補充維生素 D 對氣喘兒童的影響：統合分析

Front. Pediatr., 29 June 2022 Sec Volume 10 .
https://doi.org/10.3389/fped.2022.840617

Frontiers in pediatrics.

SYSTEMATIC REVIEW article

The Effect of Vitamin D Supplementation in Children With Asthma: A Meta-Analysis

Meiqi Hao [1,2], Ruoxin Xu [1,2], Nachuan Luo [1,2], Miaowen Liu [1,2], Junping Xie [3] and Wenxiong Zhang [1*]*

引言人：謝雨軒護理師/許翠芳護理長

日期：2023年4月11日

前言[1]

- ★ 氣喘是全世界也是台灣兒童最重要的慢性呼吸道疾病。
- ★ 根據國民健康署106年國民健康訪問調查(NHIS)，未滿12歲兒童，氣喘盛行率為5.6%，引發氣喘之過敏原及刺激物前五名為：病毒感染 (56.7%)、塵蟎(44.5%)、氣溫急遽變化(42.7%)、空氣汙染(24.6%)、冰冷食物(21.6%)。

前言[2]

- ★ 隨著全球兒童氣喘率不斷上升，兒童氣喘越來越引起研究人員的關注，而關於維生素 D 治療兒童氣喘療效的結論一直不一致。
- ★ 維生素 D 被認為是一種複雜的免疫調節分子，在抗炎和調節免疫反應中均有作用，因此越來越受到關注。
- ★ 探索補充維生素 D 對兒童氣喘的影響和安全性。故搜尋到相關文獻指出補充維生素 D 可降低氣喘惡化 (p=0.007)(Wang, et al ., 2019)。

背景

★ 5 歲以下兒童，急性期的初期處置

治療	劑量和使用方式
氧氣輔助性治療	以面罩給予 24%（通常為 1 L/min）以維持血氧飽和度 94-98%
吸入型 SABA	每 20 分鐘給予一次 2-6 puffs 的 salbutamol（以吸入輔助器給予）或 2.5 mg（以霧化劑給予），持續一小時，之後再次評估嚴重度。若症狀維持或復發，每小時再另外給予 2-3 puffs。住院時間 3-4 小時內給予 >10 puffs。
全身性類固醇	給予口服使用 prednisolone 起始劑量 1-2 mg/kg（<2 歲兒童的最高劑量 20 mg；2-5 歲兒童的最高劑量 30 mg）
治療第 1 小時的其他選擇	
Ipratropium bromide	對於中度至重度發作，每 20 分鐘給予一次 2 puffs 的 ipratropium bromide 80 mcg 或 2.5 mg（以霧化劑給予），持續一小時

Global Initiative for Asthma. 2020 GINA Report, Global Strategy for Asthma Management and Prevention.

本院現況

★ 大多數入院病童，醫療處置針對兒童氣喘除了入院使用類固醇給藥及蒸氣吸入，來緩解症狀。

兒童補充維生素D是否可以降低氣喘不良事件？

Front. Pediatr., 29 June 2022 Sec Volume 10 .
https://doi.org/10.3389/fped.2022.840617

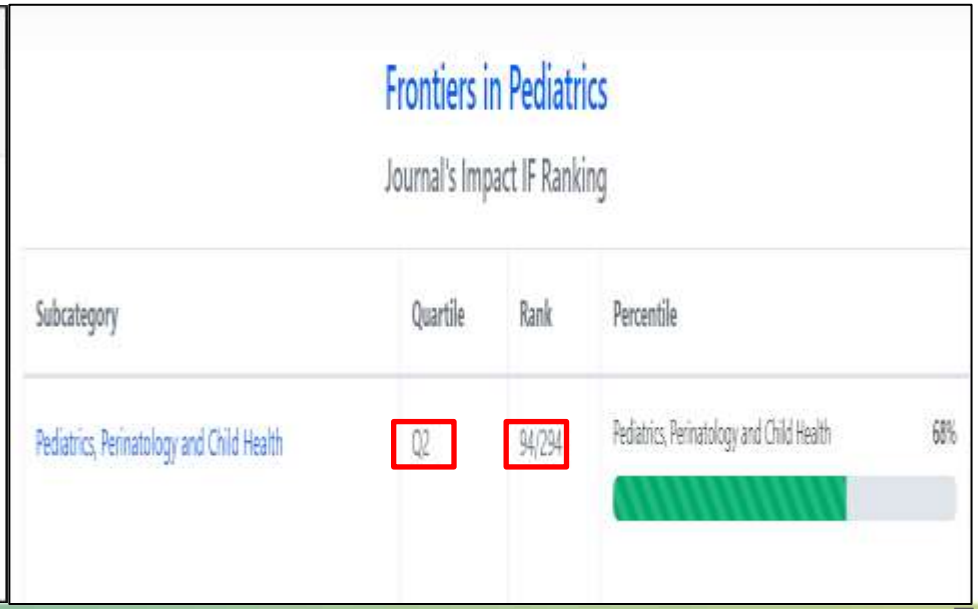
Frontiers in pediatrics.

SYSTEMATIC REVIEW **article**

The Effect of Vitamin D Supplementation in Children With Asthma: A Meta-Analysis

Meiqi Hao[1,2], *Ruoxin Xu*[1,2], *Nachuan Luo*[1,2], *Miaowen Liu*[1,2], *Junping Xie*[3*] and *Wenxiong Zhang*[1*]

影響係數IF:3.569



快速評讀 [FAITH的工具]

快速評讀 [系統性文獻回顧 Systematic Review]

步驟 1：系統性文獻回顧探討的問題為何？

研究族群 / 問題 (Population/ Problem)：

介入措施 (Intervention)：

比較 (Comparison)：

結果 (Outcomes)：

步驟 2：系統性文獻回顧的品質如何？(FAITH)

F - 研究是否找到 (Find) 所有的相關證據？

最好的狀況是？	我可以在哪裡找到這些資訊？
良好的文獻搜尋至少應包括二個主要的資料庫(如：Medline, Cochrane 考科藍實證醫學資料庫, EMBASE 等)，並且加上文獻引用檢索(參考文獻中相關研究、Web of Science, Scopus 或 Google Scholar)、試驗登錄資料等。文獻搜尋應不只限於英文，並且應同時使用 MeSH 字串及一般檢索詞彙 (text words)。	在文章的**方法(Methods)**章節，可以找到詳細搜尋策略的說明，包括使用的名詞，**結果(Results)**章節中可以找到本篇系統性文獻回顧評估的摘要及全文文獻數目、文獻納入與排除的數量及原因。資料可能會以圖表或 PRISMA 的流程圖呈現。

評讀結果：☐是 ☐否 ☐不清楚
說明：

A - 文獻是否經過嚴格評讀 (Appraisal)？

最好的狀況是？	我可以在哪裡找到這些資訊？
應根據不同臨床問題的文章類型，選擇適合的評讀工具，並說明每篇研究的品質(如針對治療型的臨床問題，選用隨機分配、盲法、及完整追蹤的研究類型)。	在文章的**方法**章節，可以找到所使用的文獻品質評讀標準的描述，而**結果**章節則會列出每篇研究品質的評讀結果。

評讀結果：☐是 ☐否 ☐不清楚
說明：

I - 是否只納入 (included) 具良好效度的文章？

最好的狀況是？	我可以在哪裡找到這些資訊？
僅進行文獻判讀是不足夠，系統性文獻回顧只納入至少要有一項研究結果是極小偏誤的試驗。	在文章的**方法**章節，可以找到文章評估的方式，以及是由誰完成評估的，在**結果**章節則會提供審查者意見一致性的程度。

