



三軍總醫院
Tri-Service General Hospital

實證醫學競賽

組別：第三組

時間：108年6月11日

我們的成員



陳怡文 藥師



楊君琦 藥師



秦侑楨 藥師

臨床情境

對象	65歲男性曾中風過
情況	反覆性泌尿道感染
	發燒、腹痛、腹瀉
	<i>Clostridium difficile</i>
家屬期望	治療與副作用
家屬預知	糞便菌叢移植法有效嗎?副作用?

背景資訊



困難梭菌 Clostridium difficile 腹瀉之口服抗生素治療 (Nonsevere)

QQ 推薦
M E D

首次	Metronidazole 500 mg Q8H或250 mg Q6H	10-14*	
	或 Vancomycin 125 mg Q6H	10-14	
復發	重複首次選項	10-14	
	或 Fidaxomicin 200 mg Q12H	10	
再復發	Vancomycin 125 mg 降階	1. Q6H	7-14
		2. Q12H→QD→QOD	7+7+7
		3. Q3D	14
	或 Fidaxomicin 200 mg Q12H	10	

*單位為天

UpToDate®

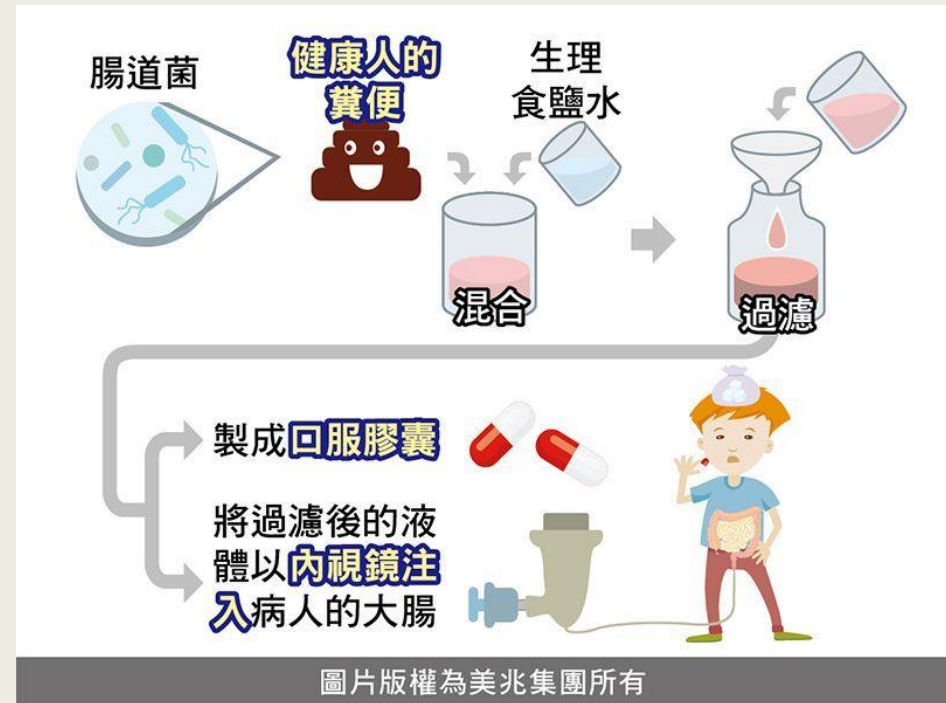
- 為革蘭氏陽性、厭氧芽孢桿菌，會分泌毒素破壞腸黏膜、引起腸道發炎，造成腹瀉。此感染的產生常因抗生素的使用破壞了腸道正常菌叢，導致 Clostridium difficile 大量繁殖。
- 可經由糞便傳染，引起群聚感染。

Fecal Microbiota Transplantation(FMT)

- We administer oral vancomycin (500 mg twice daily) for seven days prior to the procedure.

The last dose of vancomycin should be 24 hours before the procedure. Patients should be kept fasting overnight.

- The day of the procedure, administer 200 to 300g of donor stool suspended in 200 to 300mL of sterile normal saline via colonoscopy into the cecum or terminal ileum, within 10 minutes of preparation.



問題
ASK

檢索
Acquire

評讀
Appraisal

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Apply

臨床問題

	PICO 1	PICO 2
P	65歲男性困難縮狀桿菌感染	65歲男性困難縮狀桿菌感染
I	Fecal microbiota transplantation	Risk prediction model
C	antibiotic	其他工具
O	腹瀉復發率/緩解率	結果
類型	治療型問題	診斷型問題

問題
ASK

檢索
Acquire

評讀
Appraisal

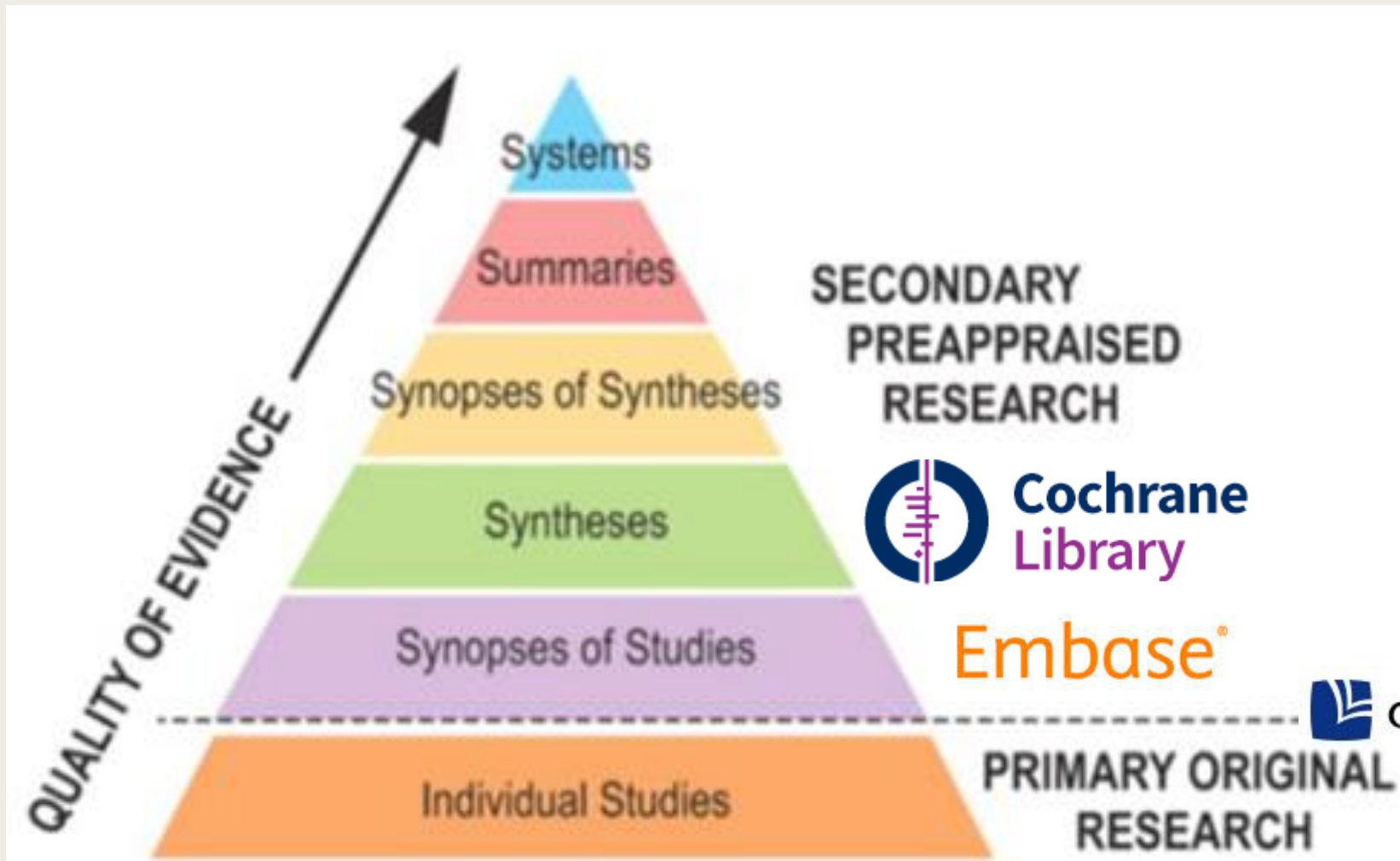
應用
Apply

臨床問題

我們選擇第一個PICO

	中文關鍵字	英文關鍵字	同義字 /MeSH/Emtree
P	困難縮狀桿菌	Clostridium difficile	CD
I	糞便菌叢移植法	Fecal Microbiota Transplantation	FMT
C	抗生素	antibiotics	vancomycin
O	腹瀉	diarrhea	scour

