IRCCS Sacro Cuore Don Calabria
Cancer Care Center
Negrar - Verona

ESMO
Designated Centers of Integrated Oncology and Palliative Care

Con il Patrocinio di

AIOM
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SICO
Società Italiana di Psico-Oncologia

STUDI CLINICI: METODOLOGIA

Coordinatore
Dr.ssa Stefania Gori

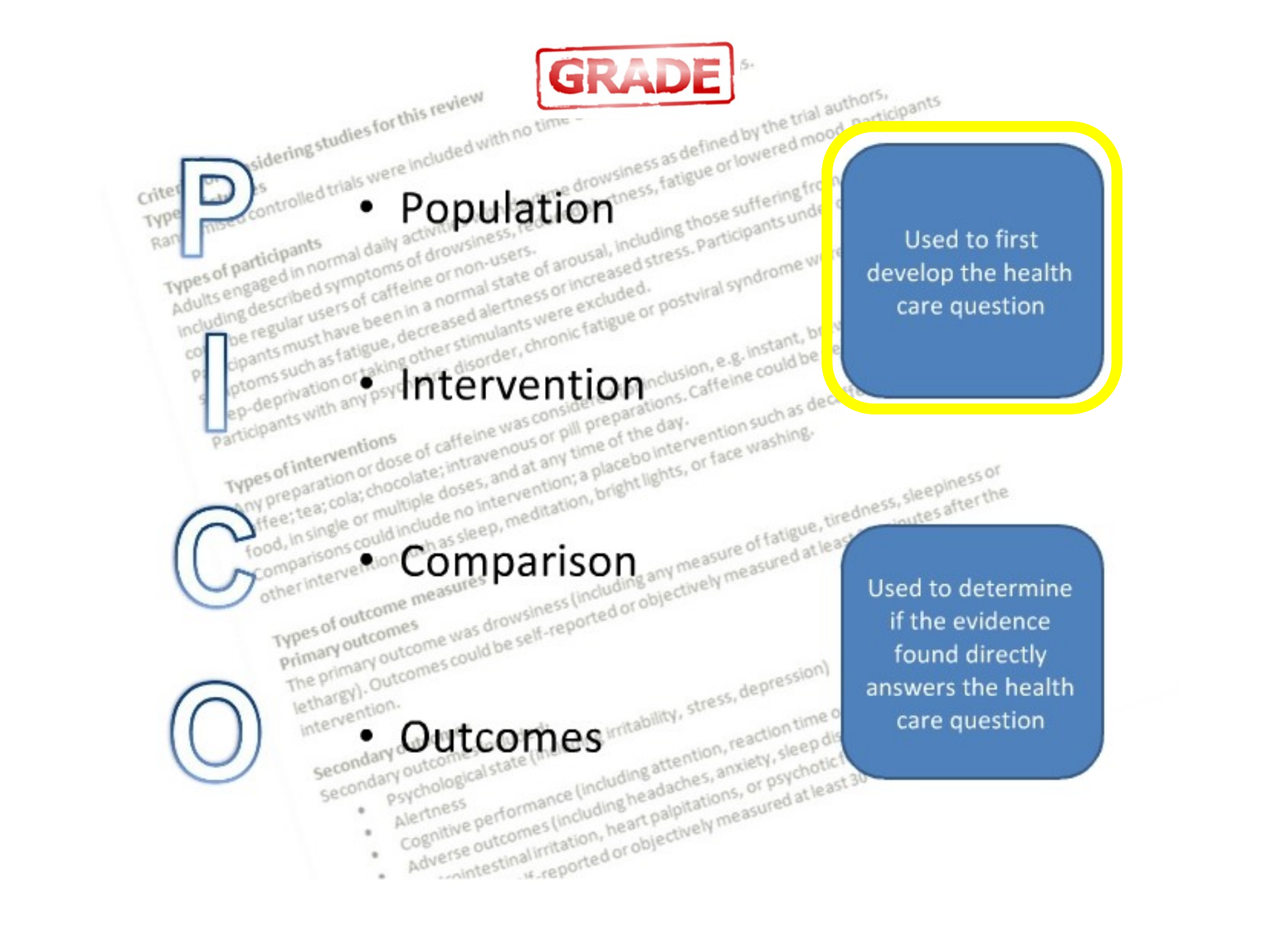
Evento ECM MODULO 2

FORMAZIONE AVANZATA

NEGRAR
8/9 Marzo
2019

Centro Formazione
IRCCS Ospedale Sacro Cuore
Don Calabria

Introduzione


GRADE
P
• Population
I
• Intervention
C
• Comparison
O
• Outcomes
Used to first develop the health care question
Used to determine if the evidence found directly answers the health care question

Il percorso verso la proposta terapeutica…

- Una volta definito con chiarezza il quesito clinico…

Il percorso verso la proposta terapeutica…

- Una volta definito con chiarezza il quesito clinico…
- sarà necessario verificare:
  - l'affidabilità delle evidenze (***confidence***)
  - la diretta (o meno) trasferibilità delle evidenze disponibili alla tipologia di paziente oggetto del quesito clinico (***directness***)
  - la rilevanza clinica degli effetti osservati (***relevance***)

