

# 麩醯胺酸(Glutamine) 可以改善放療 引起的口腔黏膜炎嗎？

**Glutamine in Alleviation of Radiation-Induced  
Severe Oral Mucositis: A Meta-Analysis**

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# Head and neck cancer (HNC) and mucositis

- 80% of HNC patients who receive radiotherapy experience oral mucositis.
- Over 50% of patients experienced severe OM (grade 3-4).

Vera-Llonch et al., 2006

# WHO Oral Mucositis Grading Scale

Grade	Description
0 (none)	None
I (mild)	Oral soreness, erythema
II (moderate)	Oral erythema, ulcers, solid diet tolerated
III (severe)	Oral ulcers, liquid diet only
IV (life-threatening)	Oral alimentation impossible

# Question

- Problem
  - Whether glutamine decreases the incidence and severity of radiation-induced oral mucositis (OM) in patients with head and neck cancer (HNC).
- Population
  - Oral mucositis in patients with head and neck cancer who received radiotherapy or chemoradiotherapy.

# Question

- Intervention
  - Radiotherapy: total RT dose 60-70Gy
  - Glutamine:10g~30g/day

**Table 1.** Characteristics of patients with mucositis (Grade 4) in included studies.

Study	Study Ddesign	Cancer type/Stage	Age of patients Tx /Control	Event No /No. of patients		Relative effect, RR 95% CI	Total RT dose (Gy)	Glu Tx dose /day	Treatment regimens per arm
16. Chattopadhyay 2014	Randomized case-control study	HN/NA	56/57.8	Glutamine 1/35	Non -Glu 6/35	0.17 [0.02, 1.31]	60	10g	RT+10g/1000 ml oral glutamine suspension daily 2 hours before radiation
17. Huang, 2000	Randomized trial	HN/NA	47 ±8 /54 ± 12	0/8	1/9	0.37 [0.02, 7.99]	45	16 g	RT+2 g glutamine in 30 ml normal saline
18. Cerchietti 2006	RCT	HN/III,IV	56/55	0/14	5/15	0.10 [0.01, 1.61]	70	24 g	CRT+ 55 IV infusions of 0.3 to 0.4 g/kg body weight of L-alanyl-L-glutamine in saline
19. Tsujimoto, 2015	RCT	HN/II-IV	60.5±10.8 /63.2±5.4	0/20	5/20	0.09[0.01, 1.54]	66–70	30 g	CRT+glutamine 10 G thrice daily
Sub-total				1/77	17/79				
20. Vidal-Casariago, 2013	Cohort study	HN/NA	62.2±13.6	2/61	3/18	0.20 [0.04, 1.09]	60–70	30g	RT+glutamine 30 g/day, orally
Total				3/138	20/97				

RCT = randomized controlled trial; HN = Head and neck; Gy = gray; Tx = treatment; No = number; Ev = mucositis; RR = risk ratio  
 NA: not available. Glu:glutamine. Grade 4: pain and inability to swallow solid foods or even liquids.

- Comparison
  - Glutamine & control group
  - the risk and severity of OM
    - duration of grade-3 & grade-4 OM
    - onset of grade-4 OM

OM: oral mucositis

- Outcomes
  - Glutamine treatment showed statistically significant benefit with respect to **reducing the risk and severity of OM** induced by radiotherapy or chemoradiotherapy compared to either placebo or no treatment.



**FAITH**





# F - 研究是否找到 (Find) 所有的相關證據？

## Methods

### *Search strategy and inclusion criteria*

We performed a systematic literature search of PubMed (1990 to January 2015), Embase (1990 to January 2015), and Cochrane Library (2013, Issue 2) to identify all original studies that investigated the effect of glutamine in the alleviation of radiation-induced OM. The search strategy was based on combinations of (“oral mucositis” or “mucositis” [Mesh]), (“radiation therapy” or “radiotherapy”) and (glutamine[Mesh] (“randomized studies” [Mesh] or clinical trials). In addition, we manually examined the titles of all references within the selected articles to identify potentially overlooked material. The corresponding full-text articles were located through the databases and independently evaluated by two reviewers, who used the same inclusion and exclusion criteria. The following inclusion and exclusion criteria were used: clinical studies published in English that evaluated the