檢索策略



airiti Library 華藝線上圖書館

PubMed.gov

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
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檢索策略

關鍵字

- ① 運用布林邏輯
- ② 以「P & I」搜尋
- ③ 依結果加入其他關鍵字

文章類型

- ① Systematic review(SR)
- ② Randomized control trial (RCT)
- ③ Cohort study

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檢索
Acquire

評讀
Appraisal

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Secondary Database: **Cochrane**

The screenshot shows the Cochrane Library website. At the top left is the Cochrane Library logo with the tagline "Trusted evidence. Informed decisions. Better health." The top right shows "Access provided by: National Defense Medical Center", "English" language selection, "Cochrane.org" link, and "Sign In" button. A search bar contains "Title Abstract Keyword" and has "Browse" and "Advanced search" buttons. A navigation menu includes "Cochrane Reviews", "Trials", "Clinical Answers", "About", and "Help". A "Content Language Selection" notification states: "Your language preference is set to Chinese. Where translations are available, article sections will display in this language. Return to English." The main content area features a large image of a blister pack of pills with the text "Do different doses or types of nicotine replacement therapy affect smoking cessation? Read the Review". To the right, there are two smaller promotional tiles: "World No Tobacco Day Read the Special Collection" and "Cochrane's new Editor in Chief Dr Karla Soares-Weiser".

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ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

Secondary Database: Cochrane

Access provided by: National Defense Medical Center English Cochrane.org Sign In

Cochrane Library Trusted evidence. Informed decisions. Better health.

Cochrane Reviews Trials Clinical Answers About Help

Advanced Search

Search Search manager Medical terms (MeSH)

Save this search View saved searches Search help

+						Print
-	+	#1	clostridium difficile	S	MeSH	Limits 1206
-	+	#2	elder			Limits 51691
-	+	#3	urinary tract infection			Limits 7680
-	+	#4	fecal microbiota transplantation			Limits 318
-	+	#5	#1 and #2 and #3 and #4			Limits 0
-	+	#6	#1 and #4 and #2			Limits 8
-	+	#7	Type a search term or use the S or MeSH	S	MeSH	Limits N/A

Clear all

Save this search View saved searches Search help

Highlight orphan lines

1. 使用Search Manager 搜尋
加入布林邏輯 AND與OR 作搜尋連結
2. Search limit : 未限制年份、語言

Secondary Database: Cochrane

Filter your results

Year ⓘ

Year first published

2019 0

2018 2

2017 0

2016 3

2015 2

Custom Range:

yyyy to yyyy

Apply Clear

Date ⓘ

Date added to CENTRAL trials database

The last 3 months 1

The last 6 months 1

The last 9 months 2

The last year 3

The last 2 years 4

Custom Range:

dd/mm/yyyy to dd/mm/yyyy

Apply Clear

Source ⓘ

Cochrane Reviews 1	Cochrane Protocols 0	Trials 7	Editorials 0	Special collections 0	Clinical Answers 0	Other Reviews
-----------------------	-------------------------	-------------	-----------------	--------------------------	-----------------------	---------------

7 Trials matching "#6 - #1 and #4 and #2"
Did you mean: [Rand](#) | [band](#) | [hand](#)

Cochrane Central Register of Controlled Trials
Issue 6 of 12, June 2019

Select all (7) Export selected citation(s)

Order by Relevancy ▾ Results per page 25 ▾

- Faecal microbiota transplantation for relapsing Clostridium difficile infection**
EUCTR2015-003004-24-DK
Http://www.who.int/trialsearch/trial2.aspx? Trialid=euctr2015-003004-24-dk, **2015** | added to CENTRAL: 31 March 2019 | 2019 Issue 3
- Effect of Fecal Microbiota Transplantation on Recurrence in Multiply Recurrent Clostridium difficile Infection: a Randomized Trial**
CR Kelly, A Khoruts, C Staley, MJ Sadowsky, M Abd, M Alani, B Bakow, P Curran, J McKenney, A Tisch, SE Reinert, JT Machan, LJ Brandt
Annals of internal medicine, **2016**, 165(9), 609-616 | added to CENTRAL: 31 January 2017 | 2017 Issue 1
[PubMed](#) | [Embase](#)
- Faecal microbiota transplantation in relapsing clostridium difficile colitis**
B Ramsauer, C König, T Sabelhaus, J Ockenga, J-M Otte
Mmw-fortschritte der medizin, **2016**, 158, 17-20 | added to CENTRAL: 28 February 2017 | 2017 Issue 2
[PubMed](#) | [Embase](#)
- Faecal microbiota transpla**
B Ramsauer, C König, T Sabelhaus
MMW fortschritte der medizin,
[PubMed](#)
- Microbial Restoration for Individuals With One or More Recurrences of Clostridium Difficile Associated Disease (CDAD)**

搜索結果：1篇 RCT文獻，0篇SR文獻
7篇 Cochrane Review

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

Secondary Database: Embase

The screenshot displays the Embase PICO Search interface. The top navigation bar includes 'Search', 'Emtree', 'Journals', 'Results', 'My tools', 'Register', and 'Login'. The main header is 'PICO Search' with a language selection dropdown. Below the header, there are tabs for 'Quick', 'PICO', 'PV Wizard', 'Advanced', 'Drug', 'Disease', 'Device', 'Article', and 'Authors'. The 'PICO' tab is active, showing a search strategy for 'fecal microbiota transplantation'. The strategy is defined by four fields: Population (Clostridium infection /exp + 8 synonyms :all), Intervention (fecal microbiota transplantation /exp + 58 synonyms :all), Comparison (e.g. placebo), and Outcome (e.g. risk). A 'Default search strategy' section shows radio buttons for /mj, /de, /exp (selected), and /br. At the bottom right, a button indicates 'Show 1,670 results >'. A red-bordered box in the bottom left corner contains four numbered points in Chinese.