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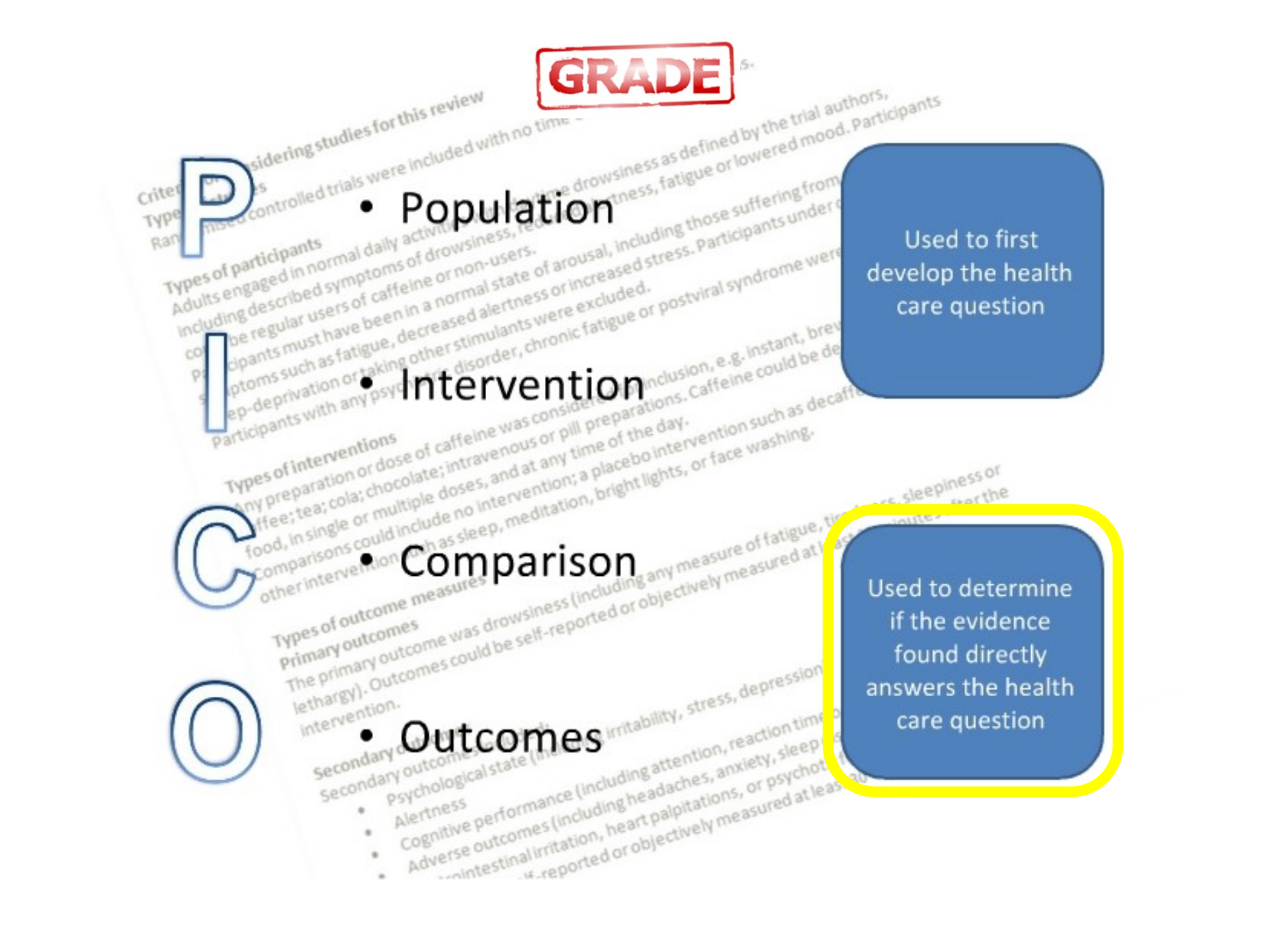
Directness

P.I.C.O.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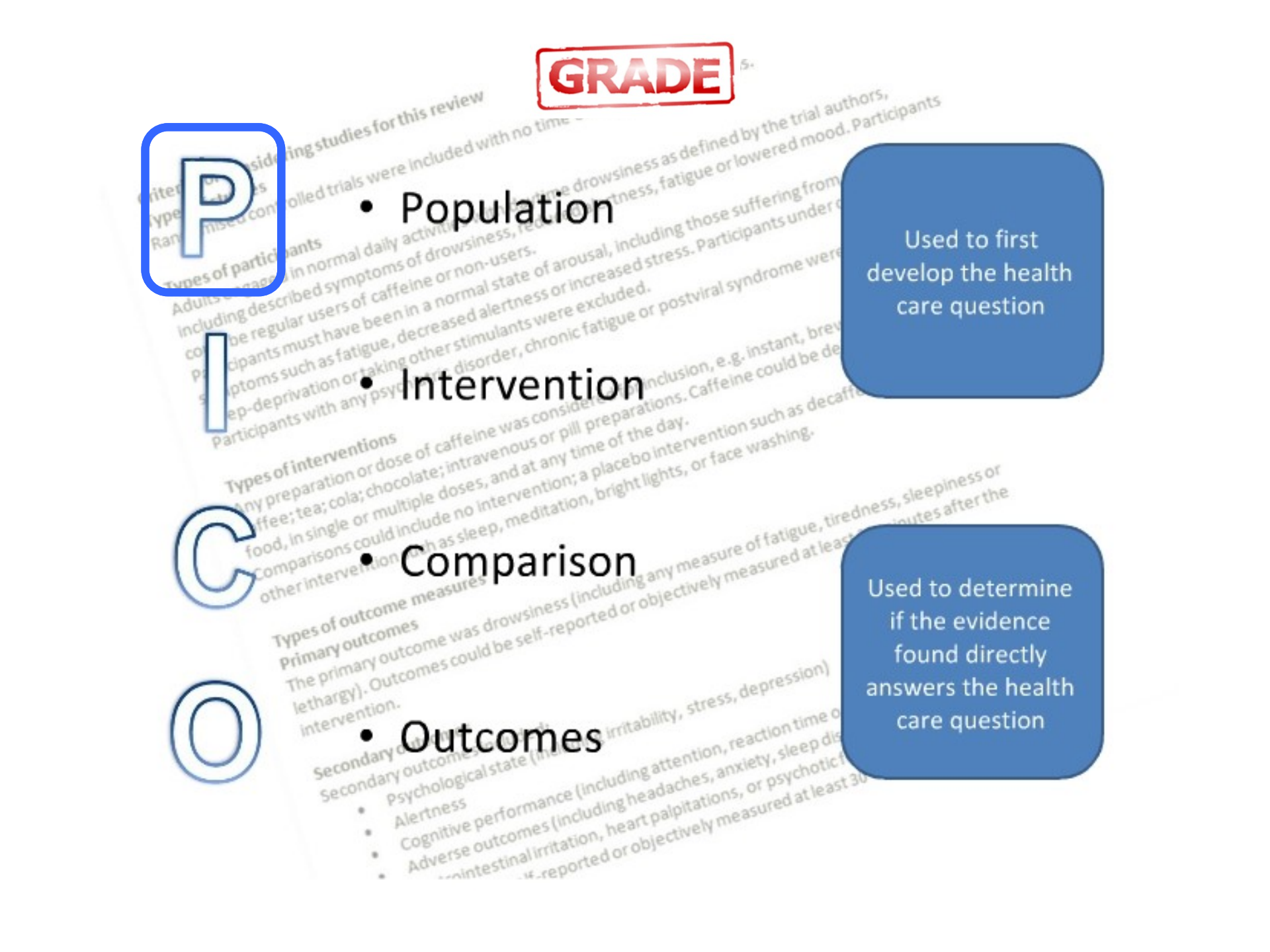
Direct evidence…

…comes from research that:

- is conducted in the **Population** that we are providing answers for;
- includes the **Intervention** that we are interested in…
- …and compares these interventions with the appropriate **Alternatives**;
- measures the **Outcomes** in which we are interested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Strutturazione del Quesito Clinico sec. modello P.I.C.O.

