黃相瀚
麻醉部
第三年住院醫師

楊子賢
麻醉部
第二年住院醫師

奉綺薇
麻醉部
第一年住院醫師

三軍總醫院麻醉部

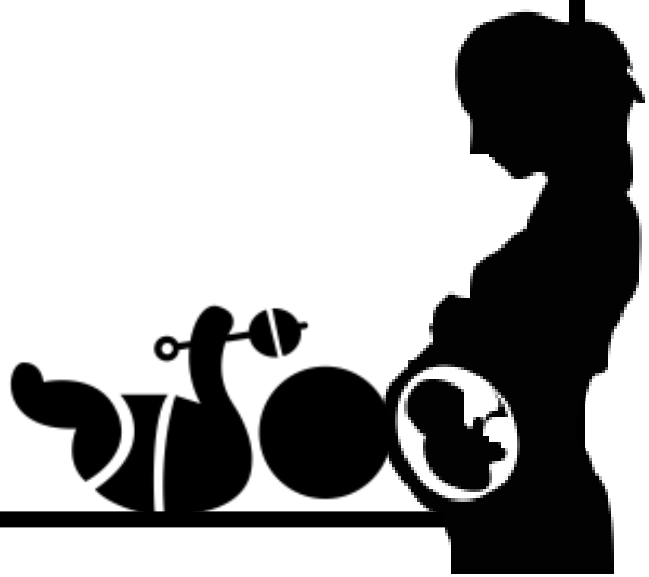
實證醫學競賽

臨床情境

35歲黃女士，懷孕39周，接受莫德納疫苗2劑已滿三個月，因出現產兆至醫院待產，發現有發燒、咳嗽症狀，經PCR採檢陽性而確診新冠病毒感染，PCR-Ct值12。

黃女士獲知確診後非常擔心自己是不是**會將病毒傳給胎兒，造成胎兒感染?胎兒出生後可以接受任何治療嗎?**

因預產期在即，原本預計要母乳哺餵，現在**產後是否還能哺餵母乳?**



背景知識

懷孕確診對孕媽咪的影響

有較高的死亡風險:確診COVID-19的孕婦其死亡率為無確診孕婦的6.09倍。

早產風險:確診 COVID-19的孕婦其早產風險為無確診孕婦的1.57倍。

死產風險: 確診 COVID-19的孕婦其死產風險為無確診孕婦的1.81倍。

子癲前症風險:確診COVID-19的孕婦發生子癲前症的風險是無確診孕婦的 1.58倍。

背景知識

懷孕確診對寶寶的影響

死亡風險:確診孕婦的胎兒其死亡風險是未確診孕婦胎兒的2.35倍。

呼吸道系統疾病風險:孕媽咪感染COVID-19的胎兒，其發生呼吸道系統疾病的風險是媽咪未感染胎兒的1.42倍。

背景知識


潮健康
「母嬰傳染」可能性確實存在!
4情況可能增加嬰兒陽性率
孕婦為重症病患
孕婦生產前
已進入重症加護病房
RIP
孕婦因確診
而死亡
孕婦生產後
才檢測出新冠病毒
資料來源:《英國醫學期刊》(BMJ)
圖片來源:潮健康

背景知識


潮健康
孕婦施打新冠疫苗的注意事項？
疾管署曝接種「4要點」
MRNA
接種疫苗不分孕期
孕婦可於懷孕任何階段接種疫苗或加強劑
優先考量mRNA疫苗
mRNA疫苗增加血栓機率較小
有副作用要注意
出現陰道出血、下腹疼痛等狀況應儘快檢查
哺乳者亦可施打
哺乳婦女可於接種疫苗前後持續哺乳
資料來源：衛福部疾管署
圖片來源：潮健康

背景知識

Breastfeeding guidelines for COVID-19-positive or exposed mothers

Breast milk is beneficial for infants because it protects against many illnesses. During the COVID-19 pandemic, some mothers may be unsure about breastfeeding their infant. It is important to use best practices when planning to breastfeed or pump.