1. 使用 **PICO search**，增加效率
2. 使用 **Emtree**，增加精準度
3. 使用內建的 **Synonyms** 系統，增加搜尋廣度
4. 使用 **Filter** 和 **Limit**

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

Secondary Database: Embase

Embase® Search Emtree Journals **Results** My tools Register Login (1)

Study types

- human 131
- systematic review 81
- controlled study 57
- randomized controlled trial 51
- nonhuman 40
- randomized controlled trial (topic) 31
- meta analysis 29
- [+ More](#) > Export

Publication types

Journal titles

Publication years

Authors

Conference Abstracts

Drug Trade Names

Drug Manufacturers

Device Trade Names

Device Manufacturers

131 results for search #3 [Set email alert](#) [Set RSS feed](#) [Search details](#) [Index miner](#)

Results View | Print | Export | Email | Order | Add to Clipboard 1 — 25

Select number of items Selected: 0 (clear) Show all abstracts | Sort by: Relevance Publication Year Entry Date

- 1 Long-term Outcomes of **Fecal Microbiota Transplantation** in Patients With Cirrhosis
Bajaj J.S., Fagan A., Gavis E.A., Kassam Z., Sikaroodi M., Gillevet P.M.
Gastroenterology 2019 156:6 (1921-1923.e3) Cited by: 1
Embase MEDLINE [No abstract available] [Index Terms](#) [View Full Text](#) [Similar records](#)
- 2 Low cure rates in controlled trials of **fecal microbiota transplantation** for recurrent clostridium difficile infection: A systematic review and meta-analysis
Tariq R., Pardi D.S., Bartlett M.G., Khanna S.
Clinical Infectious Diseases 2019 68:8 (1351-1358) Cited by: 2
Embase MEDLINE [Abstract](#) [Index Terms](#) [View Full Text](#) [Similar records](#)
- 3 **Fecal Microbiota Transplantation** Is Superior to Fidaxomicin for Treatment of Recurrent Clostridium difficile Infection
Hvas C.L., Dahl Jørgensen S.M., Jørgensen S.P., Storgaard M., Lemming L., Hansen M.M., Erikstrup C., Dahlerup J.F.
Gastroenterology 2019 156:5 (1324-1332.e3) Cited by: 5
Embase MEDLINE [Abstract](#) [Index Terms](#) [View Full Text](#) [Similar records](#)
- 4 Systematic review with meta-analysis: review of donor features, procedures and outcomes in 168 clinical studies of **faecal microbiota transplantation**
Lai C.Y., Sung J., Cheng F.,
Alimentary Pharmacology
Embase MEDLINE

搜索結果：81篇SR文獻
51篇 Cochrane Review

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

Primary Database: PubMed

The screenshot shows the PubMed website interface. At the top, there is a navigation bar with "NCBI Resources" and "How To" dropdown menus, and a "Sign in to NCBI" link. Below this is the "PubMed.gov" logo and a search bar with a "Search" button. The main content area features a large banner with the text "PubMed comprises more than 29 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full-text content from PubMed Central and publisher web sites." Below the banner are three columns of links: "Using PubMed" (including Quick Start Guide, Full Text Articles, FAQs, Tutorials, and New and Noteworthy), "PubMed Tools" (including Mobile, Citation Matchers, Clinical Queries, and Topic-Specific Queries), and "More Resources" (including MeSH Database, Journals in NCBI Databases, Clinical Trials, E-Utilities (API), and LinkOut). At the bottom, there are sections for "Latest Literature" (New articles from highly accessed journals, e.g., Blood (3)) and "Trending Articles" (PubMed records with recent increases in activity, e.g., Yogurt improves insulin resistance and liver fat in obese women).

Primary Database: PubMed

#19	Add	Search (((Clostridium difficile) OR "Clostridium difficile"[Mesh])) AND (("Fecal Microbiota Transplantation"[Mesh]) OR Fecal Microbiota Transplan*)	749	20:52:02
#18	Add	Search ("Fecal Microbiota Transplantation"[Mesh]) OR Fecal Microbiota Transplan*	1504	20:51:43
#17	Add	Search (Clostridium difficile) OR "Clostridium difficile"[Mesh]	14583	20:51:30
#16	Add	Search (Clostridium difficile) AND "Clostridium difficile"[Mesh]	8631	20:51:12
#15	Add	Search ("Clostridium difficile"[Mesh]) AND "Fecal Microbiota Transplantation"[Mesh]	287	20:50:38
#14	Add	Search (Clostridium difficile) AND Fecal Microbiota Transplan*	749	20:50:31
#12	Add	Search cure	84583	20:49:37
#11	Add	Search "Fecal Microbiota Transplantation"[Mesh]	816	20:49:01
#10	Add	Search "Clostridium difficile"[Mesh]	8631	20:48:52
#9	Add	Search Fecal Microbiota Transplan*	1504	20:48:44
#8	Add	Search Clostridium difficile	14583	20:48:28

1. 將關鍵字輸入透過**MeSH**找出最適當之Medical Terms
2. 利用**布林邏輯**“AND”“OR”等語法以免遺漏文獻搜尋分類
3. **搜尋關鍵字**：(((Clostridium difficile) OR "Clostridium difficile"[Mesh])) AND (("Fecal Microbiota Transplantation"[Mesh]) OR Fecal Microbiota Transplan*)

問題

ASK

檢索

Acquire

評讀

Appraisal

應用

Apply

Primary Database: PubMed

PubMed.gov

PubMed

(((Clostridium difficile) OR "Clostridium difficile"[Mesh])) AND ("Fecal Microbiota Transplantation"[

Search

US National Library of Medicine National Institutes of Health

Create RSS Create alert Advanced

Help

Article types clear Format: Summary Sort by: Most Recent Per page: 20

Send to Filters: Manage Filters

- Clinical Trial
- Meta-Analysis
- Randomized Controlled Trial
- Review

Search results

Items: 7

Filters activated: Systematic Reviews, Meta-Analysis, Free full text, published in the last 5 years, Humans. Clear all to show 749 items.

1. A Systematic Review of the Efficacy and Safety of Fecal Microbiota Transplant for Clostridium difficile Infection in Immunocompromised Patients.

Shogbesan O, Poudel DR, Victor S, Jehanoir A, Fadahunsi O, Shogbesan G, Donato A. 155/2018/1394379. eCollection 2018.

microbiota transplantation: Systematic

Allegretti JR. 017.1353848. Epub 2017 Sep 12. Review.

faecal microbiota transplantation for the ile infection.

Sort by: Best match Most recent

Titles with your search terms

Reducing Cost and Complexity of Fecal Microbiota Transplantation Us [Adv Ther. 2019]

Fecal Microbiota Transplantation for Clostridium difficile Infection: A [Dig Dis. 2019]

Current and future trends in clostridioides (clostridium) difficile infection [Anaerobe. 2019]

See more...

Find related data

Database: Select

Find items

17

★使用 Filter 功能以提升篩選效率

✓ 限定適當文章類型：

- 『Meta-analysis』
- 『Systematic Review』

✓ 限定搜尋範圍：

- 『5年內』 文章
- 『Free Full text』 文章
- 『human』 文章

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

Primary Database: 華藝線上圖書館

The screenshot shows the Airiti Library website interface. At the top, there is a navigation bar with 'Language' and a search bar containing the query '困難梭狀桿菌 AND 糞便移植'. Below the search bar, there are tabs for '期刊文章' (2), '會議論文' (0), '碩博士論文' (0), '電子書' (0), and '紙本書' (0). The search results section shows '共 2 筆, 1-2 筆' and '共 1 頁'. The first result is highlighted in a red box and contains the text: '1. 關鍵字：困難梭狀桿菌 AND 糞便移植'. Below this, there is a list of search results with details such as '林宜君 ; 感染控制雜誌 28卷3期 (2018/06) , 139-141' and '2 糞便微生物移植以及益生菌的治療組合'.

airiti Library 華藝線上圖書館

Language ▾

國軍醫院聯合圖書館-國防醫學院, 您好!

