



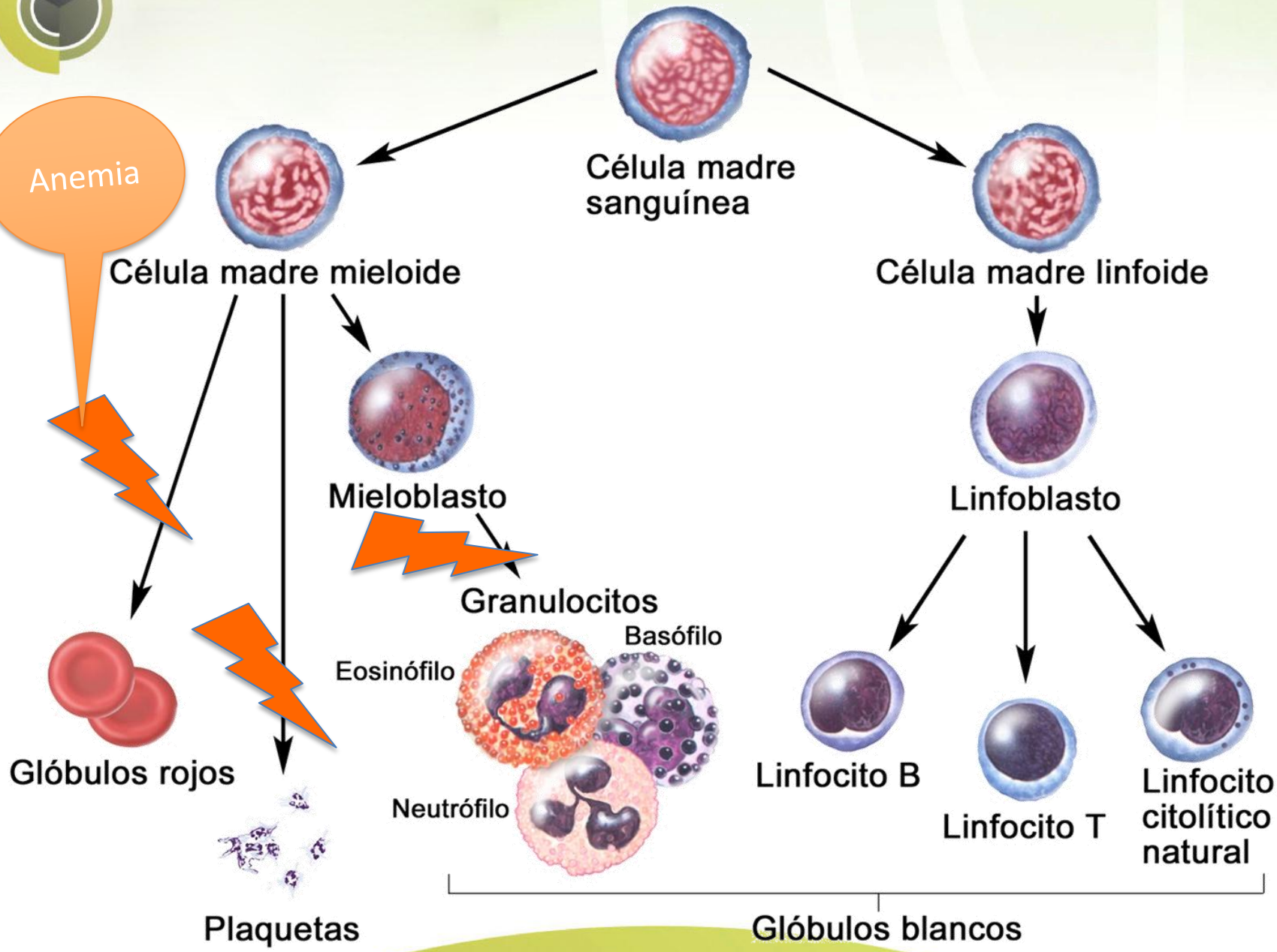
Erythropoiesis Stimulating Factors (ESAs) for the treatment of chemotherapy induced anemia in patients with Hb<11g/dl. A systematic review (SR) and meta-analysis (MA).

