# Evidence-Based Medicine
# 實證醫學

實證是守護病患健康最好的工具

# 第三組成員與單位

- 成員-精神醫學部
  - R2趙培竣
  - R2初景文
  - 專科護理師 林姵芸
- 單位內推廣實證醫學歷程
  - 每年派員參與院內外實證醫學相關比賽
  - 每月部內進行實證醫學實作：住院醫師以及實習醫學生
  - 將臨床問題於實證應學討論，並實際應用。

# 臨床教案簡述

- 林媽媽有兩個小孩，大兒子將要上小學，常常感冒拉肚子，她很怕出生不久2個多月大的女兒也會出狀況。最近聽說有一種輪狀病毒的疫苗，可以增強免疫力。她想要知道值不值的打這個疫苗，又有一點擔心副作用。
- 另外，大兒子趁著就讀小學前跟爸爸去大陸旅遊，最近的新聞報導指出今年大陸正在發生腸病毒71型的大流行。因此考慮是否到大陸當地立刻至醫院施打「腸病毒71型疫苗」？打了之後又可以提供什麼樣的保護效果呢？因為當地的網路資訊不太可靠，所以特地來電請益，想請問你這位實證醫學專家給他一些建議。

# 臨床問題(請用一句話描述)

- 問題1：
  - 兩個月大的女兒施打輪狀病毒疫苗會有哪些副作用？
- 問題2：
  - 即將上小學的男童在中國大陸施打腸病毒71型疫苗有哪些保護效果？

# 問題類型

- 問題1：
- □Therapy/Protection　□Diagnosis
- □Prognosis　■Harm

- 問題2：
- ■Therapy/Protection　□Diagnosis
- □Prognosis　□Harm

# 問題1的背景知識

- UpToDate: Rotavirus vaccines for infants
- ROTAVIRUS VACCINES
  - (Lisensed)Pentavalent human-bovine rotavirus reassortant vaccine (RV5, PRV, RotaTeq)
  - (Lisensed)Attenuated human rotavirus vaccine (RV1, HRV, Rotarix)
  - Human-bovine reassortant vaccine (116E, ROTAVAC)
  - Tetravalent human-rhesus reassortant vaccine
- ADVERSE EVENTS AND SAFETY
  - Similar rates of solicited events, including of fever (approximately 42 percent), vomiting (approximately 13 percent), and diarrhea (approximately 19 percent),
  - Intussusception-very rare
  - Kawasaki disease -case report

# 問題2的背景知識

- UpToDate: Epidemiology, pathogenesis, treatment, and prevention of enterovirus and parechovirus infections
  - PREVENTION —Effective vaccines against enteroviruses other than poliovirus are not yet clinically available. Several inactivated genotype C4 enterovirus 71 vaccines appear promising based on randomized, placebo-controlled multicenter trials in China, each involving more than 10,000 children aged 6 to 35 months (with one study including children up to 6 years old)

# 問題2的背景知識

衛生署疾病管制局

Taiwan CDC
http://www.cdc.gov.tw

- 國內CDC資料
  - 關於中國大陸腸病毒71型疫苗簡介

| 研發單位 | 國別 | 開發進度 | 病毒株 | 備註 |
|---|---|---|---|---|
| 中生集團 | 中國大陸 | 完成Phase Ⅲ | C4 | 結果顯示該疫苗對由EV71型病毒引起的手足口病具有90%的保護率。(Lancet.2013 Jun 8 ;381(9882):2024-32.) |
| 北京科興 | 中國大陸 | 完成Phase Ⅲ | C4 | 初步結果顯示疫苗具有良好的安全性和有效性對EV71型病毒導致的手足口病或疱疹性咽峽炎保護率為94.8% 。(N Engl J Med. 2014 Feb 27; 370(9):818-28.) |
| 昆明生物所 | 中國大陸 | 完成Phase Ⅲ | C4 | 結果顯示該疫苗對由EV71型病毒引起的手足口病具有97.4%的保護率。(N Engl J Med2014 Feb 27; 370(9):829-37.) |