# F - 研究是否找到 (Find) 所有的相關證據？

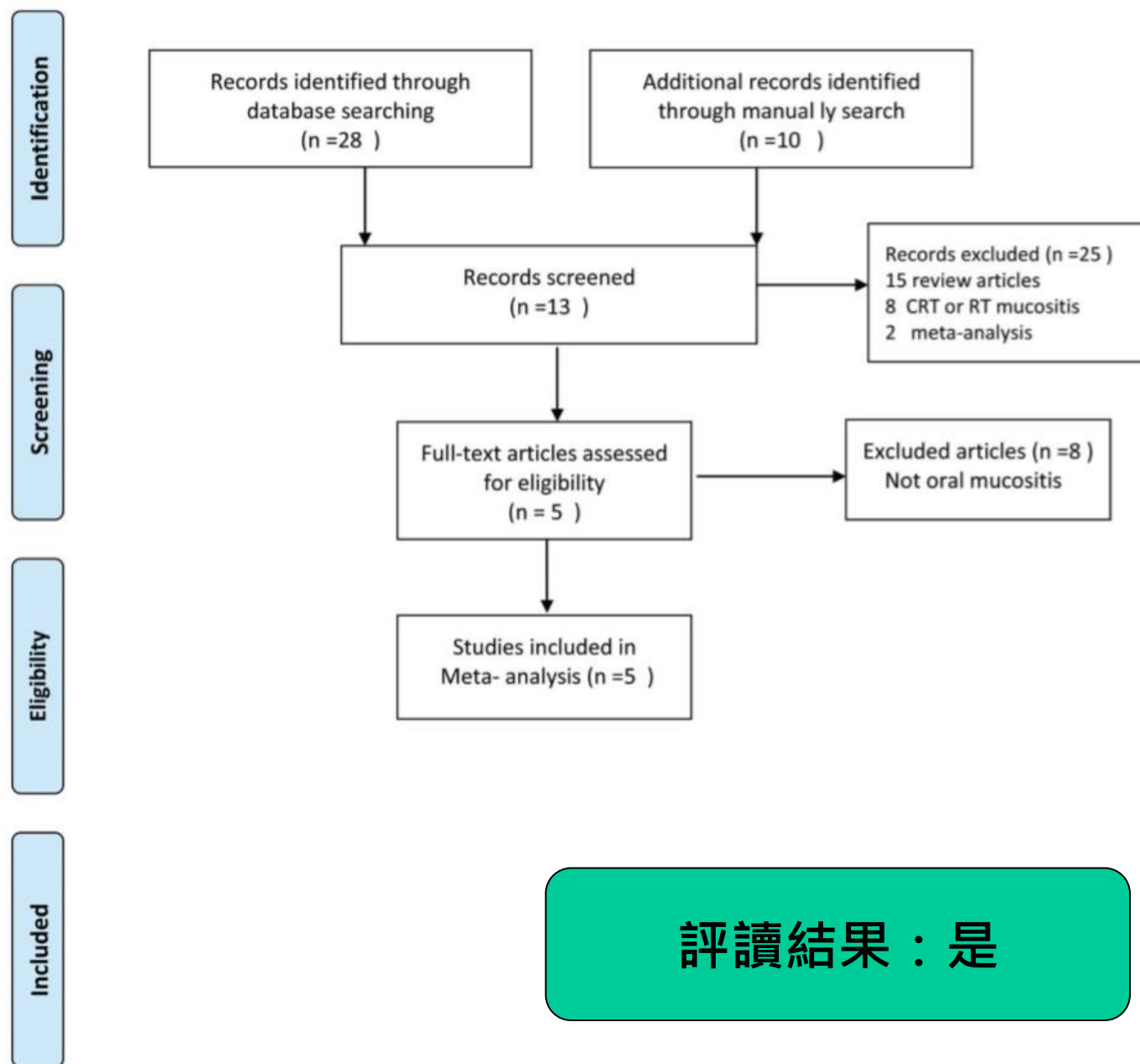
