患有支氣管擴張之成人使用吸入性抗生素是否比口服抗生素更能降低支氣管擴張的惡化程度

報告日期：2022/09/20
引言人：徐慧貞護理師/陳泳溱副護理長
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單位：12A護理之家

背景1

Bronchiectasis:

- 支氣管擴張症是一種慢性肺部發炎疾病，
  其特色為氣管及支氣管發炎、黏液纖毛清除能力下降、痰液堆積以致漸進性的結構改變，進而導致支氣管永久性擴張。
  (陳逸燕, & 歐芷瑩. 2021)
- 支氣管擴張的病理生理機制包括持續性細菌感染、免疫反應失調、粘液纖毛清除受損和氣道阻塞。
- 患者通常表現為咳痰和反覆肺部感染。
- 治療旨在減少惡化的頻率，提高生活質量和預防疾病進展。
  (Chalmers, James D., et al. 2018)

背景2

- Inhaled antibiotics
- 使用吸入性抗生素治療支氣管擴張的主要原因是，治療因細菌性感染而造成的肺部疾病，因此抗生素治療將減輕症狀。

- (Banaschewski, B., & Hofmann, T. 2019).

背景2

- 相較於全身性抗生素的使用，吸入型抗生素較無副作用且直接作用在呼吸道上，局部濃度高且殺菌效果好，是較理想的治療方式。 (Geller DE, 2009)
- 根據文獻顯示使用吸入型抗生素在支氣管擴張之患者身上可以降低呼吸道細菌總量以及急性惡化風險
- 2017 年歐洲呼吸學會所發表支氣管擴張症指引，已經建議使用吸入型抗生素在治療慢性綠膿桿菌感染之支氣管擴張症患者。 (Polverino, Eva, et al 2017).

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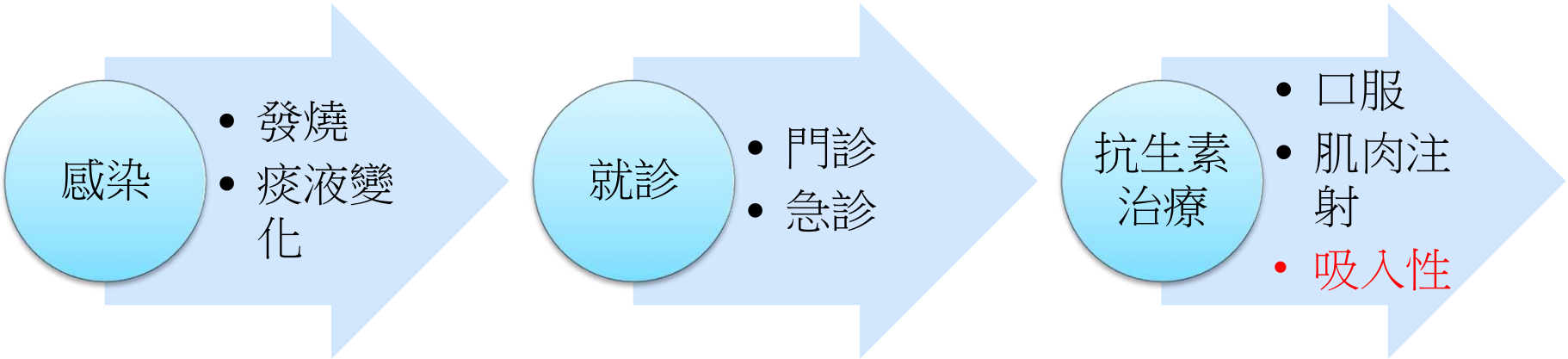
背景[3]

- 目前護理之家共有28位住民，其中有11 位住民是有使用氣切的(11/28=39.2%)。有氣切的住民在照護上的重點就是痰液的清除、維持呼吸道通暢和避免感染。
- 根據統計，入住護理之家的住民多為高齡長者，目前萬芳醫院附設護理之家住民的平均年齡為79歲。(平均76.53+21.53歲)
- 110年，住民因肺炎轉入住急性病房之比例如為48.7%
- 其中肺炎48.7%與相關研究彰化地區護理之家呼吸道感染53%相近。

(謝汶鈺, 薛雅云, & 李芳菁, 2017)

背景[4]

- 護理之家住民有反覆性支氣管發炎和肺炎發生，經過就診感染科或胸腔內科，醫師有時會選擇開立透過吸入抗生素的方式治療，(特別是針對有抗藥性菌種)。與一般病房不同，護理之家不執行抗生素經靜脈注射給藥。對於忙碌的護理臨床工作，護理師常會有知其所以，而不知所以然的困境發生。



背景4

- 目前，護理之家共有28床現存住民(總共有28床，1位住民目前入住急性病房)，就有四位住民正在執行一天兩次，使用吸入性抗生素治療(4/28=14.2%)。職希望透過此次文獻閱讀，去理解使用抗生素吸入性治療對於支氣管發炎患者的治療的效益，是否能減少支氣管發炎嚴重惡化的頻率。

The efficacy and safety of inhaled antibiotics for the treatment of bronchiectasis in adults: a systematic review and meta-analysis

Irena F Laska, MBBS • Megan L Crichton, MFM • Amelia Shoemark, PhD • Prof James D Chalmers, PhD

Published: August 09, 2019 • DOI: https://doi.org/10.1016/S2213-2600(19)30185-7 • Check for updates

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RESPIRATORY MEDICINE

Journal Impact Factor

The Journal Impact Factor (JIF) is a journal-level metric calculated from dat
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of the subject area and type of journal. The Journal Impact Factor can comp
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articles. Learn more

2019 JOURNAL IMPACT FACTOR	JOURNAL IMPACT FACTOR WITHOUT SELF CITATIONS
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Rank by Journal Impact Factor

Q2

Journals within a category are sorted in descending order by Journal Impact Factor (JIF) resulting in the Category Ranking below. A separate rank is shown for each category in which the journal is listed in JCR. Data for the most recent year is presented at the top of the list, with other years shown in reverse chronological order. Learn more

EDITION
Science Citation Index Expanded (SCIE)

CATEGORY
CARDIAC & CARDIOVASCULAR SYSTEMS
56/138

JCR YEAR	JIF RANK	JIF QUARTILE	JIF PERCENTILE
2021	55/143	Q2	61.89
2020	64/142	Q2	55.28
2019	56/138	Q2	59.78
2018	54/136	Q2	60.66
2019	56/138	Q2	59.78

EDITION
Science Citation Index Expanded (SCIE)

CATEGORY
RESPIRATORY SYSTEM
24/64

JCR YEAR	JIF RANK	JIF QUARTILE	JIF PERCENTILE
2021	25/65	Q2	62.31
2020	27/64	Q2	58.59
2019	24/64	Q2	63.28
2018	24/63	Q2	62.70
2019	24/64	Q2	63.28

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?

P 病人/對象(Population)：

患有支氣管擴張症狀之成人

I 介入(Intervention)：

使用吸入性抗生素之治療

C 對照(Comparison)

口服抗生素、肌肉注射抗生素

O 結果(Outcome)

減少支氣管擴張的惡化的頻率
(再住院率)

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?