# 問題1的PICO

| | Key words | Synonyms |
|---|---|---|
| Patient and/or problem | 2-month-old female with common cold symptoms and diarrhea | Female infant, gastrointestinal symptoms |
| Intervention | Use of rotavirus vaccination | nil |
| Comparison | Without use of vaccination | nil |
| Outcome | Side effects of gastrointestinal symptoms | Fever, vomiting, diarrhea, |

Key Word: Female infant, rotavirus vaccination, gastrointestinal symptoms

# 問題2的PICO

| | Key words | Synonyms |
|---|---|---|
| Patient and/or problem | 6-year-old healthy boy visited enterovirus type 71 pandemic region of mainland China | Male children, Chinese enterovirus type 71 |
| Intervention | Use Chinese vaccination of enterovirus 71 | nil |
| Comparison | Without use of vaccination | nil |
| Outcome | Prevention of enterovirus type 71 related symptoms | Hand-foot-mouth disease, herpangina |

Key Word: Male children, Chinese vaccination of enterovirus 71, Hand-foot-mouth disease, herpangina

# 資料庫搜尋

- Secondary database
  - Dynamed
  - Cochrane
  - Trip
- Primary database
  - PubMed
  - Medline

# 文獻搜尋歷程

# Secondary database - Dynamed


***搜尋到5篇***

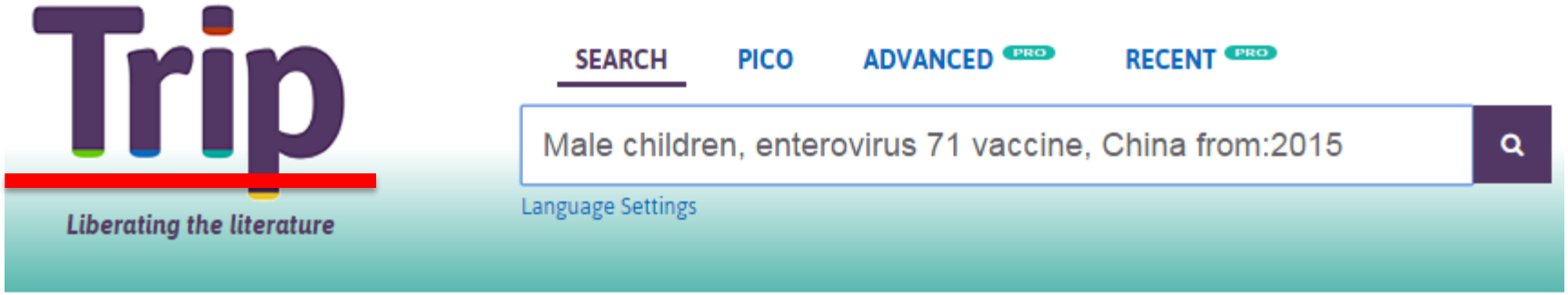
***符合PICO的文章：1篇***

# Secondary database - Cochrane


搜寻到12篇

符合PICO的文章：1篇

# Secondary database: Trip




Evidence | Images PRO | Videos PRO | Explorer PRO

**29 results for "Male children, enterovirus 71 vaccine, China from:2015", by quality**

Export | Order | Add to automated search

1. **Efficacy, safety, and immunogenicity of an oral recombinant Helicobacter pylori vaccine in children in China: a randomised, double-blind, placebo-controlled, phase 3 trial.**
   Lancet (London, England) 2015
   Tweet this | Star this | Estimate of bias: low | Prim… esearch

2. **Clinical Efficacy of Therapy with Recombinant Human Interferon α1b in Hand, Foot, and Mouth Disease with Enterovirus 71 Infection.**
   PloS one 2016 Full Text: Link to full Tex… Trip PRO

**搜尋到29篇**

**符合PICO的文章：3篇**

NCBI Resources How To Sign in to NCBI

PubMed.gov US National Library of Medicine National Institutes of Health

PubMed | Male children, enterovirus 71 vaccine, China | Search | Help

Format: Summary Sort by: Most Recent Send to

Filters: Manage Filters

**Article types**
Clinical Trial
Review
Customize ...

**Text availability** clear
Abstract
Free full text
✓ Full text

**PubMed Commons**
Reader comments
Trending articles

**Publication dates** clear
5 years
✓ 10 years
Custom range...

**Species** clear
✓ Humans
Other Animals

Clear all

Show additional filters

## Search results

**Items: 1 to 20 of 33**

<< First < Prev Page 1 of 2 Next > Last >>

Filters activated: Full text, published in the last 10 years, Humans. Clear all to show 35 items.