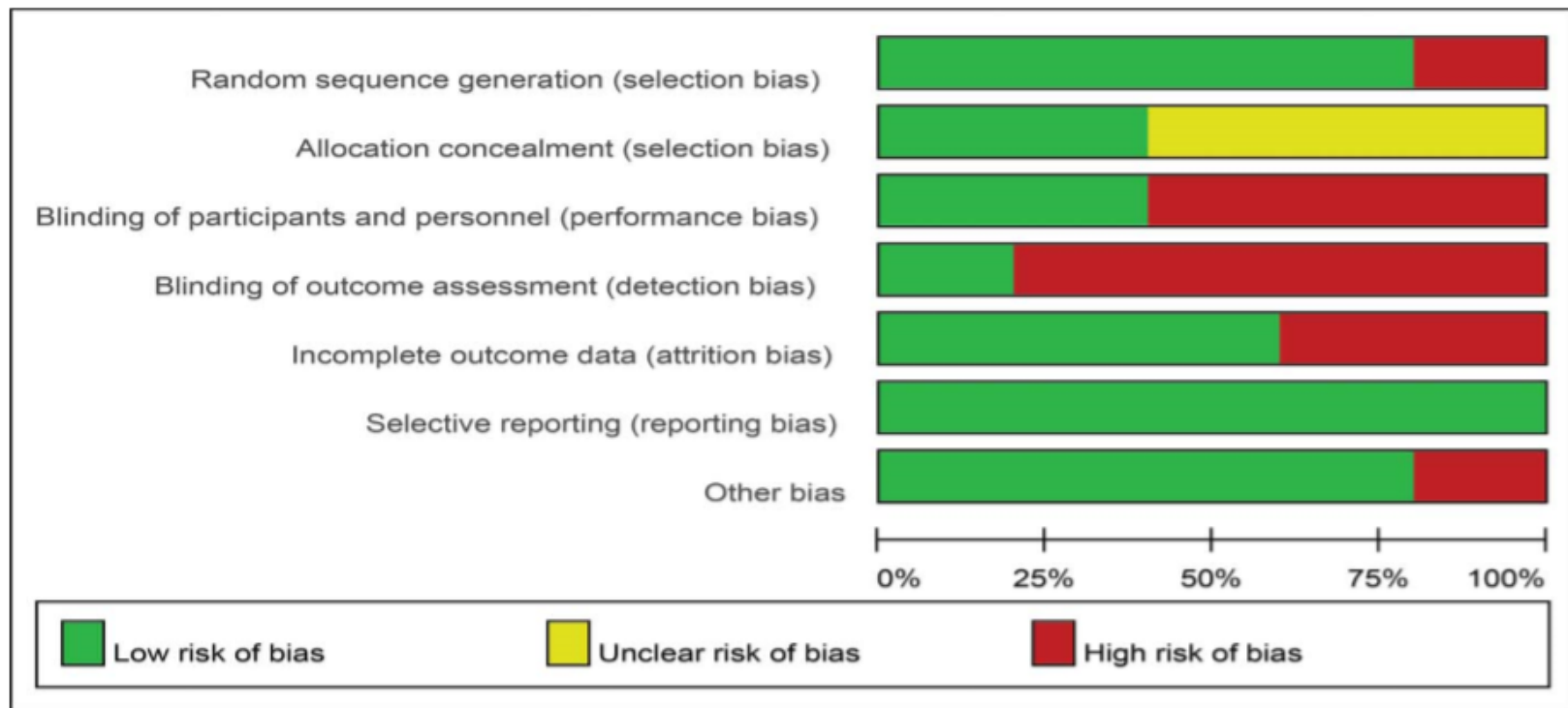


