

Linee guida ed evidenza di efficacia

Three solutions

Clinical performance can keep up to date:

- 1 by learning how to practice evidence-based medicine ourselves.
- 2 by seeking and applying evidence-based medical summaries generated by others.
- 3 by accepting evidence-based practice protocols developed by our colleagues.



Caratteristiche

- Gli *studi primari* producono l'evidenza scientifica
 - Rispondono a quesiti specifici: *trattamento per condizione per outcome*
- Le *revisioni sistematiche* la sintetizzano
 - Rispondono a quesiti più allargati: *trattamento per outcome*
- Le *linee-guida* costituiscono uno strumento di trasferimento dell'evidenza nella pratica medica
 - Rispondono a tutti i quesiti relativi a una singola *condizione* (generalmente prevenzione, diagnosi, cura, riabilitazione)

Alternative per il trasferimento

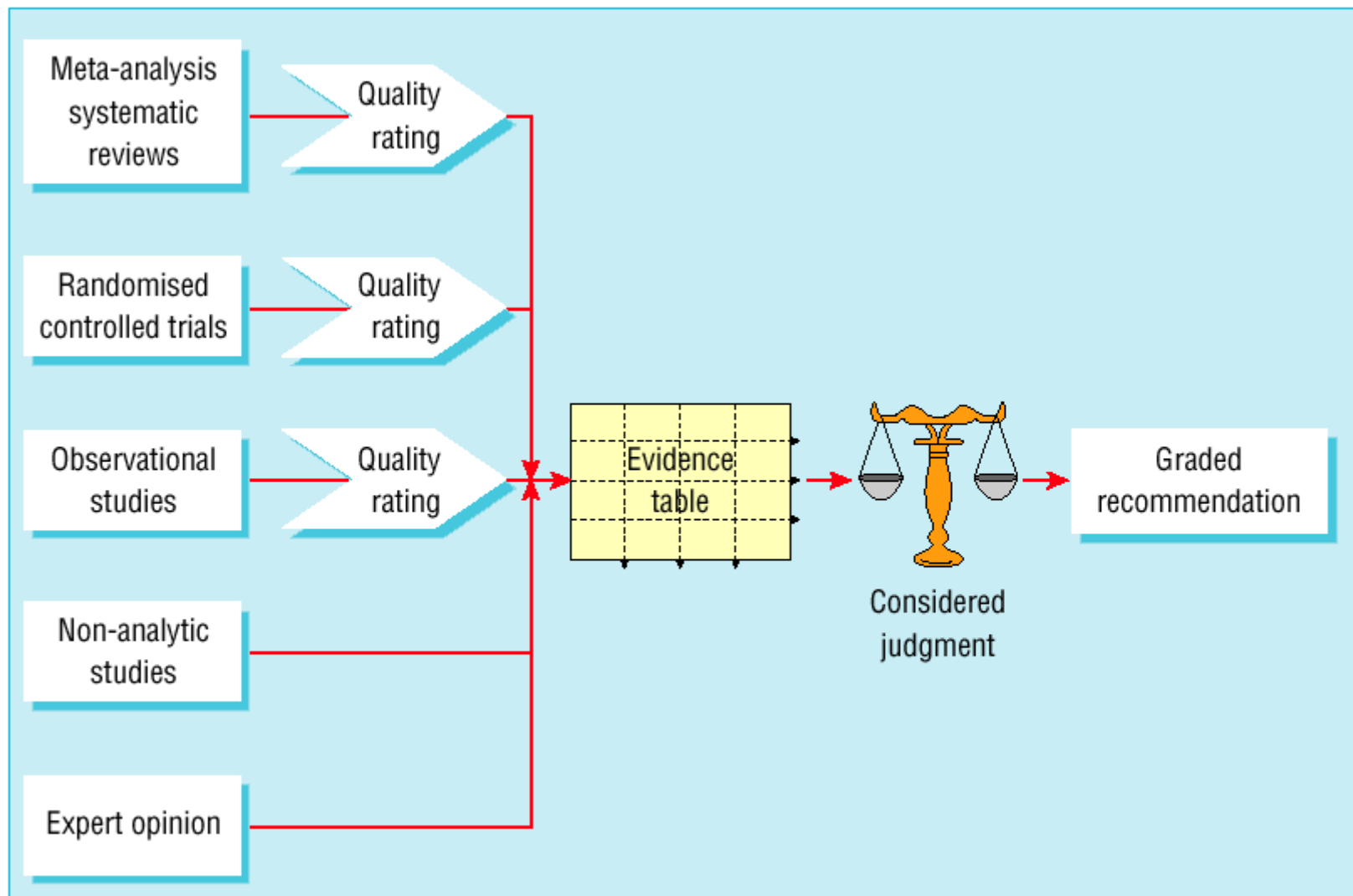
- Protocolli diagnostico-trapeutici
- Profili di cura (clinical pathways)
-
- Rappresentanti farmaceutici

Cosa sono, oggi, le linee-guida?

- *raccomandazioni di comportamento clinico, elaborate mediante un processo di revisione sistematica della letteratura e delle opinioni di esperti, con lo scopo di aiutare i medici e i pazienti a decidere le modalità assistenziali più appropriate in specifiche situazioni cliniche* (Institute of Medicine)
- **basate sulle migliori prove di efficacia esistenti**
- elaborate con **metodologia esplicita**
- da gruppi multidisciplinari
- dotate di una **gradazione**
- **peer reviewed**
- aggiornate in continuo (data di scadenza)

Produttori di LG

- Due livelli
 - Produzione a partire da studi primari (RCT) o secondari (rassegne sistematiche)
 - Ministeri della Sanità
 - Agenzie di *Technology Assessment*
 - Agenzie centrali di produzione di LG
 - Società scientifiche
 - Traduzione e adattamento di LG già esistenti
 - ASL
 - Ospedali
 - Regioni
 - (Oltre a quelle precedenti)



Overview of the process for developing and grading guideline recommendations

Alternative per l'elaborazione di raccomandazioni cliniche

- *Conferenze di consenso*
 - Elaborazione di raccomandazioni da parte di una giuria dopo consultazione di esperti che hanno l'incarico di valutare le prove disponibili
- *Valutazioni di appropriatezza delle pratiche*
 - Definizione di appropriato/non appropriato data a pratiche mediche da un panel di esperti
- *Technology assessment*
 - consiste nella valutazione di benefici, rischi e costi (clinici, sociali, economici, di sistema) del trasferimento delle tecnologie sanitarie nella pratica clinica. Mira a fornire ai decisori della sanità le informazioni necessarie per fare scelte appropriate sul piano dell'efficienza allocativa.