1. Clinical Efficacy of Therapy with Recombinant Human Interferon α1b in Hand, Foot, and Mouth Disease with **Enterovirus 71** Infection.
Huang X, Zhang X, Wang F, Wei H, Ma H, Sui M, Lu J, Wang H, Dumler JS, Sheng G, Xu B.
PLoS One. 2016 Feb 16;11(2):e0148907. doi: 10.1371/journal.pone.0148907.
PMID: 26882102 Free PMC Article
Similar articles

2. Protein microarray-mediated detection of antienterovirus antibodies in serum.
Zhang A, Xiu B, Zhang H, Li N.
J Int Med Res. 2016 Apr;44(2):287-96. doi: 10.1177/0300060515604981.
PMID: 26831405
Similar articles

3. Two-year efficacy and immunogenicity of Sinovac **Enterovirus 71 vaccine** against hand, foot and mouth disease in **children**.
Li JX, Song YF, Wang L, Zhang XF, Hu YS, Hu YM, Xia JL, Li J, Zhu FC.
Expert Rev **Vaccines**. 2016;15(1):129-37. doi: 10.1586/14760584.2016.1096782.
PMID: 26460695
Similar articles

4. Similar protective immunity induced by an inacti[illegible] rhesus macaques and **children**.
Zhang Y, Wang L, Liao Y, Liu L, Ma K, Yang [illegible] Y, Cui W, Yang H, Li Q.
**Vaccine**. 2015 Nov 17;33(46):6290-7. doi: 10.1016/j.**vaccine**.2015.09.047.
PMID: 26419198
Similar articles

搜寻到33篇

符合PICO的文章：3篇

**Find related data**
Database: Select
Find items

**Search details**
(("male"[MeSH Terms] OR "male"[All Fields]) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields]) AND ("enterovirus"[MeSH Terms] OR "enterovirus"[All
Search See more...

**Recent Activity**
Turn Off Clear
Male children, enterovirus 71 vaccine, China AND (full text[sb] A... (33) PubMed
Male children, enterovirus 71 vaccine, China AND (full text[sb] A... (33) PubMed
Male children, enterovirus 71 vaccine, China AND (Humans[Mesh]) (34) PubMed
Male children, enterovirus 71 vaccine, China (35) PubMed
See more...

# Primary database: Medline


***搜尋到16篇***

***符合PICO的文章：9篇***

airiti Library 華藝線上圖書館

Language

國軍醫院聯合圖書館-三軍總醫院，您好！

瀏覽 | 進階檢索 | 儲值&購物車 | 登入 | 加入會員 | 購買點數 | 個人化服務 | 客服中心 | 使用說明 | 網站地圖

| 文章 | 出版品 | 所有欄位 | 更多選項 | 查詢歷史

期刊文章 1 | 會議論文 0 | 碩博士論文 0 | 電子書 0

依下方條件來精確結果

來源資料庫

CEPS中文電子期刊 (1)

學科分類

醫學與生命科學 (1)

年代

2010 (1)

出版品名稱

實用兒科臨床雜誌 (1)

指標期刊

查詢 (Male children, enterovirus 71 vaccine, China ) = 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 1 筆，1 - 1 筆

共 1 頁 1

書目 追蹤 加入購物

相關程度最高

1 河北省2008年手足口病的流行病学分析

张九菊(Jiu-Ju Zhang)；张少丹(Shao-Dan Zhang)；张会丰(Hui-Feng Zhang)；田晓瑜(Xiao-Yu Tian)；

enterovirus 71

預覽摘要 加入追蹤 全文下載

**搜尋到1篇**

**符合PICO的文章：0篇**

# 搜尋結果

| Database | 搜尋到的篇數 | 符合PICO的文章篇數 |
|---|---|---|
| Dynamed | 5 | 1 |
| Cochrane | 12 | 1 |
| Trip | 29 | 3 |
| PubMed | 33 | 3 |
| Medline | 16 | 9 |
| 華藝線上 | 1 | 0 |
| | 96 | 17 |

# Flow chart for selection of articles


Search for potential relevant articles (n=96)