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)。

Methods

Search strategy and selection criteria

We did a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) recommendations.[18] Two investigators (MLC and JDC) searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and Web of Science from Jan 1, 1990, to Jan 30, 2019. Further details of the search strategy can be found in the appendix (p 1). We also searched the ClinicalTrials.gov registry using "bronchiectasis" as the only search term. Searches were supplemented by reviewing the reference lists of the publications, previous meta-analyses, and guidelines.

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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?

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)。

A priori we considered for inclusion studies that were randomised controlled trials with a placebo or other comparator, included adult patients with bronchiectasis diagnosed by CT or bronchography, used inhaled antibiotics as a treatment for stable patients (defined by the absence of exacerbation at baseline [appendix p 2]), had a duration of at least 4 weeks, and assessed at least one of the clinical endpoints of interest (listed in Outcomes). We excluded trials that included patients with cystic fibrosis, trials in children, and studies in which treatment was administered during an acute exacerbation of bronchiectasis only. Two authors (MLC and JDC) did the

納入條件

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排除條件

(FAITH)

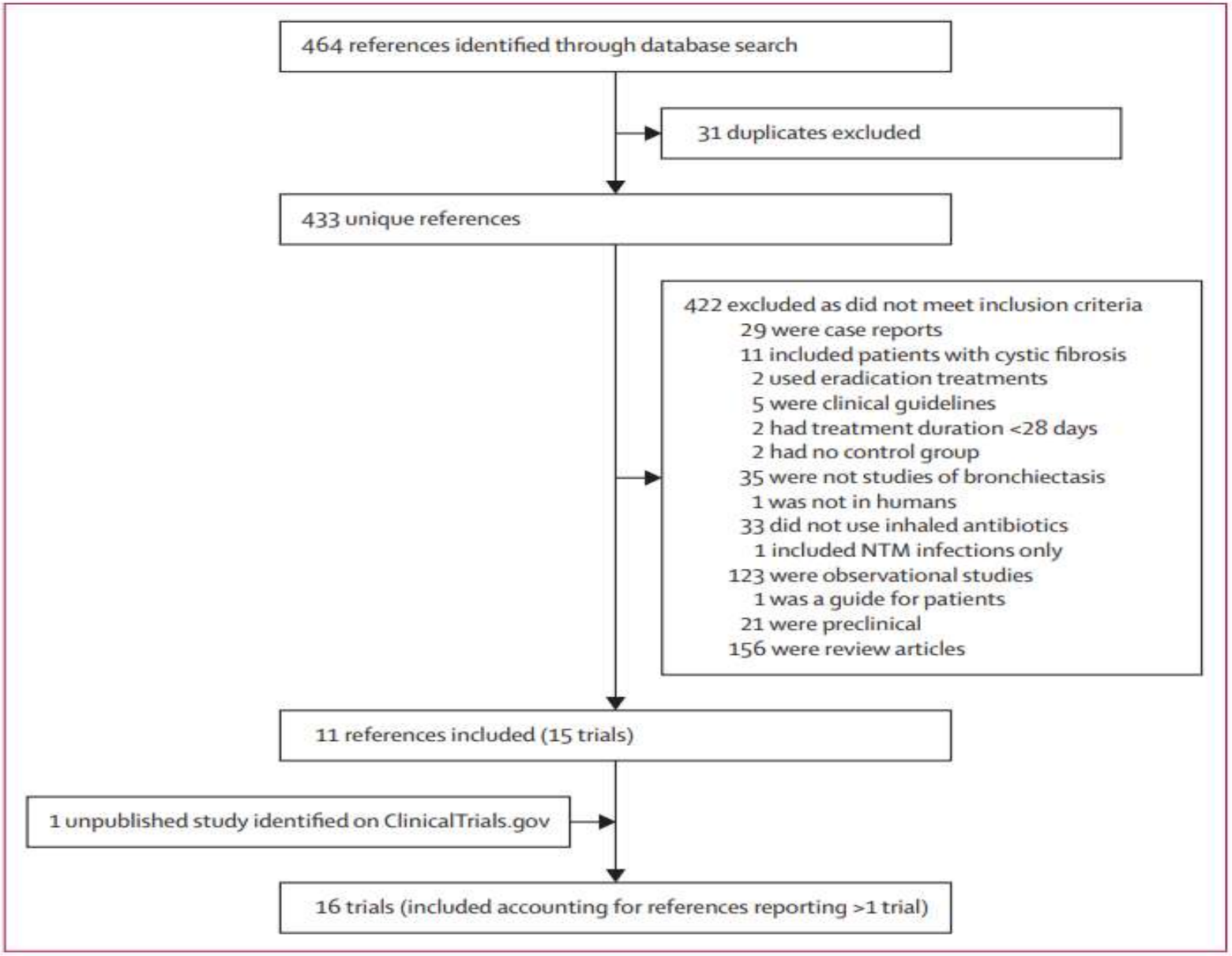

Figure 1: **Study profile**
NTM=non-tuberculous mycobacteria.

刪除重複文獻

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依標題/摘要
刪除文獻

閱讀全文後
確定刪除文獻

研究是否找到所有的相關證據 ☑是 ☐否 ☐不確定

A–文獻是否經過嚴格評讀(Appraisal)?

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 authors (IFL and MLC) independently assessed the risk of bias using the Cochrane collaboration risk of bias tool,[21] which takes account of allocation sequence generation, concealment of allocation, masking of participants and investigators, incomplete outcome reporting, selective outcome reporting, and other sources of bias. Each potential source of bias was graded as "yes", "no", or "unclear" allowing to determine whether studies were considered at high, low, or moderate risk of bias. Disagreement regarding quality assessments was resolved by a third author (AS).

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研究是否找到所有的相關證據？ ☑是 ☐否 ☐不確定

步驟二：系統性文獻回顧的品質如何？

(FAITH)