Mothers who are COVID-19-positive and want to breastfeed:

- Wash hands before and after touching the infant or feeding equipment
- Avoid using a pump shared by others
- Wear a mask or face covering during breastfeeding and pumping
- Follow manufacturer instructions to clean pump parts after each use
- Try to have a healthy caregiver (who does not have COVID-19 and lives in the same home) feed pumped breast milk to the infant

Breastfeeding mothers who have been exposed to COVID-19 should also follow the suggestions above

Breastfeeding mothers who work in settings with high risk of exposure:

- Talk to supervisors at work about limiting exposure to situations involving COVID-19-positive individuals
- Clean shared surfaces in lactation rooms before and after use
- After coming home, take off shoes, wash work clothes, and take a shower
- If the infant is high risk for COVID-19, consider isolating from the infant while providing breast milk

瞭解病人的主要問題

1. 孕婦黃女士確診後擔心是不是會將病毒傳給胎兒，造成胎兒感染?
2. 胎兒出生後可以接受任何治療嗎?
3. 產後是否還能哺餵母乳?

根據臨床問題形成PICO

	PICO/ 關鍵字	MeSH同義詞	中文關鍵字(繁/簡體)
P	• Neonate	• Infant	• 胎兒、新生兒
I	• Mother with Covid-19 infection	• Mother with SARS-CoV-2 infection	• 新冠病毒感染孕婦
C	• Mother with no exposure	• none、healthy	• 無對照組
O	• Neonate with COVID PCR positive rate	• SARS-CoV-2 positive	• 胎兒感染新冠病毒

☐治療/預防問題 ☐診斷型問題 ☑預後型問題 ☐傷害/病因型問題

根據臨床問題形成PICO

	PICO/ 關鍵字	MeSH同義詞	中文關鍵字(繁/簡體)
P	• Neonate	• Infant	• 胎兒、新生兒
I	• Breast feeding	• Breast feeding	• 哺乳
C	• No breast feeding	• No breast feeding	• 無哺乳
O	• Neonate with COVID PCR positive rate	• SARS-CoV-2 positive	• 胎兒感染新冠病毒

☐治療/預防問題 ☐診斷型問題 ☑預後型問題 ☐傷害/病因型問題

檢索策略-提升檢索效率

首先以『P』、『I』做搜尋，再依據結果適當加入關鍵字及同義詞

P	AND	I	AND	C	AND	O
Neonate		Mother with Covid-19 infection		No exposure		COVID PCR positive rate

限定搜尋範圍	Free full text、Within 5 years、Human species
限定研究類型	Systematic review、Meta-analysis、Randomized controlled trial
限定語言地區	English、中文[台灣本土文獻]

檢索策略-我們的主要目標

Clinical Queries

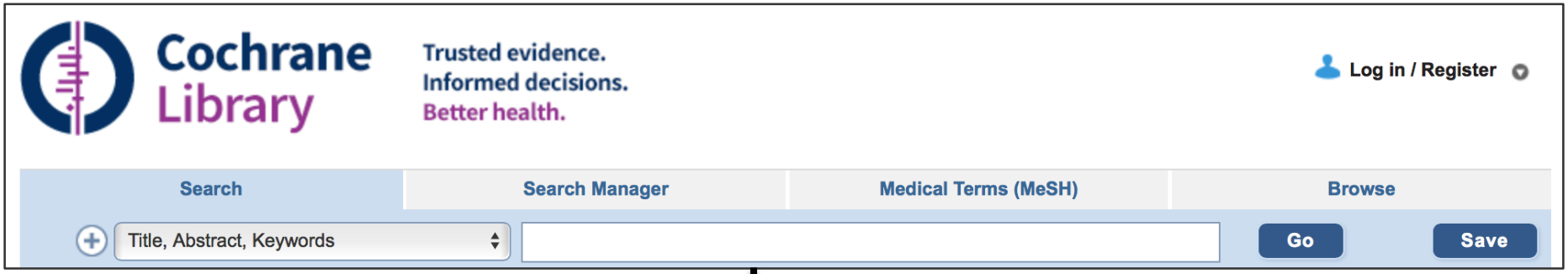
Systematic Review (**Meta-Analysis**)