評讀結果：☐是 ☐否 ☐不清楚
說明：

快速評讀 [系統性文獻回顧 Systematic Review]

T - 作者是否以表格和圖表「總結」(total up) 試驗結果？

最好的狀況是？	我可以在哪裡找到這些資訊？
應該用至少 1 個摘要表格呈現所納入的試驗結果。若結果相近，可針對結果進行統合分析(meta-analysis)，並以「森林圖」(forest plot)呈現研究結果，最好再加上異質性分析（見後文）。	在文章的**結果**章節，可以找到摘要的圖表，以及作者對系統性文獻回顧結果的解釋。

評讀結果：☐是 ☐否 ☐不清楚
說明：

H - 試驗的結果是否相近 - 異質性 (Heterogeneity)？

最好的狀況是？	我可以在哪裡找到這些資訊？
在理想情況下，各個試驗的結果應相近或具同質性，若具有異質性，作者應評估差異是否顯著(卡方檢定)。根據每篇個別研究中不同的 PICO 及研究方法，探討造成異質性的原因。	在文章的**結果**章節，可以找到研究結果是否具異質性，及造成異質性可能的原因探討。森林圖中可以找到異質性的卡方檢定結果。

評讀結果：☐是 ☐否 ☐不清楚
說明：

結果為何？

使用何種評估方式，療效有多大（是否來自隨機效果）？

其他說明？

步驟一：系統性文獻回顧探討的問題為何?

- 研究族群/問題(Population/ Problem):
  患有氣喘的兒童（18歲以下）
- 介入措施(Intervention):
  服用維生素 D
- 比較(Comparison):
  常規照護處置
- 結果(Outcomes):
  不良事件(血清Vit D濃度、氣喘急性發作控制、肺部功能、安全性)

步驟二：系統性文獻回顧的品質如何？

F-研究是否找到(Find)所有的相關證據?

P2

良好的文獻搜尋**至少**應包括**二個主要的資料庫**(如:Medline, Cochrane 考科藍實證醫學資料庫,EMBASE 等),並且加上文獻引用檢索(參考文獻中相關研究、Web of Science, Scopus 或 Google Scholar)、試驗登錄資料等。**文獻搜尋應不只限於英文**,並且應同時**使用 MeSH 字串及一般檢索詞彙**(text words)。

Search Strategy

We comprehensively searched the PubMed, The Cochrane Library, ScienceDirect, Embase, Scopus, Ovid MEDLINE, Google Scholar and Web of Science databases for eligible RCTs from inception to 24 October 2021. "Asthma," "vitamin D," and "children" were used as keywords. We also manually searched the references lists of the included RCTs for additional eligible studies (Supplementary Table S2).

搜索了 PubMed、The Cochrane Library、ScienceDirect、Embase、Scopus、Ovid MEDLINE、Google Scholar 和 Web of Science 數據庫，尋找從開始到 2021 年 10 月 24 日符合條件的 RCT。"氣喘"、"維生素 D" 和 "兒童" 是用作關鍵字。

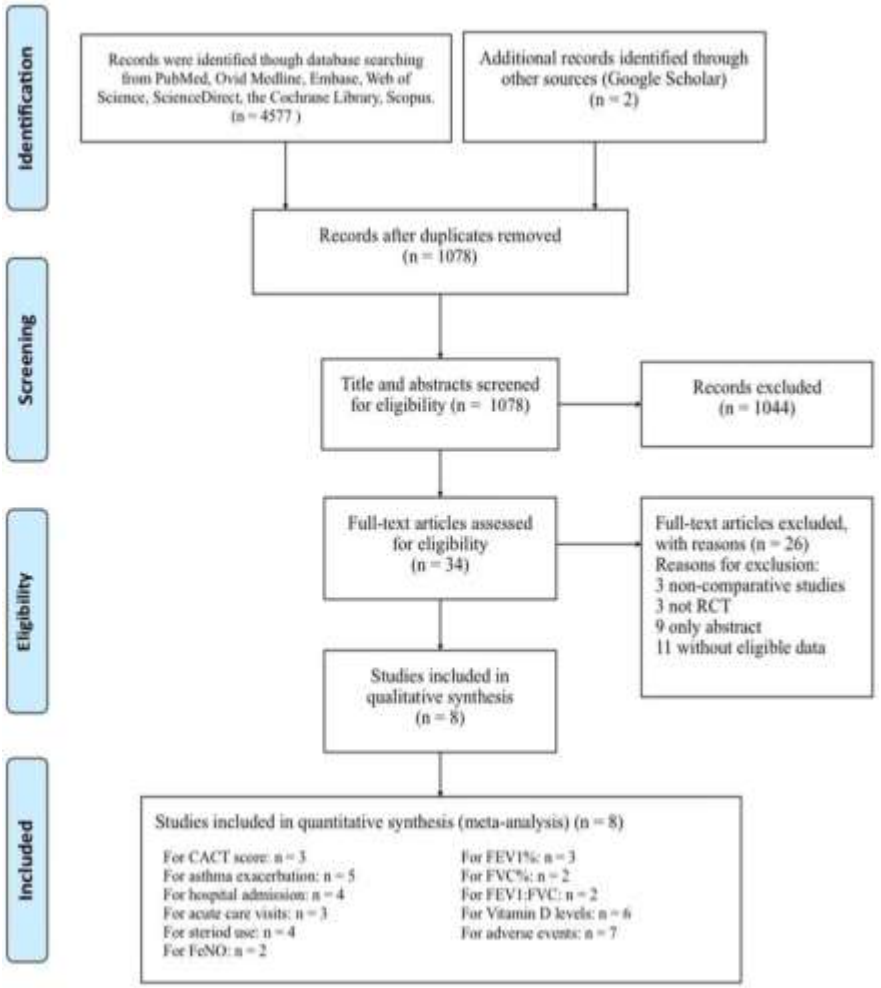
文獻搜尋只限於英文，使用一般檢索詞彙搜尋，未使用MeSH字串搜尋

評讀結果：√是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

F-研究是否找到(Find)所有的相關證據?

P2-3



Selection Criteria

Two researchers independently screened relevant articles using Endnote. The inclusion criteria were as follows: (1) population: children (up to 18 years of age) with asthma (doctor's diagnosis and/or objective criteria); (2) intervention and control: vitamin D vs.

1. 資料庫初搜尋獲得文獻4577篇，刪除了1078篇重複研究。經過標題和摘要篩選，剩下34篇可能相關的研究。
2. 經兩位研究人員獨立審查篩選相關文章最終納入8篇文獻進行研究成果整合。

quality (3 points on the Jadad scale) (**Supplementary Table S3**). The geographical distribution of studies was relatively wide, with four studies in Asia (17, 20, 21, 25) and four in North America (16, 22–24). More details on the included RCTs, including baseline characteristics and main outcome indicators, are shown in **Table 1**.

評讀結果：√是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

F-研究是否找到(Find)所有的相關證據?

P4

TABLE 1 | Summary of the baseline characteristics of the included studies.