P	Nei **P**azienti con…	Specifiche caratteristiche di malattia (stadio, classe di rischio, ecc.)
I	l'**I**	ggetto
C	(è impiego) in **C**onfronto con…	derabile in alternativa all'inter-vento in esame
O	riguardo agli **O**utcome di beneficio/danno…	Parametri clinico-laboratoristici ritenuti essenziali per la decisio-ne terapeutica

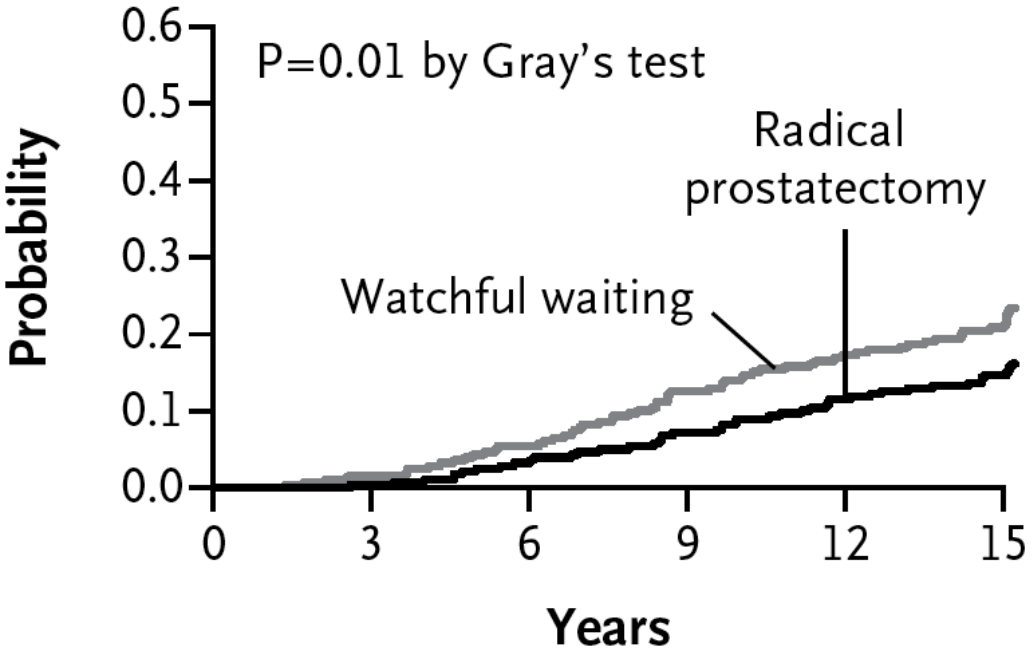
Non necessariamente corrispondenti ai criteri di selezione delle evidenze disponibili!

Radical Prostatectomy versus Watchful Waiting in Early Prostate Cancer

Anna Bill-Axelson, M.D., Ph.D., Lars Holmberg, M.D., Ph.D., Mirja Ruutu, M.D., Ph.D., Hans Garmo, Ph.D., Jennifer R. Stark, Sc.D., Christer Busch, M.D., Ph.D., Stig Nordling, M.D., Ph.D., Michael Häggman, M.D., Ph.D., Swen-Olof Andersson, M.D., Ph.D., Stefan Bratell, M.D., Ph.D., Anders Spångberg, M.D., Ph.D., Juni Palmgren, Ph.D., Gunnar Steineck, M.D., Ph.D., Hans-Olov Adami, M.D., Ph.D., and Jan-Erik Johansson, M.D., Ph.D., for the SPCG-4 Investigators*

N Engl J Med 2011;364:1708-17.

Death from Prostate Cancer, Total Cohort



Diagnostic and Prognostic Factors in Non-Muscle-Invasive Bladder Cancer and Their Influence on Treatment and Outcomes

Willem Oosterlinck [a,*], *Fred Witjes* [b], *Richard Sylvester* [c]

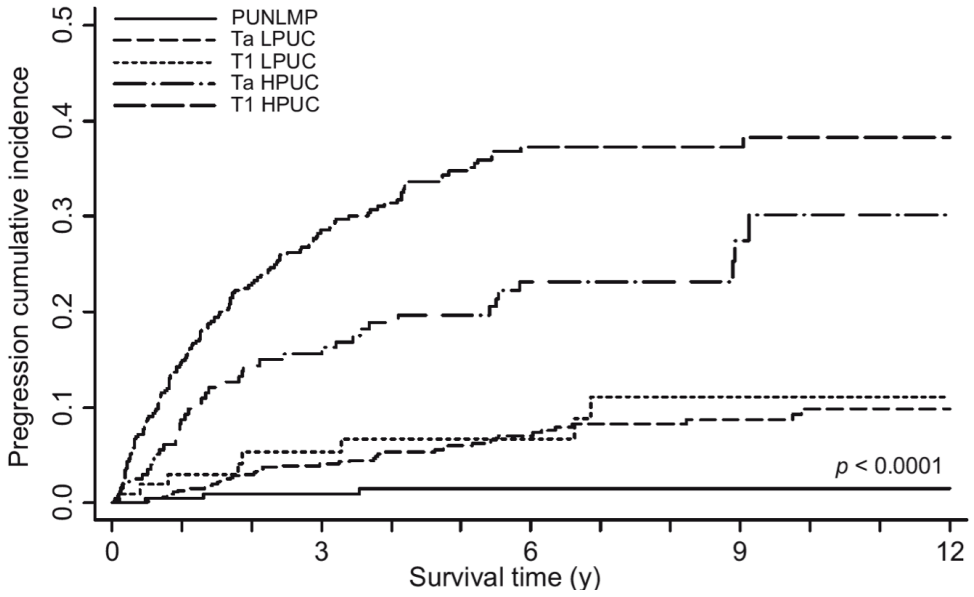
EUROPEAN UROLOGY SUPPLEMENTS 7 (2008) 516–523