Studies excluded (n=79)

Not fitting with our PICO

Articles retrieved for further evaluation (n=17)

Studies excluded (n=16)

Before 2011

Repeated

Not Available

Case number

Article selected for inclusion (n=1)

# 嚴格評讀(Critical appraisal)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## An Inactivated Enterovirus 71 Vaccine in Healthy Children

這篇文獻「納入理由」

- V 最符合臨床問題
- V 發表年份較新
- V 最佳的研究設計
- V 有全文可供評讀

## Critical Appraisal Worksheets

### English

- Systematic Reviews Critical Appraisal Sheet
- Diagnostics Critical Appraisal Sheet
- Prognosis Critical Appraisal Sheet
- Randomised Controlled Trials Critical Appraisal Sheet

Was the assignment of patients to treatments randomised?

病人治療之分配是否隨機？

**STUDY DESIGN AND PARTICIPANTS**

This randomized, double-blind, placebo-controlled clinical study was designed by the Institute of Medical Biology, the Center for Drug Evaluation in the State Food and Drug Administration, and the Center for Disease Control and Prevention

All eligible participants were stratified according to age (6 to 23 months vs. 24 to 71 months). Randomization was performed in a 1:1 ratio in blocks of eight. Identical labels with computer-generated random numbers were used on all study-agent vials. Two doses of either vaccine or placebo were administered intramuscularly, with a 4-week interval between doses.

**This paper: Yes ■ No □ Unclear □**

# Were the groups similar at the start of the trial?
# 不同族群於開始時是否相似？

The demographic characteristics of the participants were similar in the two groups (Table 1, and Table S1 in the Supplementary Appendix).

**Table 1. Demographic Characteristics of the Participants Included in the Intention-to-Treat Analysis.***

| Characteristic | Efficacy Cohort | | Immunogenicity Subgroup | |
|---|---|---|---|---|
| | Vaccine Group (N=6000) | Placebo Group (N=6000) | Vaccine Group (N=549) | Placebo Group (N=550) |
| Sex — no. (%) | | | | |
| Male | 3151 (52.5) | 3099 (51.6) | 279 (50.8) | 296 (53.8) |
| Female | 2849 (47.5) | 2901 (48.4) | 270 (49.2) | 254 (46.2) |
| Age at entry — mo | | | | |
| Mean | 23.7±15.2 | 23.7±15.2 | 21.2±12.9 | 21.3±12.8 |
| Range | 6.0–71.9 | 6.1–71.9 | 6.1–71.3 | 6.1–69.1 |
| Weight at entry — kg | | | | |
| Mean | 11.9±3.1 | 11.9±3.1 | 11.3±2.7 | 11.4±2.8 |
| Range | 4.2–33.6 | 4.5–30.0 | 5.0–22.0 | 5.0–23.0 |
| Ethnic group — no (%)† | | | | |
| Han | 5278 (88.0) | 5201 (86.7) | 494 (90.0) | 477 (86.7) |
| Zhuang | 434 (7.2) | 485 (8.1) | 28 (5.1) | 38 (6.9) |
| Yao | 207 (3.4) | 227 (3.8) | 22 (4.0) | 27 (4.9) |
| Miao | 27 (0.4) | 31 (0.5) | 1 (0.2) | 5 (0.9) |
| Other | 54 (0.9) | 56 (0.9) | 4 (0.7) | 3 (0.5) |