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文章 | 出版品 | 所有欄位

期刊文章 2 會議論文 0 碩博士論文 0 電子書 0 紙本書 0

依下方條件來精確結果

來源資料庫

CEPS中文電子期刊 (2)

學科分類

醫藥衛生 (2)

年代

查詢 (困難梭狀桿菌 AND 糞便移植) = 所有欄位

篇名-關鍵字-摘要 作者 刊名 起始年 結束年 檢索結果再查詢

每頁 10 筆

共 2 筆, 1-2 筆

共 1 頁

書目匯出 加入追蹤 加入購物車

相關程度最高

2016年以後 (2)
2014年以後 (2)

出版品名稱

感染控制雜誌 (1)

林宜君 ;
感染控制雜誌 28卷3期 (2018/06) , 139-141

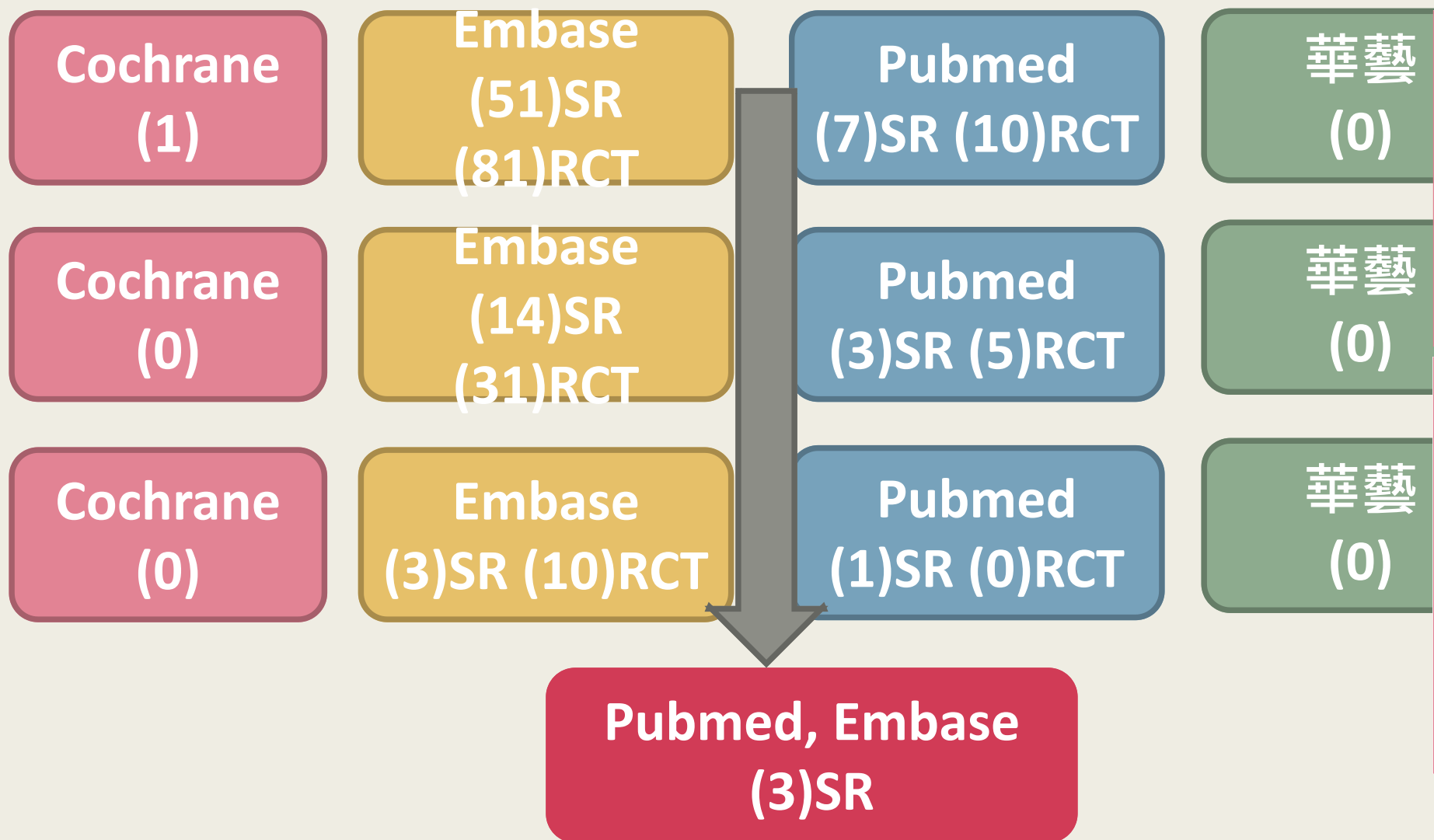
加入追蹤 全文下載

2 糞便微生物移植以及益生菌的治療組合

1. 關鍵字：困難梭狀桿菌 AND 糞便移植



篩選結果



排除條件1

- ✓ 有全文
- ✓ 與PICO相符
- ✓ 近三年

排除條件2

- ✓ 最佳證據等級
- ✓ 刪除重複的文章

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

文章篩選

文章	S	P	I	C	O
Fecal microbiota transplantation for treatment of recurrent C. difficile infection: An updated randomized controlled trial meta-analysis	●	●	●	●	●
Fecal microbiota transplantation for eradicating carriage of multidrug-resistant organisms: a systematic review	●	●	●	●	●
[2017]Systematic review with meta-analysis: the efficacy of faecal microbiota transplantation for the treatment of recurrent and refractory Clostridium difficile infection.	●	●	●	●	●

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

篩選結果



RESEARCH ARTICLE

Fecal microbiota transplantation for treatment of recurrent *C. difficile* infection: An updated randomized controlled trial meta-analysis

Wenjia Hui¹, Ting Li¹, Weidong Liu¹, Chunyan Zhou², Feng Gao^{1*}

¹ Department of Gastroenterology, People's Hospital of Xin jiang Uygur Autonomous Region, Urumqi, Xinjiang, China, ² State Key Laboratory of Food Science and Technology, Nanchang University, Nanchang, Jiangxi, China

* xjgf@sina.com

Abstract

Objectives

Although systematic evaluation has confirmed the efficacy of fresh fecal microbiota trans-

這篇文獻「**納入的理由**」

- ✓ 最符合臨床問題
- ✓ 發表年份較新
- ✓ 最佳的研究設計 (治療型-RCT)
- ✓ 有全文可供評讀



我們的文獻工具是

CASP SR critical appraisal tool !!

1. Did the review address a clearly focused question?
此研究是否問了一個清楚明確的問題?

Yes No Can't tell

Methods

We reviewed studies in PubMed, Medline, Embase, the Cochrane Library and Cochrane Central written in English. The retrieval period was from the establishment of the databases to September 20th, 2018. The retrieval objectives were published RCTs of RCDI treated by fresh FMT. The intervention group was fresh FMT group, while the control group included antibiotic therapy or placebo or frozen FMT or capsule. The primary and secondary outcomes were the clinical remission of diarrhea without relapse after 8–17 weeks and the occurrence of severe adverse events, respectively. Subgroup analysis analyzed the effect of single and multiple fecal infusions. Two authors independently completed the information extraction and assessed risk of bias and overall quality of the evidence.

C

I

P

O

1. Did the review address a clearly focused question? 此研究是否問了一個清楚明確的問題?

Yes No Can't tell

	此篇研究	臨床情境	是否相符
P	recurrent and/or refractory and/or relapse C. difficile infection (RCDI)	Clostridium difficile infection	是 否
I	fresh FMT	faecal microbiota transplantation	是 否
C	antibiotic therapy or placebo or frozen FMT or capsule	antibiotic therapy or placebo	是 否
O	clinical remission of diarrhea without relapse after 8–17 weeks the occurrence of severe adverse events	clinical remission of diarrhea without relapse the occurrence of severe adverse events	是 否

2. Did the authors look for the right type of papers? 作者是否收納適當的研究類型？

Yes No Can't tell

Inclusion and exclusion criteria

Inclusion criteria: (I) Patients of any age who had at least one incidence of *C. difficile* infection, confirmed by pathology or laboratory or endoscopy, and at least one course of oral metronidazole or vancomycin; (II) There was a clear intervention group by fresh FMT and a control group, and the control group could be antibiotic therapy or placebo or frozen FMT or capsule; (III) There was a clear primary outcome, and the primary outcome was the remission rate of diarrhea 8 to 17 weeks later; (IV) Only randomized controlled trials in full text reported by peer review were included.

