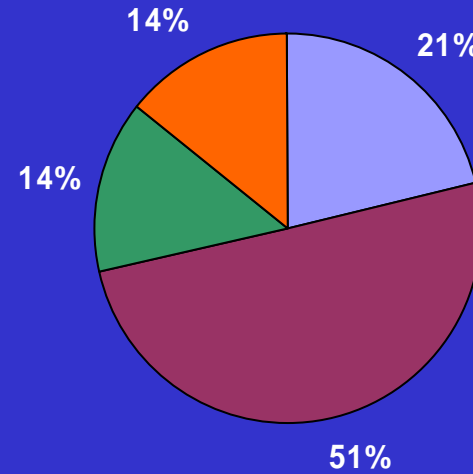- trade off between benefits and harms
- unlikely to be beneficial
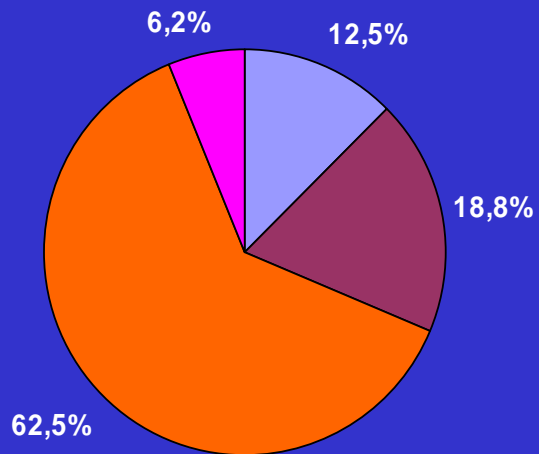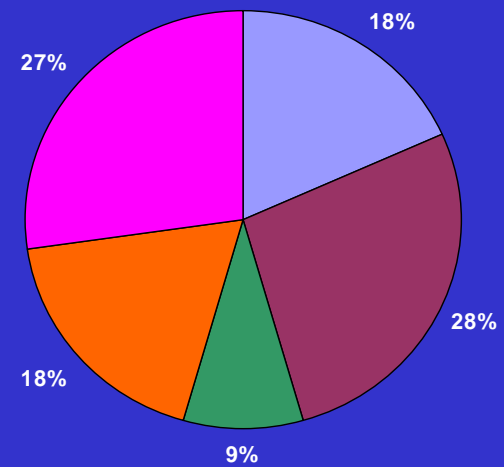
Effectiveness of all interventions

OPIATES
- 45%
- 26%
- 8%
- 18%
- 3%

ALCOHOL
- 21%
- 51%
- 14%
- 14%
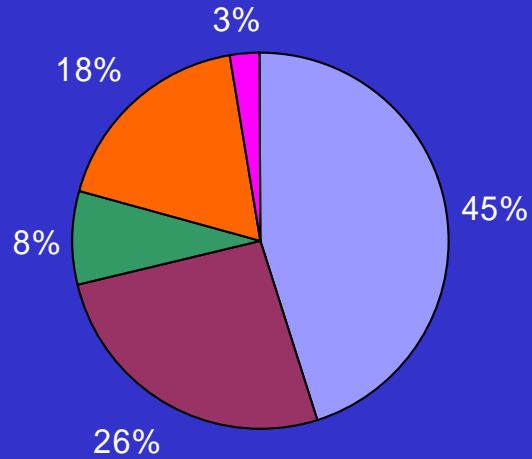
COCAINE
- 12,5%
- 18,8%
- 6,2%
- 62,5%

PREVENTION
- 18%
- 28%
- 9%
- 18%
- 27%

Legend:
- □ beneficial or likely to be beneficial
- □ trade off between benefits and harms
- □ unknown effectiveness
- □ unlikely to be beneficial
- □ likely to be ineffective or harmful

Does all this matter for research indications?

Implicazioni per la ricerca
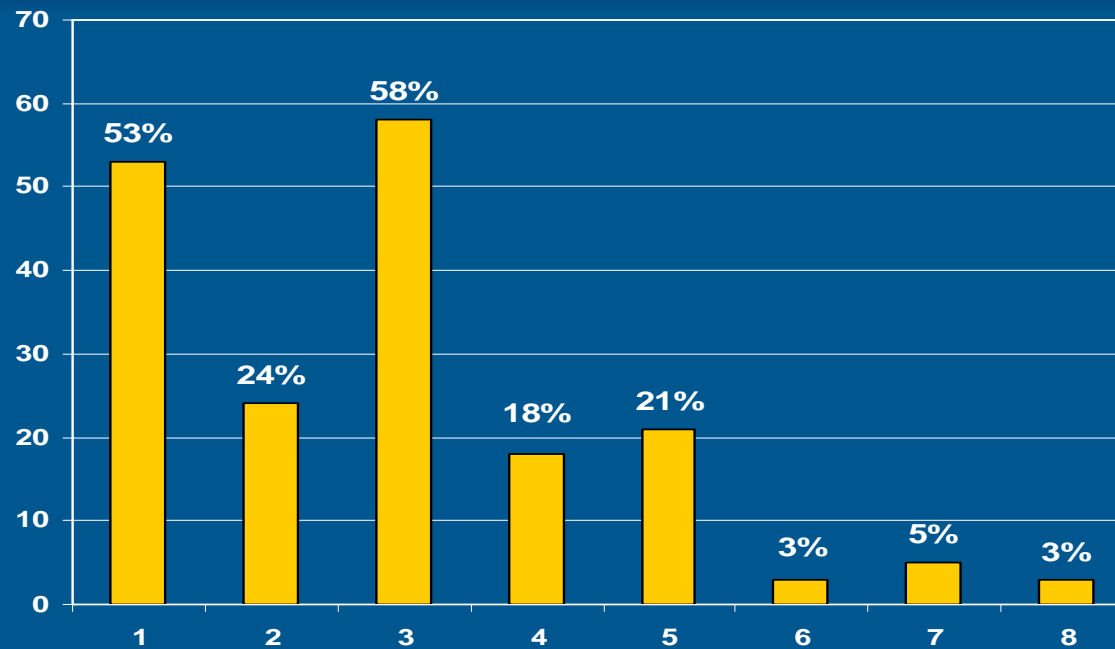
1: inserisce suggerimenti su uno specifico tipo di intervento da considerare
2: inserisce suggerimenti sul tipo di partecipanti da includere
3: inserisce suggerimenti sulle misure d'esito da considerare
4: inserisce suggerimenti sui tutti e tre i primi punti
5: non dà suggerimenti per nessuno dei primi tre punti
6: afferma la necessità di una nuova o aggiornata revisione
7: conclude che non vi è necessità di ulteriori ricerche
8: cita trial in corso