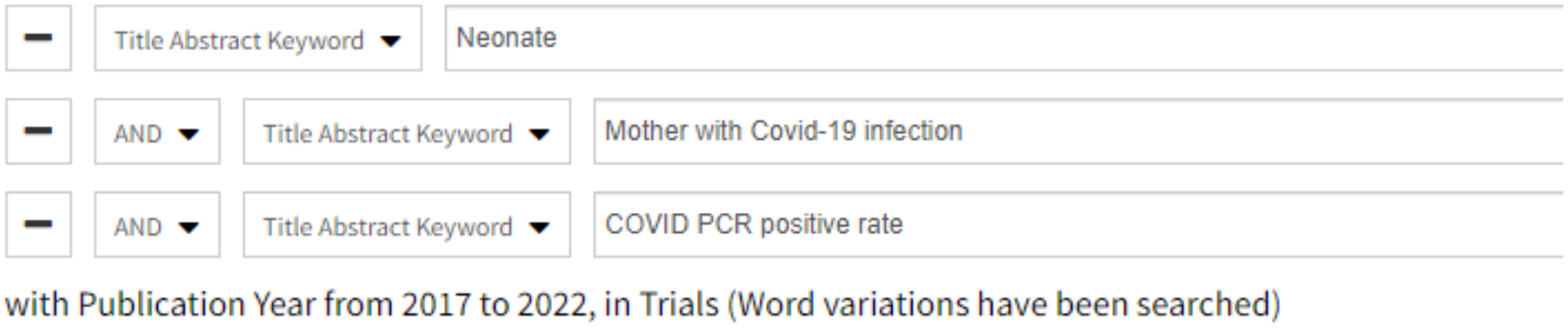
Randomized Controlled Trial/ Cohort Study