Forza delle raccomandazioni (1)

Category of evidence:

- Ia) from meta-analysis of randomised controlled trials
- Ib) from at least one randomised controlled trial
- IIa) from at least one controlled study without randomisation
- IIb) from at least one other type of quasi-experimental study
- III) from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies
- IV) from expert committee reports or opinions or clinical experience of respected authorities, or both

Forza delle raccomandazioni (2)

Strength of recommendation:

- A) directly based on category I evidence
- B) directly based on category II evidence or extrapolated recommendation from category I evidence
- C) directly based on category III evidence or extrapolated recommendation from category I or II evidence
- D) directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence

Argomenti delle linee-guida

Table 1.1 **Types of clinical and public health questions, ideal study types and major appraisal issues**

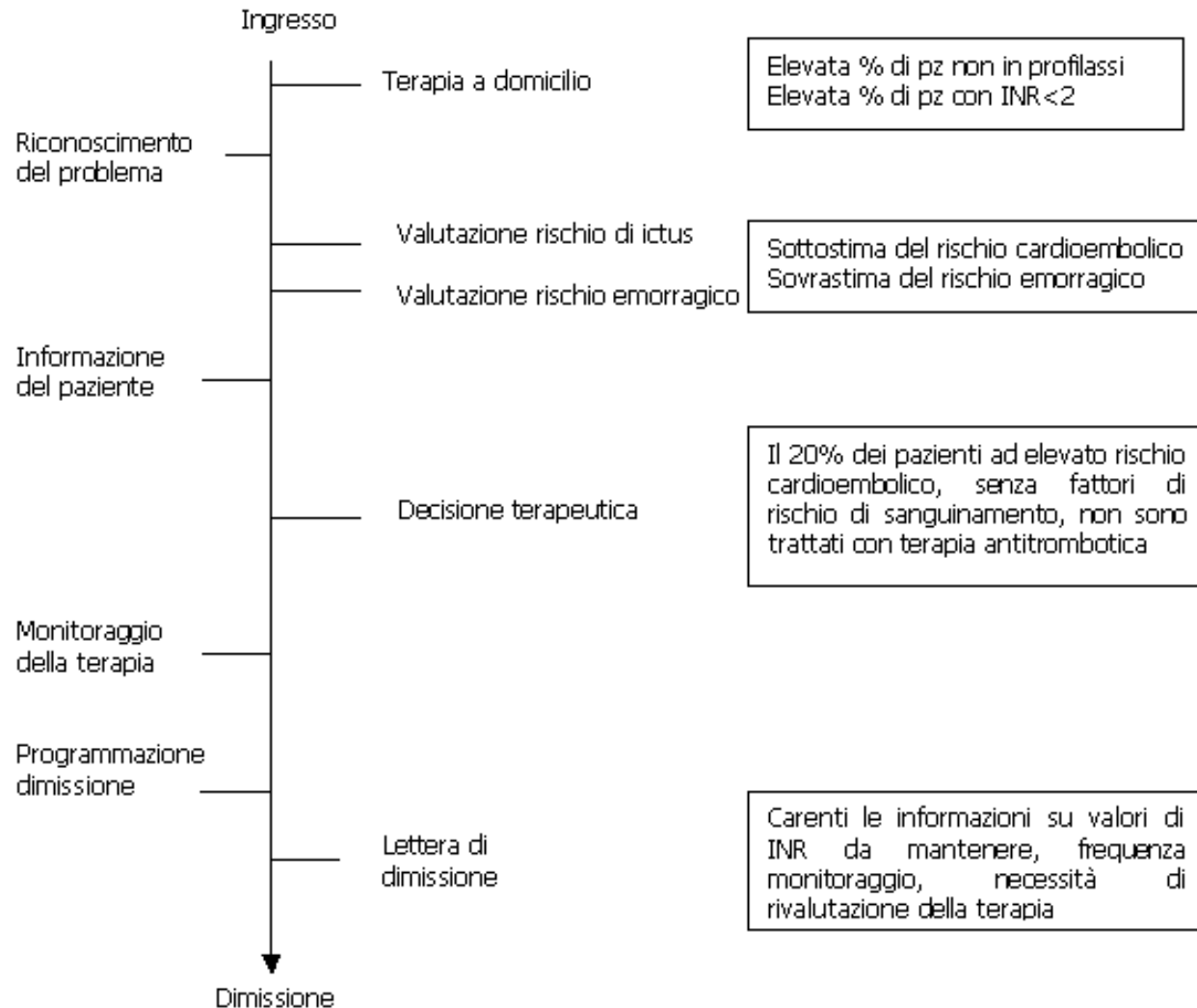
Question	Study types	Major appraisal issues
1. Intervention	Systematic review RCT's Cohort study Case-control study	Randomisation Follow-up complete Blinding of patients and clinicians
2. Frequency/ rate (burden of illness)	Systematic review Cohort study Cross-sectional study	Sample frame Case ascertainment Adequate response/ follow-up achieved
3. Diagnostic test performance	Systematic review Cross-sectional study (random or consecutive sample)	Independent, blind comparison with 'gold standard' Appropriate selection of patients
4. Aetiology and risk factors	Systematic review Cohort study Case-control study	Groups only differ in exposure Outcomes measurement Reasonable evidence for causation
5. Prediction and prognosis	Systematic review Cohort/survival study	Inception cohort Sufficient follow-up

Criteria per la scelta degli argomenti

(ASO Molinette)

- **aree con ampia variabilità della pratica clinica o degli esiti (a livello locale)**
- terapia anticoagulante nella prevenzione degli eventi cardioembolici nei pazienti con fibrillazione atriale cronica o la profilassi della TVP
- **aree con improprio utilizzo delle risorse**
- indagini strumentali effettuate in assenza di prevedibile utilità come la radiografia del cranio nei traumi cranici minori o alcuni farmaci prescritti al di là della loro utilità (ad esempio i gastroprotettori o i "neuroprotettori")
- **condizioni per le quali esistono trattamenti di provata efficacia ed in cui la morbilità o la mortalità possono essere ridotte**
- β -bloccanti nello scompenso cardiaco
- **rischio di danno iatrogeno o rischi significativi o costi elevati**
- ad esempio l'uso di antibiotici a rischio di creare resistenze o l'uso di certi antineoplastici
- **aree di priorità clinica per l'azienda o priorità indicate dal SSN**
- prevenzione delle lesioni da decubito, la riduzione delle degenze per particolari patologie o la Day Surgery
- **necessità di una Linea Guida espressa dalla comunità scientifica locale o da parte dell'utenza o delle sue rappresentanze (URP, Associazioni di pazienti)**

Paziente affetto da fibrillazione atriale non-valvolare
- Esempio di analisi del problema -



LG Piemontesi

Linee Guida

TUMORI DEL COLON-RETTO - linee guida clinico organizzative per la Regione Piemonte

Regione Piemonte Assessorato Sanità - Commissione Oncologica Regionale - Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte
Settembre 2001

TUMORE DELLA MAMMELLA - linee guida clinico organizzative per la Regione Piemonte

Regione Piemonte Assessorato Sanità - Commissione Oncologica Regionale - Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte
Luglio 2002

LINEE-GUIDA SULL'ICTUS ISCHEMICO

Gruppo di lavoro multidisciplinare per le linee-guida sull'ictus ischemico - Gruppo Evidence-Based Medicine
Azienda Sanitaria Ospedaliera San Giovanni Battista di Torino
Settembre 2002