Study 研究		Country 國家	Period (year) 期間	Groups 群組	Patients 病患	Sex (M/F) 性別	Age (Mean, year) 年齡	Duration 期間	Oral dose 口服劑量	Baseline characteristics 基準特性					Quality (score) 質量評估	Follow up 後續追蹤
										Vitamin D levels	CACT (score)	Lung fuction (%)				
											FEV1%	FVC%	FEV1:FVC			
2021	Thakur (25)	India 印度	2018.07–2019.11	Vitamin D	30	16/14	9.0	12 weeks	2,000 IU/day	15.8 ±8.2	18.0 ± 2.9	75.3 ± 26.5	NA	NA	5	3 months
				Placebo	30	18/12	8.7			16.5 ± 9.9	15.5 ± 2.7	75.6 ± 15.7				
2021	Jat (17)	India	2017.05–2019.08	Vitamin D	125	89/36	8.2	9 months	1,000 IU/day	11.6 ± 4.6	21.7 ± 4.2	92.5 ± 21.7	92.7 ± 21.7	98.5 ± 10.9	5	9 months
				Placebo	125	91/34	7.8			10.8 ± 4.4	21.9 ± 3.6	97.0 ± 17.5	94.6 ± 17	99.3 ± 10.1		
2020	Forno (24)	USA 美國	2016.02–2019.03	Vitamin D	96	52/44	9.9	48 weeks	4,000 IU/day	22.5 ± 4.6	22.0 ± 3.2	93.9 ± 15.8	NA	91.5 ± 9.3	5	48 weeks
				Placebo	96	63/33	9.7			22.8 ± 4.6	21.3 ± 3.6	90.6 ± 17.3		89.6 ± 10.1		
2019	Ducharme (23)	Canada 加拿大	2014.09–2015.11	Vitamin D	23	16/7	2.9	0, 3.5 months	100,000 IU at baseline and 3.5 months	28.5 ± 5.8	NA	NA	NA	NA	5	7 months
				Placebo	24	14/10	2.9			29.4 ± 11.1						
2016	Tachimoto (21)	Japan 日本	2010.10–2013.04	Vitamin D	54	28/26	10.0	2 months	800 IU/day	28.1 ± 7.6	25.0 ± 3.0	87.2 ± 6.1	98.1 ± 11.4	87.6 ± 5.3	5	6 months
				Placebo	35	22/13	9.8			29.7 ± 7.7	26.0 ± 1.5	87.1 ± 5.4	96.6 ± 11.6	86.4 ± 7.0		
2016	Kerley (16)	Ireland 愛爾蘭	2013.11–2014.04	Vitamin D	17	11/6	10	15 weeks	2,000 IU/day	20.45 ± 7.43	19.0 ± 3.2	105.0 ± 16.3	94.1 ± 11.3	94.2 ± 8.9	3	15 weeks
				Placebo	22	13/9	7			20.45 ± 8.92	16.7 ± 3.7	96.0 ± 10.37	91.6 ± 9.5	93.3 ± 6.3		
2016	Jenson (22)	Canada	2013.11–2014.08	Vitamin D	11	4/7	2.2	6 months	100 000 IU bolus then 400 IU/day	24.8 ± 2.5	NA	NA	NA	NA	5	6 months
				Placebo	11	3/8	3.1		400 IU vitamin D / day	27.2 ± 2.5						
2015	Bar (20)	Israel 以色列	unclear	Vitamin D	20	12/8	13.5	6 weeks	14,000 IU/week	20.8 ± 6.5	NA	NA	NA	NA	4	6 weeks
				Placebo	18	13/6	12.4			20.0 ± 7.1						

CACT, childhood asthma control test; Data are mean (±SD); FEV1%, predicted percentage of forced expiratory volume in first second; FVC%, percentage of predicted forced vital capacity; IU, international unit; M/F, male/female; NA, not available.

評讀結果：√是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

A-文獻是否經過嚴格評讀(Appraisal)?

P3-5

應根據不同臨床問題的文章類型,選擇適合的評讀工具,並說明每篇研究的品質(如針對治療型的臨床問題,選用隨機分配、盲法、及完整追蹤的研究類型)。

Two reviewers assessed the quality of the 8 studies based on the Cochrane Handbook (26). The handbook clarified that the risk of bias in RCTs needs to be assessed by examining following criteria: random sequence generation, allocation concealment, blinding of the participants and personnel, blinding of the outcome assessment, incomplete outcome data, selective reporting, and other bias (**Supplementary Figure S1**). Six studies (17, 21–25) described random sequence generation and were regarded as having a low risk of bias, but two studies (16, 20) had an unclear risk of bias because of a lack of description. Seven studies (17, 20–25) described the allocation concealment process and were regarded as having a low risk of bias, and only one study (16) was considered to have an unclear risk of bias. In the domain of blinding of participants and personnel and outcome assessment, all studies described blinding assignments, researchers, and patients. Thus, all the studies were regarded as having a low risk of bias. For incomplete outcome data, two (21, 23) had an unclear risk of bias because of the lack of outcome data. For the domain of selective reporting and other biases, all the studies were regarding as having a low risk of bias. Disagreements between the two reviewers were resolved *via* discussion or by consulting a third researcher.

In addition, to evaluate the quality of evidence for each terminal, we adopted the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system (27). This system divided the quality of evidence into four levels by evaluating the risk of bias, inconsistency, indirectness, imprecision, and publication bias. **Supplementary Table S4** summarizes the statistical results and the quality of evidence. We assessed the quality of all outcome measures, and the associated qualities of evidence were rated as very low or low. Consequently, the results should be interpreted cautiously.

1.兩位研究人員運用cochrane handbook risk of bias進行8篇RCT研究文章品質評估。

2.經過審查標準來評估 RCT 中的偏倚風險：隨機序列生成、分配隱藏、參與者和人員的盲法、結果評估的盲法、結果數據不完整、選擇性報告和其他誤差。

3.由二位研究員獨立進行評讀，意見不一致時透過和第三位研究員進行討論採共識決。

評讀結果： √是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

A-文獻是否經過嚴格評讀(Appraisal)?