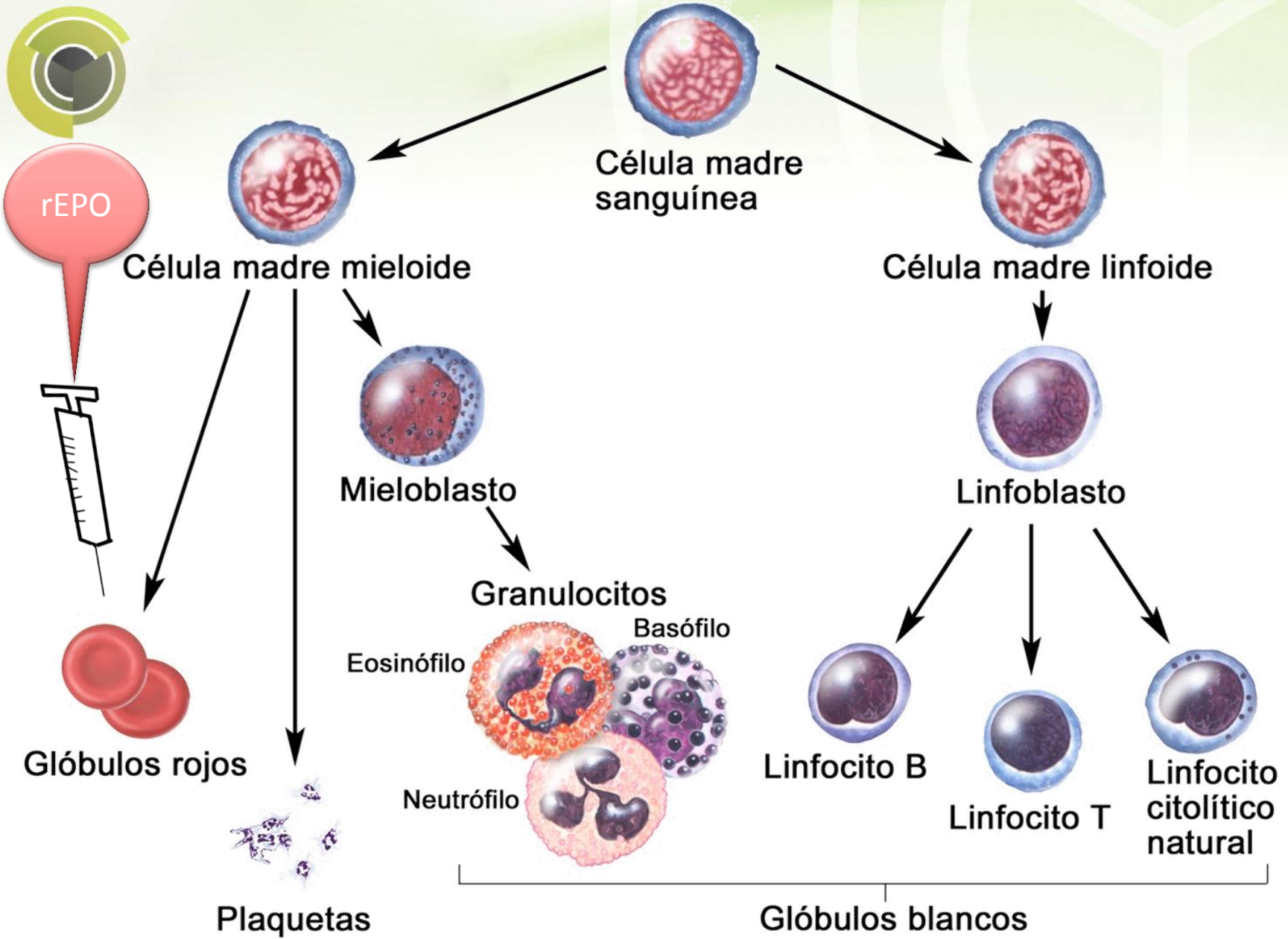
Otávio Clark, Luciano Paladini, Camila Pepe, Tobias Engel, Enéas Faleiros, Luciana Clark
otavio.clark@evidencias.com.br

*Editais MCT/CNPq/CT-Saúde/MS/SCTIE/DECIT Nº 067/2009
Avaliação de tecnologias em saúde*