作者 藥物 期限 人數 平均年齡 FEV1% PA菌落數 其他菌種 主要結果 次要結果

	Drug	Duration	Number of participants, intervention vs control	Age, years (SD), intervention vs control	FEV$_1$% predicted (SD), intervention vs control	*Pseudomonas aeruginosa* present, intervention vs placebo	Other pathogens present, intervention vs placebo	Primary outcome	Secondary outcomes
Wilson et al (2013)[16]	Ciprofloxacin DPI (32·5 mg) vs placebo twice per day	84 days	60 (39 female and 21 male) vs 64 (43 female and 21 male)	64·7 (11·8) vs 61·4 (11·9)	57·2 (13·7) vs 54·6 (14·8)	32 (53%) vs 35 (55%)	*Haemophilus influenzae*: 14 (23%) vs 16 (25%); *Staphylococcus aureus*: 8 (13%) vs 17 (27%); *Streptococcus pneumoniae*: 7 (12%) vs 2 (3%); *Moraxella catarrhalis* 5 (8%) vs 3 (5%)	Effect of ciprofloxacin DPI on total bacterial density of predefined potential respiratory pathogens in sputum (CFU per g) after the 28-day treatment period	Time to exacerbation; emergence of new potential respiratory pathogens; emergence of resistance among baseline pathogens; changes in inflammatory biomarkers; change in 24-hour sputum volume and colour; changes in FEV$_1$, FVC, and SGRQ score at days 29, 56, and 84; adverse events; results of physical examinations; vital signs; and laboratory analyses
De Soyza et al (2018, RESPIRE 1, 14 days)[14]	Ciprofloxacin DPI (32·5 mg) vs placebo twice per day	12 months	137 (88 female and 49 male) vs 68 (44 female and 24 male)	65·2 (13·5) vs 65·5 (12·9)	59·42 (16·7) vs 57·37 (15·5)	83 (61%) vs 41 (60%)	≥1 prespecified microorganism for recruitment: *H influenzae*, *M catarrhalis*, *S aureus*, *S pneumoniae*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*	Time to first exacerbation, frequency of exacerbations	Less stringent definition of an exacerbation microbiological outcomes, QOL assessments (SGRQ and QOL-B), lung function
De Soyza et al (2018, RESPIRE 1, 28 days)[14]	Ciprofloxacin DPI (32·5 mg) vs placebo twice per day	-	141 (101 female and 40 male) vs 70 (52 female and 18 male)	64·2 (12·1) vs 64·0 (13·5)	59·48 (15·1) vs 61·7 (16·7)	83 (59%) vs 45 (64%)	≥1 prespecified microorganism for recruitment: *H influenzae*, *M catarrhalis*, *S aureus*, *S pneumoniae*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*	Time to first exacerbation, frequency of exacerbations	Less stringent definition of an exacerbation, microbiological outcomes, QOL assessments (SGRQ and QOL-B), lung function
Aksamit et al (2018, RESPIRE 2, 14 days)[14]	Ciprofloxacin DPI (32·5 mg) vs placebo twice per day	-	176 (96 female, 80 male) vs 88 (62 female, 26 male)	60·4 (13·7) vs 60·4 (15·0)	54·3 (17·3) vs 55·8 (18·6)	107 (61%) vs 55 (63%)	≥1 prespecified microorganism for recruitment: *H influenzae*, *M catarrhalis*, *S aureus*, *S pneumoniae*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*	Time to first exacerbation, frequency of exacerbations	Less stringent definition of an exacerbation, microbiological outcomes, QOL assessments (SGRQ and QOL-B), lung function
Aksamit et al (2018, RESPIRE 2, 28 days)[14]	Ciprofloxacin DPI (32·5 mg) vs placebo twice per day	-	171 (92 female, 79 male) vs 86 (52 female, 34 male)	59·3 (14·2) vs 60·6 (13·7)	56·4 (18·8) vs 56·2 (18·2)	99 (58%) vs 54 (63%)	≥1 prespecified microorganism for recruitment: *H influenzae*, *M catarrhalis*, *S aureus*, *S pneumoniae*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*	Time to first exacerbation, frequency of exacerbations	Less stringent definition of an exacerbation, microbiological outcomes, QOL assessments (SGRQ and QOL-B), lung function
Serisier et al (2013, ORBIT-2)[15]	Liposomal ciprofloxacin (liposome encased ciprofloxacin [135 mg] and free ciprofloxacin [54 mg]) vs placebo (empty liposomes in 0·9% saline) once per day	24 weeks	20 (10 female, 10 male) vs 22 (13 female, 9 male)	70 (5·6) vs 59·5 (13·2)	60·7 (24·1) vs 53·1 (22·7)	20 (100%) vs 22 (100%)	*Klebsiella*: 2 (10%) vs 2 (9%), *Achromobacter xylosoxidans*: 0 vs 2 (9%)	Mean change in sputum *P aeruginosa* bacterial density (CFU per g) from baseline to end of first treatment cycle (28 days)	Time to first pulmonary exacerbation, FEV$_1$, 6MWT, SGRQ, safety, and tolerability

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步驟二：系統性文獻回顧的品質如何？

(FAITH)

作者 藥物 期限 人數 平均年齡 FEV1% PA菌落數 其他菌種 主要結果 次要結果

	Drug	Duration	Number of participants, intervention vs control	Age, years (SD), intervention vs control	FEV$_1$, % predicted (SD), intervention vs control	*Pseudomonas aeruginosa* present, intervention vs placebo	Other pathogens present, intervention vs placebo	Primary outcome	Secondary outcomes
(Continued from previous page)									
Haworth et al (2019; ORBIT-3)[17]	Liposomal ciprofloxacin (liposome encased ciprofloxacin [135 mg] and free ciprofloxacin [54 mg]) vs placebo (empty liposomes in 0·9% saline) once per day	48 weeks	183 (127 female, 56 male) vs 95 (67 female, 28 male)	64·3 (13·6) vs 66·7 (10·7)	57·3 (21·9) vs 57·4 (20·2)	183 (100%) vs 95 (100%)	*S aureus*: 31 (17%) vs 22 (23%); *Escherichia coli* and coliforms: 11 (6%) vs 5 (5%); *S pneumoniae*: 5 (3%) vs 3 (3%); *H influenzae*: 5 (3%) vs 1 (1%); *M catarrhalis*: 2 (1%) vs 0	Time to first pulmonary exacerbation	Number and frequency of pulmonary exacerbations, number of patients requiring intravenous antibiotics, QOL-B-RSS, change in *P aeruginosa* bacterial density (CFU per g)
Haworth et al (2019; ORBIT-4)[17]	Liposomal ciprofloxacin (liposome encased ciprofloxacin [135 mg] and free ciprofloxacin [54 mg]) vs placebo (empty liposomes in 0·9% saline) once per day	..	206 (134 female, 72 male) vs 98 (63 female, 35 male)	63·3 (13·5) vs 64·2 (12·6)	62·6 (22·2) vs 59·8 (20·8)	206 (100%) vs 98 (100%)	*S aureus*: 50 (24%) vs 23 (24%); *E coli* and coliforms: 9 (4%) vs 3 (3%); *S pneumoniae*: 10 (5%) vs 3 (3%); *H influenzae*: 7 (3%) vs 4 (4%)	Time to first pulmonary exacerbation	Number and frequency of pulmonary exacerbations, number of patients requiring intravenous antibiotics, QOL-B-RSS, change in *P aeruginosa* bacterial density (CFU per g)
Barker et al (2014; AIR-BX 1)[18]	Nebulised aztreonam (75 mg) vs placebo three times per day	28 weeks	134 (84 female, 50 male) vs 132 (97 female, 35 male)	64·2 (12·9) vs 64·9 (12·1)	60·4 (22·6) vs 64·5 (18·7)	112 (84%) vs 105 (80%)	History of *Mycobacterium*: 16 (12%) vs 14 (10%); no data for other organisms	Change in QOL-B-RSS from baseline to week 4	Change in QOL-B-RSS from baseline to week 12, time to first exacerbation by week 16, change in CFU per g, presence or absence of respiratory pathogens, changes in MIC of aztreonam
Barker et al (2014; AIR-BX2)[18]	Nebulised aztreonam (75 mg) vs placebo three times per day	..	136 (89 female, 47 male) vs 138 (101 female, 37 male)	63·3 (14·2) vs 62·7 (13·3)	63·8 (19·5) vs 63·4 (21·6)	116 (85%) vs 103 (75%)	History of *Mycobacterium*: 8 (6%) vs 12 (9%); no data for other organisms	Change in QOL-B-RSS from baseline to week 4	Change in QOL-B-RSS from baseline to week 12, time to first exacerbation by week 16, change in CFU per g, presence or absence of respiratory pathogens, changes in MIC of aztreonam
Drobnic et al (2005)[19]	Nebulised tobramycin (300 mg) vs placebo (0·9% saline) twice per day; crossover trial	13 months	10 vs 10 in the PP population of 30 participants included in the ITT population (sex breakdown not reported)	64·5 (range 38–75)	51·78 (16·5)	10 (100%) vs 10 (100%)	No data	Not specifically stated but presumed to be number of exacerbations	Number of hospital admissions, number of hospital admission days, antibiotic use, pulmonary function, SGRQ, tobramycin toxicity, density of *P aeruginosa* in sputum, emergence of bacterial resistance, and emergence of other opportunistic bacteria
Barker et al (2000)[20]	Nebulised tobramycin (300 mg) vs placebo (1·25 mg quinine in saline) twice per day	6 weeks	37 (23 female, 14 male) vs 37 (22 female, 15 male)	66·6 (13·0) vs 63·2 (13·5)	56·2 (21·2) vs 53·3 (22·1)	37 (100%) vs 37 (100%)	No data	Change in *P aeruginosa* density (CFU per g) from baseline to week 4	Change in *P aeruginosa* density from baseline to week 2 and to week 6, investigator's subjective assessment of change in patients' general medical condition, percentage change in FEV, and FVC % predicted, and safety measurements