Within **5** Years

Meet our 『**PICO**』

搜尋Cochrane Library-提升檢索效率





使用Limit功能

限定『Review』之文章

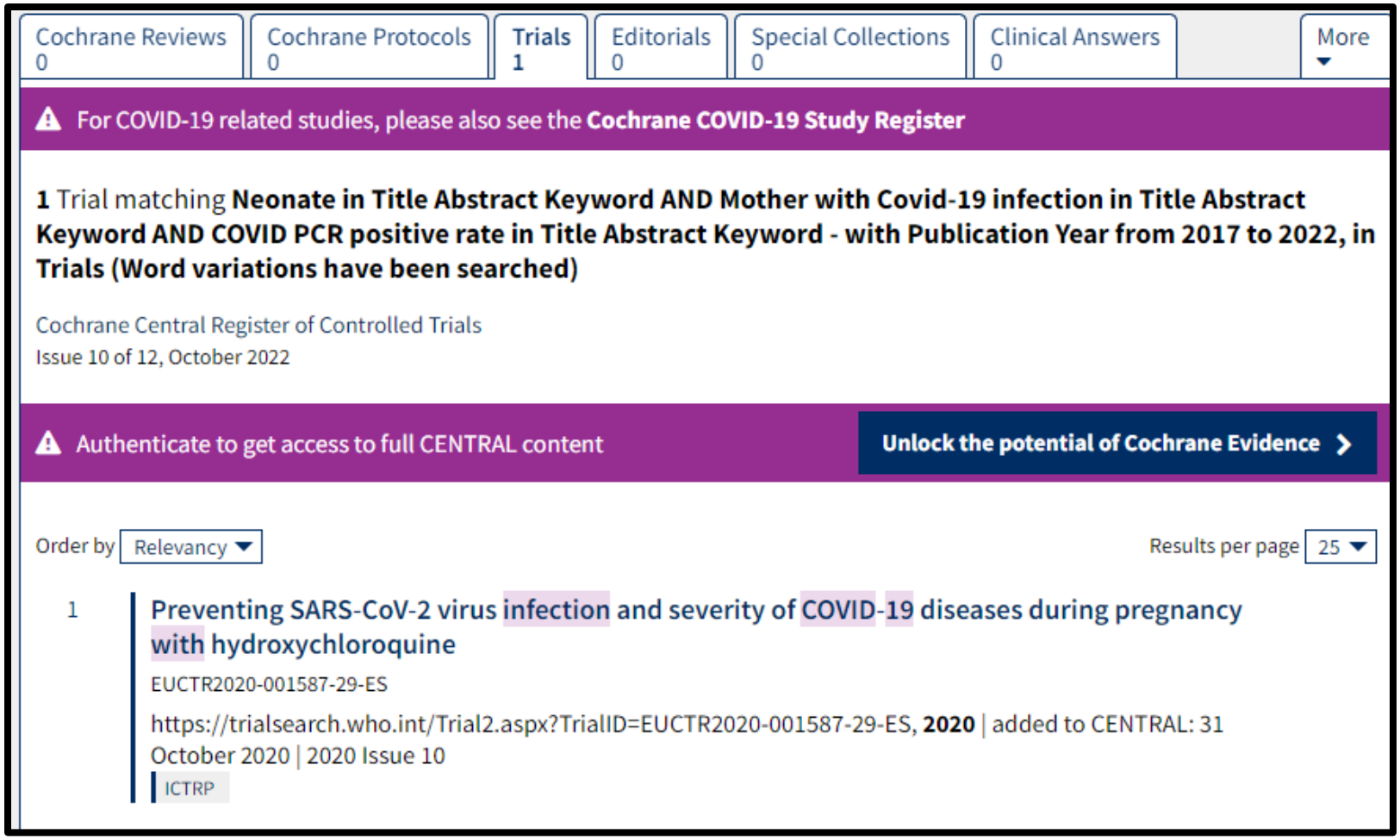
限定『2017-2022』文章

輸入關鍵字、適當使用Truncation*

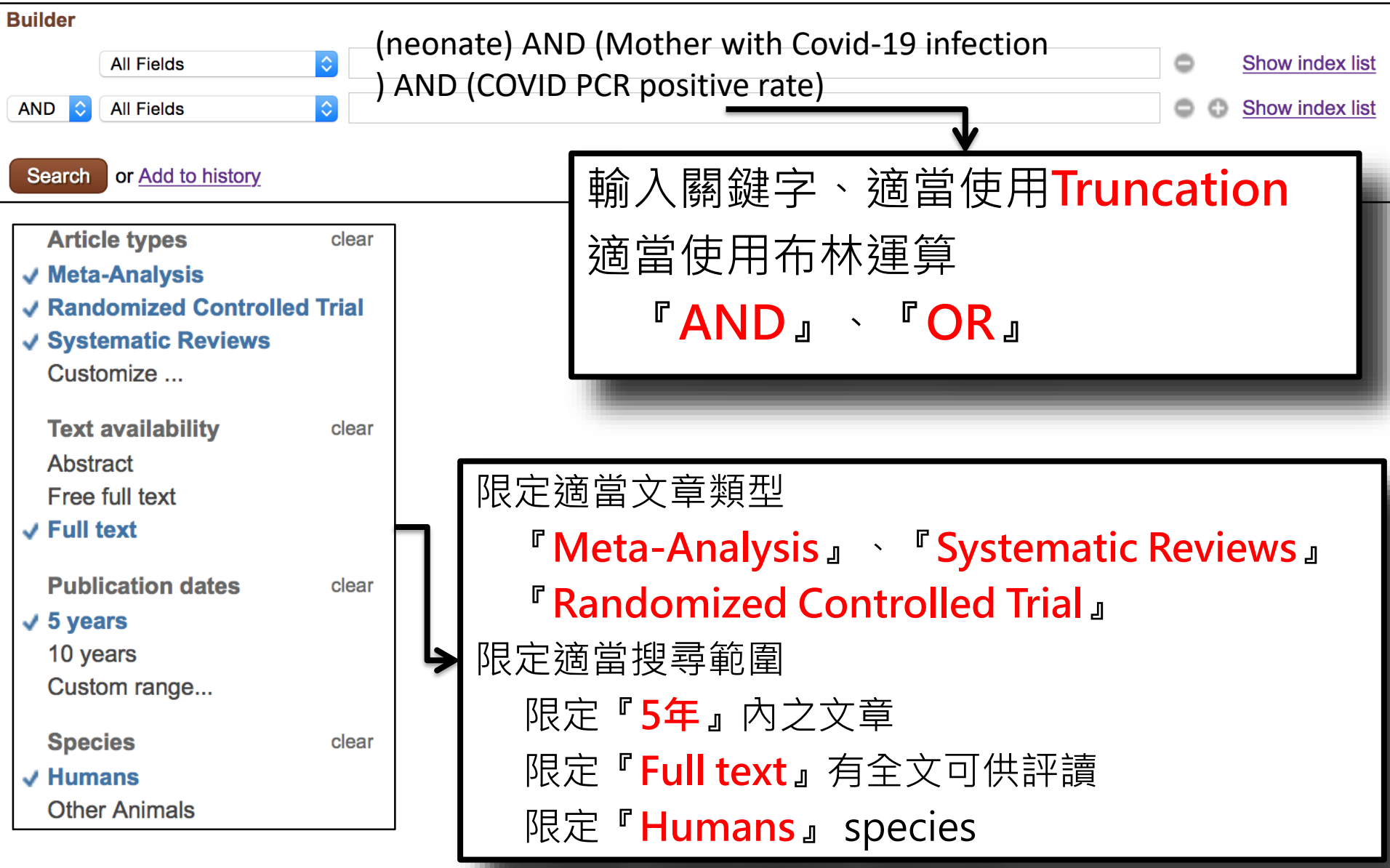
適當使用布林運算

『AND』

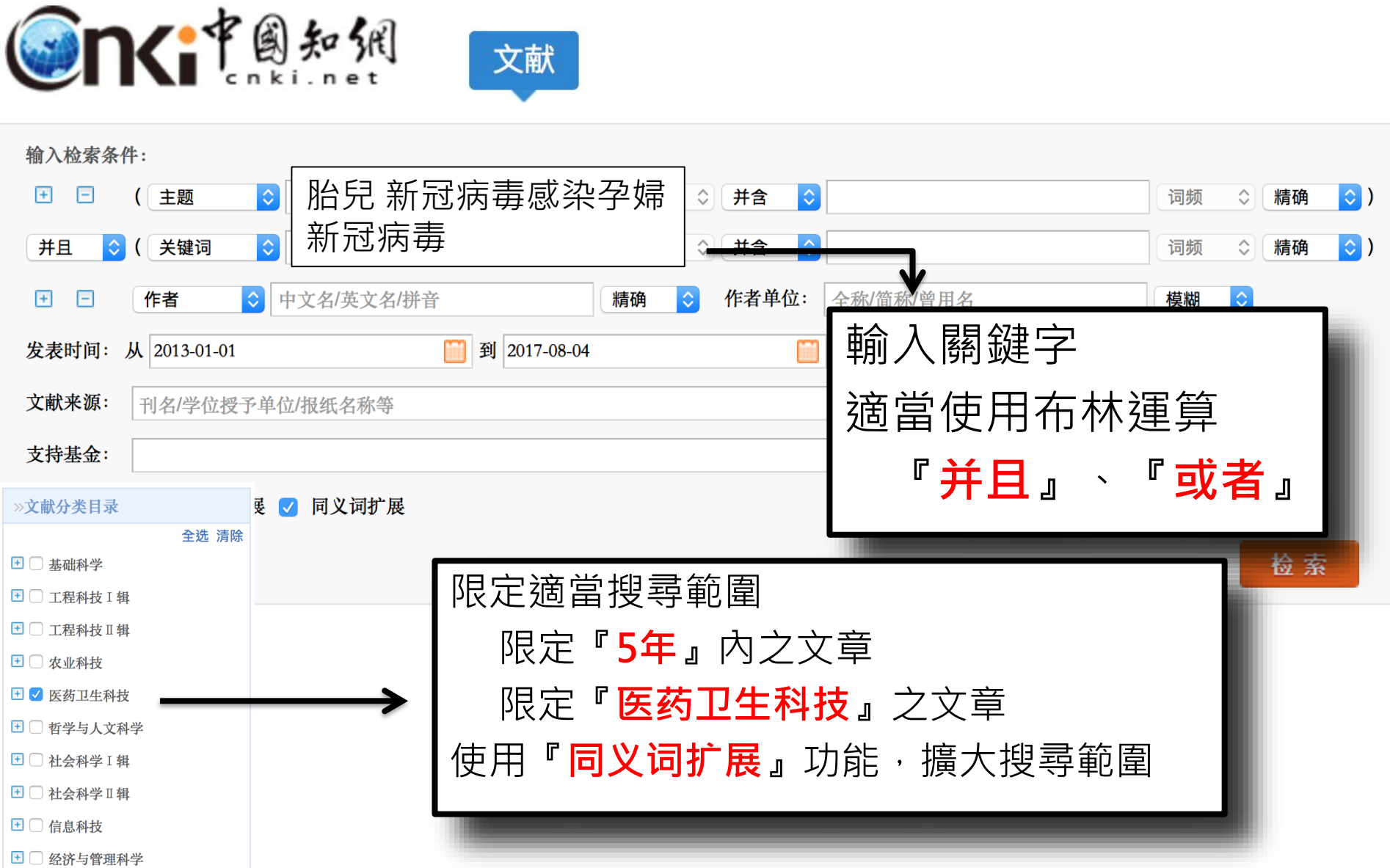
搜尋Cochrane Library-提升檢索效率



搜尋Pubmed-利用限定縮小檢索範圍



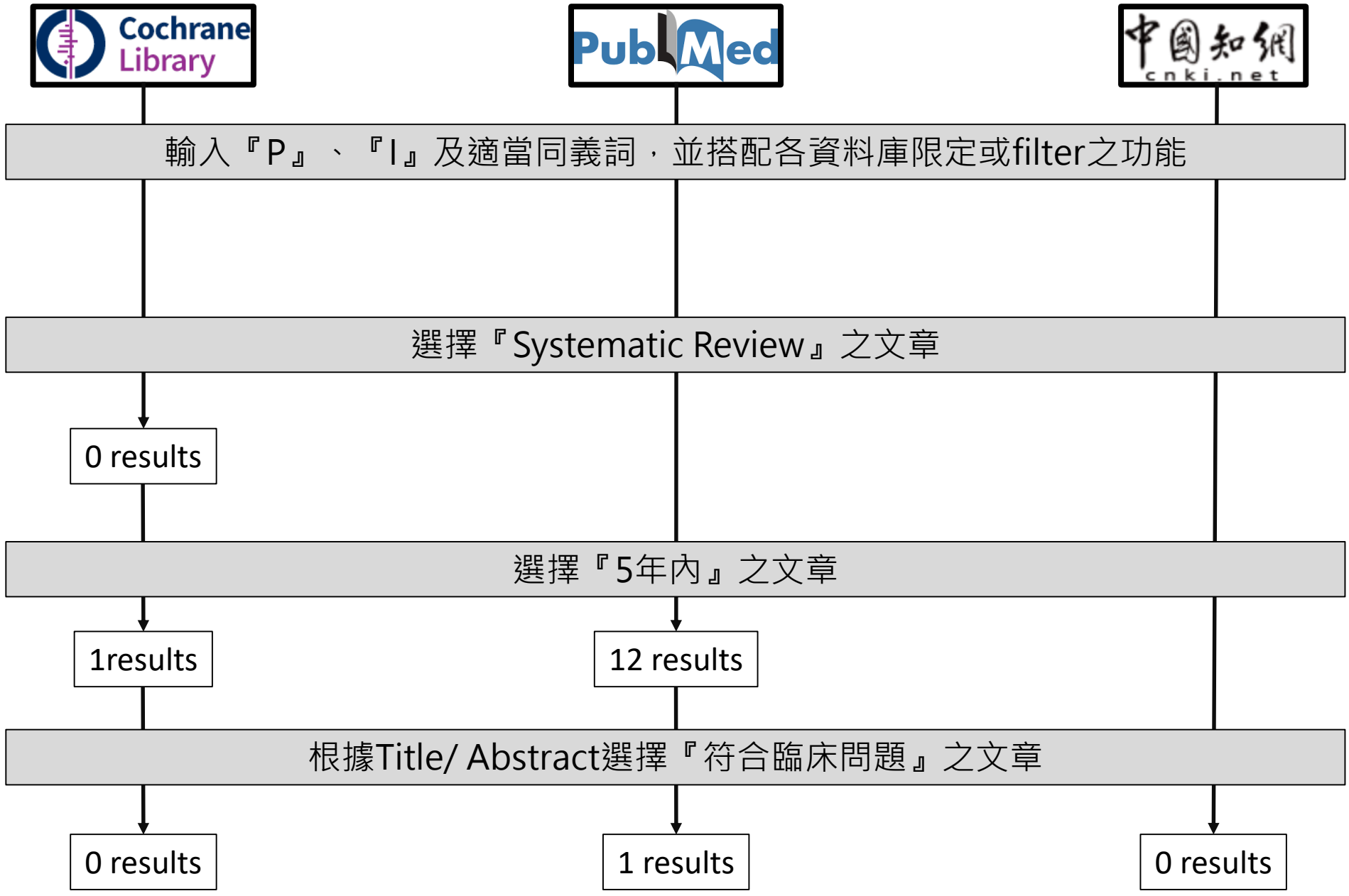