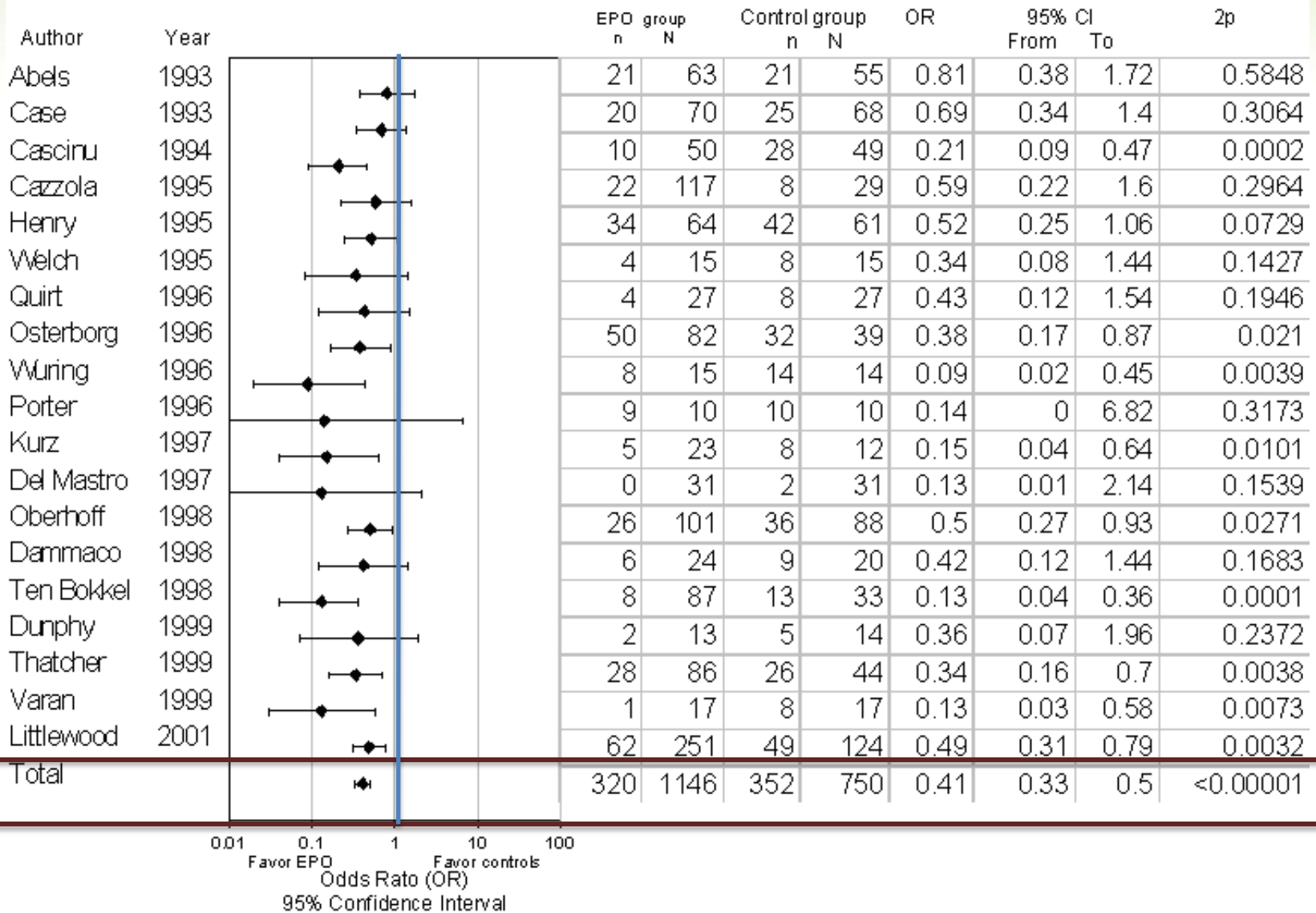
Anemia







Meta-analysis of EPO trials: Number of patients requiring transfusions





r-EPO

- **Increases** Hb Level
- **Diminishes** transfusion needs



2009

- Cochrane meta-analysis
- Increase in mortality associated to EPO use



Treatment-Related Anemia

Throuvalas et al. ⁵⁵ 2000	0/28 (0)	1/27 (4)	0.01	0.13 [0-332.66]
Dunphy et al. ³⁰ 1999	0/15 (0)	1/15 (7)	0.05	0.14 [0-6.88]
Vadhan-Raj et al. ⁵⁶ 2004	0/28 (0)	1/31 (3)	0.01	0.15 [0-415.90]
Dammacco et al. ³³ 2001	3/69 (4)	11/76 (14)	0.59	0.32 [0.11-0.95]
Del Mastro et al. ³⁴ 1997	1/31 (3)	3/31 (10)	0.19	0.36 [0.05-2.56]
Cazzola et al. ³¹ 1995	2/117 (2)	1/29 (3)	0.22	0.37 [0.06-2.27]
P-174, ¹¹ 2004	1/33 (3)	1/12 (8)	0.11	0.41 [0.03-5.76]
Thatcher et al. ⁵⁴ 1999	1/42 (2)	1/22 (5)	0.09	0.49 [0.03-8.71]
Kotasek et al. ²⁰ 2003	7/198 (4)	3/51 (6)	0.29	0.55 [0.11-2.71]
Oberhoff et al. ⁴⁴ 1998	4/114 (4)	12/104 (12)	0.80	0.61 [0.24-1.55]
Blohmer et al. ²⁴ 2003 (AGO/NOGG)	16/33 (48)	23/116 (20)	1.43	0.67 [0.34-1.33]
Henry and Abels, ³⁶ 1994	8/67 (12)	10/65 (15)	0.72	0.75 [0.28-2.01]
Vansteenkiste et al. ² 2002	100/155 (65)	119/159 (75)	6.01	0.78 [0.60-1.01]
Littlewood et al. ⁴¹ 2001	155/251 (62)	82/124 (66)	5.82	0.81 [0.62-1.06]
Taylor et al. ²¹ 2005 (DA 232)	NR	NR	1.84	0.85 [0.45-1.60]
EPO-CAN-17, ¹² 2007	24/176 (14)	27/178 (15)	1.85	0.88 [0.49-1.59]
Amgen DA 145, ¹³ 2007	NR	NR	10.44	0.93 [0.82-1.05]
Razzouk et al. ⁴⁹ 2004	2/112 (2)	2/110 (2)	0.19	0.98 [0.14-6.90]
Savonije et al. ⁵¹ 2004	12/211 (6)	6/104 (6)	0.70	0.98 [0.36-2.67]
ten Bokkel Huinink et al. ⁵³ 1998	4/87 (5)	2/33 (6)	0.26	1.01 [0.19-5.31]
Osterborg et al. ⁴⁶ 1996	15/47 (32)	12/49 (24)	1.38	1.02 [0.51-2.04]