(Table continues on next page)

P860

步驟二：系統性文獻回顧的品質如何？

(FAITH)

作者　藥物　期限　人數　平均年齡　FEV1%　PA菌落數　其他菌種　主要結果　次要結果

	Drug	Duration	Number of participants, intervention vs control	Age, years (SD), intervention vs control	FEV_1, % predicted (SD), intervention vs control	*Pseudomonas aeruginosa* present, intervention vs placebo	Other pathogens present, intervention vs placebo	Primary outcome	Secondary outcomes
(Continued from previous page)									
Orriols et al (1999)[31]	Nebulised ceftazidime (1000 mg) and tobramycin (100 mg) twice per day vs standard care	12 months	7 (1 female, 6 male) vs 8 (4 female, 4 male)	62·0 (SEM 8·5) vs 61·4 (10·3)	62·3 (SEM 19·9) vs 56·2 (21·4)	7 (100%) vs 8 (100%)	No data	Not specifically stated but presumed to be number of hospital admissions	Number of hospitalisation days, use of oral antibiotics, FVC, FEV_1, P_aO_2, P_aCO_2, drug toxicity, and emergence of bacterial resistance
Murray et al (2011)[32]	Nebulised gentamicin (80 mg) vs placebo (0·9% saline) twice per day	15 months	32 vs 33 randomly assigned; 27 (18 female, 9 male) vs 30 (15 female, 15 male) completed and included in analysis	58 (53–67) vs 64 (56–69) (median, interquartile range)	72·9 (60–81·2) vs 63·4 (45·5–80·4) (median, interquartile range)	13 (48%) vs 11 (37%)	*H influenzae* 11 (41%) vs 15 (50%); *S aureus* 2 (7%) vs 1 (3%); *S pneumoniae* 1 (4%) vs 0; *M catarrhalis* 0 vs 2 (7%); coliforms 0 vs 1 (3%)	Quantitative bacteriology in CFU per g	Sputum purulence and 24-hour volume, pulmonary function tests, exercise capacity, LCQ and SGRQ, exacerbation frequency, inflammatory biomarkers
Haworth et al (2014)[33]	Nebulised colistin (1 million international units) vs placebo (0·45% saline) twice per day	26 weeks	73 (46 female, 27 male) vs 71 (37 female, 34 male)	58·3 (15·3) vs 60·3 (15·8)	55·9 (24·3) vs 57·6 (24·9)	73 (100%) vs 71 (100%)	*H influenzae*: 0 vs 1 (1%); *S aureus*: 3 (4%) vs 5 (7%); *S pneumoniae*: 2 (3%) vs 0; *S maltophilia*: 0 vs 0; *M catarrhalis*: 3 (4%) vs 2 (3%)	Time to exacerbation	Time to exacerbation (based on adherence recorded by the I-neb), severity of exacerbation, CFUs of *P aeruginosa*, 24-hour sputum weight, SGRQ, bronchoconstriction in 30 min after first dose of study drug, FEV_1, sensitivity of *P aeruginosa* to colistin, CFUs of other potentially pathogenic organisms, and adverse event reporting
TR02-107 (NCT00775138)	Nebulised liposomal amikacin (280 mg and 560 mg) vs placebo (empty liposomes in 1·5% saline) once per day	56 days	24 (10 female, 14 male) vs 19 (11 female, 8 male) vs 19 (9 female, 10 male)*	49·9 (21·1) vs 58·5 (16·0) vs 49·4 (13·3)*	64·5 (20·7) vs 71·4 (23·9) vs 62·6 (15·7)*	24 (100%) vs 19 (100%) vs 19 (100%)*	No data	Safety of liposomal amikacin as measured by proportion of adverse events, change in oxygen saturations, change in FEV_1	Frequency of cough with expectoration, PSSS, SGRQ, bacterial density of *P aeruginosa* (CFU per g), pulmonary exacerbations

Data are n (%) unless otherwise specified. DPI=dry powder for inhalation. CFU=colony-forming units. FVC=forced vital capacity. SGRQ=St George's Respiratory Questionnaire. QOL=quality of life. QOL-B=the Quality of Life Questionnaire-Bronchiectasis. 6MWT=6-min walk test. RSS=respiratory symptoms domain scale. MIC=minimum inhibitory concentration. PP=per protocol. ITT=intention to treat. LCQ=Leicester Cough Questionnaire. SEM=standard error of the mean. P_aO_2=partial pressure of O_2 in alveoli. P_aCO_2=partial pressure of CO_2 in alveoli. PSSS=Pulmonary Symptom Severity Score. *280 mg group vs 560 mg group vs placebo group.

Table: Characteristics of included studies

P861

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?