P3-5

應根據不同臨床問題的文章類型,選擇適合的評讀工具,並說明每篇研究的品質(如針對治療型的臨床問題,選用隨機分配、盲法、及完整追蹤的研究類型)。

評讀工具：

1.考科藍針對 randomized parallel-group trials 的誤差風險評估工具RoB 2.0

2.納入文獻的研究品質以紐卡索渥太華品質評估量表（Newcastle Ottawa Quality Assessment Scale，簡稱NOS）來進行評析

3. GRADE證據品質表 (GRADE evidence profile)

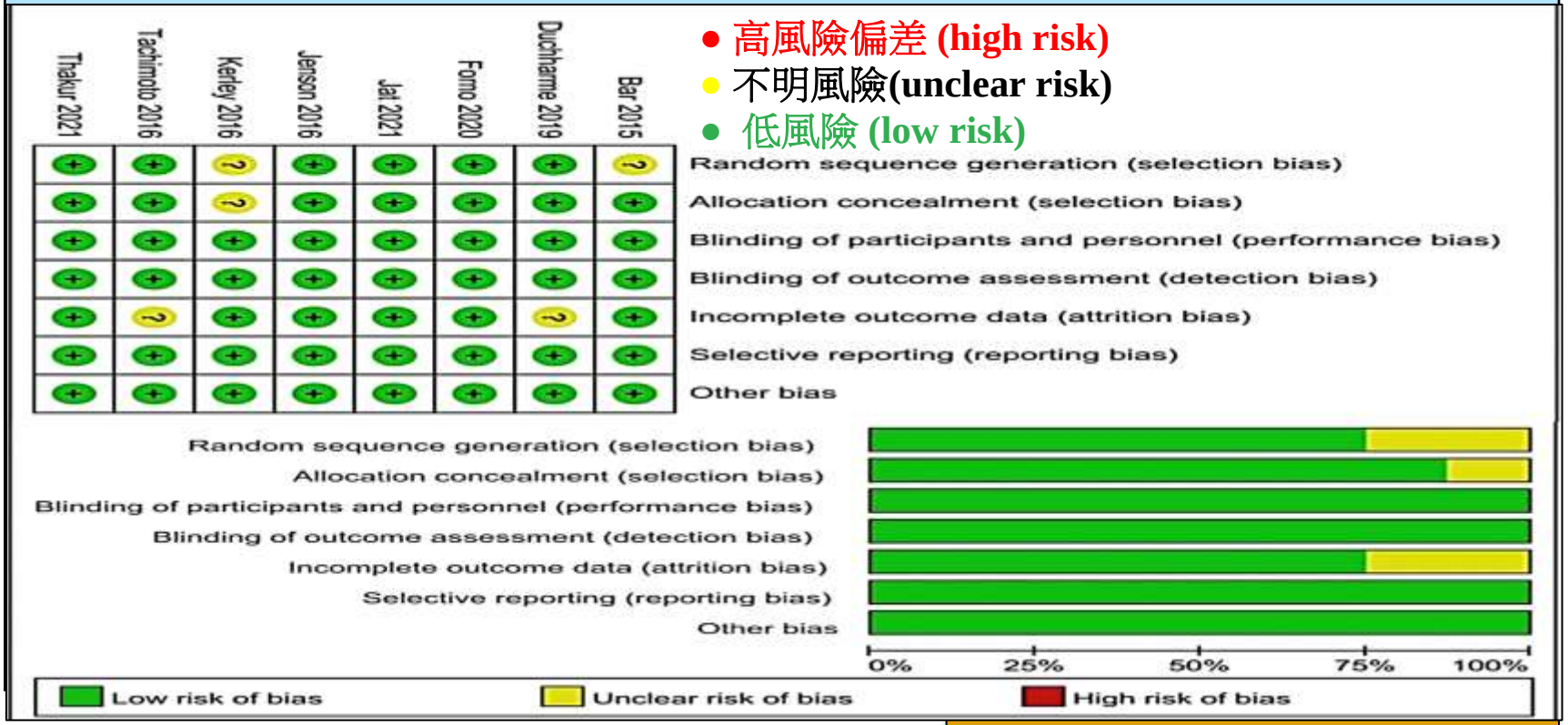
評讀結果： √是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

I-是否只納入(Included)具良好效度文章?

P10

僅進行文獻判讀是不足夠,系統性文獻回顧需納入至少要有一項研究結果是極小偏誤的試驗。



評讀結果： √是 □否□不清楚

步驟二：系統性文獻回顧的品質如何？

I-是否只納入(Included)具良好效度文章?

P2

僅進行文獻判讀是不足夠,系統性文獻回顧需納入至少要有一項研究結果是極小偏誤的試驗

Table S3 Quality assessment of all included studies

Study		Randomization	Masking	Accountability of all patients	Quality (score)
2021	Thakur [25]	★★	★★	★	5
2021	Jat [17]	★★	★★	★	5
2020	Forno [24]	★★	★★	★	5
2019	Ducharme [23]	★★	★★	★	5
2016	Tachimoto [21]	★★	★★	★	5
2016	Keyley [16]				3
2016	Jenson [22]				5
2015	Bar [20]				4

Newcastle-Ottawa Scale for risk of bias
3 or less was considered poor
4–6 was considered moderate
7–9 was deemed high quality

步驟二：系統性文獻回顧的品質如何？

P5

I-是否只納入(Included)具良好效度文章?

僅進行文獻判讀是不足夠,系統性文獻回顧需納入至少要有一項研究結果是極小偏誤的試驗。

Table S4 GRADE Quality assessment by therapeutic strategy and study design for the outcomes of asthma control, lung function, safety and vitamin D levels.

Primary outcomes	No. of Studies	No. of participants: Vitamin D	No. of participants: Placebo	Differences* (95% CI) 絕對風險差異	Quality assessment: Risk of bias[b] 基礎風險	Inconsistency	Indirectness	Imprecision	Publication bias[c]	Quality 證據品質
Vitamin D levels										
Baseline	8	375	362	0.14 [-1.13, 1.42]	Serious (-1)	Serious (-1)	No indirectness	Serious (-1)	Unlikely	Very Low
After intervention	6	262	272	13.51 [4.24, 22.79]	Serious (-1)	Very Serious (-2)	No indirectness	Serious (-1)	Unlikely	Very Low
Asthma control										
CACT score										
Baseline	5	322	308	0.29 [-0.21, 0.79]	Serious (-1)	Very Serious (-2)	No indirectness	No imprecision	Unlikely	Very Low
After intervention	3	157	158	0.15 [-0.43, 0.74]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
Asthma exacerbation	5	310	294	0.92 [0.68, 1.25]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
Hospitalizations for asthma exacerbation	4	189	170	1.20 [0.48, 2.96]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low
Acute care visits	3	62	63	1.13 [0.77, 1.65]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low
Steriod use	4	122	109	1.03 [0.41, 2.57]	Serious (-1)	Serious (-1)	No indirectness	Serious (-1)	Unlikely	Very Low
FeNO										
Baseline	2	50	49	-4.78 [-14.64, 5.07]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
After intervention	2	48	47	1.98 [-3.54, 7.50]	Serious (-1)	Serious (-1)	No indirectness	Serious (-1)	Unlikely	Very Low
Lung function										
FEV1%										
Baseline	5	322	308	0.18 [-1.72, 2.08]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
After intervention	3	135	134	-4.77 [-9.35, -0.19]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
FVC%										
Baseline	3	196	182	0.35 [-2.71, 3.41]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
After intervention	2	107	106	-4.67 [-9.52, 0.18]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
FEV1/FVC										
Baseline	4	292	278	0.73 [-0.75, 2.21]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low
After intervention	2	107	106	-0.86 [-3.52, 1.79]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low
Serious adverse events	4	184	166	1.00 [0.43, 2.33]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low
Hypercalciuria	3	62	63	0.58 [0.22, 1.53]	Serious (-1)	No inconsistency	No indirectness	Serious (-1)	Unlikely	Low
Hospital admission	4	160	161	0.84 [0.37, 1.87]	Serious (-1)	No inconsistency	No indirectness	Very Serious (-2)	Unlikely	Very Low

Abbreviations: CACT: childhood asthma control test; FEV1%: predicted percentage of forced expiratory volume in first second; FVC%: percentage of predicted forced vital capacity; CI: confidence interval.

[a] Differences: mean difference (MD) for CACT scores, FeNO, lung function and vitamin D levels; odds ratios (OR) for safety, asthma exacerbation, hospitalizations for asthma exacerbation, acute care visits and steriod use.

[b] Blinding method and selective reporting and other types of some included trials were not offered.

[c] Publication bias were reported by incomplete outcome data.