Coiffier et al. ³² 2001	8/133 (6)	8/129 (6)	0.73	1.02 [0.38-2.73]
Debus et al. ¹⁶ 2007 (EPO-GER-22)	NR	NR	2.17	1.02 [0.60-1.74]
Osterborg et al. ⁴⁷ 2005	110/170 (65)	119/173 (69)	5.91	1.04 [0.80-1.35]
EPO-GBR-7, ¹² 2007	52/151 (34)	50/149 (34)	3.87	1.07 [0.73-1.57]
Case et al. ³⁰ 1993	10/81 (12)	9/76 (12)	0.86	1.08 [0.44-2.66]
Witzig et al. ⁵⁷ 2005	105/166 (63)	103/164 (63)	5.74	1.09 [0.83-1.43]
Moebus et al. ¹⁸ 2007	NR	NR	3.50	1.14 [0.77-1.69]
Strauss et al. ²³ 2007	NR	NR	2.28	1.16 [0.69-1.95]
Thomas et al. ³⁶ 2007 (GOG-191)	8/58 (14)	9/55 (16)	1.54	1.25 [0.65-2.41]
Thatcher et al. ⁵⁴ 1999	5/44 (11)	2/22 (9)	0.27	1.26 [0.24-6.60]
Overgaard et al. ¹⁴ 2007 (DAHANCA 10)	NR	NR	5.59	1.28 [0.97-1.69]
Hedeker et al. ³⁷ 2009	74/175 (42)	61/169 (36)	4.54	1.36 [0.98-1.89]
Leyland-Jones et al. ⁴⁰ 2005 (INT-76)	148/469 (32)	115/470 (24)	6.39	1.37 [1.07-1.75]
Henke et al. ²⁶ 2003	109/180 (61)	89/171 (52)	5.53	1.39 [1.05-1.84]
Machtay et al. ⁴² 2007 (RTOG 99-03)	27/71 (38)	21/70 (30)	1.97	1.41 [0.80-2.49]
PREPARE, ⁴⁸ 2007	50/356 (14)	37/377 (10)	2.92	1.50 [0.96-2.34]
Grote et al. ⁴³ 2005 (N93-004)	100/109 (92)	101/115 (88)	0.94	1.53 [0.65-3.61]
INT-3, ¹¹ 2004	9/135 (7)	3/65 (5)	0.42	1.56 [0.42-5.79]
INT-1, ¹¹ 2004	6/164 (4)	2/80 (3)	0.28	1.58 [0.32-7.82]
Rose et al. ⁵⁰ 1994	16/142 (11)	6/79 (8)	0.80	1.68 [0.66-4.29]
Barnias et al. ²⁸ 2003	7/72 (10)	4/72 (6)	0.48	1.80 [0.53-6.12]
Wright et al. ⁵⁸ 2007 (EPO-CAN-20)	32/33 (97)	34/37 (92)	1.79	1.84 [1.01-3.35]
EPO-CAN-15, ¹¹ 2004	21/53 (40)	10/53 (19)	0.99	2.70 [1.17-6.23]
Wilkinson et al. ²⁰ 2006	NR	NR	0.13	4.54 [0.40-51.20]
O'Shaughnessy et al. ⁴⁵ 2005	1/47 (2)	0/47 (0)	0.05	7.39 [0.15-366.10]