Exclusion criteria: (I) Animal tests or in vitro tests; (II) Non-English literature; (III) Gastrointestinal diarrhea not caused by CDI, or diarrhea caused by multiple etiology including *C. difficile*; (IV) Data that were published more than one journal; (V) Unpublished data at the trial phase, such as abstracts, conference reports.

1. 收錄包含有同儕審查、已經出版、且有全文的RCT文章
2. 定義 inclusion, exclusion

2. Did the authors look for the right type of papers? 作者是否收納適當的研究類型？

Yes No Can't tell

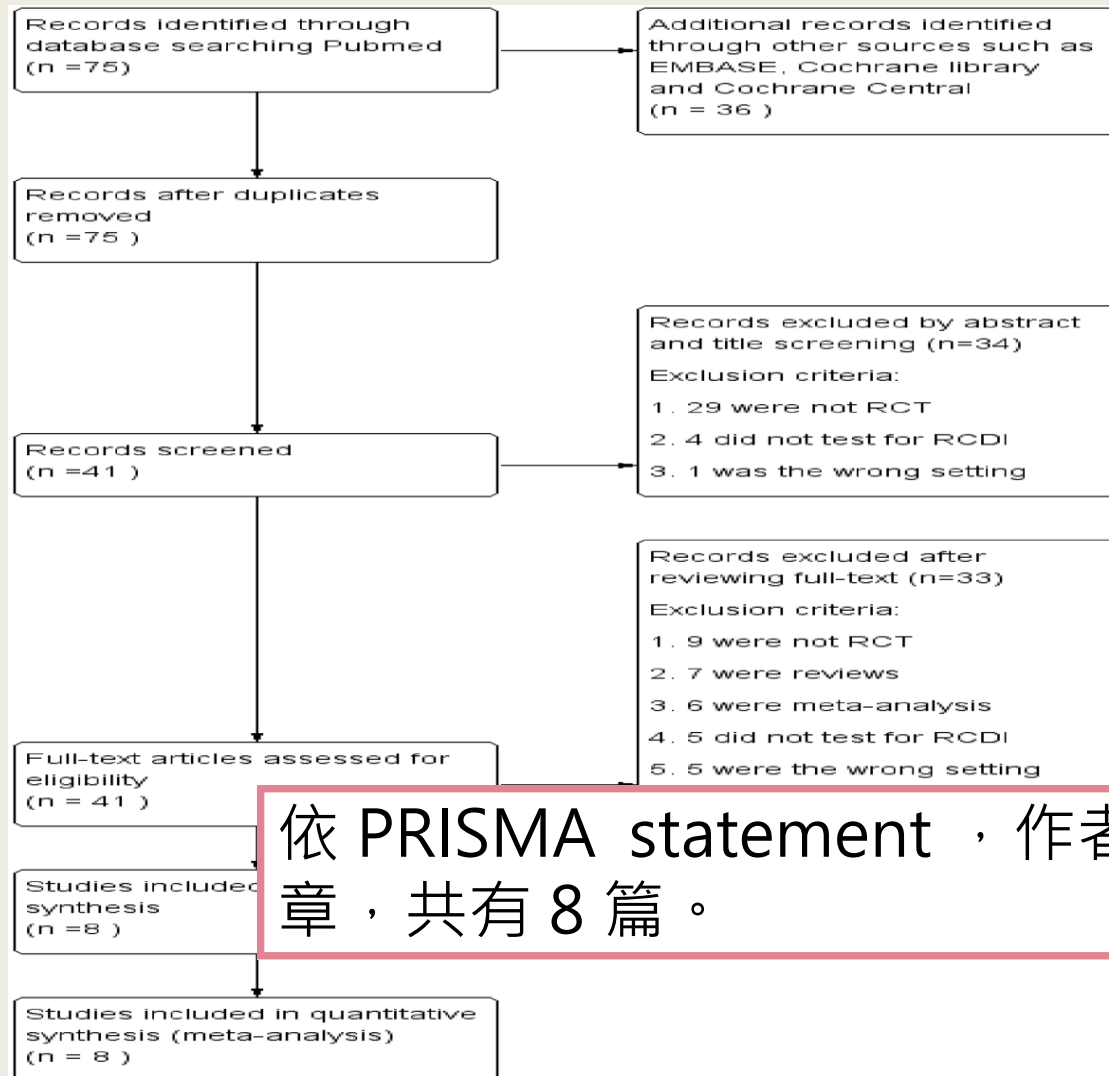
First author, year	Location	Sample	FMT formula (FMT group)	Times of infusion	Mean dose (FMT)	Donor	Follow-up, wk	The median time of the recurrence	Age, intervention group		Age, control group		Female sex, experimental group		Female sex, control group	
									N	Mean (SD or range)	N	Mean (SD or range)	N	No. (%)	N	No. (%)
SS. Hota, 2016 [53]	Ontario, Canada	28	Fresh feces by E	1	50g	R	17	9 days	16	75.7(14.5)	12	68.8(14.2)	16	11 (68.8)	12	8 (66.7)
CR. Kelly, 2016 [49]	NY and RI	46	Fresh feces by C	2	64g	H	8	10 days	22	48 (16)	24	55 (14)	22	18 (82)	24	19 (79)
E Nood, 2013 [48]	Amsterdam.	29	Fresh feces by N	2	141g	H	10	23 days	16	73(13)	13	66(14)	16	8 (50)	13	7 (54)
D Kao, 2017 [50]	Alberta	116	Fresh feces by C	1	90g	H	12	NR	59	57.4 (19.1)	57	58.7 (18.5)	59	36 (61)	57	43 (75.4)
G. Ianiro, 2018 [51]	Rome	56	Fresh faces by C	4	50g	H	8	10 days	28	75 (59–91)	28	74 (49–93)	28	18 (64)	28	21 (75)
C H. Lee, 2016 [52]	Canada	178	Fresh feces by E	1	100g	H	13	NR	87	72.9 (15.4)	91	72.2 (15.9)	87	54(62.1)	91	58(63.7)
G. Cammarota, 2015 [54]	Rome	39	Fresh feces by C	4	152g	RIH	10	7 days	20	71 (29–89)	19	75 (49–93)	20	12 (60)	19	11 (58)
ZD Jiang 2017 [55]	Texas	49	Fresh feces by C	1	50g	H	9	7 days	25	75 (19–97)	24	62.5 (33–88)	25	21 (84.0)	24	18 (75.0)

NR: Not reported;

FMT: fecal microbiota transplantation; C: colonoscopy; E: enema; N: nasoduodenal; NY: New York; RI: Rhode Island; RIH: relatives or intimates or healthy volunteers; H: healthy donor; R: relatives or lived together.

2. Did the authors look for the right type of papers? 作者是否收納適當的研究類型？

Yes No Can't tell



依 PRISMA statement，作者只收納證據等級較高的 RCT 文章，共有 8 篇。

3. Do you think all the important, relevant studies were included?

作者有沒有可能遺漏掉重要、相關的研究？

Yes No **Can't tell**

Exclusion criteria: (I) Animal tests or in vitro tests; (II) Non-English literature; (III) Gastro-intestinal diarrhea not caused by CDI, or diarrhea caused by multiple etiology including *C. difficile*; (IV) Data that were published more than one journal; (V) **Unpublished data** at the trial phase, such as abstracts, conference reports.