步驟二：系統性文獻回顧的品質如何？

P6

T-作者是否以表格和圖表總結(Total up)試驗結果?	H-試驗的結果是否相近-異質性(Heterogeneity)?
應該用至少 1 個摘要表格呈現所納入的試驗結果。若結果相近,可針對結果進行統合分析(meta-analysis),並以「森林圖」(forest plot)呈現研究結果,最好再加上異質性分析。	在理想情況下,各個試驗的結果應相近或具同質性,若具有異質性,作者應評估差異是否顯著(卡方檢定)。根據每篇個別研究中不同的 PICO 及研究方法,探討造成異質性的原因。

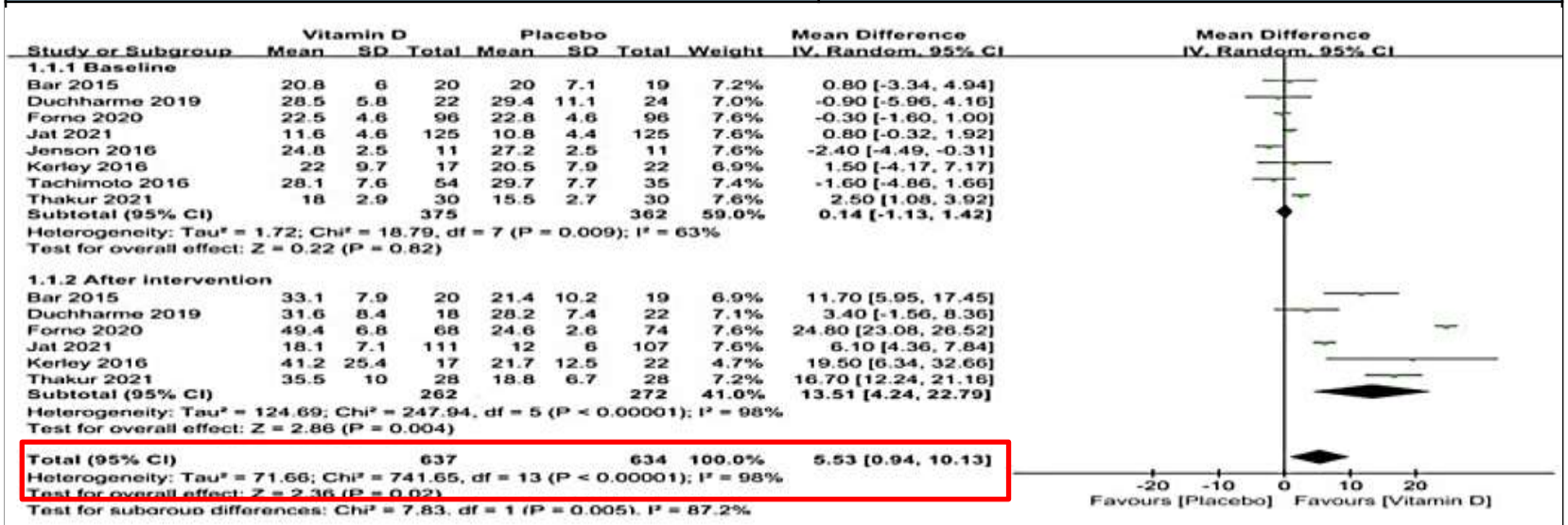


FIGURE 2 | Forest plots of MD of vitamin D levels associated with vitamin D vs. placebo

步驟二：系統性文獻回顧的品質如何？

P7

T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?

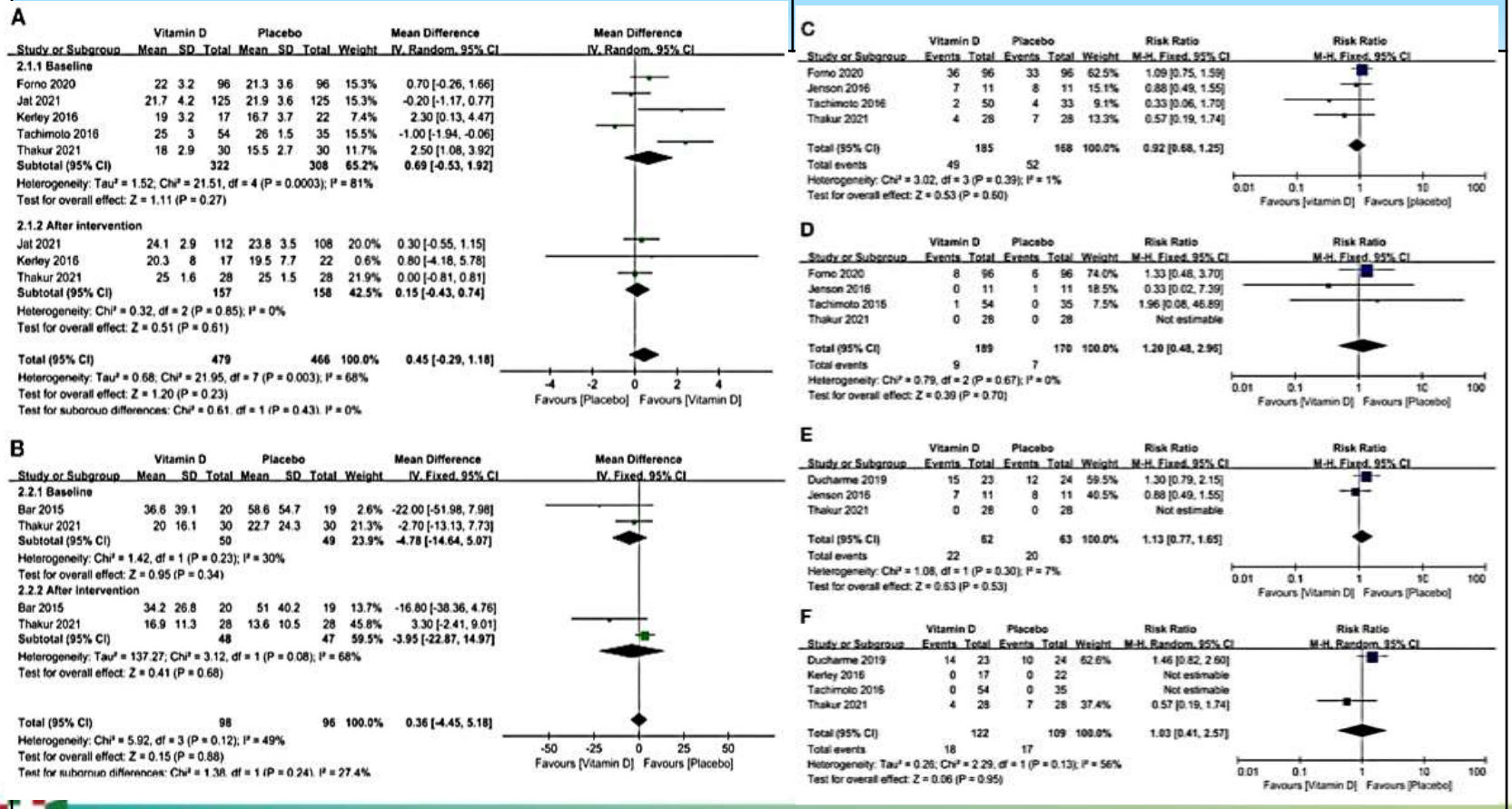


FIGURE 3 | Forest plots of MD of CACT scores (A) and FeNO (B), and RR of asthma exacerbation (C), hospitalizations for asthma exacerbation (D), acute care visits (E), and steroid use (F) associated with vitamin D vs. placebo.

步驟二：系統性文獻回顧的品質如何？

P8

T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?