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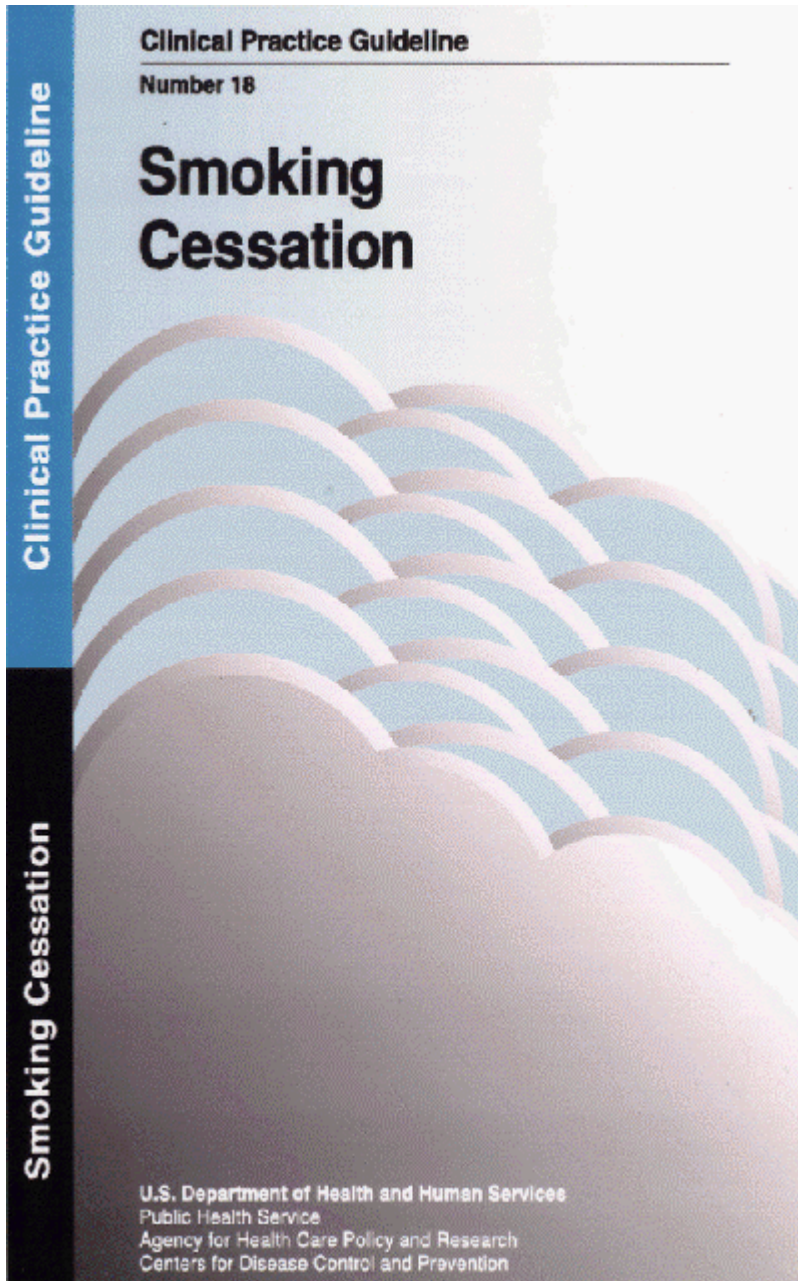
Commissione Oncologica Regionale

CPO

Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

TUMORI DEL COLON-RETTO

linee guida clinico organizzative per la Regione Piemonte



Agency for Health
Care Policy and
Research (AHCPR)

Smoking cessation
guideline

AHCPR - Clinical practice guideline # 18

Smoking Cessation

- **1. Overview**

- Organization of the Guideline and Other Products
- Guideline Development Methodology
 - Guideline Development Process
 - Search and Review of the Literature
 - Inclusion Criteria / Selection of Evidence.
 - Preparation of Evidence Tables / Analysis of Treatment Effect.
 - Outcome Data.
 - Meta-Analytic Techniques
 - Methodology and Limitations.
 - **Strength of Evidence**
 - Interpretation of Meta-Analysis Results
 - Caveats to Recommendation Use
 - External Review of the Guideline

Strenght of evidence

- A. Multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings.
- B. Some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal.
- C. Important clinical situations where the panel achieved consensus on the recommendation in the absence of relevant randomized controlled trials.

- **2. Recommendations for Three Target Audiences**
- Primary Care Clinicians
 - Training Clinicians To Intervene With Their Patients Who Smoke
 - Recommendations for Primary Care Clinicians
- Tobacco Cessation Specialists and Programs
 - Recommendations for Tobacco Cessation Specialists and Programs
- Health Care Administrators, Insurers, and Purchasers
 - Cost-Effectiveness of Smoking Cessation Interventions
 - Recommendations for Health Care Administrators, Insurers, and Purchasers

- **3. Evidence**

- Screen for Tobacco Use
- Advice To Quit Smoking
- Specialized Assessment
- Interventions
 - Type of Clinician
 - Treatment Formats
 - Efficacy of Self-Help Treatment Alone
 - Intensity of Person-to-Person Clinical Intervention
 - Content of Smoking Cessation Interventions
 - Person-to-Person Treatment: Duration and Number of Sessions
 - Smoking Cessation Pharmacotherapy
 - Transdermal Nicotine / Nicotine Gum / Other Nicotine Replacements
 - Over-the-Counter Nicotine Replacement Therapy.
 - Clonidine / Antidepressants / Anxiolytics/Benzodiazepines
 - Silver Acetate.
- Followup Assessment and Procedures
- Reimbursement for Smoking Cessation Treatment

Advice To Quit Smoking

- **Recommendation:** All *physicians* should strongly advise every patient who smokes to quit because evidence shows that physician advice to quit smoking increases abstinence rates. (Strength of Evidence = A)
- **Recommendation:** All *clinicians* should strongly advise their patients who use tobacco to quit. Although studies have not independently addressed the impact of advice to quit by all types of nonphysician clinicians, it is reasonable to believe that such advice is effective in increasing their patients' long-term quit rates. (Strength of Evidence = B)

Table 11. Meta-analysis: Efficacy of and estimated abstinence rates for advice to quit by a physician (n = 7 studies)

Advice	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No advice to quit (reference group)	9	1.0	7.9
Physician advice to quit	10	1.3 (1.1-1.6)	10.2 (8.5-12.0)

Intensity of Clinical Interventions

- **Recommendation: Minimal interventions lasting less than 3 minutes increase abstinence rates. Every tobacco user should be offered at least a minimal intervention. (Strength of Evidence = A)**
- **Recommendation: There is a strong dose-response relation between the session length of person-to-person contact and successful treatment outcomes. Intensive interventions are more effective than less intensive interventions and should be used whenever possible. (Strength of Evidence = A)**

Table 12. Meta-analysis: Efficacy of and estimated abstinence rates for various intensity levels of person-to-person contact (n = 43 studies)