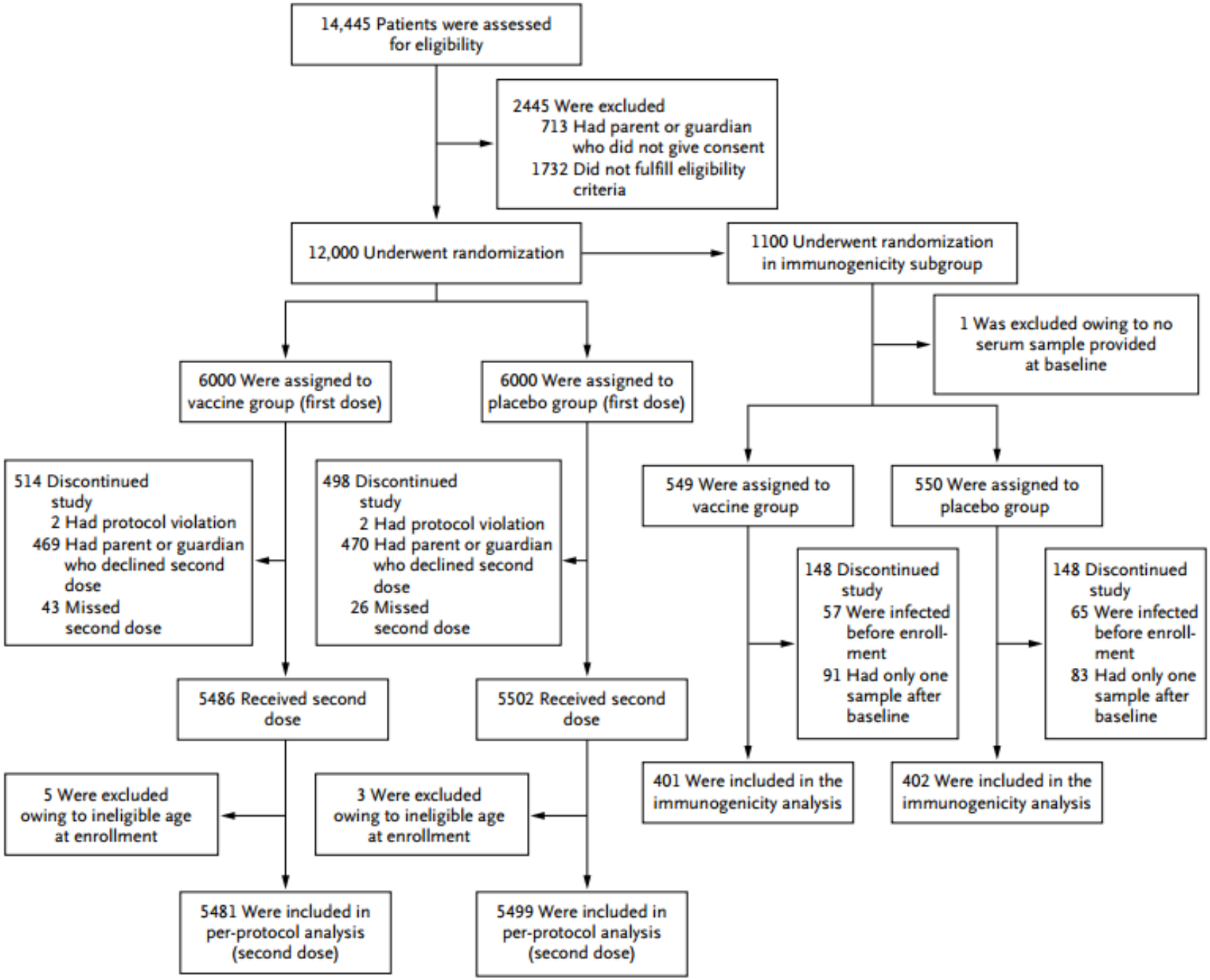
**This paper: Yes ■ No □ Unclear □**

* Plus–minus values are means ±SD. There were no significant between-group differences at baseline. The intention-to-treat analysis included data from all participants who received at least one dose of vaccine or placebo.
† Ethnic group was reported by a parent or guardian and verified by a study investigator.

Aside from the allocated treatment, were groups treated equally?
除了主要治療外，其他治療是否相同？

| 2a. A – Aside from the allocated treatment, were groups treated equally? | |
|---|---|
| What is best? | Where do I find the information? |
| Apart from the intervention the patients in the different groups should be treated the same, eg., additional treatments or tests. | Look in the ***Methods*** section for the follow-up schedule, and permitted additional treatments, etc and in ***Results*** for actual use. |