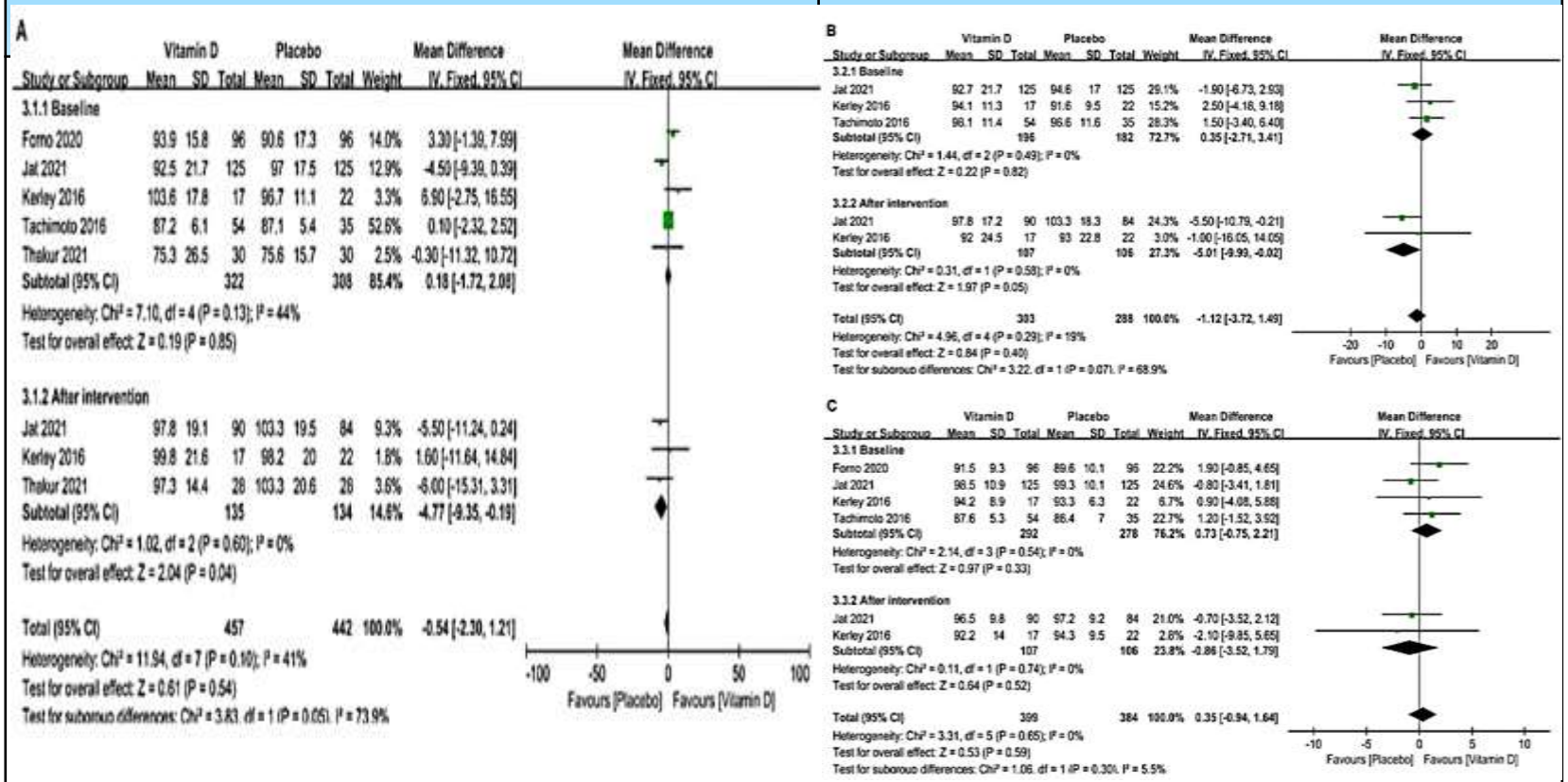


FIGURE 4 | Forest plots MD of FEV1% (A), FVC% (B), and FEV1: FVC (C) associated with vitamin D vs. placebo

步驟二：系統性文獻回顧的品質如何？

P5

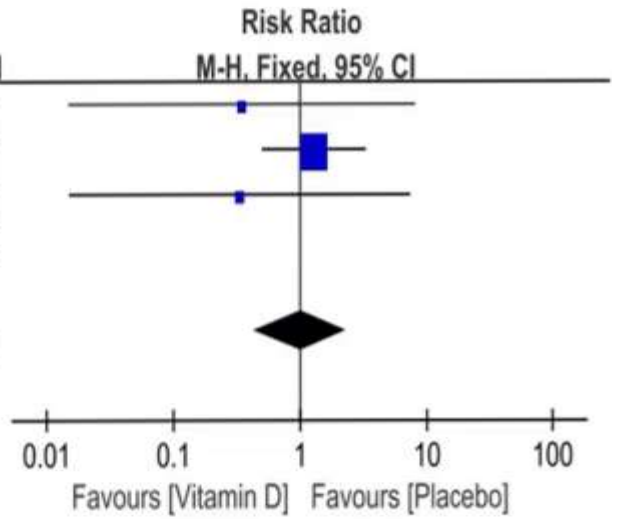
T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?

Study or Subgroup	Vitamin D Events	Vitamin D Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ducharme 2019	0	23	1	24	14.7%	0.35 [0.01, 8.11]
Forno 2020	9	96	7	96	70.2%	1.29 [0.50, 3.31]
Jenson 2016	0	11	1	11	15.0%	0.33 [0.02, 7.39]
Tachimoto 2016	0	54	0	35		Not estimable
Total (95% CI)		**184**		**166**	**100.0%**	**1.00 [0.43, 2.33]**
Total events	9		9			

Heterogeneity: $Chi^2 = 1.18$, $df = 2$ ($P = 0.55$); $I^2 = 0\%$

Test for overall effect: $Z = 0.01$ ($P = 0.99$)



步驟二：系統性文獻回顧的品質如何？

P5

T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?

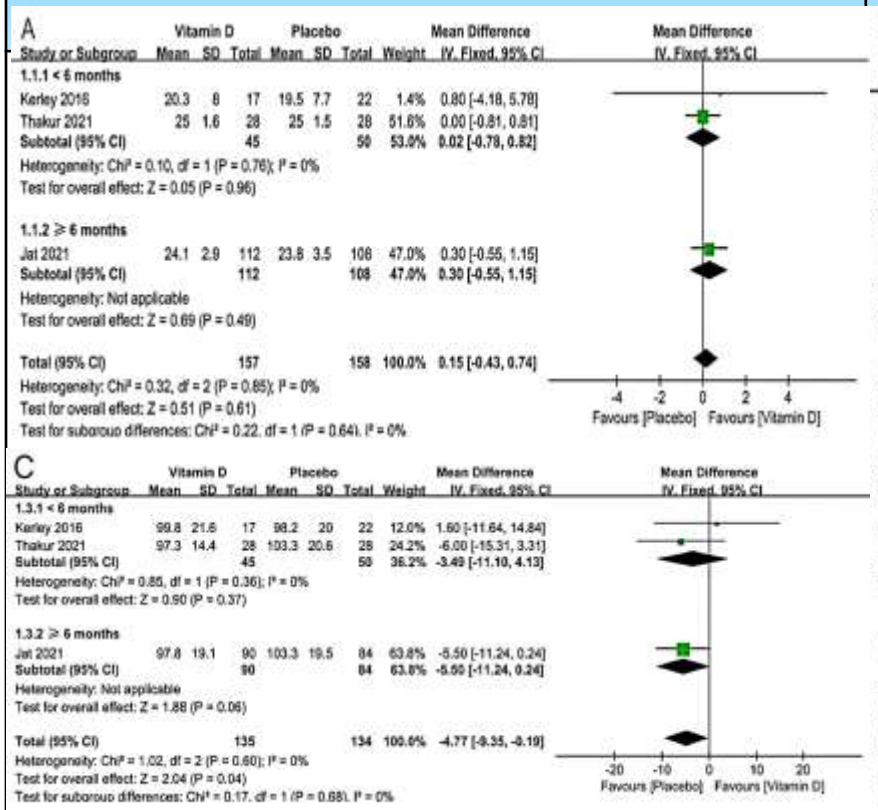
TABLE 2 | Adverse effects (all grade) associated with vitamin D vs. placebo.