Level of contact	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No contact	30	1.0	10.9
Minimal counseling (< 3 minutes)	19	1.3 (1.01, 1.6)	13.4 (10.9, 16.1)
Low intensity counseling (3 – 10 minutes)	16	1.6 (1.2, 2.0)	16.0 (12.8, 19.2)
Higher intensity counseling (> 10 minutes)	55	2.3 (2.0, 2.7)	22.1 (19.4, 24.7)

Formats of Psychosocial Treatments

- **Recommendation: Proactive telephone counseling, group counseling, and individual counseling formats are effective and should be used in smoking cessation interventions. (Strength of Evidence = A)**
- **Recommendation: Smoking cessation interventions that are delivered in multiple formats increase abstinence rates and should be encouraged. (Strength of Evidence = A)**

Table 17. Meta-analysis: Efficacy of and estimated abstinence rates for various types of format (n = 58 studies)

Format	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No format	20	1.0	10.8
Self-help	93	1.2 (1.02, 1.3)	12.3 (10.9, 13.6)
Proactive telephone counseling	26	1.2 (1.1, 1.4)	13.1 (11.4, 14.8)
Group counseling	52	1.3 (1.1, 1.6)	13.9 (11.6, 16.1)
Individual counseling	67	1.7 (1.4, 2.0)	16.8 (14.7, 19.1)

Bupropion SR (Sustained Release Bupropion)

- **Recommendation: Bupropion SR is an efficacious smoking cessation treatment that patients should be encouraged to use. (Strength of Evidence = A)**

Table 25. Meta-analysis: Efficacy of and estimated abstinence rates for bupropion SR (n = 2 studies)

Pharmacotherapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	2	1.0	17.3
Bupropion SR	4	2.1 (1.5, 3.0)	30.5 (23.2, 37.8)

Nicotine replacement

- **Recommendation: Nicotine gum, patch, nasal spray are efficacious smoking cessation treatments that patients should be encouraged to use. (Strength of Evidence = A)**
- **Recommendation: Clinicians should offer 4 mg rather than 2 mg nicotine gum to highly dependent smokers. (Strength of Evidence = B)**

Table 26. Meta-analysis: Efficacy of and estimated abstinence rates for 2 mg nicotine gum (n = 13 studies)

Pharmacotherapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	16	1.0	17.1
Nicotine gum	18	1.5 (1.3, 1.8)	23.7 (20.6, 26.7)

Table 27. Meta-analysis: Efficacy of and estimated abstinence rates for nicotine inhaler (n = 4 studies)

Pharmacotherapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	4	1.0	10.5
Nicotine inhaler	4	2.5 (1.7, 3.6)	22.8 (16.4, 29.2)

Table 28. Meta-analysis: Efficacy of and estimated abstinence rates for nicotine nasal spray (n = 3 studies)

Pharmacotherapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	3	1.0	13.9
Nicotine nasal spray	3	2.7 (1.8, 4.1)	30.5 (21.8, 39.2)

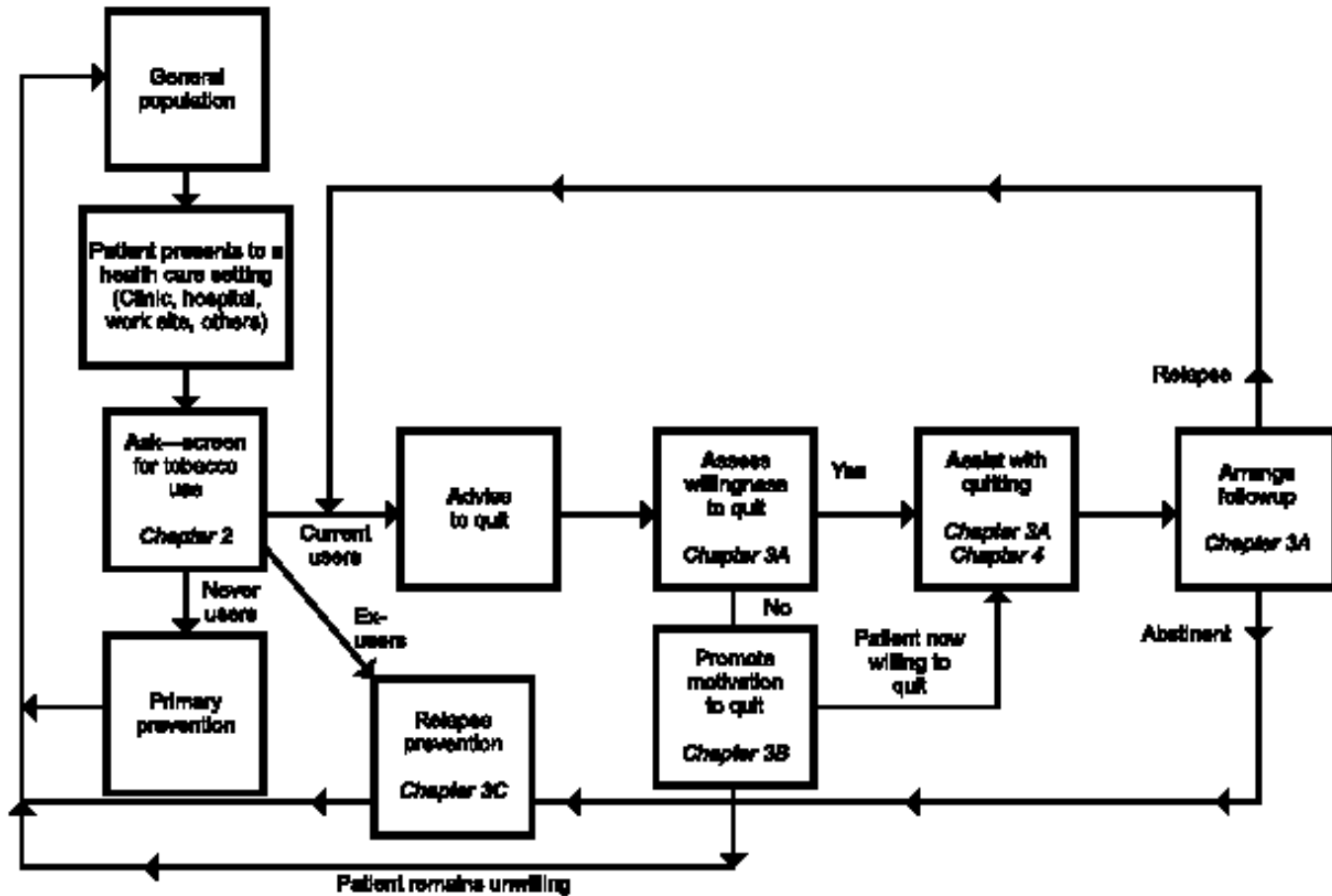
Organizzazione dell'intervento raccomandato

Table 3. The "5 A's" for brief intervention

Ask about tobacco use.	Identify and document tobacco use status for every patient at every visit. (Brief Strategy A1)
Advise to quit.	In a clear, strong and personalized manner urge every tobacco user to quit. (Brief Strategy A2)
Assess willingness to make a quit attempt.	Is the tobacco user willing to make a quit attempt at this time? (Brief Strategy A3)
Assist in quit attempt.	For the patient willing to make a quit attempt, use counseling and pharmacotherapy to help him or her quit. (Brief Strategy A4)
Arrange followup.	Schedule followup contact, preferably within the first week after the quit date. (Brief Strategy A5)