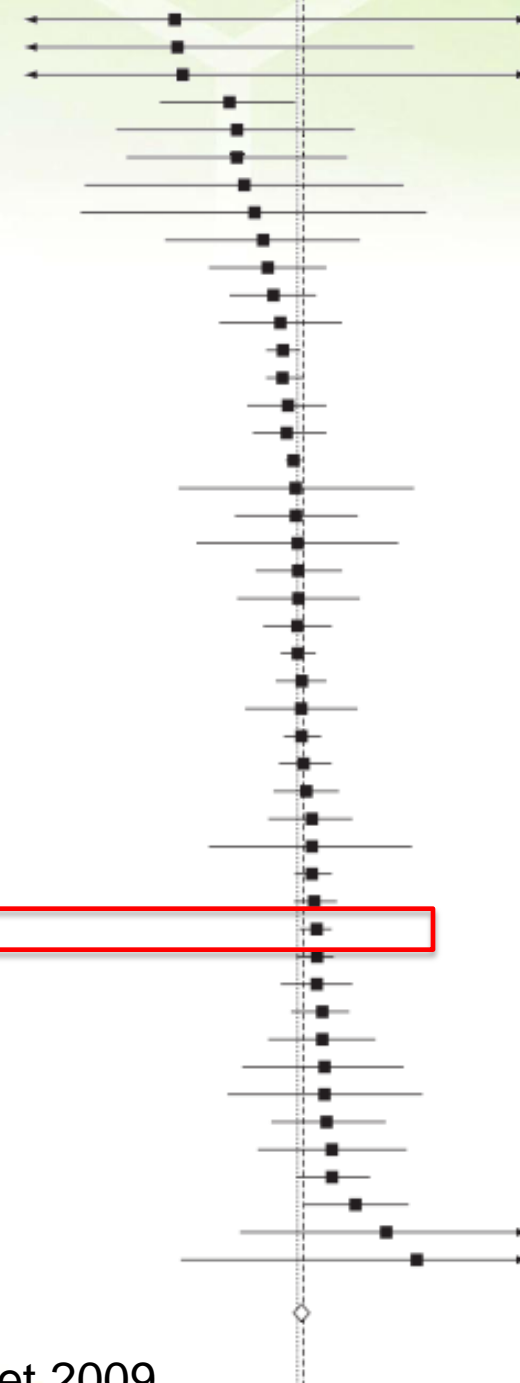
Subtotal

92.28

1.09 [0.99-1.19]

$I^2 = 21.1\%$; $P = .11$

Heterogeneity between groups, $P = .13$





Does EPO increase mortality?