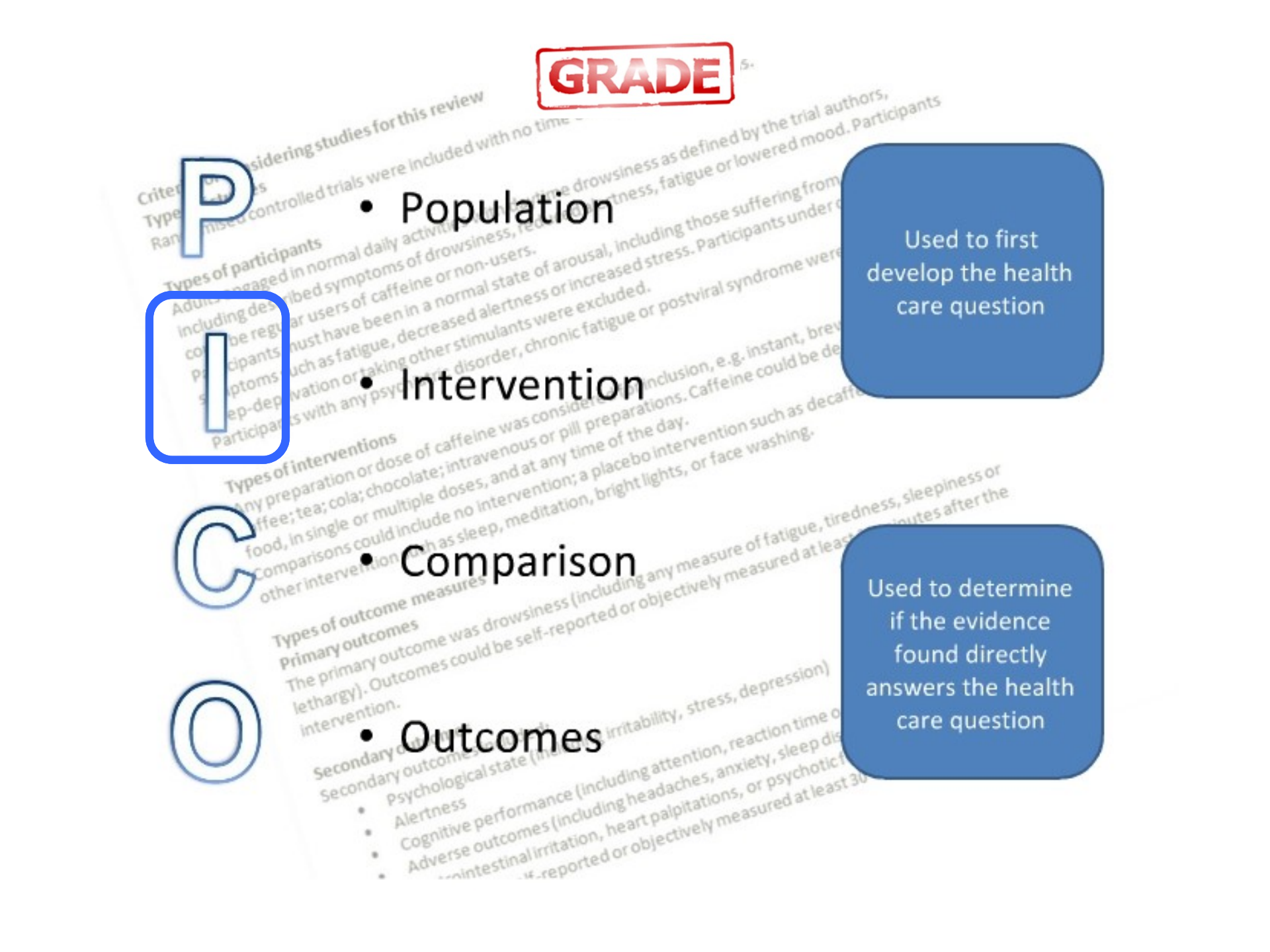
Table 1 – Weighting used to calculate recurrence and progression scores

Factor	Recurrence	Progression
Number of tumours		
Single	0	0
2–7	3	3
≥8	6	3
Tumour diameter		
<3 cm	0	0
≥3 cm	3	3
Prior recurrence rate		
Primary tumour	0	0
≤1 recurrence/year	2	2
>1 recurrence/year	4	2
Category		
Ta	0	0
T1	1	4
CIS		
No	0	0
Yes	1	6
	0	0
	1	0
	2	5
Total score	0–17	0–23

The 2004 World Health Organization/International Society of Urological Pathology classification system for non-muscle-invasive bladder cancer☆

Urological Science 24 (2013) 96–100

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Strutturazione del Quesito Clinico sec. modello P.I.C.O.

P	Nei **P**azienti con…	Specifiche caratteristiche di malattia (stadio, classe di rischio, ecc.)
I	l'**I**ntervento…	Intervento terapeutico oggetto del quesito clinico
C	(è suscettibile di …	T… …to altrimenti consi- … …ativa all'inter- …
O	riguardo agli **O**utcome di beneficio/danno…	Parametri clinico-laboratoristici ritenuti essenziali per la decisio-ne terapeutica

Non sempre l'intervento descritto nelle evidenze corrisponde all'intervento oggetto del quesito clinico!

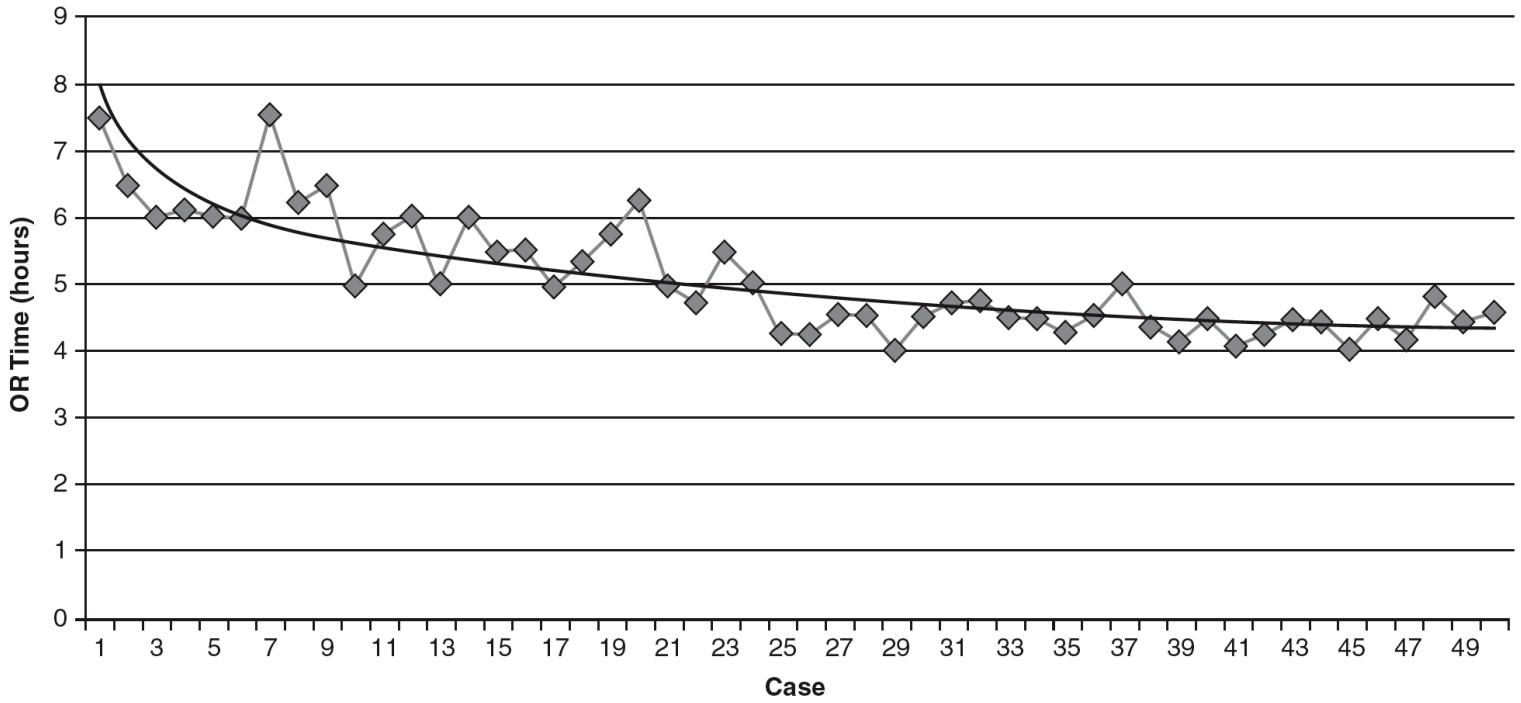
2.2. *Indirectness: differences in interventions*