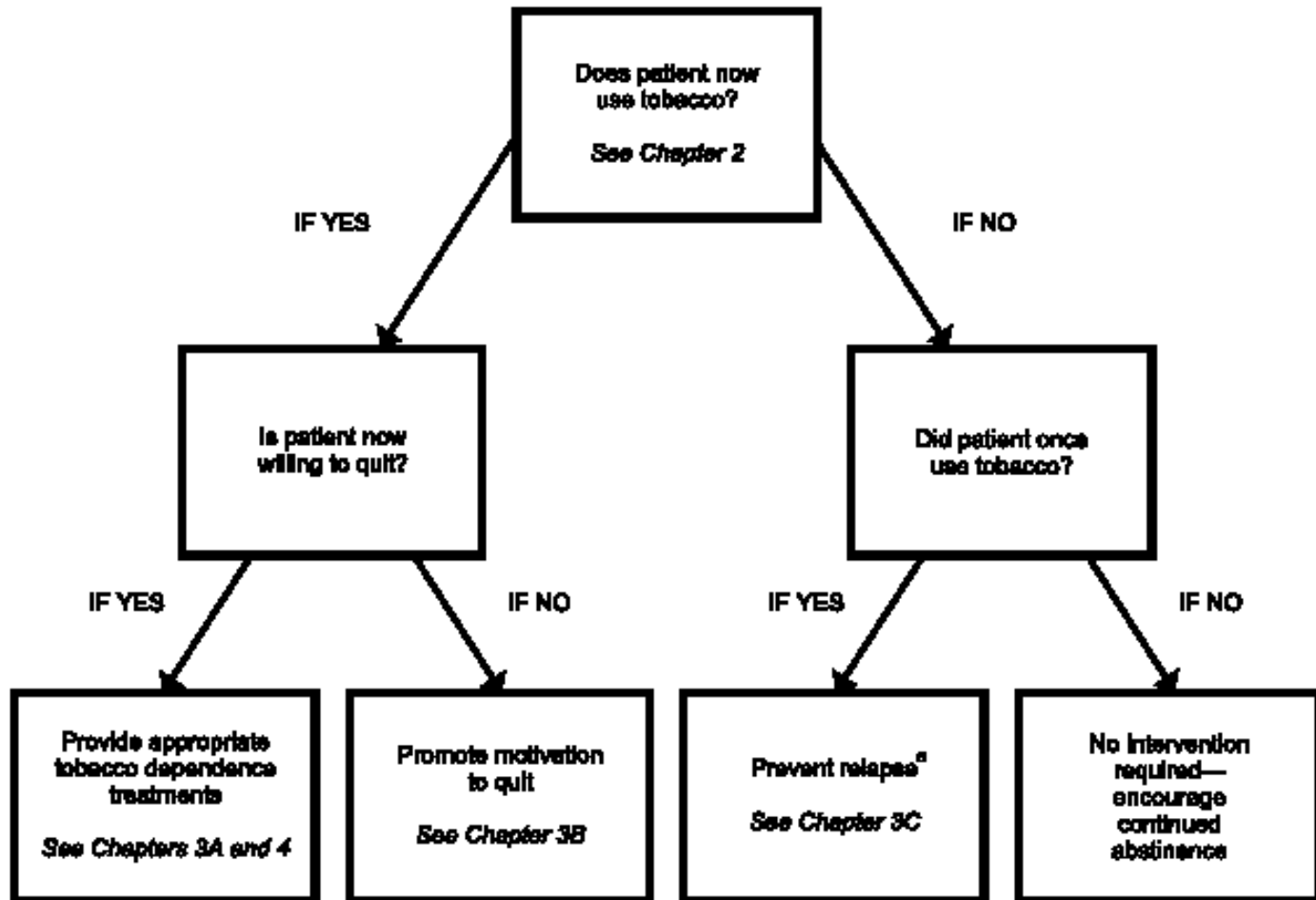
a livello di popolazione ...

Figure 2. Model for treatment of tobacco use and dependence



...e a livello individuale

Figure 3. Algorithm for treating tobacco use



^a Relapse prevention interventions are not necessary in the case of the adult who has not used tobacco for many years.

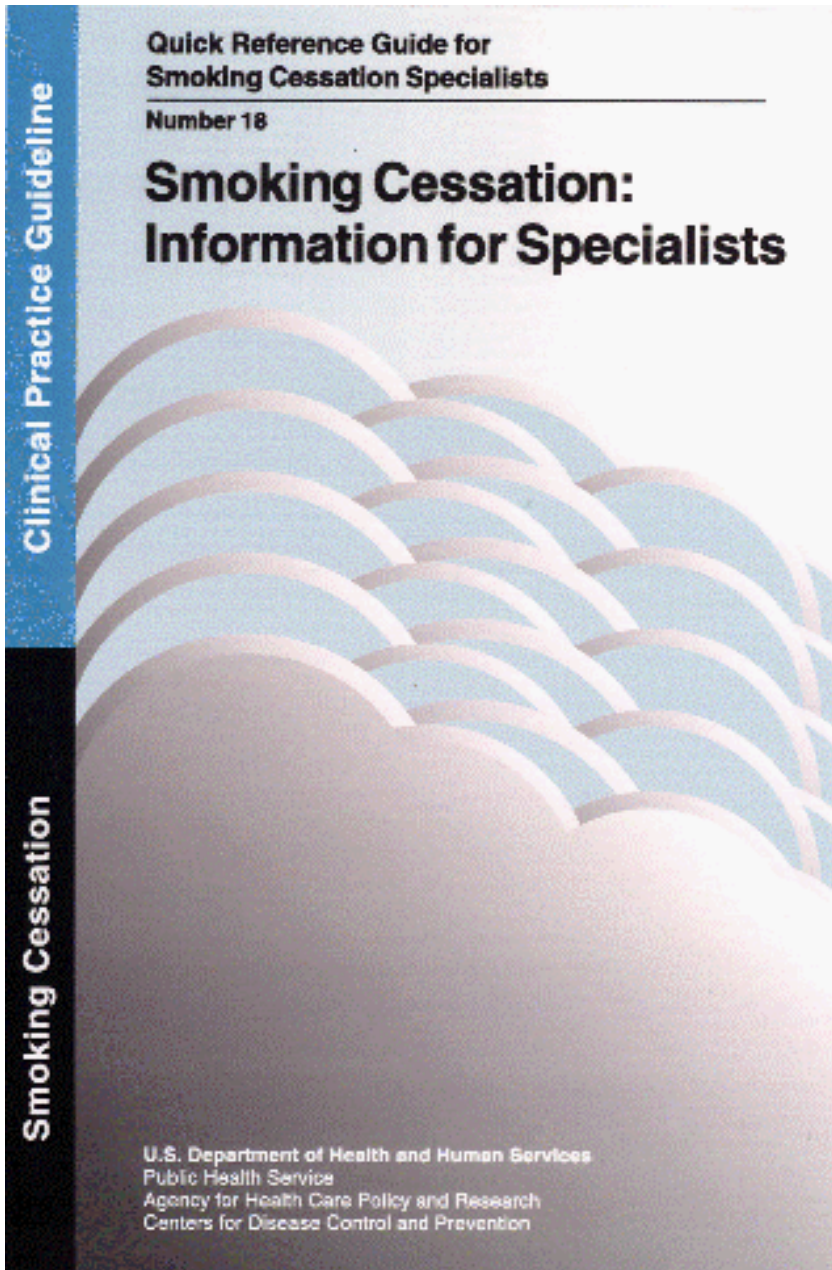
- **4. Promoting the Motivation To Quit and Preventing Relapse**