Search strategy

Electronic databases including **PubMed, EMBASE, the Cochrane library and Cochrane Central** were searched. All databases were searched up to **September 20, 2018**. The following terms were used: “recurrent / refractory/relapse *clostridium difficile* infection” or “recurrent / refractory/relapse *C. difficile*” or *clostridium difficile* or *C. difficile* (as free words) and with studies identified by “fecal microbiota transplantation” (**[Mesh]** and free text) and randomized controlled trial (**[Mesh]** and free text) (**S2 Table**). **Only English language articles were considered.**

- ✓ 搜尋的資料庫：
PubMed, EMBASE, the Cochrane library and Cochrane Central
- ✓ 有用MeSH term
- ✓ 文章區間~2018.9.20
- ✓ 未收錄未發表或摘要或會議相關的文章
- ✓ 語言：只有英文₂₇

4. Did the review's authors do enough to assess quality of the included studies?

作者是否有評估收納研究的品質？

Yes No Can't tell

Data collection

Two authors (WJ Hui and Ting Li) independently extracted information from the included articles. The following information was extracted from all articles: (1) First author, date of publication and location; (2) Sample size; (3) Fecal transmission route, transmission dosage form and transmission dose, the most infusion numbers; (4) Donor; (5) Follow-up time; and (6) General basic information including age and gender.

Methodology quality appraisal

The quality of articles was evaluated independently by two reviewers (WJ Hui and WD Liu) according to the *Cochrane Handbook for Systematic Review of Interventions*. When the two reviewers could not reach a consensus on an evaluation, the third reviewer (Feng Gao) gave the final decision. And the specific contents of the assessment included the following seven points: (1) Random sequence generation or not or unclear? (2) Allocation concealment or not or unclear? (3) Blindness of participants and personnel or not or unclear? (4) Blindness of outcome assessment or not or unclear? (5) Incomplete outcome data or not or unclear? (6) Selective reporting or not or unclear? (7) Other bias. The GRADE system was used to evaluate the overall quality of the evidence, and the integrity of the above seven points was regarded as the evaluation standard. If the above bias did not exist, it was defined as low-risk; the existence of the above bias was identified as high risk. If no reference was mentioned in the article, it was defined as unclear [16, 17].

1. 兩位作者 (WJ Hui and Ting Li) 根據六個項目進行首次篩選
2. 文章的品質由兩位作者 (WJ Hui and WD Liu) 獨立評估，使用 *Cochrane Handbook for Systematic Review of Interventions*
3. 若以上兩者意見相左，則諮詢第三作者 (Feng Gao) 來解決分歧
4. 最後有使用 **GRADE system** 來評估證據等級。



4. Did the review's authors do enough to assess quality of the included studies?

作者是否有評估收納研究的品質？

Yes No Can't tell

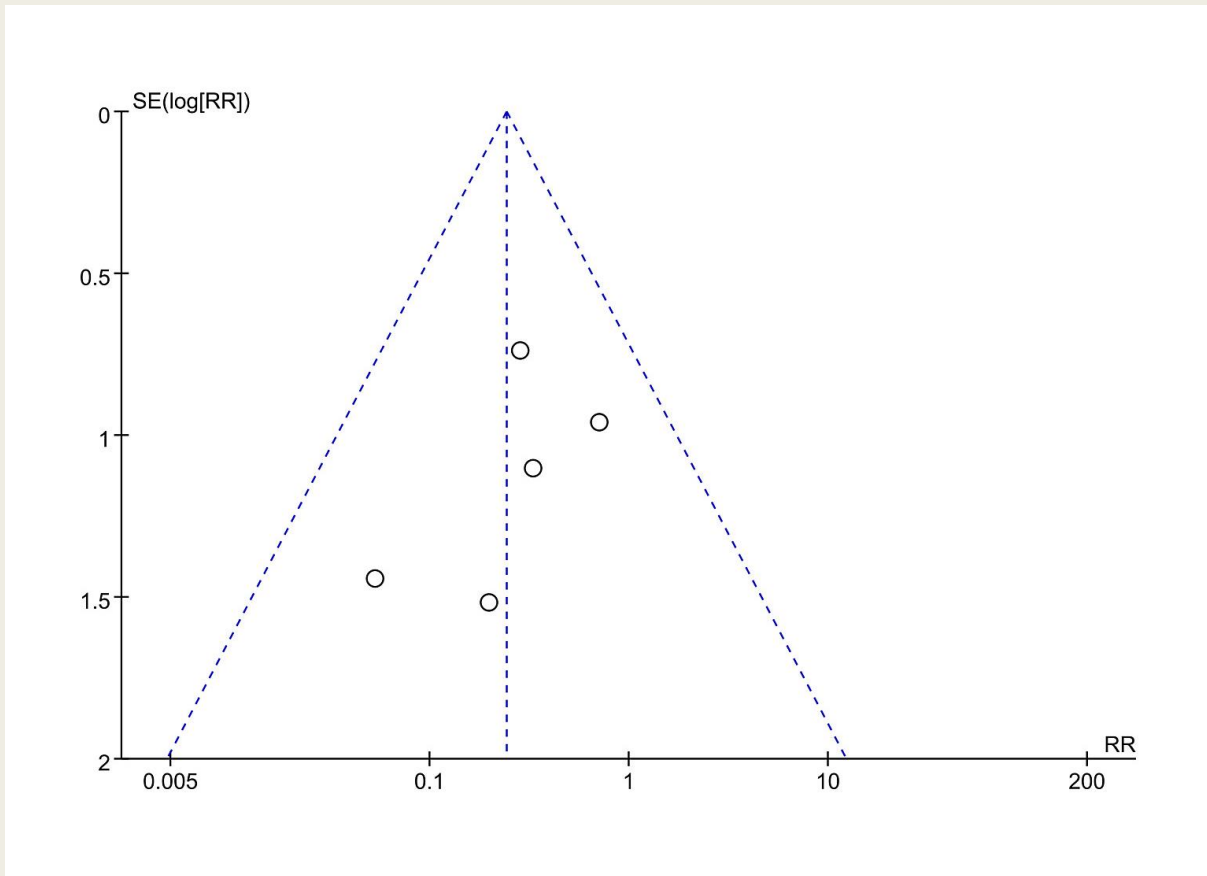
Author	Z. D. Jiang 2017	Susy S. Hota 2016	G. Ianiro 2018	G. Cammarota 2015	Els van Nood 2013	Dina Kao 2017	Colleen R. Kelly 2016	Christine H. Lee 2016	
Random sequence generation (selection bias)	+	+	+	+	+	+	+	+	
Allocation concealment (selection bias)	+	+	+	+	+	+	?	+	
Blinding of participants and personnel (performance bias)	?	-	?	+	+	+	+	+	
Blinding of outcome assessment (detection bias)	+	+	+	+	+	+	+	+	
Incomplete outcome data (attrition bias)	+	+	+	+	+	+	+	+	
Selective reporting (reporting bias)	+	+	+	+	+	+	+	+	
Other bias	+	+	+	+	+	+	+	+	

研究的Risk of bias score的建議等級是以Cochrane handbook建議為主。the whole risk of bias was low, and the quality and the evidence level were high。

4. Did the review's authors do enough to assess quality of the included studies?

作者是否有評估收納研究的品質？

Yes No Can't tell



✓ Funnel plot大致算對稱，表示 publication bias是可以接受的。

4. Did the review's authors do enough to assess quality of the included studies?

作者是否有評估收納研究的品質？

Yes No Can't tell

- ✓ 用Cochrane Handbook for Systematic Review of Interventions評估文章品質(quality)
- ✓ 有爭議性文章有請第三人共同討論文章留存
- ✓ 漏斗圖大致對稱，publication bias可接受
- ✓ 最後有使用**GRADE system**來評估證據等級。

5. If the results of the review have been combined, was it reasonable to do so? 作者是否有把各個研究的結果合併起來？這樣的合併是合理的嗎？

Yes No Can't tell

Statistical methods

The relative risk ratio and 95% confidence interval were obtained by comparing the ratio of patients whose diarrhea did not receive relief by FMT in the intervention group to patients who did not respond to diarrhea in the control group. When $I^2 \geq 50\%$, which indicated the existence of the heterogeneity, and a random effects model was used and sensitivity analysis was needed; otherwise, the fixed effect model was used [18]. The same situation applied to subgroup analysis. All of the above statistical analyses were conducted in Review Manager 5.3.5 (RevMan; the Nordic Cochrane Centre) including forest plots of pooled RRs and funnel plots.