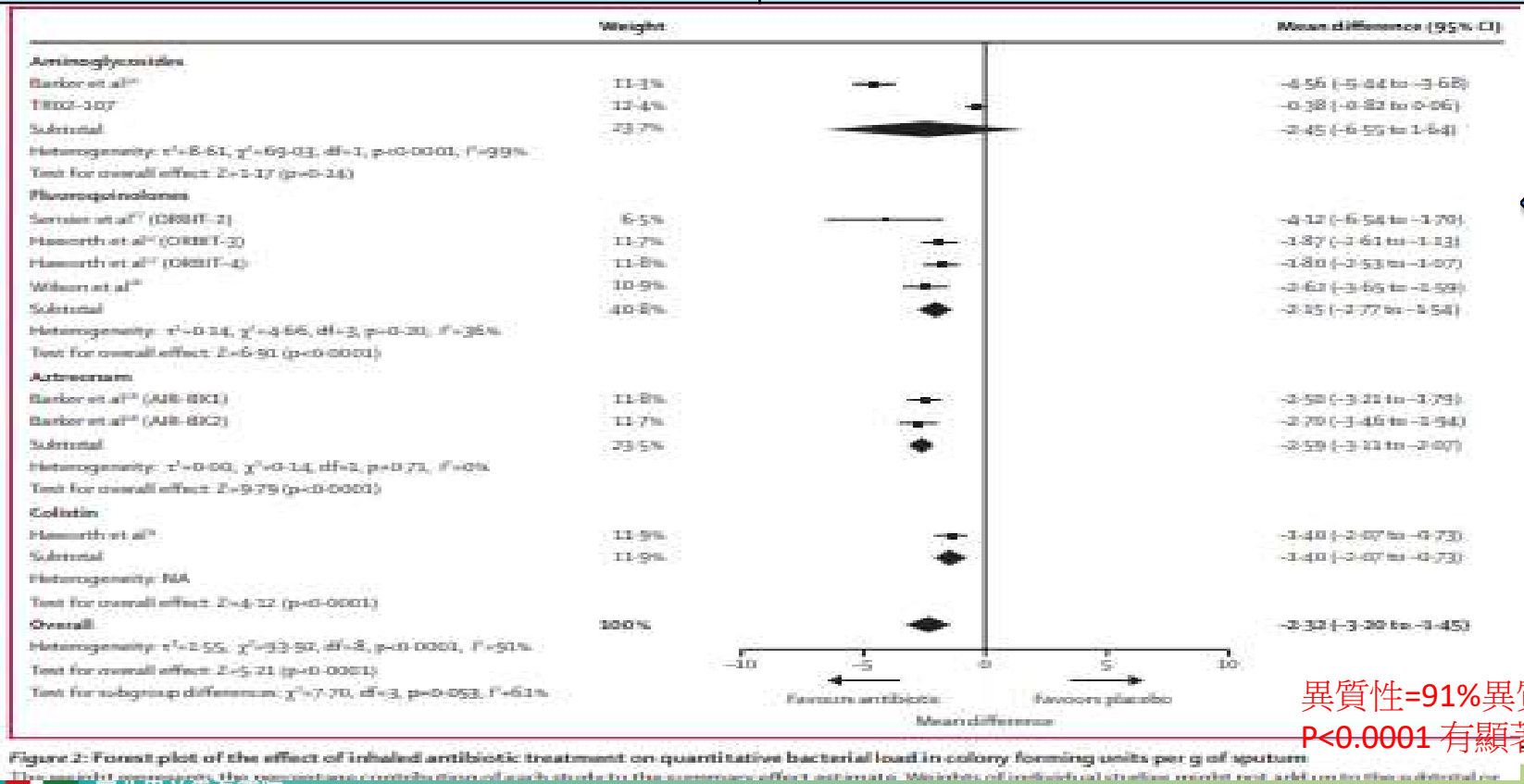
僅進行文獻判讀是不足夠,系統性文獻回顧需納入至少要有一項研究結果是極小偏誤的試驗。

P857

研究是否找到所有的相關證據？ ☑是 ☐否 ☐不確定

步驟二：系統性文獻回顧的品質如何？(FAITH)

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。



P862

異質性=91%異質性高
P<0.0001 有顯著差異

Figure 2: Forest plot of the effect of inhaled antibiotic treatment on quantitative bacterial load in colony forming units per g of sputum

(FAITH)

步驟二：系統性文獻回顧的品質如何？

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)?
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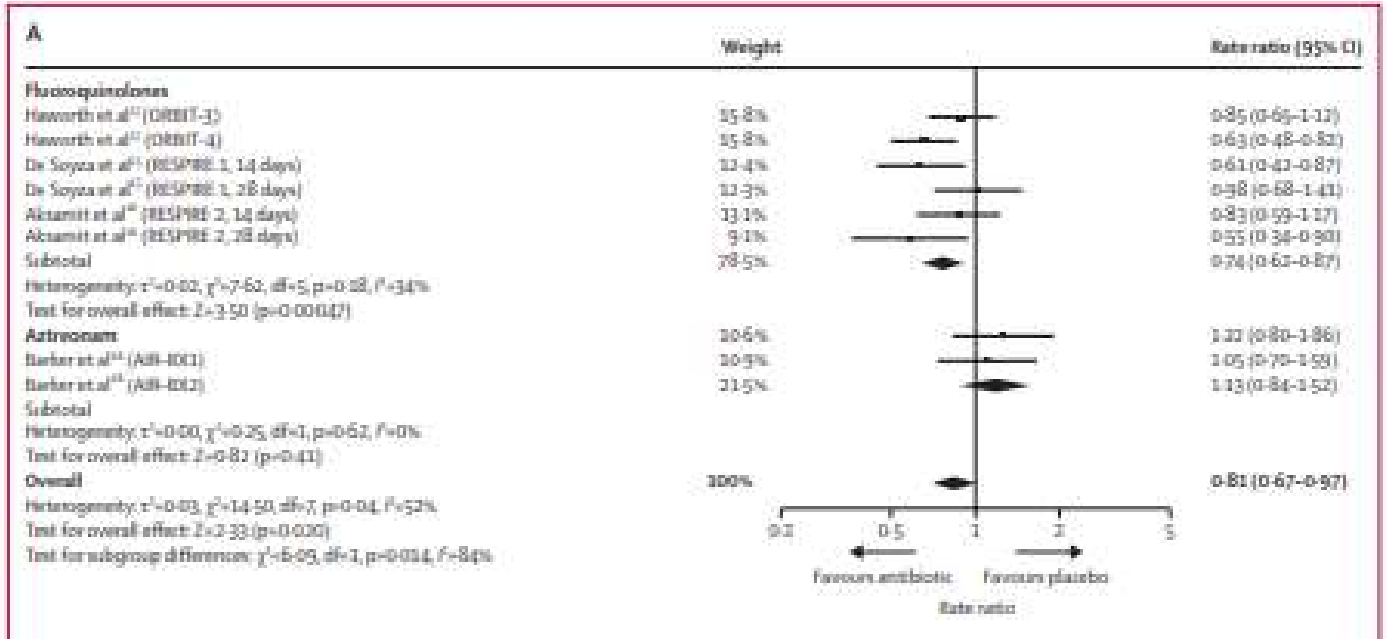


P863

病情惡化的頻率
異質性=52% 中度
p-=0.020 有顯著差異

步驟二：系統性文獻回顧的品質如何？

(FAITH)