搜尋中國知網Cnki-不遺漏重要亞洲文獻



胎兒 新冠病毒感染孕婦
新冠病毒

輸入關鍵字
適當使用布林運算
『并且』、『或者』

限定適當搜尋範圍
限定『5年』內之文章
限定『医药卫生科技』之文章
使用『同义词扩展』功能，擴大搜尋範圍


Cochrane Library
PubMed
中國知網 cnki.net
輸入『P』、『I』及適當同義詞，並搭配各資料庫限定或filter之功能
選擇『Systematic Review』之文章
0 results
選擇『5年內』之文章
1results
12 results
根據Title/ Abstract選擇『符合臨床問題』之文章
0 results
1 results
0 results

比較收納文獻-選出最佳文獻，並提出我們的理由

PubMed

SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission: living systematic review and meta-analysis		
M	meta-analysis	●
P	Neonate	●
I	Mother with Covid-19 infection	●
C	Mother with No exposure	●
O	Neonate with COVID PCR positive rate	●
T	1 December 2019 and 3 August 2021.	●

嚴格評讀之文章及評讀工具

PubMed.gov

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User Guide

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☑高影響力期刊
☑最符合臨床情境

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Meta-Analysis > BMJ. 2022 Mar 16;376:e067696. doi: 10.1136/bmj-2021-067696.

SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission: living systematic review and meta-analysis