a surgical procedure would have different effects when undertaken by subspecialists in referral centers compared with general surgeons in the community.

JOURNAL OF ENDOUROLOGY
Volume 22, Number 11, November 2008

Evaluating the Learning Curve for Robot-Assisted Laparoscopic Radical Cystectomy

Raj S. Pruthi, M.D., Angela Smith, M.D., and Eric M. Wallen, M.D.



Long-term oncologic outcomes of postoperative adjuvant versus salvage radiotherapy in prostate cancer: Systemic review and meta-analysis of 5-year and 10-year follow-up data

Ja Yoon Ku[1], Chan Ho Lee[1], Hong Koo Ha[1,2]

Korean J Urol 2015;56:735-741.

The present systemic review has the following limitations that must be taken into account.

The first limitation is that we heterogeneously recruit randomized controlled studies and retrospective studies: in retrospective studies, the initiation timing of radiotherapy is somewhat different in each study.

The second limitation is that (2-dimensional, 3-dimensional, or intensity modulated radiation therapy) which may alter oncologic outcomes.

The third limitation ... were different in ea... of long-term outcome be...

Indirectness per I. (di P.I.C.O.)

EUROPEAN UROLOGY 59 (2011) 775–783

A Systematic Review and Meta-analysis of the Relationship Between Hospital/Surgeon Volume and Outcome for Radical Cystectomy: An Update for the Ongoing Debate

Catharina A. Goossens-Laan [a,], Gea A. Gooiker [b], Willem van Gijn [b], Piet N. Post [c], J.L.H. Ruud Bosch [a], Paul J.M. Kil [d], Michel W.J.M. Wouters [b,e]*

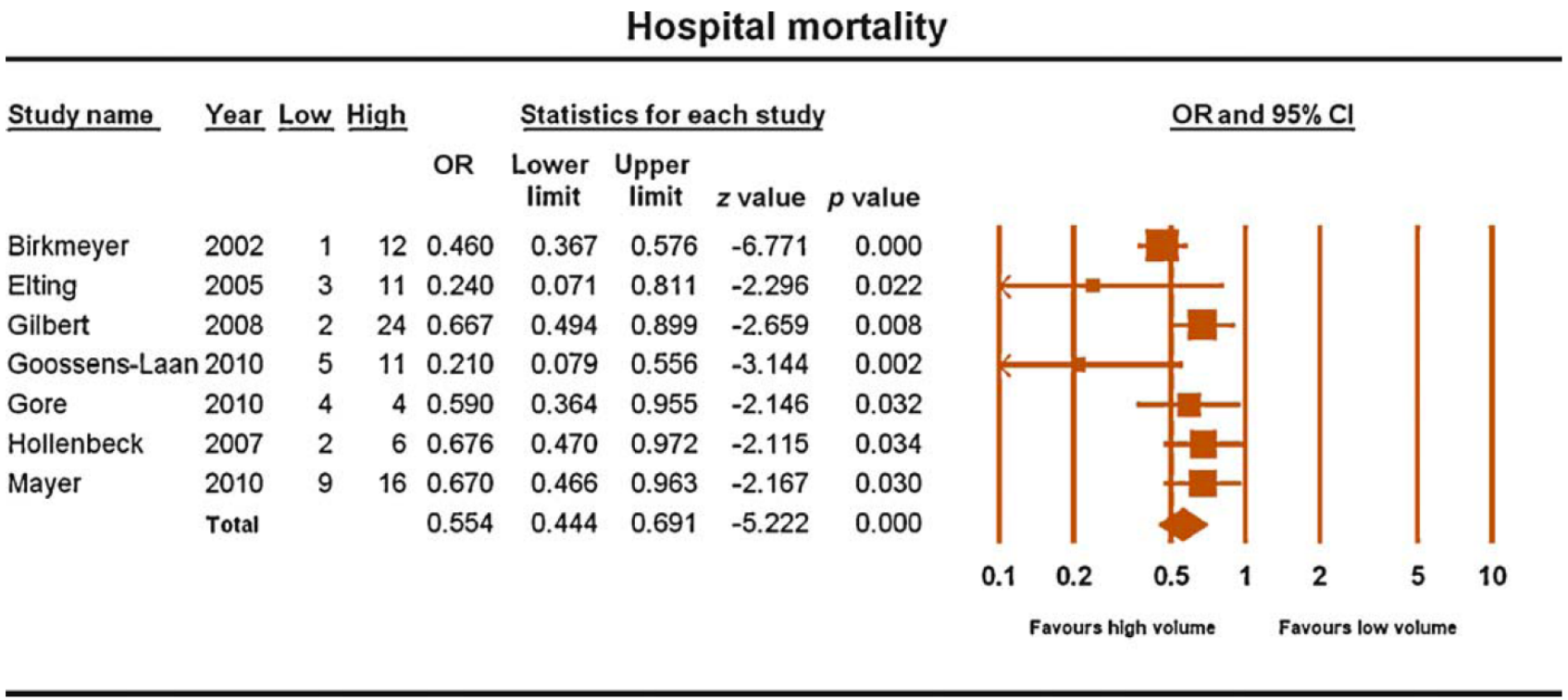
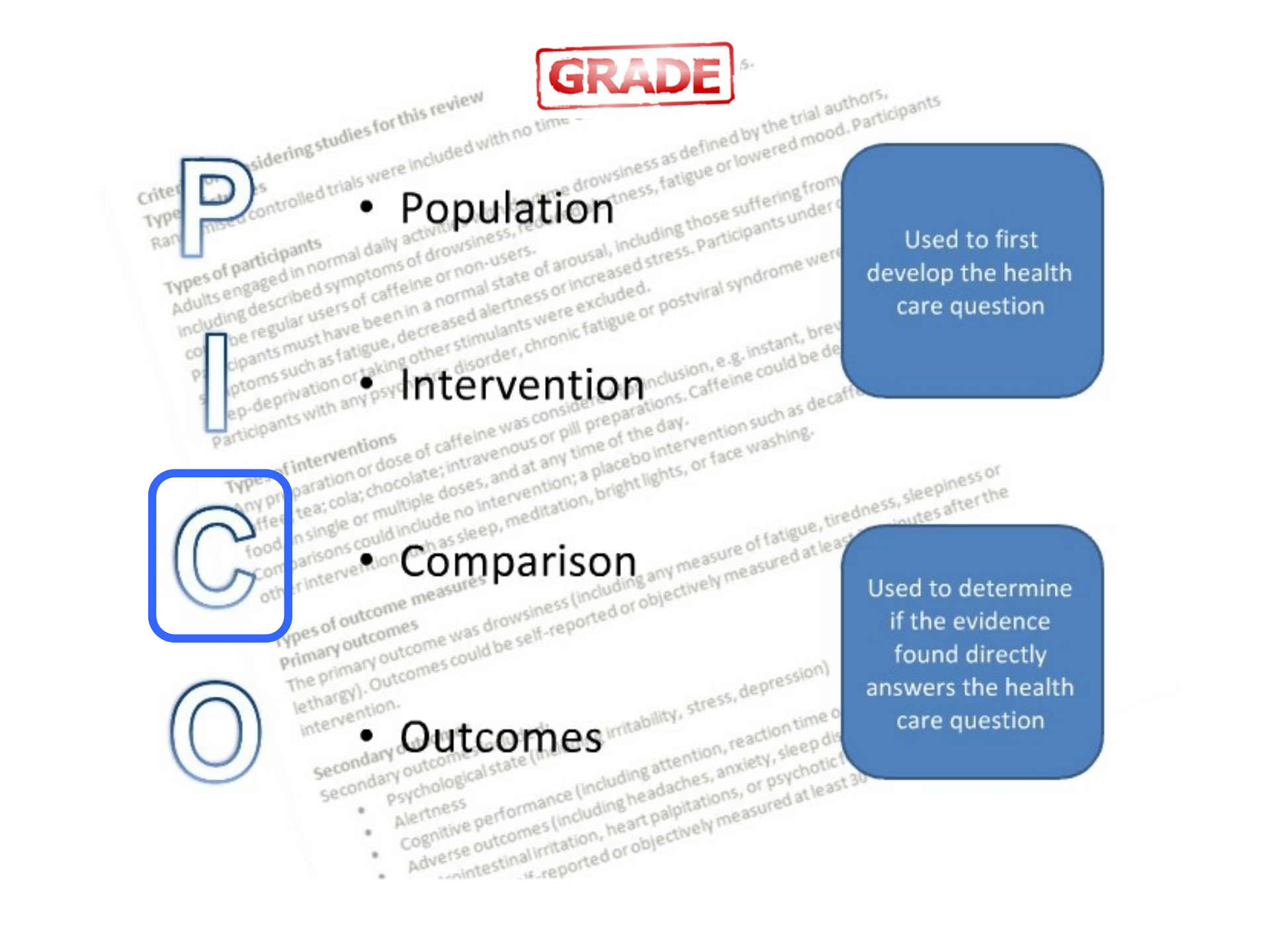