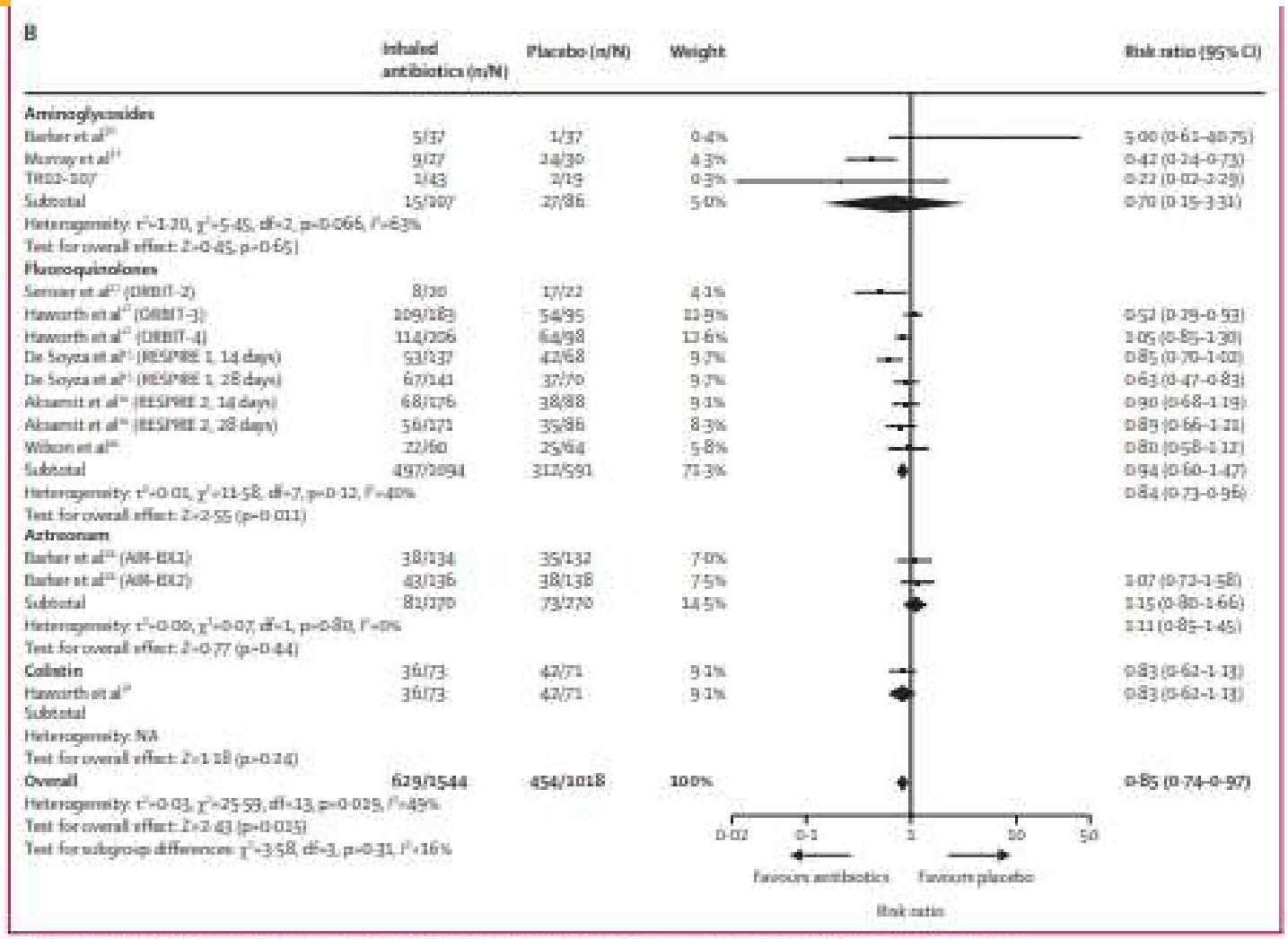


Figure 3: Forest plot of frequency of exacerbations (A) and number of participants experiencing at least one exacerbation (B)
The weight represents the percentage contribution of each study to the summary effect estimate. Weights of individual studies might not add up to the subtotal or overall weights because of rounding. df=degrees of freedom. NA=not applicable.

P863

至少有一次惡化的比例下降
異質性=49%
P=0.015有顯著差異

(FAITH)