- Cochrane meta-analysis
- Included patients with anemia and patients with normal Hb levels
- Different profile of patients



Objectives

- Systematic review and meta-analysis
 - Is rEPO linked to an increase in mortality when given to patients, according to the label indication?
 - HB<11g/Dl
 - On chemotherapy

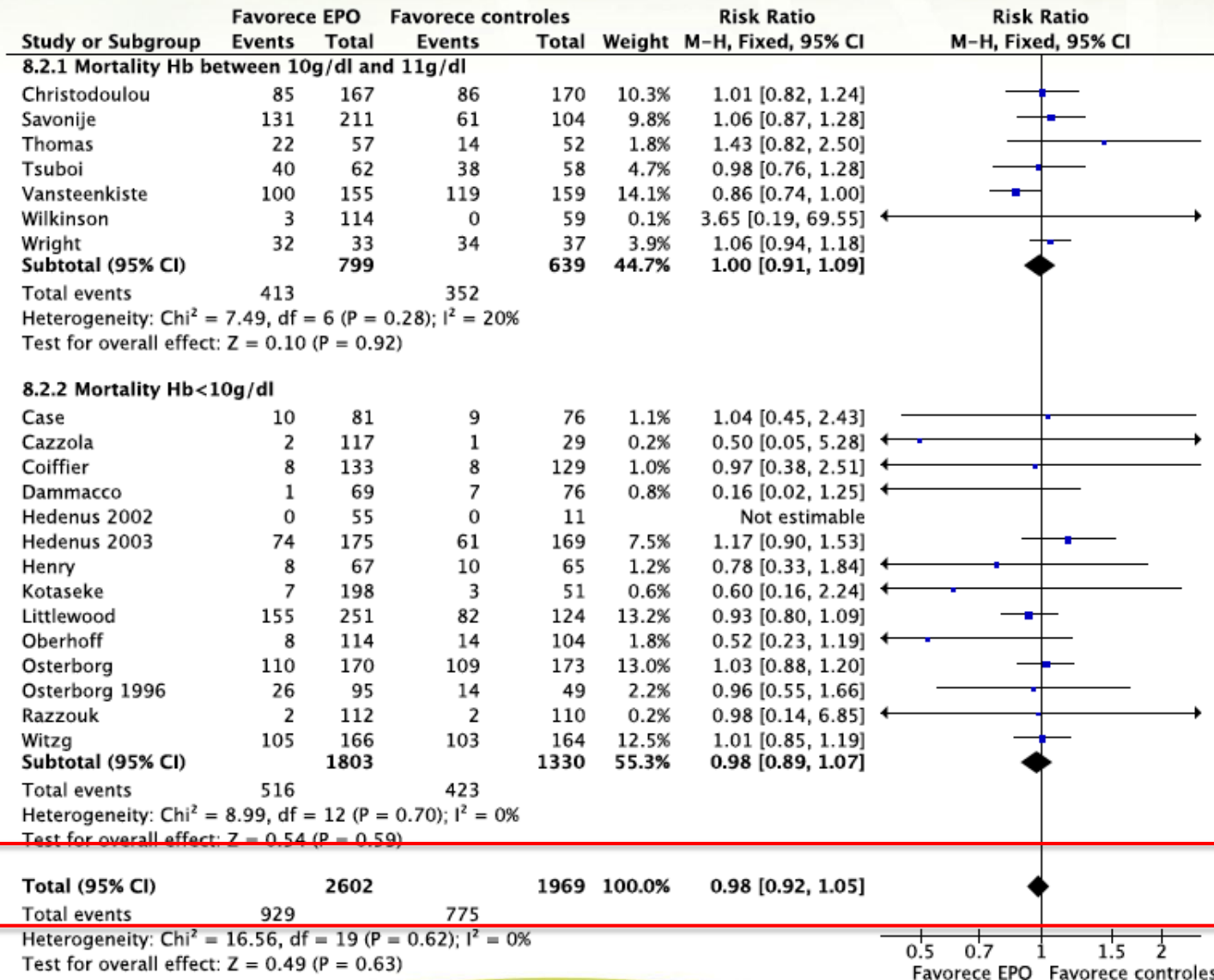


rEPO

- Included studies:
 - Randomized controlled trials
 - Patients with cancer
 - In use of chemotherapy
 - With anemia
 - $HB < 11\text{g/dl}$
- 21 studies were included



Meta-analysis





Results

- r-EPO, when used according to the label indications does not increase mortality
- RR= 0.98 (0.92-1.05)
- No statistical heterogeneity



Discussion

- This meta-analysis highlights the importance of evaluating the heterogeneity of patients
- Not only statistical heterogeneity
- Danger of mixing “apples and oranges”



Conclusion

r-EPO when administered according to the label indication does not increase mortality



otavio.clark@evidencias.com.br



@otavioclark



Otávio clark



@otavioclark



19 8149 5375