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Who does all this?
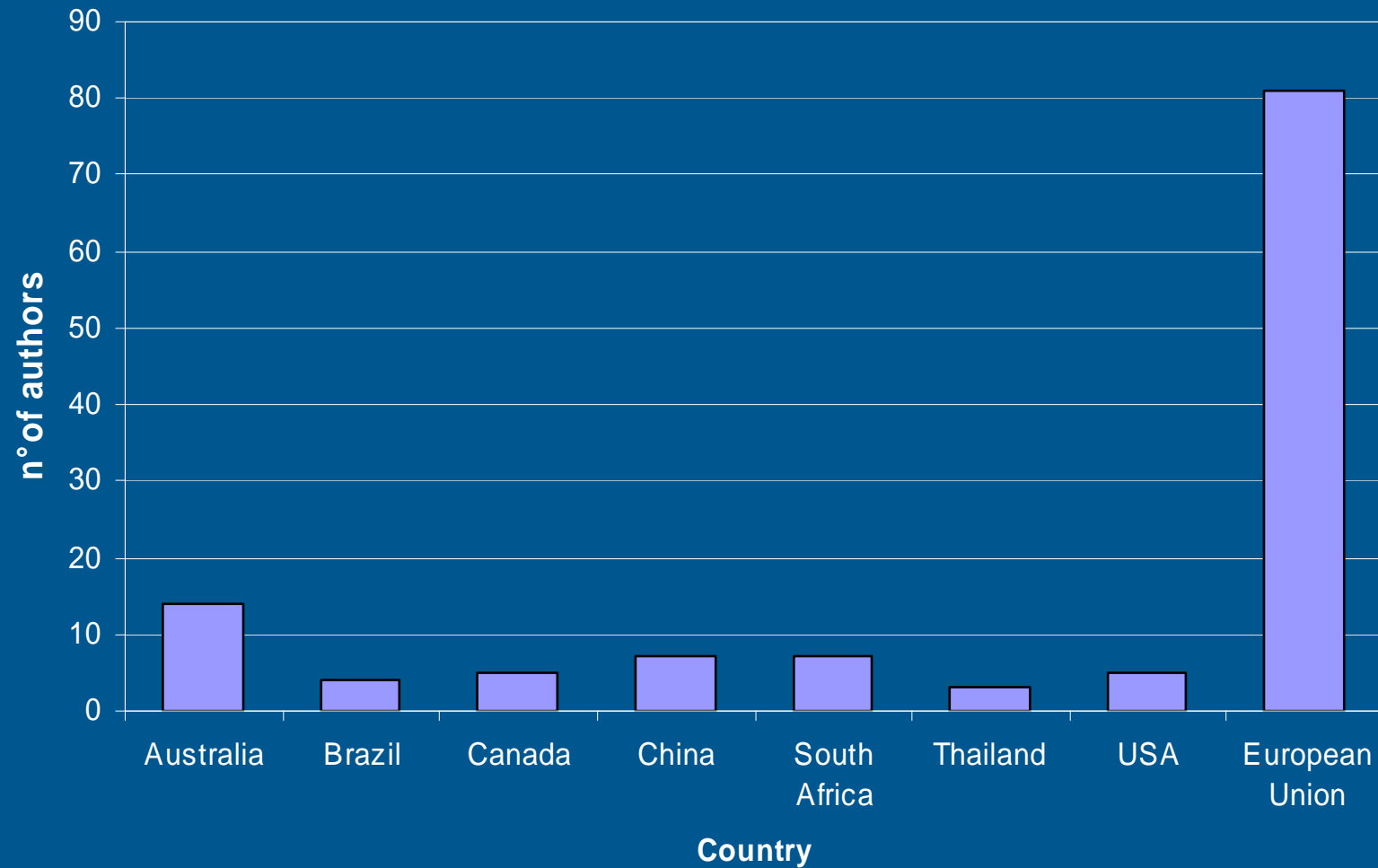
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CONCLUSIONS

- Cochrane reviews provide the "best available evidence" addressing the questions they are planned to answer

- Cochrane reviews sometimes provide useful results to identify effective treatments

- They also identify a wide range of interventions unlikely to be beneficial and even likely to be ineffective or harmful

- Cochrane reviews also help in identifying areas where more systematic reviews are necessary and areas where more primary research is required

Future challenges

- Maintain high quality standard of updated evidence
- Better balance between extreme attention to "*bias hunting*" and broader view towards impact
- Interact with all stakeholders to prioritize questions to be addressed by systematic reviews in order to be relevant for:
  - Patients and their families
  - Care givers
  - Policy maker
- Make the best possible use of evidence coming from different sources (long term effect, diagnostics, other technologies)
- Make the evidence available and accessible
- and….hope that sometime in the future Italian policy makers would be interested