Fig. 1 – Forest plot of the included studies on hospital volume and postoperative mortality. OR = odds ratio; CI = confidence interval.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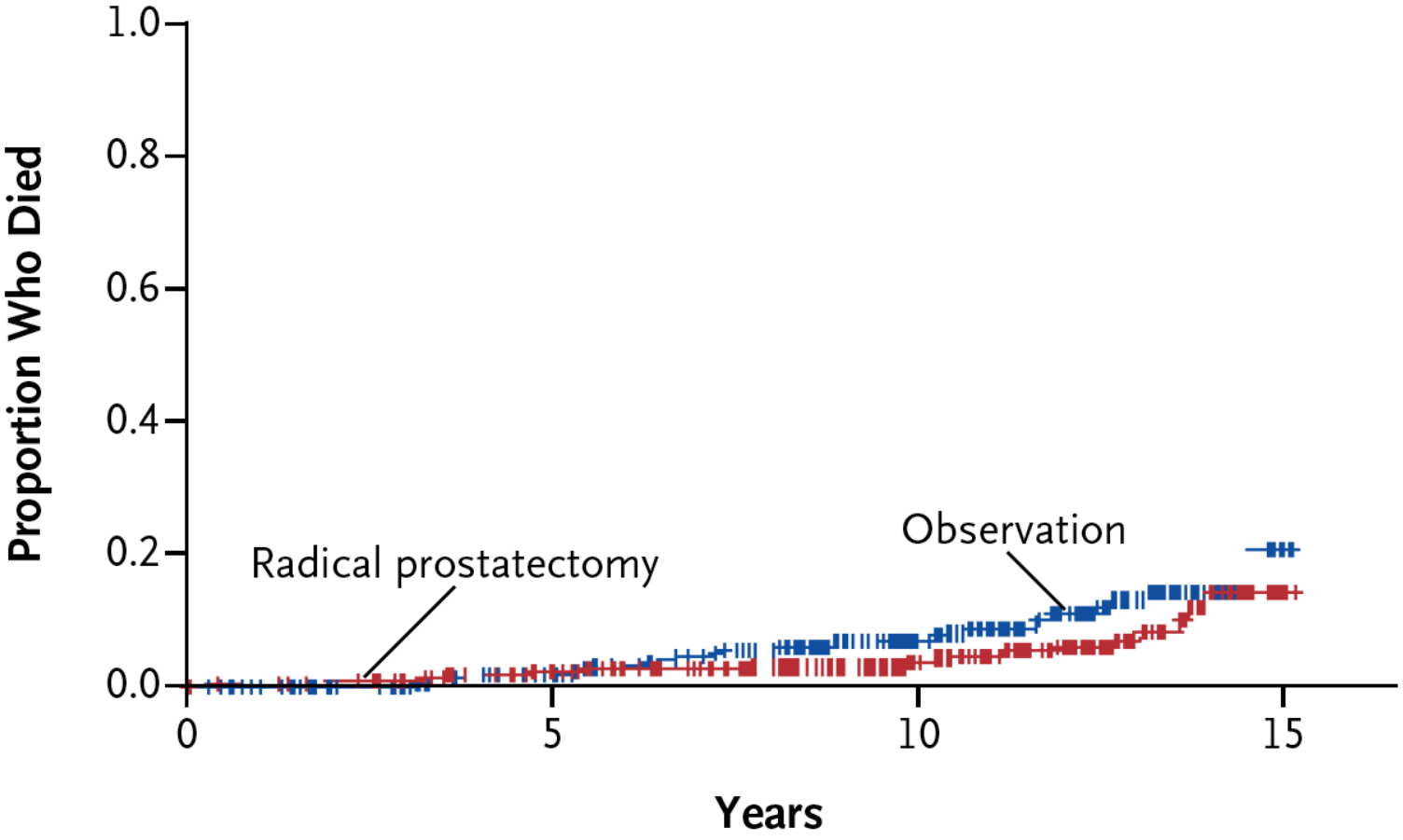
P	Nei **P**azienti con…	Specifiche caratteristiche di malattia (stadio, classe di rischio, ecc.)
I	l'**I**ntervento…	Intervento terapeutico oggetto del quesito clinico
C	(è suscettibile di impiego) in **C**onfronto con…	Trattamento altrimenti considerabile in alternativa all'intervento in esame
O	riguardo ag **O**utcome c beneficio/c	