步驟二：系統性文獻回顧的品質如何？

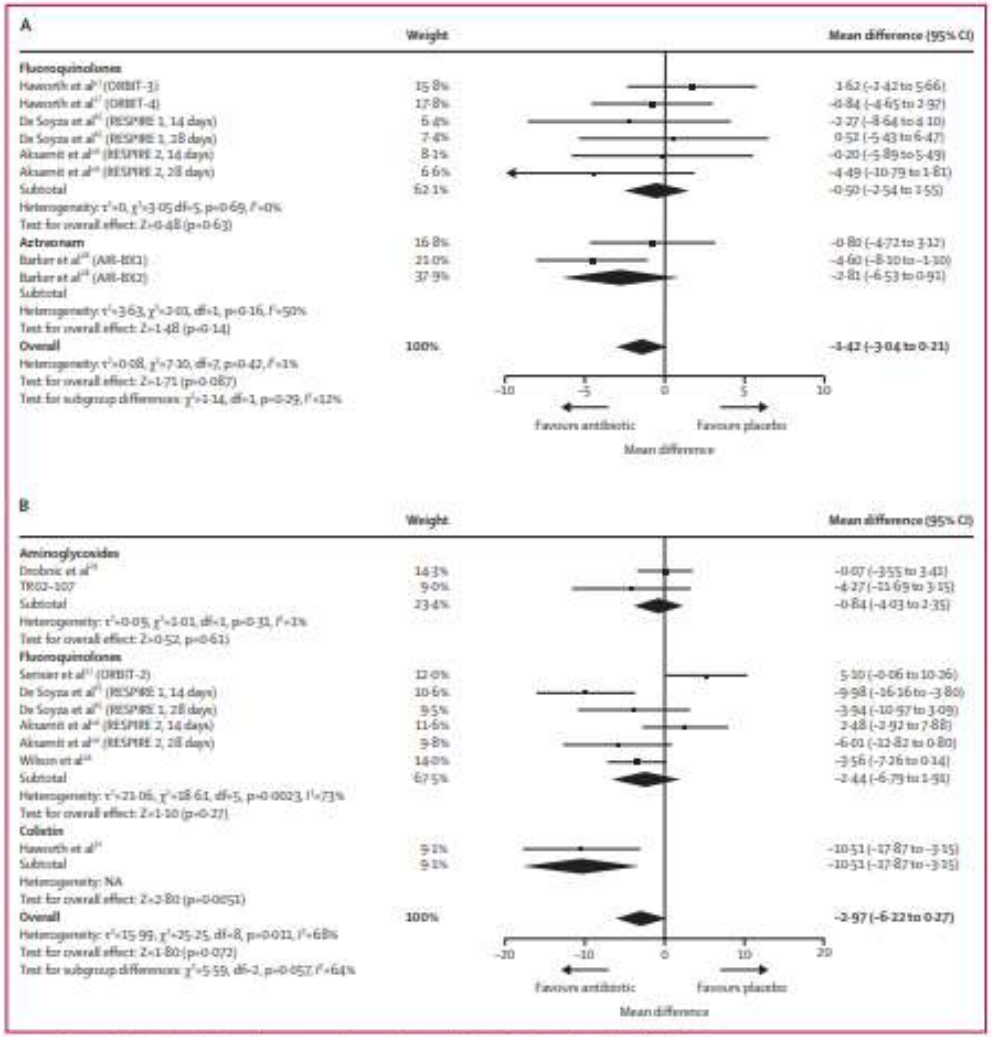


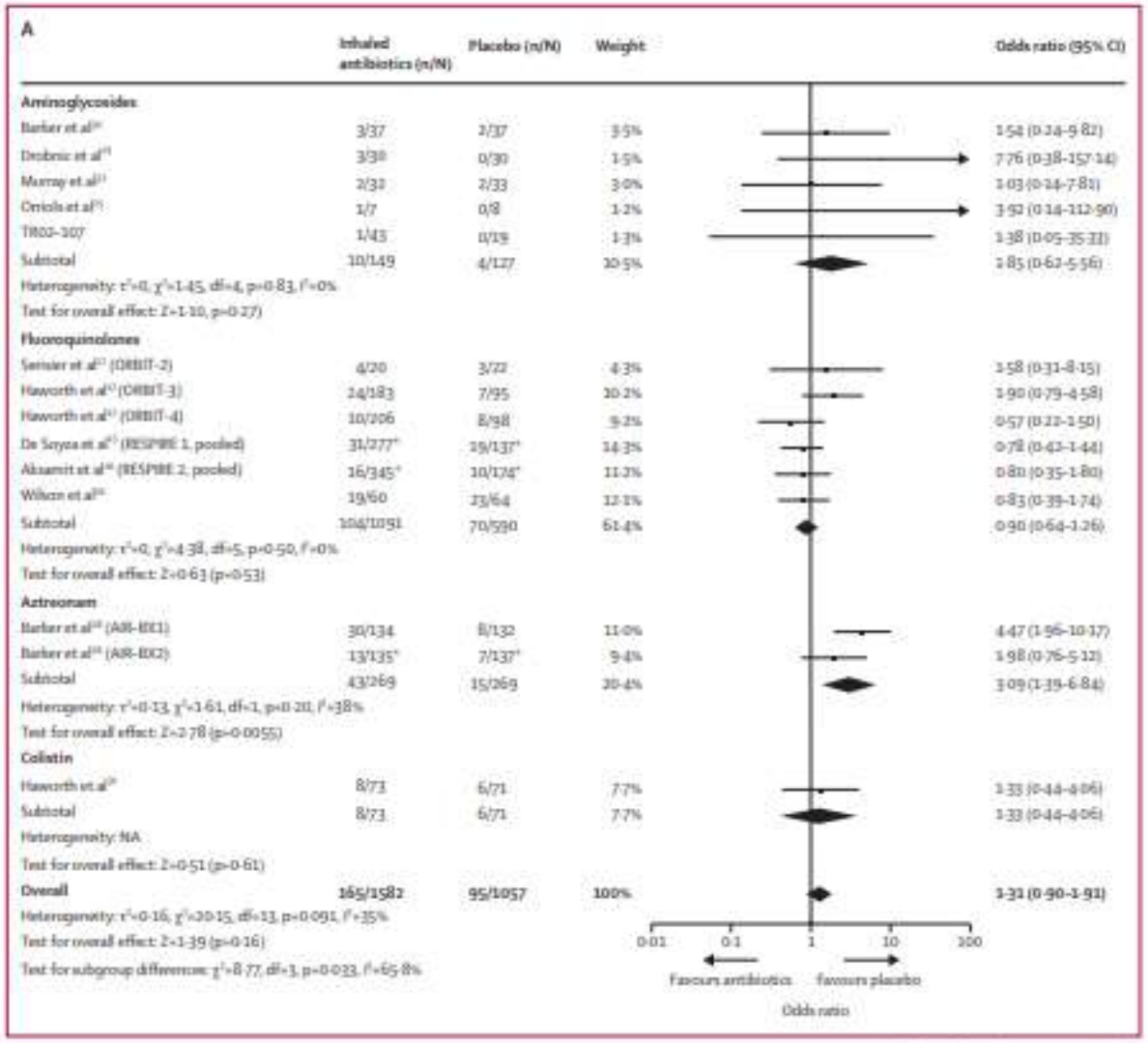
Figure 4: Forest plot of quality of life and symptom scales according to the QOL-B questionnaire (A) and SGRQ (B)
For both QOL-B and SGRQ, a negative score has been shown as a reduction in symptoms for ease of interpretation. In the scales themselves a reduction in the scale indicates an improvement in symptoms with SGRQ but a worsening with QOL-B. The weight represents the percentage contribution of each study to the summary effect estimate. Weights of individual studies might not add up to the subtotal or overall weights because of rounding. df=degrees of freedom. NA=not applicable. QOL-B=Quality of life—Bronchiectasis. SGRQ=St George's Respiratory Questionnaire.

生活品質
異質性=1%異質性低
P=0.087沒有顯著差異

P864

異質性=68% 異質性高
P=0.072 沒有顯著差異

步驟二：系統性文獻回顧的品質如何？



A	Inhaled antibiotics (n/N)	Placebo (n/N)	Weight	Odds ratio (95% CI)
Aminoglycosides				
Barker et al[20]	3/37	2/37	3·5%	1·54 (0·24–9·82)
Drobnic et al[21]	3/30	0/30	1·5%	7·76 (0·38–157·14)
Murray et al[22]	2/32	2/33	3·0%	1·03 (0·14–7·81)
Orriols et al[23]	1/7	0/8	1·2%	3·92 (0·14–112·90)
TRIO-307	1/43	0/19	1·3%	1·38 (0·05–35·33)
Subtotal	10/149	4/127	10·5%	1·85 (0·62–5·56)
Heterogeneity: τ^2=0, χ^2=1·45, df=4, p=0·83, I^2=0%				
Test for overall effect: Z=1·10, p=0·27)				
Fluoroquinolones				
Serisier et al[17] (ORBIT-2)	4/20	3/22	4·3%	1·58 (0·31–8·15)
Haworth et al[17] (ORBIT-3)	14/183	7/95	10·2%	1·90 (0·79–4·58)
Haworth et al[17] (ORBIT-4)	10/206	8/98	9·2%	0·57 (0·22–1·50)
De Soyza et al[24] (RESPIRE 1, pooled)	31/277*	19/137*	14·3%	0·78 (0·42–1·44)
Aksamit et al[18] (RESPIRE 2, pooled)	16/345*	10/174*	11·3%	0·80 (0·35–1·80)
Wilcox et al[25]	19/60	23/64	12·1%	0·83 (0·39–1·74)
Subtotal	104/1091	70/590	61·4%	0·90 (0·64–1·26)
Heterogeneity: τ^2=0, χ^2=4·38, df=5, p=0·50, I^2=0%				
Test for overall effect: Z=0·63 (p=0·53)				
Aztreonam				
Barker et al[19] (AIR-EX1)	30/134	8/132	11·0%	4·47 (1·96–10·17)
Barker et al[19] (AIR-EX2)	13/135*	7/137*	9·4%	1·98 (0·76–5·12)
Subtotal	43/269	15/269	20·4%	3·09 (1·39–6·84)
Heterogeneity: τ^2=0·13, χ^2=1·61, df=1, p=0·21, I^2=38%				
Test for overall effect: Z=2·78 (p=0·0055)				
Colistin				
Haworth et al[26]	8/73	6/71	7·7%	1·33 (0·44–4·06)
Subtotal	8/73	6/71	7·7%	1·33 (0·44–4·06)
Heterogeneity: NA				
Test for overall effect: Z=0·51 (p=0·61)				
Overall	**165/1582**	**95/1057**	**100%**	**1·31 (0·90–1·91)**
Heterogeneity: τ^2=0·16, χ^2=20·15, df=13, p=0·091, I^2=35%				
Test for overall effect: Z=1·39 (p=0·16)				
Test for subgroup differences: χ^2=8·77, df=3, p=0·033, I^2=65·8%				