Adverse effects	Vitamin D group (event/total)	Placebo group (event/total)	RR (95% CI)	*P* value	Heterogeneity	
					I^2 (%)	*P* value
Hypercalciuria	5/62	9/63	0.58 [0.22, 1.53]	0.27	0	0.65
Blood and lymphatic system disorders	5/119	1/120	3.76 [0.64, 22.11]	0.14	0	0.80
Infection	19/23	17/24	1.17 [0.85, 1.60]	0.34	Not applicable	
General disorders	13/23	17/24	0.80 [0.51, 1.24]	0.32	Not applicable	
Investigations	7/23	9/24	0.81 [0.36, 1.82]	0.61	Not applicable	
Nausea	7/249	8/249	0.82 [0.53, 1.27]	0.38	Not applicable	
Constipation	11/249	12/249	0.92 [0.42, 2.00]	0.83	Not applicable	
Vomiting	28/249	34/249	0.82 [0.53, 1.27]	0.38	Not applicable	
Pain abdomen	41/249	40/249	1.02 [0.72, 1.47]	0.89	Not applicable	
Headache	25/153	25/153	1.00 [0.61, 1.64]	1.00	Not applicable	
Ear and labyrinth disorders	0/23	2/24	0.21 [0.01, 4.12]	0.30	Not applicable	
Eye disorders	0/23	1/24	0.35 [0.01, 8.11]	0.51	Not applicable	
Gastrointestinal disorders	3/23	8/24	0.39 [0.12, 1.30]	0.12	Not applicable	
Immune system disorders	2/23	5/24	0.42 [0.09, 1.94]	0.27	Not applicable	
Musculoskeletal disorders	0/23	1/24	0.35 [0.01, 8.11]	0.51	Not applicable	
Nervous system disorders	1/23	1/24	1.04 [0.07, 15.72]	0.98	Not applicable	
Altered sensorium	1/125	0/125	3.00 [0.12, 72.94]	0.50	Not applicable	
Seizures	0/125	1/125	0.33 [0.01, 8.10]	0.50	Not applicable	
Reproductive system and breast disorders	1/23	0/24	3.13 [0.13, 73.01]	0.48	Not applicable	
Respiratory, thoracic and mediastinal disorders	4/23	7/24	0.60 [0.20, 1.77]	0.35	Not applicable	
Skin and subcutaneous tissue disorders	7/23	4/24	1.83 [0.62, 5.42]	0.28	Not applicable	
Surgical and medical procedure	1/23	1/24	1.04 [0.07, 15.72]	0.98	Not applicable	

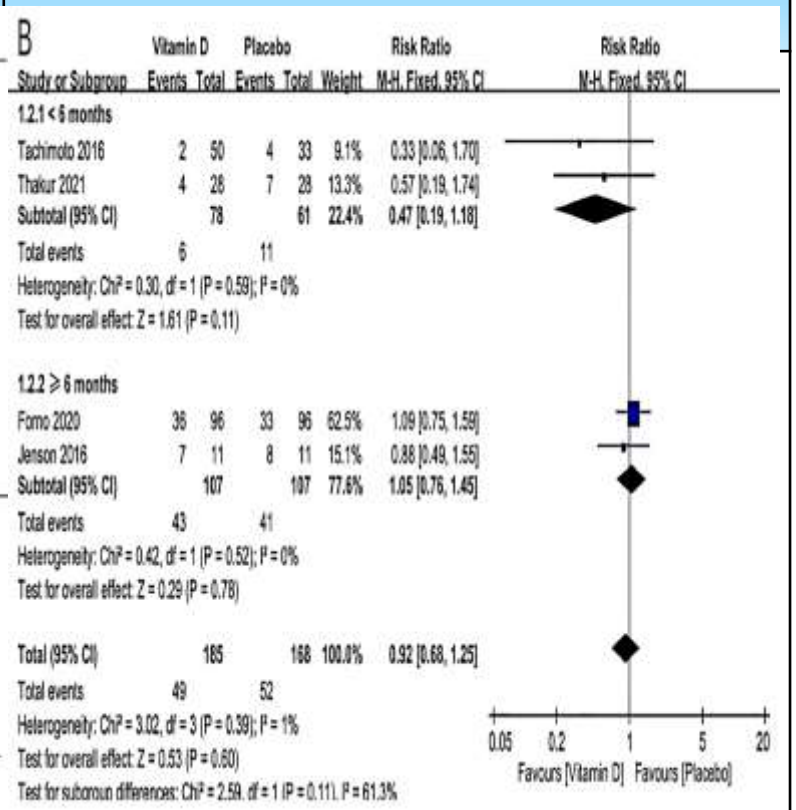
步驟二：系統性文獻回顧的品質如何？

P5

T-作者是否以表格和圖表總結(Total up)試驗結果?



H-試驗的結果是否相近-異質性(Heterogeneity)?



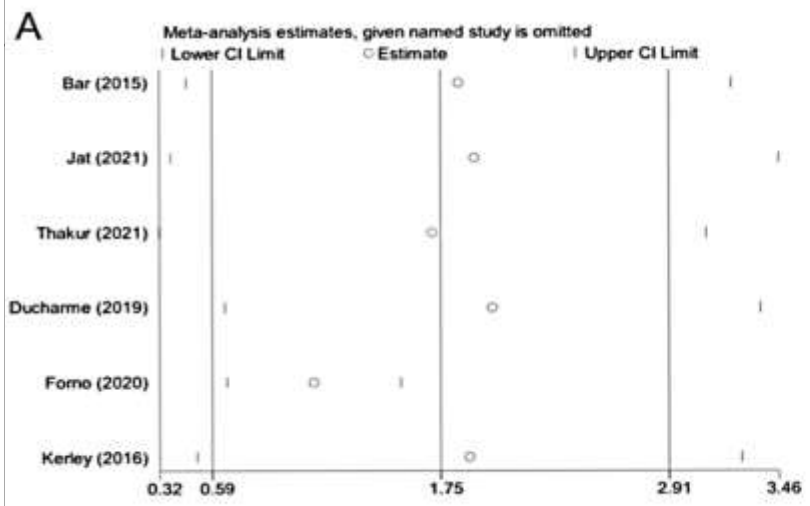
Supplementary Figure S3：Subgroup analysis of CACT scores, asthma exacerbation and FEV1%.

步驟二：系統性文獻回顧的品質如何？

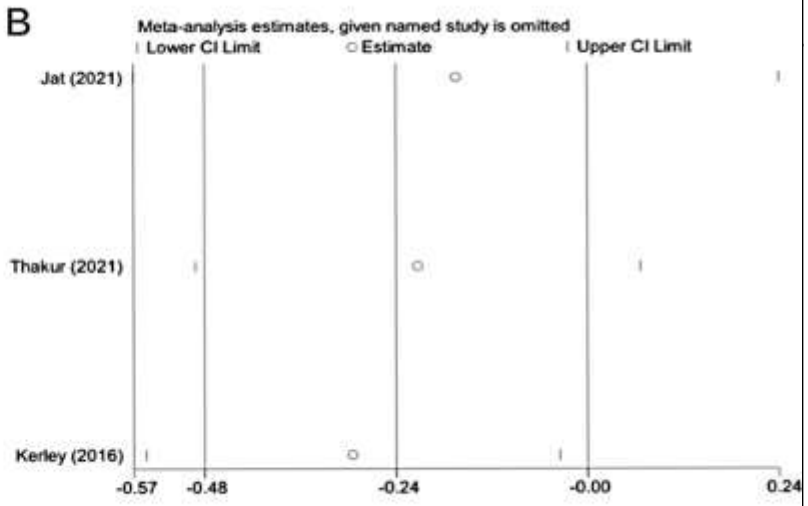
P5

T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?