Non necessariamente (quasi mai!) il braccio di controllo dello studio RND di riferimento!

Radical Prostatectomy versus Observation for Localized Prostate Cancer

Timothy J. Wilt, M.D., M.P.H., Michael K. Brawer, M.D., Karen M. Jones, M.S., Michael J. Barry, M.D., William J. Aronson, M.D., Steven Fox, M.D., M.P.H., Jeffrey R. Gingrich, M.D., John T. Wei, M.D., Patricia Gilhooly, M.D., B. Mayer Grob, M.D., Imad Nsouli, M.D., Padmini Iyer, M.D., Ruben Cartagena, M.D., Glenn Snider, M.D., Claus Roehrborn, M.D., Ph.D., Roohollah Sharifi, M.D., William Blank, M.D., Parikshit Pandya, M.D., Gerald L. Andriole, M.D., Daniel Culkin, M.D., and Thomas Wheeler, M.D., for the Prostate Cancer Intervention versus Observation Trial (PIVOT) Study Group

N Engl J Med 2012;367:203-13.



Phase III Trial of Vinflunine Plus Best Supportive Care [redacted] After a Platinum-Containing Regimen i[redacted] Patients With Advanced Transitional Cell Carcinom[redacted]e Urothelial Tract

Joaquim Bellmunt, Christine Théodor[redacted]ris Komyakov, Lisa Sengelov, Gedske Daugaard, [redacted]cois-Michel Delgado, [redacted]ine, and Hans von der Maase

[redacted] *Oncology*

Second-line therapy in bladder cancer

Mark Bachner and Maria De Santis

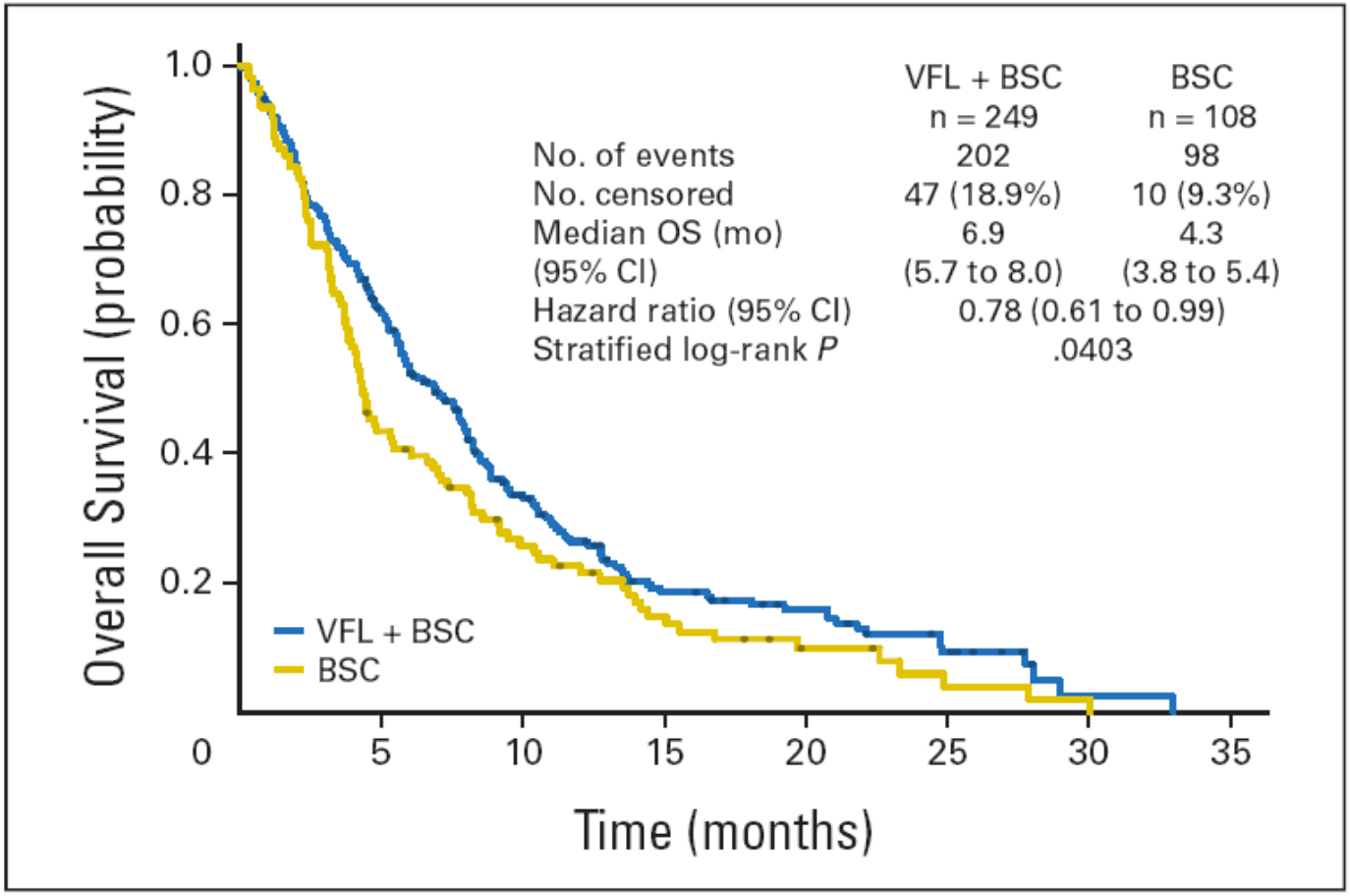
Current Opinion in Urology 2009, 19:533–539