**This paper: Yes ☐ No ☐ Unclear ■**


14,445 Patients were assessed for eligibility
2445 Were excluded
713 Had parent or guardian who did not give consent
1732 Did not fulfill eligibility criteria
12,000 Underwent randomization
1100 Underwent randomization in immunogenicity subgroup
1 Was excluded owing to no serum sample provided at baseline
6000 Were assigned to vaccine group (first dose)
6000 Were assigned to placebo group (first dose)
514 Discontinued study
2 Had protocol violation
469 Had parent or guardian who declined second dose
43 Missed second dose
498 Discontinued study
2 Had protocol violation
470 Had parent or guardian who declined second dose
26 Missed second dose
549 Were assigned to vaccine group
550 Were assigned to placebo group
148 Discontinued study
57 Were infected before enrollment
91 Had only one sample after baseline
148 Discontinued study
65 Were infected before enrollment
83 Had only one sample after baseline
5486 Received second dose
5502 Received second dose
5 Were excluded owing to ineligible age at enrollment
3 Were excluded owing to ineligible age at enrollment
401 Were included in the immunogenicity analysis
402 Were included in the immunogenicity analysis
5481 Were included in per-protocol analysis (second dose)
5499 Were included in per-protocol analysis (second dose)

Were measures objective or were the patients and clinicians kept "blind" to which treatment was being received?

All eligible participants were stratified according to age (6 to 23 months vs. 24 to 71 months). Randomization was performed in a 1:1 ratio in blocks of eight. Identical labels with computer-generated random numbers were used on all study-agent vials. Two doses of either vaccine or placebo were administered intramuscularly, with a 4-week interval between doses.

**END POINTS**

The primary end point was efficacy against EV71-associated hand, foot, and mouth disease according to the case definition described above. Efficacy was assessed from 2 weeks after completion of the two-dose schedule until 1 year after receipt of the first dose. The secondary end points were efficacy against severe hand, foot, and mouth disease within the same study period and the proportion of participants in whom EV71-neutralizing antibodies developed at 56 days and 180 days after the initial vaccination.

**This paper: Yes ■ No □ Unclear □**

# What were the results?

# 結果如何？

**Table 2. Efficacy of the Enterovirus 71 (EV71) Vaccine against Overall Hand, Foot, and Mouth Disease and EV71-Associated Hand, Foot, and Mouth Disease over an 11-Month Period, According to the Intention-to-Treat Analysis.**

| Cases of Hand, Foot, and Mouth Disease | Vaccine Group (N=6000) | | Placebo Group (N=6000) | | Vaccine Efficacy* | P Value |
|---|---|---|---|---|---|---|
| | Participants | Incidence *no. of cases/ 1000 participants/yr* | Participants | Incidence *no. of cases/ 1000 participants/yr* | *% (95% CI)* | |
| Clinically diagnosed and pathogenically confirmed cases | | | | | | |
| Caused by EV71 — no. | 4 | 0.7 | 151 | 25.2 | 97.4 (92.9 to 99.0) | <0.001 |
| Age 6–23 mo — no./total no. | 2/3500 | 0.6 | 94/3500 | 26.9 | 97.9 (91.4 to 99.5) | <0.001 |
| Age 24–72 mo — no./total no. | 2/2500 | 0.8 | 57/2500 | 22.8 | 96.5 (85.6 to 99.1) | <0.001 |
| Caused by coxsackievirus A16 — no. | 48 | 8.0 | 54 | 9.0 | 11.1 (–30.8 to 39.6) | 0.55 |
| Caused by other enterovirus — no. | 106 | 17.7 | 128 | 21.3 | 17.2 (–6.0 to 35.8) | 0.15 |
| Clinically diagnosed cases — no. | 202 | 33.7 | 392 | 65.3 | 48.5 (39.2 to 56.3) | <0.001 |

* The calculation of overall vaccine efficacy was adjusted for study center.

# What were the results?
# 結果如何？

- Relative Risk(RR): (0.8/1000) / (22.8/1000) =0.035
- Absolute Risk Reduction (ARR): 22.8/1000-0.8/1000=2.2%
- Relative Risk Reduction (RRR) = 1-RR= 1-0.035=0.965
- Number Needed to Treat (NNT): 1/ARR=45.45

# Will the results help me in caring for my patient?

- Is my patient so different to those in the study that the results cannot apply? No
- Is the treatment feasible in my setting? Not yet in Taiwan, but available in China

## 中國研發腸病毒疫苗上市 標榜全球首個

建立於 2016/03/28　上稿編輯： 鄒敏惠

摘錄自2016年3月27日中央社報導

中國大陸研發的全球首個腸道病毒71型（EV71）滅活疫苗日前獲批上市，專家表示，接種此疫苗將有效降低腸病毒兒童手足口病的發病率。在大陸手足口病高發區廣西，今天也完成此疫苗的接種。