- Promoting the Motivation To Quit
- Relapse Prevention

- **5. Special Populations and Topics**

- Gender
- Racial and Ethnic Minorities
- Pregnancy
- Hospitalized Smokers
- Smokers With Psychiatric Comorbidity
- Weight Gain After Smoking Cessation
- Smokeless Tobacco Use
- Children and Adolescents: Primary Prevention of Tobacco Addiction

- References
- Glossary
- Contributors
 - Smoking Cessation Guideline Panel
 - Consultants
 - Project Staff
 - Additional Project Staff
 - Federal Liaisons
 - Canadian Government Liaison
 - Article Reviewers
 - AHCPR Staff
 - Contract Support
 - Peer Reviewers
- Annexes
 - Strategies for the Primary Care Physician
 - Strategies for the Tobacco Cessation Specialist
 - Strategies for Health Care Administrators, Insurers, and Purchasers
 - General Strategies



Quick Reference Guide for
Smoking Cessation Specialists

Number 18

Smoking Cessation: Information for Specialists

Clinical Practice Guideline

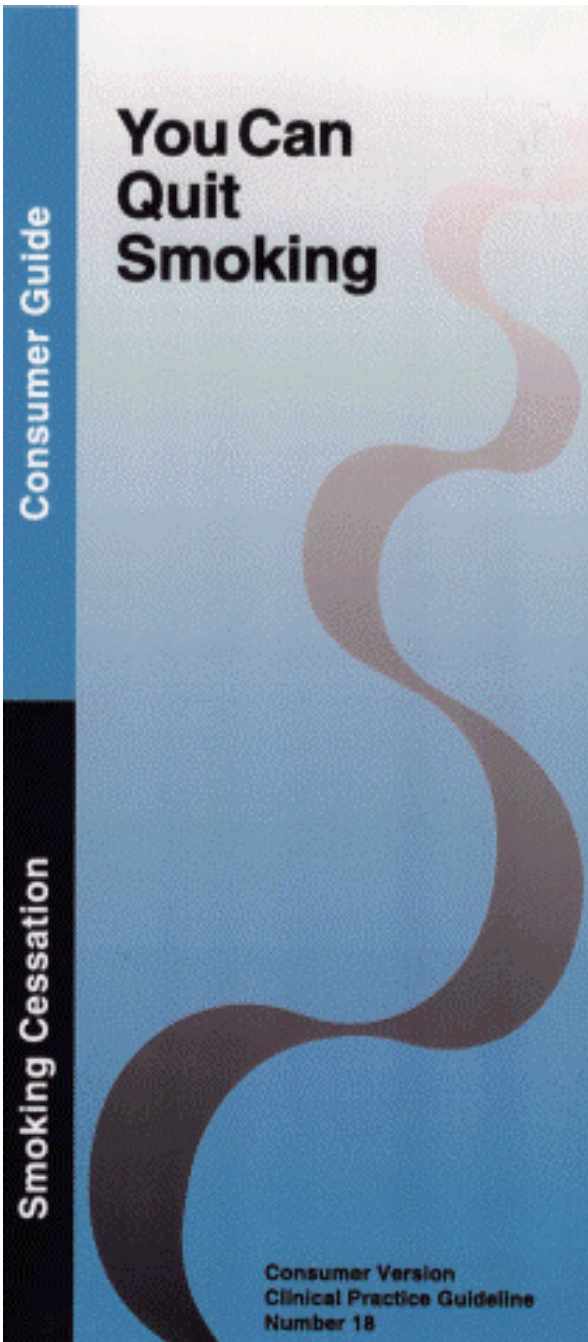
Smoking Cessation

U.S. Department of Health and Human Services
Public Health Service
Agency for Health Care Policy and Research
Centers for Disease Control and Prevention

AHCPR

Smoking cessation
guideline

Versione per gli
specialisti



You Can Quit Smoking

Consumer Guide

Smoking Cessation

Consumer Version
Clinical Practice Guideline
Number 18

AHCPR

Smoking cessation
guideline

Versione per gli
utenti

Guía para el público

**Si quiere,
puede
dejar
de fumar**

Dejar de fumar

Version para el público
Guía de práctica clínica
Número 18

AHCPR

Smoking cessation
guideline

Versione per gli
utenti (lingua spagnola)

Come valutare la qualità delle LG?

Appraisal of Guidelines for Research & Evaluation (AGREE)

- **Checklist per la valutazione della qualità di linee guida per la pratica clinica**
- <http://www.regione.emilia-romagna.it/agenziasan/colldoss/index.htm>
- <http://www.agreecollaboration.org>
- *Frutto di una collaborazione internazionale finanziata da fondi europei e coordinata da F. Cluzeau*
- *Tradotta dalla regione Regione Emilia Romagna*

Struttura di AGREE

- ***Obiettivo e motivazione (item 1-3)***
 - obiettivi quesiti e popolazione
- ***Coinvolgimento delle parti in causa (item 4-7)***
- ***Rigore della elaborazione (item 8-14)***
 - processo per identificare e sintetizzare le informazioni e per formulare le raccomandazioni e per mantenerle aggiornate.
- ***Chiarezza e presentazione (item 15-18)***
 - formulazione e formato della linea guida.
- ***Applicabilità (item 19-21)***
 - implicazioni organizzative, economiche e sui comportamenti professionali
- ***Indipendenza editoriale (item 22-23)***
 - l'indipendenza e esplicito riconoscimento di conflitti di interesse



Siti istituzionali per la ricerca di linee-guida

- Piano nazionale linee-guida:
www.pnlg.it/
- Agency for Health Research and Quality
www.ahrq.gov/
www.guideline.gov/index.asp
- Health Technology Assessment UK
www.hta.nhsweb.nhs.uk/internat.htm
- Center for Disease Control
www.cdc.gov
- Scottish Intercollegiate Guidelines Network (SIGN)
www.sign.ac.uk
- Canadian Medical Association Clinical Practice Guidelines Infobase
<http://www.cma.ca/cpgs/>
- GIMBE Gruppo Italiano Medicina Basata sull'Evidenza
www.gimbe.org