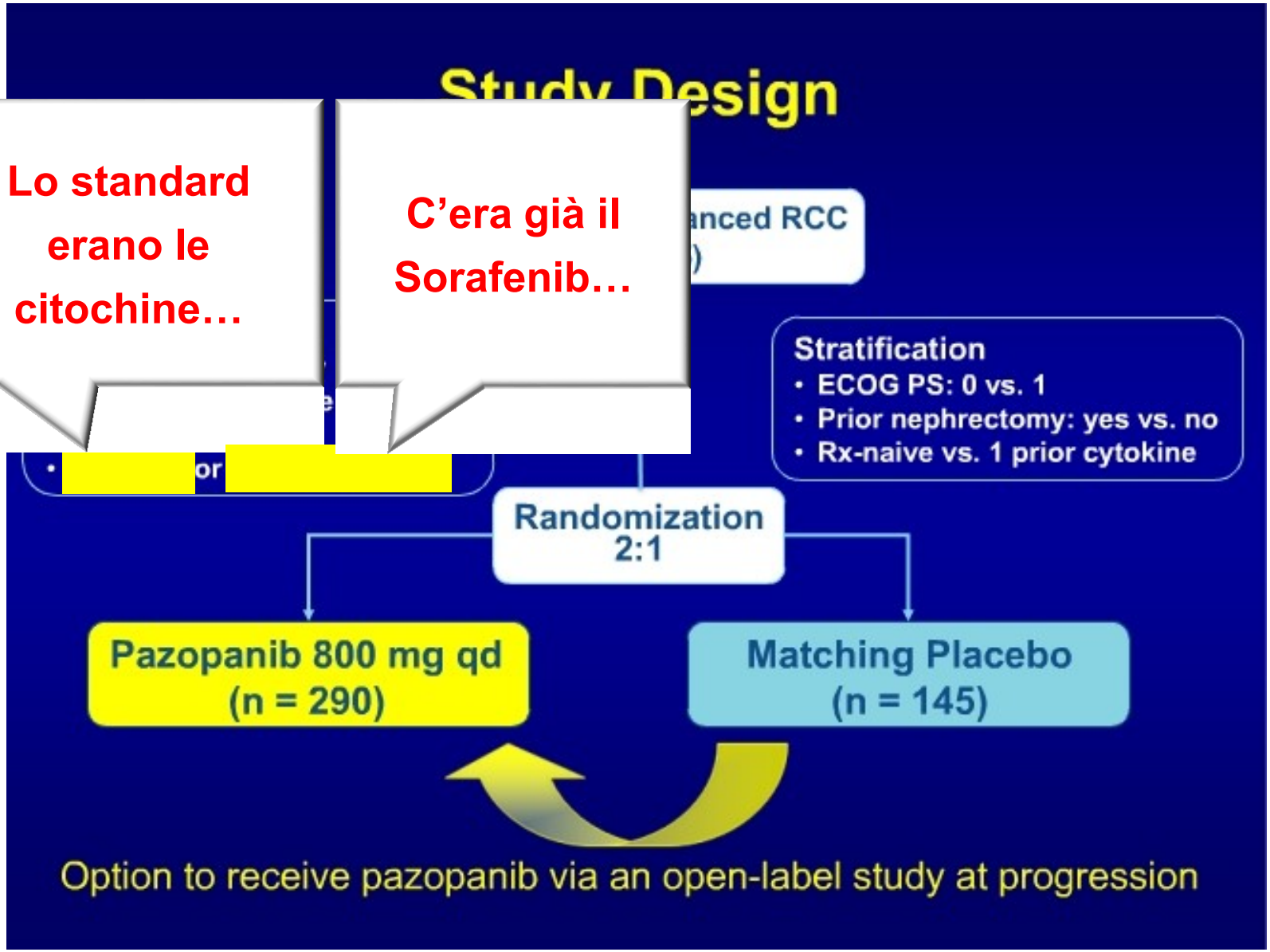
So far no standard therapy has been established for pretreated patients with transitional cell carcinoma.

Phase III Trial of Vinflunine Plus Best Supportive Care After a Platinum-Containing Regimen in Patients With Advanced Transitional Cell Carcinoma of the Urothelial Tract

Joaquim Bellmunt, Christine Théodore, Tomasz Demkov, Boris Komyakov, Lisa Sengelov, Gedske Daugaard, Armelle Caty, Joan Carles, Agnieszka Jagiello-Gruszfeld, Oleg Karyakin, François-Michel Delgado, Patrick Hurteloup, Eric Winquist, Nassim Morsli, Yacine Salhi, Stéphane Culine, and Hans von der Maase

J Clin Oncol 27:4454-4461. © 2009 by American Society of Clinical Oncology




Study Design
Lo standard erano le citochine…
C'era già il Sorafenib…
anced RCC
)
Stratification
• ECOG PS: 0 vs. 1
• Prior nephrectomy: yes vs. no
• Rx-naive vs. 1 prior cytokine
or
Randomization 2:1
Pazopanib 800 mg qd (n = 290)
Matching Placebo (n = 145)
Option to receive pazopanib via an open-label study at progression

Abiraterone Acetato - Prednisone e Docetaxel nel mHSPC: l'importanza della formulazione del Quesito

P. Pazienti con mHSPC ad alto volume/rischio

I. AAP/Doce + ADT

C. ADT

O. OS, PFS, QoL, Tollerabilità

Evidenze **direttamente trasferibili** nel caso la sola ADT rappresenti l'alternativa terapeutica *standard*

GRADE

Important Questions

Should be from practice NOT evidence driven

Abiraterone Acetato - Prednisone e Docetaxel nel mHSPC: l'importanza della formulazione del Quesito

P. Pazienti con mHSPC ad alto volume/rischio
I. AAP/Doce + ADT
C. ADT
O. OS, PFS, QoL, Tollerabilità

Evidenze **direttamente trasferibili** nel caso la sola ADT rappresenti l'alternativa terapeutica *standard*

P. Pazienti con mHSPC ad alto volume/rischio
I. AAP + ADT
C. Doce + ADT
O. OS, PFS, QoL, Tollerabilità

Evidenze **NON direttamente trasferibili** in quanto la sola ADT NON rappresenta più l'alternativa terapeutica *standard*

Indirect comparisons of competing interventions

AM Glenny,[1*] DG Altman,[2] F Song,[3] C Sakarovitch,[2] JJ Deeks,[2] R D'Amico,[2] M Bradburn[2] and AJ Eastwood[4]

Health Technology Assessment 2005; Vol. 9: No. 26

When conducting systematic reviews to evaluate the effectiveness of interventions, direct evidence from good-quality RCTs should be used wherever possible. If little or no such evidence exists, it may be necessary to look for indirect comparisons from RCTs. The reviewer needs, however, to be aware that the results may be susceptible to bias.