Figure 1. Flow chart of study selection.

# A - 文獻是否經過嚴格評讀 (Appraisal) ?



A. Risk of bias assessment graph for each risk of bias domain presented as percentages across all included studies

# A - 文獻是否經過嚴格評讀 (Appraisal) ?

Risk of bias summary:

each risk of bias domain for  
each included study.

評讀結果：是



B.

Figure 4

# I - 是否只納入 (included) 具良好效度的文章？

## **Data collection and extraction**

Based on the inclusion criteria, the two reviewers (HWCL and ALFC) independently assessed the titles and abstracts of potentially relevant studies. Any discrepancies in auditing data were judged by consensus. The abstracts and full-text articles of the selected titles were collected for review.

The overall parameters of the clinical studies were summarized in a standardized table, including the study's first author, year of publication, characteristics of the population, interventions, and outcomes (Table 1).

## **Assessment of risk of bias and study quality**

Two review authors independently graded the relevant clinical studies based on the domains described in the *Cochrane Handbook for Systematic Reviews of Interventions* 5.0.2 (updated September 2009) (13).

The review authors then reported their assessments in a risk of bias table using Review Manager 5 (RevMan) software.

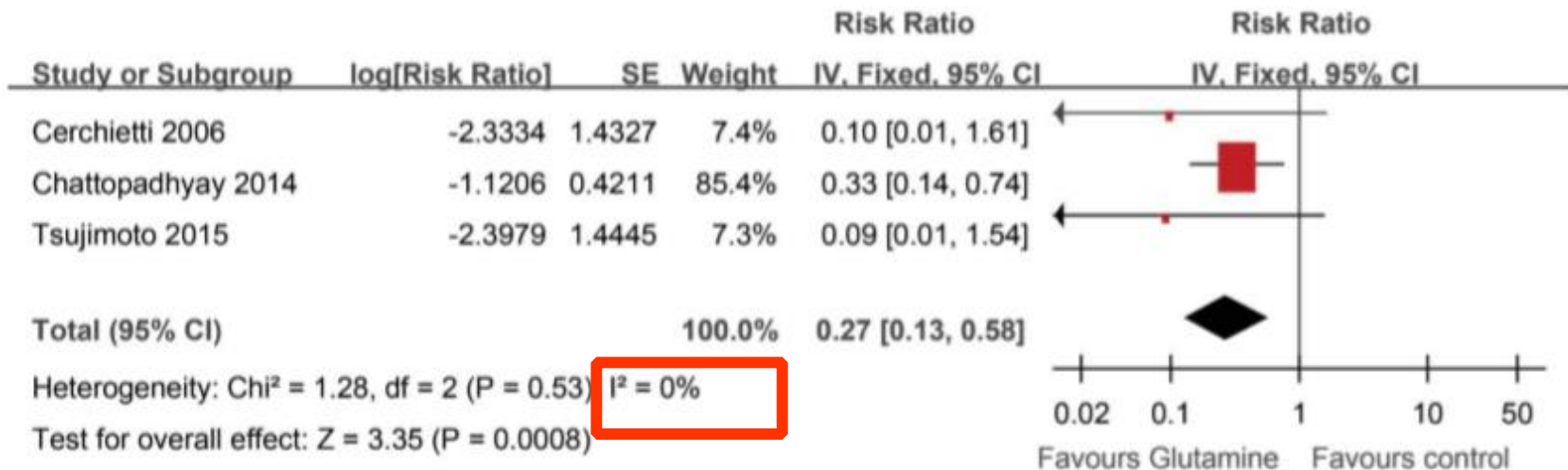
The studies were assessed as at low, high, or unclear risk of bias according to the following six domains: 1). adequate sequence generation; 2). allocation concealment; 3). blinding of subjects, caregivers, and outcome assessors;

4). incomplete outcome data addressed; 5). freedom from selective outcome reporting; and 6). freedom from other biases by categorization. Any discrepancies in assessment were resolved by discussion and consensus.

We also assessed the quality of evidence in these studies using GRADE profiler software (GRADE Working Group, version 3.6.1) (14), which allowed us to create a summary of findings table. Data from the systematic review and meta-analysis could be retrieved from a Review Manager 5 file and then combined with data we entered; a summary of findings table was then exported, ready for import into Review Manager 5. The GRADE software performed many of the calculations necessary to present the key results from systematic reviews in a table format and guided us through the process of grading the quality of the evidence using the GRADE approach.

**評讀結果：是**

# T - 作者是否以表格和圖表「總結」 (total up) 試驗結果



A.

Figure 3. Comparison of glutamine versus control, outcome: alleviation of OM oral mucositis (grade 4) in patients with A: Chemoradiation, B: Radiotherapy only.