Cercare l'EBN sul web

- Joanna Briggs Institute (JBI) Evidence Based Nursing and Midwifery www.joannabriggs.edu.au
- Uk Centre for Evidence Based Nursing
www1.york.ac.uk/healthsciences/centres/evidence/cebn.htm
- Canadian Centre for Evidence Based Nursing
- New Zeland Centre of Evidence Based Nursing (Coll JBI)
- Victorian Centre for Nursing Practice Research (Coll JBI)
- Sarah Cole Hirsh Institute for Best Nursing Practices Based on Evidence (Germania)
- Scottish Intercollegiate Guidelines Network (SIGN)
www.sign.ac.uk/guidelines/published/index.html

Clinica e ricerca

	Gerarchia evidenza	Percorso	
		Clinica	Ricerca
Opinione di esperti	0		
Case report, case series	1		
Studi osservazionali	2		
Singoli RCT	3		
Rassegne sistematiche	4		
Linee-guida	-		
L-g locali, altri materiali E-B	-		

Il caso della radioterapia nel trattamento del tumore della mammella

Ipotesi di partenza

- La recidiva locale riduce del 50% la sopravvivenza a 5 anni (Fortin 1999)
- La radioterapia dopo la chirurgia potrebbe aumentare il controllo locale della malattia

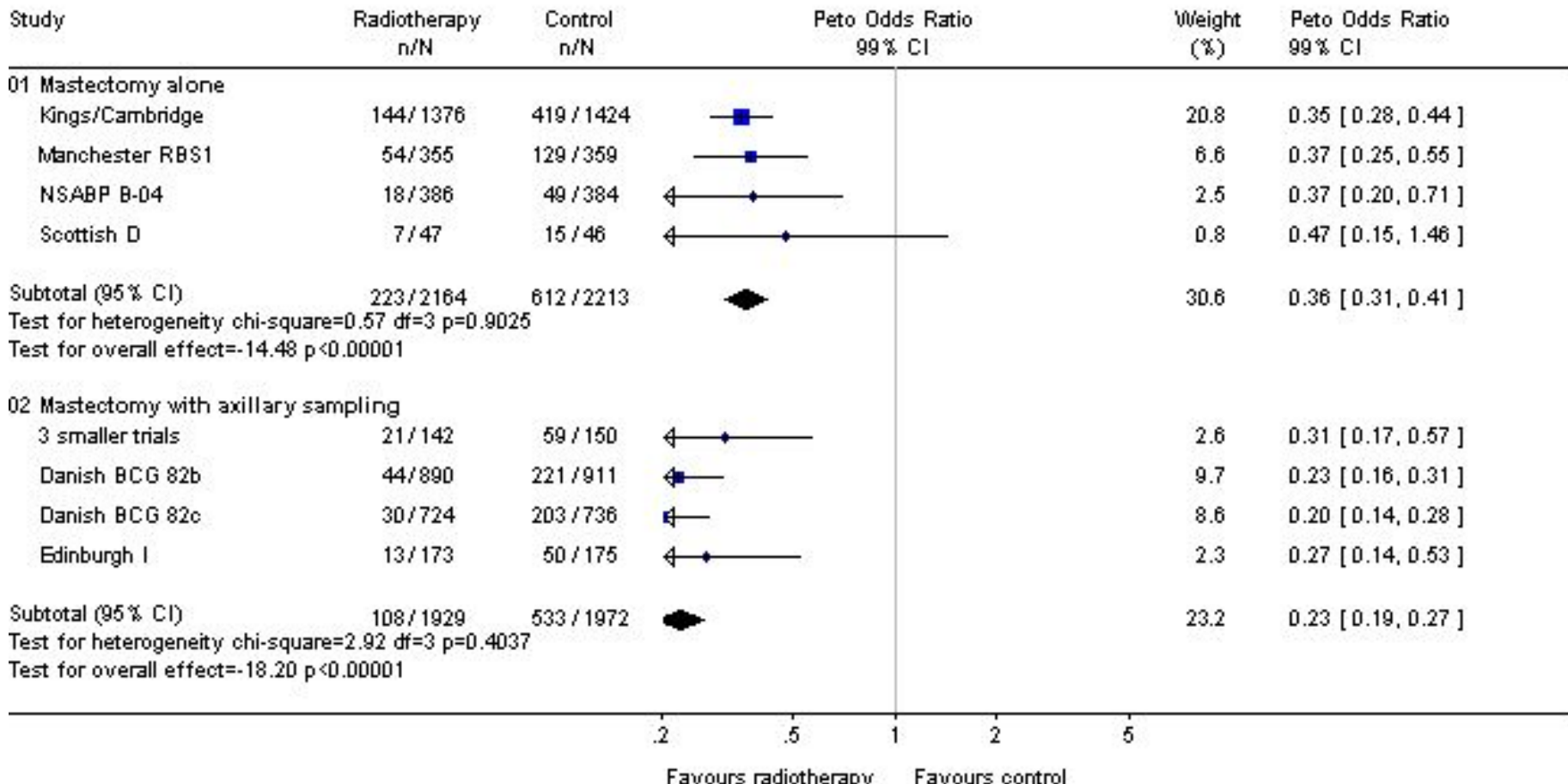
RCT e altri studi

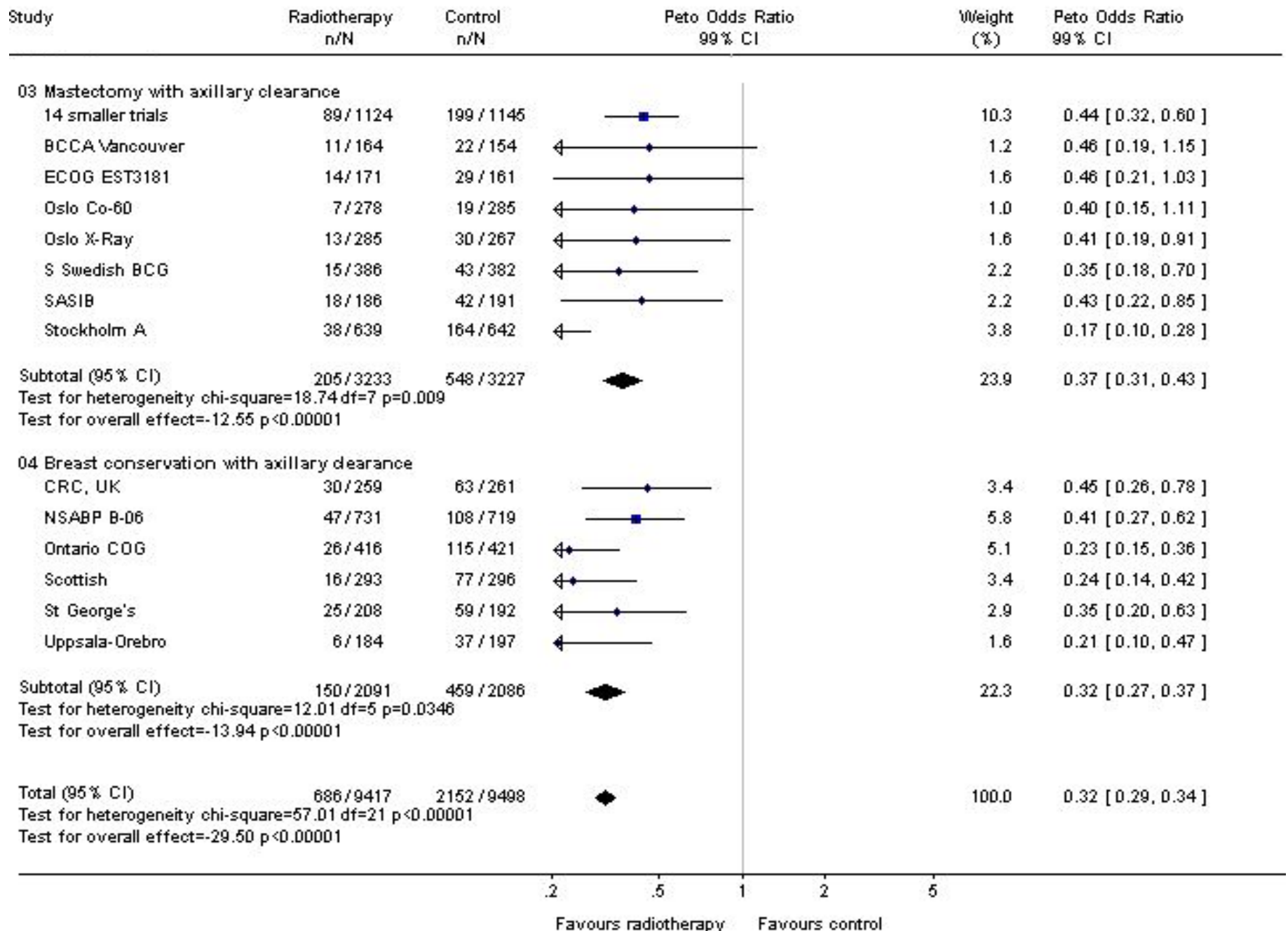
A u t o r e	T i p o	R i s u l t a t i
V a n d e S t e e n e 2000	R e v i s i o n e d i R C T	R T post-operatoria riduce il rischio di ripresa locale in chirurgia conservativa
B a r t e l i n k 2001	R C T	Il sovradosaggio riduce del 40% le recidive locali
R e c h t 1991	C O O	Il trattamento R T precedente la 16° riduce di 2/3 le recidive locali La R T riduce di 2/3 il rischio di morte dopo mastectomia nelle pazienti a rischio

Revisione Cochrane

Early Breast Cancer Trialists' Collaborative Group 2003

Review: Radiotherapy for early breast cancer
 Comparison: 01 Radiotherapy versus no radiotherapy
 Outcome: 02 Isolated local recurrence





SIGN: Breast cancer in women - 1998

9.1 RADIOTHERAPY AFTER WIDE LOCAL EXCISION OR QUADRANTECTOMY

Several randomised trials have compared limited breast surgery to the same with radiotherapy.^{69,90-92} All show that radiotherapy to the breast after wide local excision or quadrantectomy significantly reduces the risk of recurrence within the breast.

Evidence level Ib

A Radiotherapy should normally be given to the breast after wide local excision.

SIGN: Breast cancer in women - 1998

9.2 RADIOTHERAPY AFTER MASTECTOMY

(See section 8.1.2 for factors affecting the decision to proceed with mastectomy.)

Radiotherapy after mastectomy reduces the risk of local recurrence, but has very little effect on overall survival due to increased cardiac morbidity.⁹⁶ Two more recent papers^{97,98} show that, in premenopausal women receiving adjuvant chemotherapy, postmastectomy radiotherapy significantly improves survival. An overview showed that the rate of local recurrence is three times lower after radiotherapy compared to surgery alone.⁹⁹ Those patients at high risk of local recurrence are the group in whom survival benefit is most likely. Among the factors associated with high risk of recurrence are tumour size (> 5 cm), grade, nodal status, lymphatic invasion and involvement of deep margins; risk is a summation of these factors.