Study omitted	Estimate	[95% Conf.	Interval]
Bar (2015)	1.8390081	.45616913	3.2218471
Jat (2021)	1.9186608	.37728754	3.4600341
Thakur (2021)	1.7053956	.31892699	3.0918641
Ducharme (2019)	2.0100303	.65409625	3.3659642
Forno (2020)	1.1049004	.66439027	1.5454104
Kerley (2016)	1.8927523	.50907254	3.276432
Combined	1.7469114	.58768711	2.9061357



Study omitted	Estimate	[95% Conf.	Interval]
Jat (2021)	-.16755523	-.57291418	.23780374
Thakur (2021)	-.21582024	-.49503043	.06338996
Kerley (2016)	-.29782245	-.55787569	-.0377692
Combined	-.24368031	-.48423392	-.0031267

Supplementary Figure S4：Meta-based influence analyses for vitamin D levels **(A)** and FEV1% **(B)**.

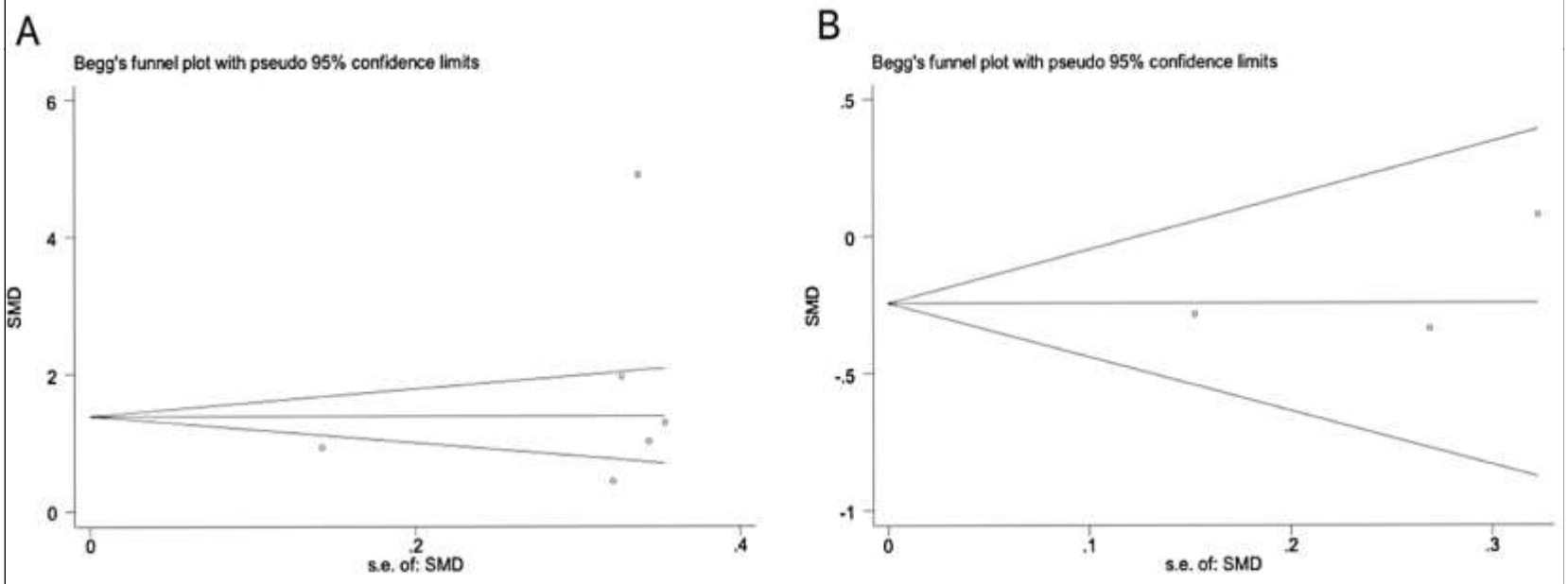
步驟二：系統性文獻回顧的品質如何？

P6

評讀結果：□是 □否□不清楚

T-作者是否以表格和圖表總結(Total up)試驗結果?

H-試驗的結果是否相近-異質性(Heterogeneity)?



Egger's test

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	.1864831	1.410436	0.13	0.901	-3.729515	4.102481
bias	5.144386	5.564894	0.92	0.408	-10.30624	20.59501

Egger's test

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	-.4875946	.3272427	-1.49	0.376	-4.645607	3.670418
bias	1.211293	1.539379	0.79	0.576	-18.34837	20.77096

Supplementary Figure S5： Egger's and Begg's tests for comparisons of vitamin D levels (A) and FEV1% (B).

總結[系統性文獻回顧 Systematic Review]

	FAITH系統性文獻回顧快速評讀表		結果
F	研究是否找到 (Find) 所有的相關證據？	至少二個主要資料庫(PubMed，EMBASE，and Cochrane Library)，加上文獻引用檢索(Web of Science)，不限英文，使用MeSH字串及一般檢索詞彙(text words)	是
A	文獻是否經過嚴格評讀 (Appraisal)？	以the Cochrane Risk of Bias assessment tool進行嚴格評讀，並以表格呈現各篇納入文獻品質	是
I	是否只納入 (Included) 具良好效度的文章？	由二位研究員獨立進行評讀，意見不一時和第三位研究員進行討論採共識決	是
T	作者是否以表格和圖表「總結」(Total up)？	Table (characteristics of enrolled studies, subgroup analysis), forest plot of probiotics overall effects and adverse events	是
H	試驗的結果是否相近 - 異質性 (Heterogeneity)？	因異質性大套用random effects model，進行sensitivity analyses and subgroup analyses，funnel plot、Begg test、Egger test to assess publication bias	是

研究結果

1.補充維生素D對於維持血清維生素 D 濃度有改善。

2.補充維生素D在改善肺功能方面沒有明顯效益。

3.補充維生素D的兒童相比未補充維生素D，氣喘的發生率相當，故推斷補充維生素D是安全的。

研究限制

1.納入的文章數量少，只納入了八個 RCTS。

2.樣本數少，分析中納入的兒科患者樣本量有限可能會影響結果的品質。

3.分析結果氣喘發作的次數和嚴重度相似，納入試驗中氣喘發作存有差異性，故使得結果受影響。

4.研究中使用的劑量和持續時間不明確。

5.納入研究的氣喘類型較廣，導致樣本異質性高。

此文獻的實證證據可以用於本院嗎？

1.使用維生素 D 治療兒童氣喘的看法？

2. 本院進兒童LiquiD P&B 400IU/drop(5ml/瓶=178滴，自費2160元)，是否可以用錠劑來取代呢？效果是否相近

3.文獻中表示補充維生素 D 甚至可能會降低患者的肺功能？

4.使用維生素 D 治療兒童氣喘的安全劑量？建議服用持續時間？

議題討論

是否贊成兒童補充維生素D來降低氣喘不良事件發生？

同意: 0票

需再評估:13票

不同意:15票

THANK YOU!