# T - 作者是否以表格和圖表「總結」 (total up) 試驗結果

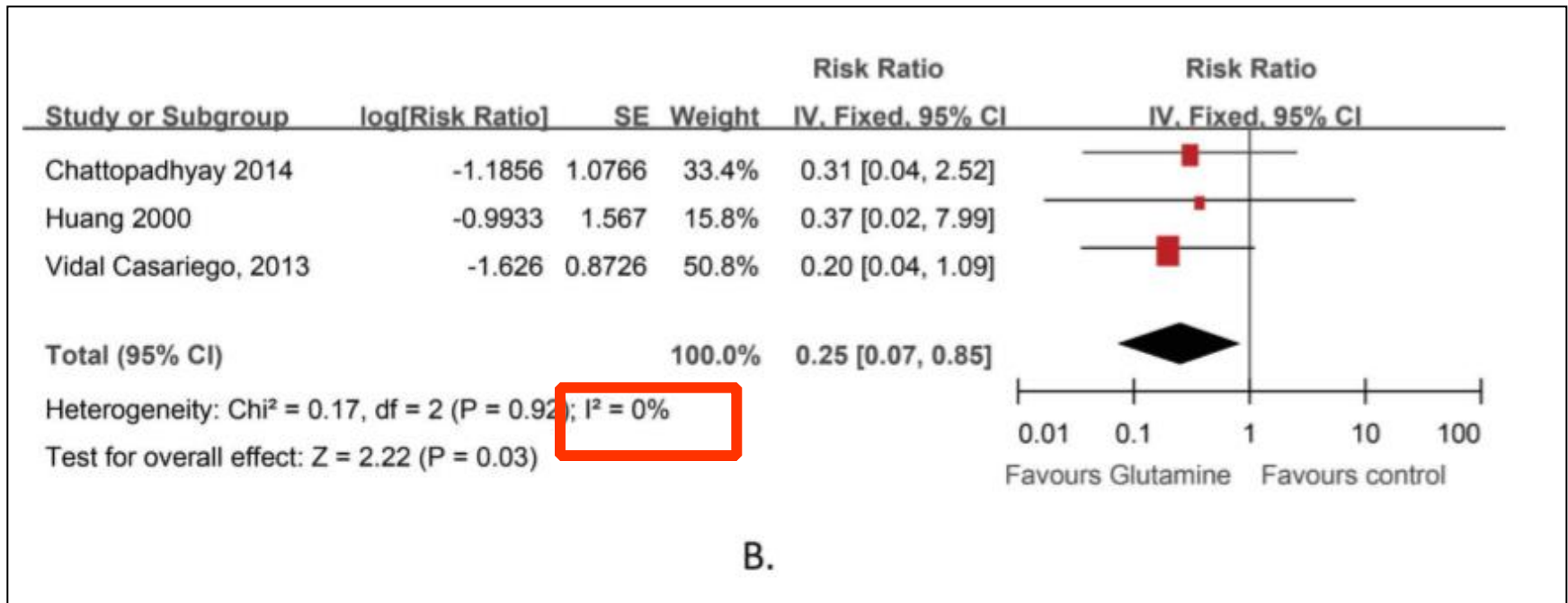
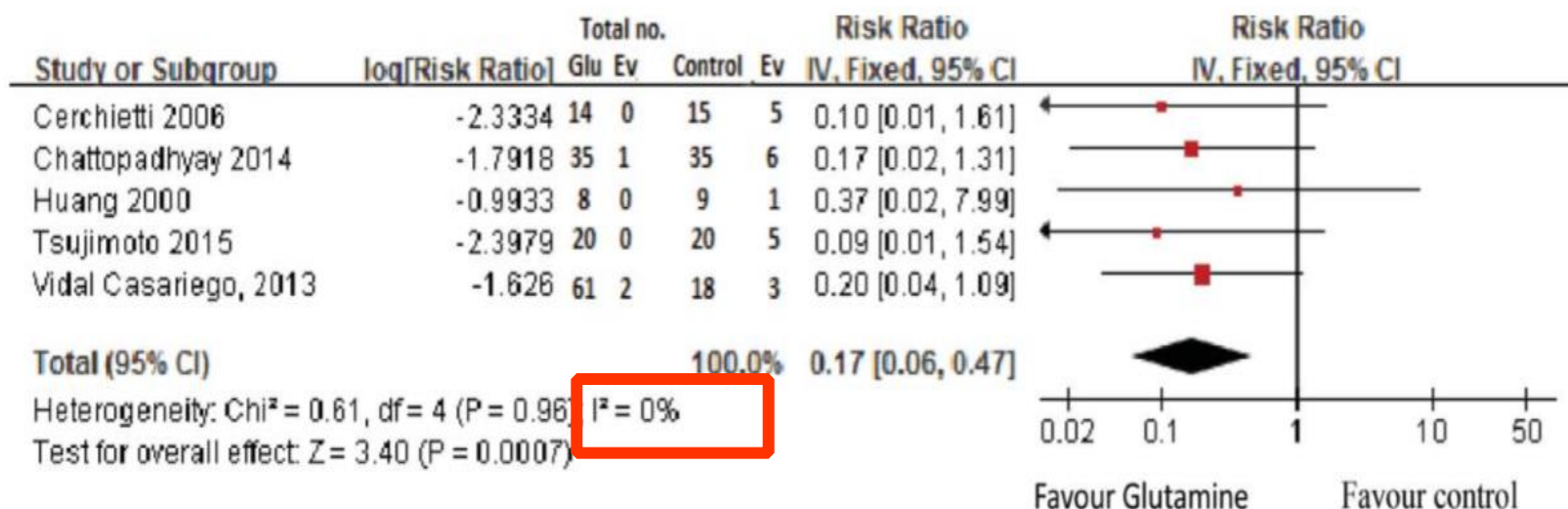


Figure 3. Comparison of glutamine versus control, outcome: alleviation of OM oral mucositis (grade 4) in patients with A: Chemoradiation, B: Radiotherapy only.

評讀結果：是

# H - 試驗的結果是否相近 - 異質性 (Heterogeneity) ?

- No heterogeneity



**Figure 2.** Comparison of glutamine versus control, alleviation of mucositis (Grade 4) in patients with CRT or RT. Glu: glutamine; Ev: events, grade- 4 mucositis.



# Question

- 放射治療前，是否例行性建議使用 Glutamine (10-30g/day)，以緩解口腔黏膜炎的嚴重度？