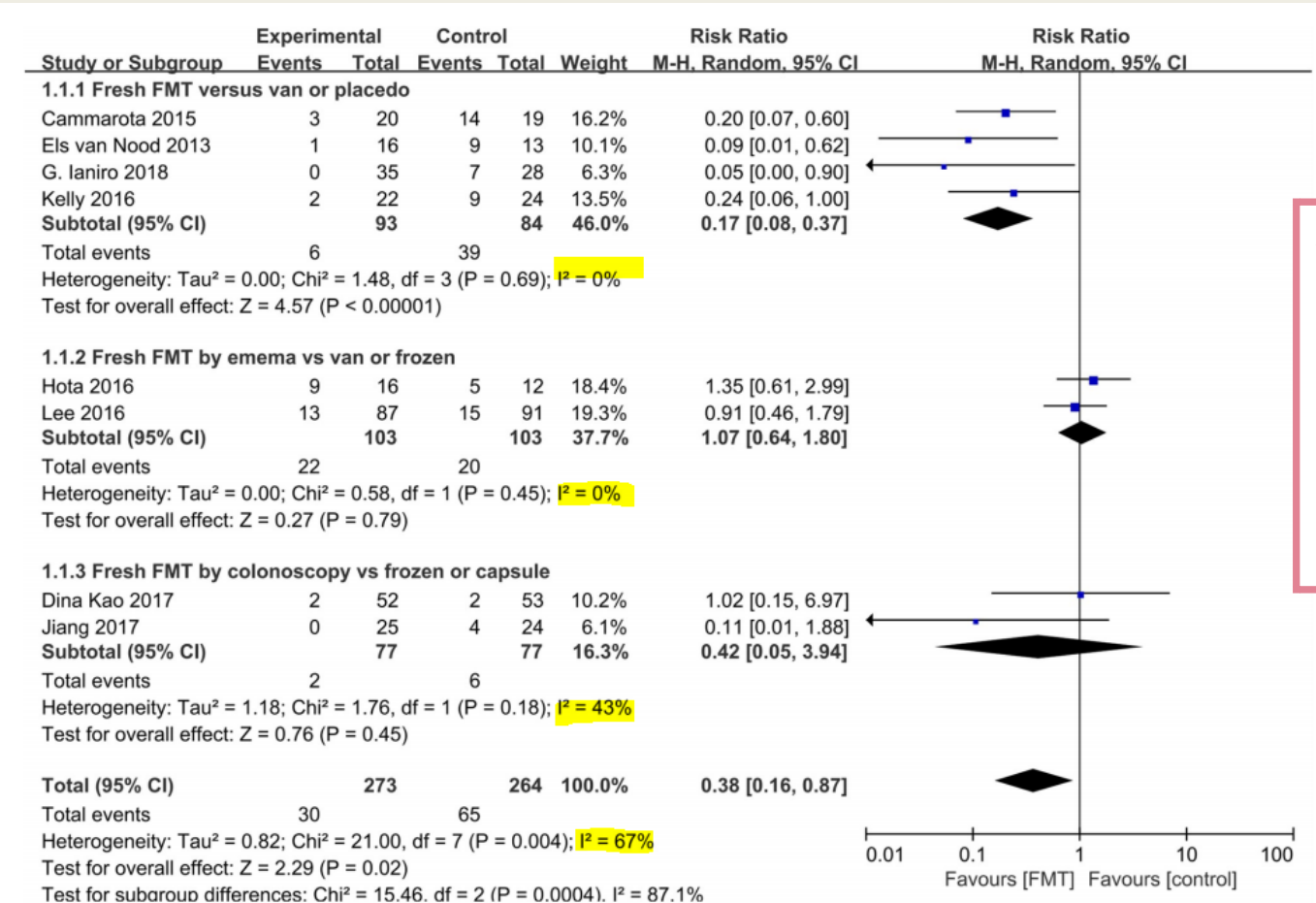
- ✓ 使用Review Manager 5.3.5 (RevMan; the Nordic Cochrane Centre)來分析研究間的異質性 (heterogeneity)。
- ✓ 異質性 $I^2 > 50\%$ ，採用random-effects model進行meta-analysis；異質性 $I^2 < 25\%$ ，採fixed effect model。

Section A: Are the results of the review valid?



5. If the results of the review have been combined, was it reasonable to do so? 作者是否有把各個研究的結果合併起來？這樣的合併是合理的嗎？

Yes No Can't tell



✓ 雖然各個結果單項來看異質性小(0、0、43)，但是整體異質性大(67)，I²>50%，因此採用random-effects model進行meta-analysis合理。

Fig 3. Meta-analysis of the RR between the intervention group and the control group.

6. What are the overall results of the review?
這篇回顧呈現了什麼結果？

7. How precise are the results?
結果精準嗎？

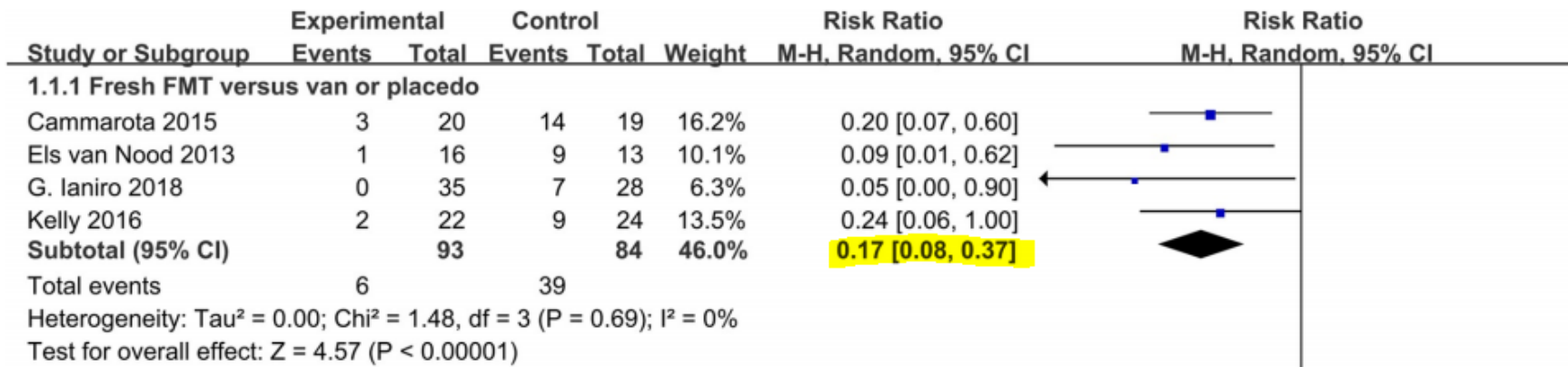
Section B: What are the results?