- Will the potential benefits of treatment outweigh the potential harms of treatment for my patient? It generally less or no difference harmed of severe events

**Table 3. Adverse Events and Serious Adverse Events.**

| Event | All Adverse Events | | | Adverse Events of Grade 3 or Higher* | | |
|---|---|---|---|---|---|---|
| | Vaccine Group (N=6000) | Placebo Group (N=6000) | P Value | Vaccine Group (N=6000) | Placebo Group (N=6000) | P Value |
| | *no. of participants with event (%)* | | | *no. of participants with event (%* | | |
| Adverse event ≤7 days after injection | | | | | | |
| Systemic event | 2916 (48.6) | 2574 (42.9) | <0.001 | | | |
| Fever | 2498 (41.6) | 2111 (35.2) | <0.001 | 147 (2.4) | 149 (2.5) | 0.95 |
| Diarrhea | 498 (8.3) | 535 (8.9) | 0.24 | 8 (0.1) | 12 (0.2) | 0.50 |
| Nausea, vomiting, or anorexia | 530 (8.8) | 475 (7.9) | 0.08 | 6 (0.1) | 7 (0.1) | 1.00 |
| Irritability, drowsiness, or weakness | 360 (6.0) | 303 (5.0) | 0.03 | 3 (<0.1) | 7 (0.1) | 0.34 |
| Allergy | 166 (2.8) | 156 (2.6) | 0.61 | 2 (<0.1) | 0 | 0.50 |
| Local event | 356 (5.9) | 138 (2.3) | <0.001 | | | |
| Pain | 211 (3.5) | 80 (1.3) | <0.001 | 1 (<0.1) | 0 | 1.00 |
| Redness | 130 (2.2) | 34 (0.6) | <0.001 | 1 (<0.1) | 0 | 1.00 |
| Itching | 59 (1.0) | 31 (0.5) | 0.004 | 0 | 0 | — |
| Swelling | 106 (1.8) | 22 (0.4) | <0.001 | 0 | 0 | — |
| Adverse event ≤28 days after injection | 2841 (47.4) | 2985 (49.8) | 0.009 | 136 (2.3) | 136 (2.3) | 1.00 |
| Serious adverse event | — | — | — | 68 (1.1) | 125 (2.1) | <0.001 |
| Death† | — | — | — | 1 (<0.1) | 1 (<0.1) | 1.00 |
| Hospitalization‡ | — | — | — | 67 (1.1) | 124 (2.1) | <0.001 |
| Hand, foot, and mouth disease | — | — | — | 41 (0.7) | 88 (1.5) | <0.001 |
| Injection-related cause§ | — | — | — | 2 (<0.1) | 2 (<0.1) | 1.0 |
| Other cause¶ | — | — | — | 24 (0.4) | 34 (0.6) | 0.34 |

# 證據等級(Levels of evidence)

**Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence**

| 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 *n*-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, *n*-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 *n*-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 |

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

# 建議分級(Grades of recommendation)

| Grades of Recommendation | |
|---|---|
| A | consistent level 1 studies |
| B | consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies |
| C | level 4 studies ***or*** extrapolations from level 2 or 3 studies |
| D | level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level |

| 建議等級 | 說明 |
|---|---|
| A | 有好的證據支持此建議<br>(level 1研究有一致結論) |
| B | 有相當的證據支持此建議<br>(level 2或3研究有一致結論，或根據level 1研究之推論) |
| C | 沒有充分證據支持或反對此建議<br>(level 4研究，或根據level 2或3研究之推論) |
| D | 有level 5的證據，或研究沒有一致結論 |

# 臨床回覆

- 林媽媽您好，根據團隊依據實證醫學證據搜尋評讀以及討論現有文獻，特別針對中國大陸當地之文獻指出，您的大兒子於大陸地區施打之腸病毒疫苗，有相當證據支持可降低罹患腸病毒71型所引起之疾病，可降低約96.5%之罹病風險，且由疫苗引起之嚴重副作用機率無明顯差別，僅輕微副作用機率較高，應可安心施打疫苗。