0·01 0·1 1 10 100

Favours antibiotics Favours placebo

Odds ratio

(Figure 5 continues on next page)

導致停藥的不良事件
異質性=35%異質性低
P=0.16沒有顯著差異

P865

步驟二：系統性文獻回顧的品質如何？

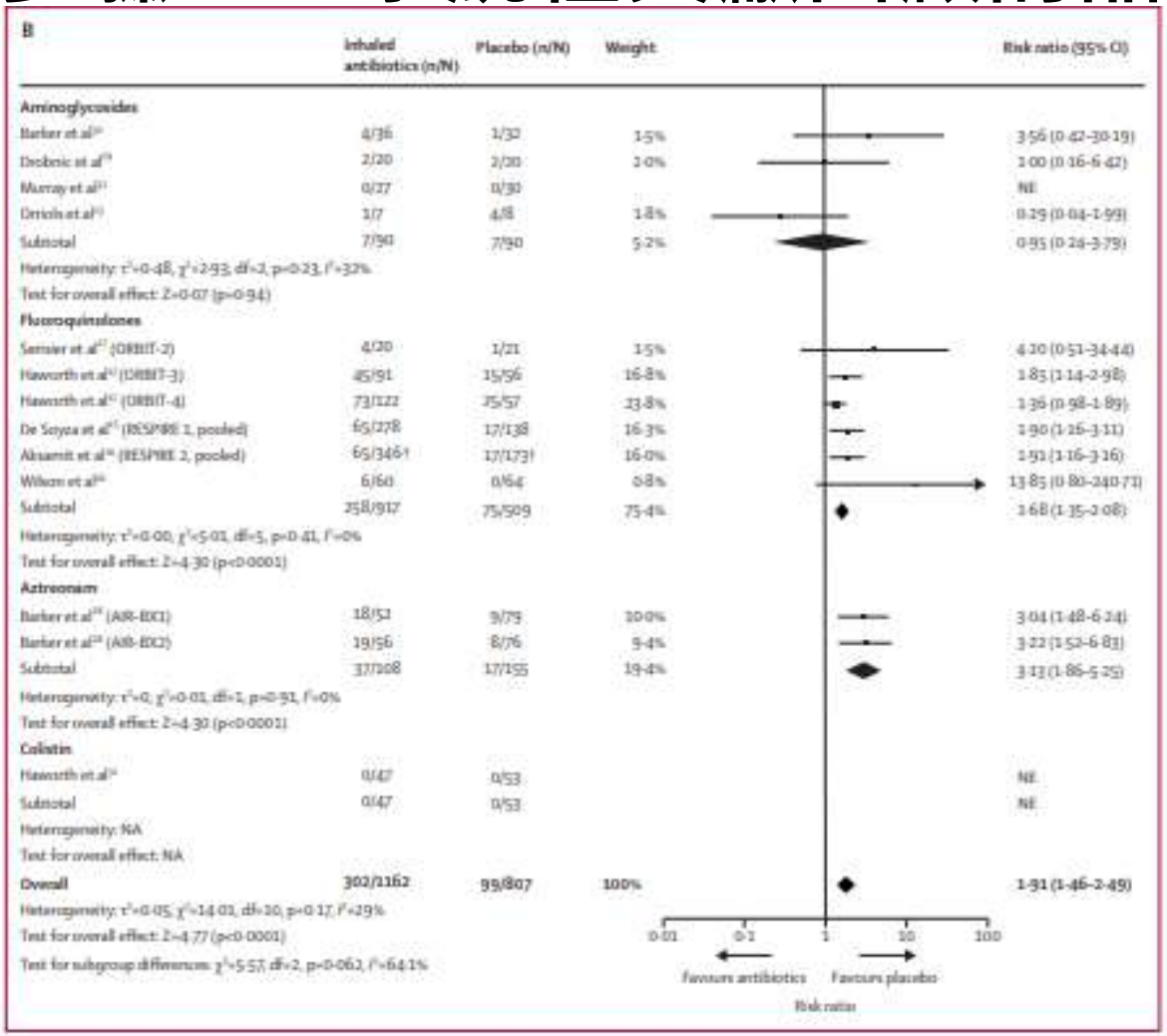


Figure 5: Forest plot of adverse events leading to study drug discontinuation (A) and of isolated bacteria with a minimum inhibitory concentration above the resistant breakpoint at the end of treatment (B)

The weight represents the percentage contribution of each study to the summary effect estimate. Weights of individual studies might not add up to the subtotal or overall weights because of rounding. df=degrees of freedom. NA=not applicable. NE=not estimable. *A few participants in these studies did not receive any dose and were not included this analysis. †Data for one patient in each group were missing.

導致停藥的不良事件
異質性=29%異質性低
P<0.0001有顯著差異
對照組較容易停藥

P866

步驟二：系統性文獻回顧的品質如何？

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)?
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研究是否有圖表? ☑是 ☐否 ☐不確定

試驗的結果是否相近? ☑是 ☐否 ☐不確定

總結[系統性文獻回顧 Systematic Review]

Systematic Review	是	否	不確定
F	✓		
A	✓		
I	✓		
T	✓		
H	✓		

研究結果

1成人使用吸入性抗生素治療肺炎及支氣管炎的有效性:

顯著差異:

- ✓ 結果顯示使用吸入性抗生素的病人平均痰中細菌量可下降 2.32 log units、
- ✓ 細菌清除率可增加 3.36倍、
- ✓ 可以降低 19% 急性發作的風險、
- ✓ 不管是治療至第一次急性發作的時間或是急性發作的頻率都會有明顯的改善；

研究結果

1成人使用吸入性抗生素治療肺炎及支氣管炎的有效性:

無顯著差異:

- ✓ 生活品質
- ✓ FEV_1變化
- ✓ 因治療出現不良反應
- ✓ 支氣管痙攣發生頻率
- ✓ 治療結束時細菌的抗藥性

研究限制

1.研究設計的差異性很大:

- ✓ 研究的時間長短
- ✓ 使用的抗生素藥物種類不同
- ✓ 受試者平均年齡不同

建議:研究時間可延長至一年，可經歷季節的變化，

可能會發生的病情改變。

2.招募的對象為支氣管擴張(症狀)，但是，支氣管擴張的原因，

是很重要的因素，也會影響到後續的研究結果。

經驗分享

Discussion

是否贊成使用吸入性抗生素來治療支氣管擴張的患者?

同意	13票
不同意	0票
不確定	5票

參考資料:

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THANK YOU!