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply



Fresh FMT versus van or placebo
0.17 [0.08, 0.37]

實驗組事件發生率 (EER, experimental event rate)

對照組事件發生率 (CER, control event rate)

絕對風險下降率 (ARR, absolute risk reduction)

相對風險下降率 (RRR, relative risk reduction)

需要被治療的病人數 (NNT, number needed to treat)

6/39=0.15

39/84=0.46

0.31

0.32

3.22

8. Can the results be applied to the local population? 此研究是否可應用到你的病患？

Yes No Can't tell

First author, year	Location	Sample	FMT formula (FMT group)	Times of infusion	Mean dose (FMT)	Donor	Follow-up, wk	The median time of the recurrence	Age, intervention group		Age, control group		Female sex, experimental group		Female sex, control group	
									N	Mean (SD or range)	N	Mean (SD or range)	N	No. (%)	N	No. (%)
SS. Hota, 2016 [53]	Ontario, Canada	28	Fresh feces by E	1	50g	R	17	9 days	16	75.7(14.5)	12	68.8(14.2)	16	11 (68.8)	12	8 (66.7)
CR. Kelly, 2016 [49]	NY and RI	46	Fresh feces by C	2	64g	H	8	10 days	22	48 (16)	24	55 (14)	22	18 (82)	24	19 (79)
E Nood, 2013 [48]	Amsterdam.	29	Fresh feces by N	2	141g	H	10	23 days	16	73(13)	13	66(14)	16	8 (50)	13	7 (54)
D Kao, 2017 [50]	Alberta	116	Fresh feces by C	1	90g	H	12	NR	59	57.4 (19.1)	57	58.7 (18.5)	59	36 (61)	57	43 (75.4)
G. Ianiro, 2018 [51]	Rome	56	Fresh faces by C	4	50g	H	8	10 days	28	75 (59-91)	28	74 (49-93)	28	18 (64)	28	21 (75)
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ZD Jiang 2017 [55]	Te								25	75 (19-97)	24	62.5 (33-88)	25	21 (84.0)	24	18 (75.0)

文獻研究分析是以反覆型或難治型困難縮狀桿菌患者。且收錄的內容平均年齡層介於48~75歲，但大部分為女性(50~84%)追蹤8~17周。大致符合本題目的背景，故可應用到病患身上。

NR: Not reported; FMT: fecal microb or lived together.

RIH: relatives or intimates or healthy volunteers; H: healthy donor; R: relatives

9. Were all clinically important outcomes considered? 是否所有重要的臨床結果都被考量到？

Yes No Can't tell

Methods

We reviewed studies in PubMed, Medline, Embase, the Cochrane library and Cochrane Central written in English. The retrieval period was from the establishment of the databases to September 20th, 2018. The retrieval objects were published RCTs of RCDI treated by fresh FMT. The intervention group was fresh FMT group, while the control group included antibiotic therapy or placebo or frozen FMT or capsule. The primary and secondary outcomes were the clinical remission of diarrhea without relapse after 8–17 weeks and the occurrence of severe adverse events, respectively. Subgroup analysis analyzed the effect of single and multiple fecal infusions. Two authors independently completed the information extraction and assessed risk of bias and overall quality of the evidence.

文獻研究以腹瀉的臨床緩解作為主要評估工具，也有評估使用過後的嚴重不良反應

10. Are the benefits worth the harms and costs? 這些好處隨之而來的傷害和花費是否值得？

Yes No Can't tell

優點 - 療效

相對於一般抗生素的治療，對於腹瀉改善情況風險比率降低83%，療效顯著；且無明顯之不良反應

缺點 - 花費

相較於一般抗生素治療，費用較昂貴(但有符合成本效益)



10. Are the benefits worth the harms and costs? 這些好處隨之而來的傷害和花費是否值得？

Yes No Can't tell

Recurrent CDI							
Konijeti ¹³ (2014)	MET: 0.710 VAN: 0.916	MET: 0.421 VAN: 0.355	• Hospitalization, tx, outpt visit	MET: \$25 VAN: \$754	FMT colonoscopy: \$18,865/ QALY (\$17,016)	FMT duodenal available	• Cure and recurrence rate of outpt oral VAN, FMT colonoscopy
United States Public	FID: 0.937 FMT colonoscopy: 0.945 FMT duodenal infusion: 0.813 FMT enema: 0.815	FID: 0.197 FMT colonoscopy: 0.091 FMT duodenal infusion: 0.063 FMT enema: 0.091	• Clinical diagnostic laboratory fee schedule from Centers for Medicare and Medicaid Services, literature • 2012	FID: \$3,104 FMT colonoscopy: \$2,495 FMT duodenal infusion: \$2,386 FMT enema: \$2,048		• FMT duodenal: \$107,927/QALY (\$97,352); • FID: \$109,136/QALY (\$98,443) FMT enema available • FID: \$110.709/QALY (\$99,862)	• Costs of colonoscopy, FID, outpt oral VAN • Probability of severe CDI if tx failure • PSA: no

Decision threshold: 50000 USD/QALY
符合成本效益

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

綜合評讀結果

	問題	結果
有效性	1 清楚明確的問題？	●YES ○NO ○UNCLEAR
	2 收納適當的研究類型？	●YES ○NO ○UNCLEAR
	3 包含所有重要、相關的研究？	○YES ○NO ●UNCLEAR
	4 評估收納研究的品質？	●YES ○NO ○UNCLEAR
	5 是否合併？合併的合理性？	●YES ○NO ○UNCLEAR
重要性	6 適當的呈現結果？	●YES ○NO ○UNCLEAR
	7 結果精準嗎？	●YES ○NO ○UNCLEAR
應用性	8 應用到臨床情境？	●YES ○NO ○UNCLEAR
	9 所有重要的臨床結果都被考量到？	●YES ○NO ○UNCLEAR
	10 好處是否值得其帶來的傷害和花費？	●YES ○NO ○UNCLEAR

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

證據等級

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or *poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or <i>n</i> -of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, <i>n</i> -of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)*	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or <i>n</i> -of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

證據品質

		主要結果
研究設計		RCT
降階	1.存在誤差風險	-
	2.結果不一致	-
	3.證據不具直接性	-
	4.結果不精準	-
	5.存在發表誤差	-
生階	1.效果顯著	V
	2.降低干擾因素	-
	3.具劑量-反應效果	-
證據品質		高

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

成本效益

比較不同治療選擇，價格&副作用

選擇	優點	缺點	花費成本
糞便菌叢移植法	療效佳 副作用低	費用較昂貴	FMT colonoscopy:2495USD
傳統抗生素治療 (Vancomycin, Metronidazole)	費用較便宜	治癒率及復發率較糞 便移植法差 副作用較多 (如red man syndrome)	Vancomycin:754USD Metronidazole:25USD
新型抗生素 (Fidaxomicin)	療效介於上兩種治療方式之間， 費用最昂貴(且目前健保未給付)		Fidaxomicin:3104USD

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

病人考量觀點

病患選擇治療方式會在意的因素有什麼？以及在意的程度？

考量因素	不重要	普通	重要	非常重要
經濟考量因素		V		
較好生活品質			V	
照護的方便性			V	
病人的舒適性 (副作用)				V
病人可存活時間			V	
治療有效性				V

每一項選擇的優點、風險

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

治療方式 考量因素	糞便菌叢移植法	傳統抗生素治療	新型抗生素 (Fidaxomicin)
經濟考量因素	◎	★	○
較好生活品質	★	◎	◎
照護的方便性	◎	★	★
病人的舒適性 (副作用)	★	○	★
病人可存活時間	★	◎	◎
治療的有效性	★	◎	◎

註：★較佳 ◎普通 ○較差

問題
ASK

檢索
Acquire

評讀
Appraisal

應用
Apply

臨床回覆

✓ 臨床情況 (Environment)

目前臨床上治療困難縮狀桿菌的標準治療還是使用一般性抗生素，糞便菌叢移植法是一種比較新的治療方式，且根據國外文顯統計是一種符合成本效益的治療方式

✓ 臨床經驗 (Experience)

糞便菌叢移植法主要是取得健康捐贈者的糞便經過過濾、萃取、純化濃縮成液體，再經由大腸鏡送入腸道

✓ 最佳證據等級 (Evidence)

根據我們找到的文獻顯示，使用糞便菌叢移植法療效及復發率較傳統抗生素好，且並無嚴重的副作用發生，大約是一些發燒、噁心嘔吐、疲累等等，但都是用藥來緩解的輕微不良反應

✓ 病人期望 (Expectation)

雖然費用較傳統型抗生素昂貴一些，但若您期望要療效好、副作用少的治療方式，糞便菌叢移植法是一個可以考慮的選擇

Thank You