Evidence level Ib

A Radiotherapy should be given to the chest wall after mastectomy in those patients judged to be at high risk of local recurrence.

LG Piemontesi: raccomandazioni A

- Le donne con tumori infiltranti sottoposte a chirurgia conservativa devono essere sottoposte ad un trattamento radiante sul tessuto mammario residuo
- Il sovradosaggio del sito chirurgico è raccomandato
- Nel caso di associazione con terapie sistemiche, è preferibile iniziare la RT entro 4 mesi dall'intervento chirurgico, compatibilmente con i tempi previsti per la chemioterapia quando questa comprenda antracicline
- Dopo mastectomia la RT sulla parete toracica deve essere programmata nelle pazienti ad alto rischio di recidiva locale

INDICATORI	NHS ¹	SQTM ²	TIPOL.	OBIETTIVO
7. RADIOTERAPIA				
Percentuale di pazienti che ricevono una valutazione da parte del radioterapista			P	
Percentuale di pazienti che ricevono radioterapia a seguito di chirurgia conservativa	X	X	P	≥ 95%
Percentuale di pazienti che non effettuano chemioterapia che ricevono radioterapia entro 12 settimane dall'intervento conservativo			P	≥ 90%
Tempi di attesa per il trattamento radioterapico dopo trattamento chirurgico e/o chemioterapico			S	
Percentuale di pazienti (non incluse in terapie sistemiche adjuvanti di durata maggiore) che hanno effettuato chemioterapia adjuvante e che ricevono la radioterapia entro 4 mesi dall'intervento conservativo		X	P	≥ 90%
Percentuale di interruzione del trattamento per effetti tossici			R	

NHS= National Health System

SQTM= Scheda computerizzata sulla Qualità del trattamento del Tumore della Mammella

Tipol= P=processo; S=struttura; R=risultato

Frequenza dei percorsi di trattamento delle pazienti trattate chirurgicamente per tumore della mammella per caratteristiche individuali e strutturali. Piemonte, 2001

	NESSUNA TERAPIA		ALTRE TERAPIE :						TOTALE	
			RADIOTERAPIA		CHEMIOTERAPIA		RADIO + CHEMIOTERAPIA			
	N	%	N	%	N	%	N	%	N	%
ETA':										
▪ <70anni	229	23,0	344	34,6	161	16,2	260	26,2	994	100
▪ ≥ 70 anni	305	63,3	124	25,7	33	6,8	20	4,1	482	100
DISEASE STAGING:										
▪ N0 M0	480	37,9	410	32,4	152	12	225	17,8	1267	100
▪ N+ o M+	54	25,8	58	27,8	42	20,1	55	26,3	209	100
TIPO INTERVENTO:										
▪ Conservativo	272	27,1	444	44,3	51	5,1	236	23,5	1003	100
▪ Mastectomia	262	55,4	24	5,1	143	30,2	44	9,3	473	100
N° CASI/ANNO:										
▪ ≥100	95	23,3	162	39,7	36	8,8	115	28,2	408	100
▪ 50-99	131	40,2	101	31,0	40	12,3	54	16,6	326	100
▪ ≤50	308	41,5	205	27,6	118	15,9	111	15,0	742	100