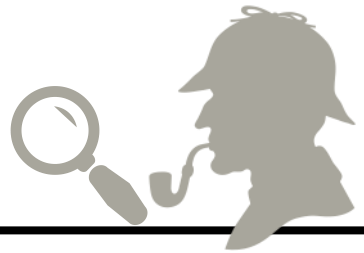
FULL TEXT LINKS

BMJ Open Access Full Text

FREE Full text PMC

ACTIONS

CASP Systematic Review Checklist



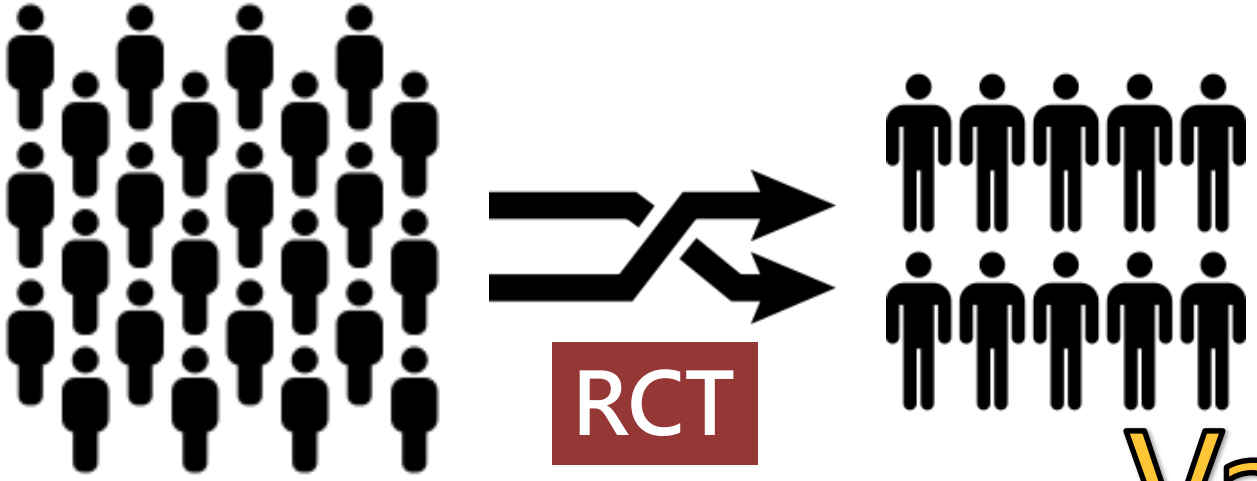
Validity

1. Did the review address a clearly focused question ?
   此回顧是否問了一個清楚、明確的臨床問題？

P	Neonate
I	Mothers with SARS-CoV-2 infection
C	Mothers with no exposure
O	Babies with SARS-CoV-2 positivity rates

作者清楚地說明了PICO，因此評讀結果為Yes。

☑Yes ☐ No ☐ Unclear



Validity

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

評讀結果

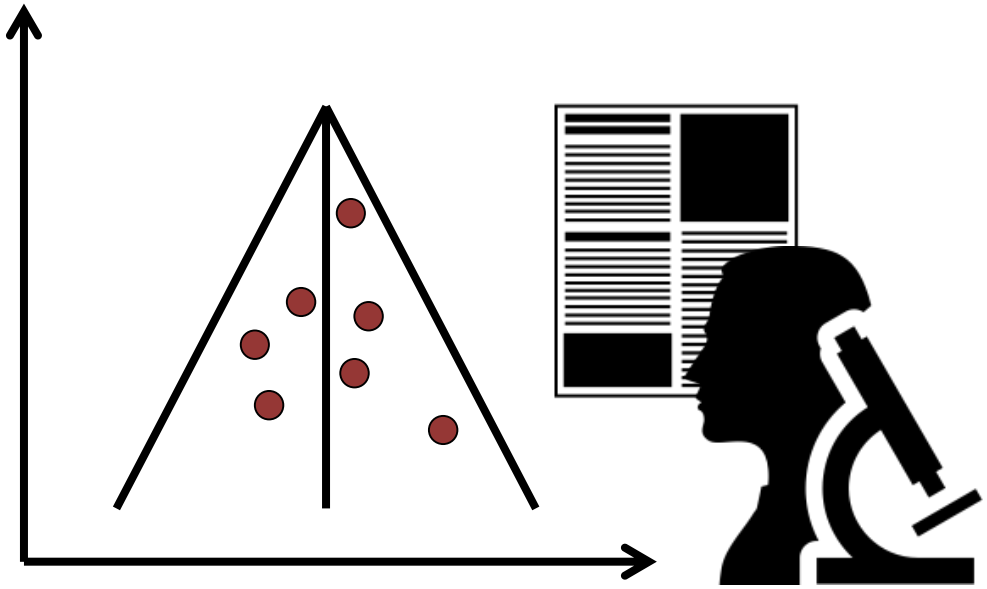
Study selection

Sixteen reviewers contributed to study selection. Two independent reviewers assessed each study using a two stage process. In the first stage, the titles and abstracts of all citations were screened and the full texts examined for inclusion in the second stage. Disagreements between reviewers were resolved through discussion with a third reviewer (ST, JA, or ES). To assess SARS-CoV-2 positivity rates in offspring, we included cohort studies of pregnant and recently pregnant women who sought hospital care for any reason and had a diagnosis of SARS-CoV-2 infection, and where SARS-CoV-2 status was ascertained in the fetus or neonate using RT-PCR (neonatal pharyngeal, rectal, or faecal swabs, neonatal or cord blood, fetal tissue, placental samples, or amniotic fluid) or serological tests (anti-SARS-CoV-2 IgM), or both. We defined cohort studies as those that sampled consecutive women, who were followed-up to ascertain the SARS-CoV-2 status of their offspring within the first 30 days after birth.[14] Unless specified otherwise, we use the term babies and offspring to denote both fetuses and neonates.

優點

1. 收錄符合治療型問題的cohort文章
2. 清楚定義了納入條件
3. 清楚定義了排除條件

☑Yes ☐ No ☐ Unclear



Validity

3. Do you think the important, relevant studies were included?
重要、相關的研究是否皆被納入？

評讀結果

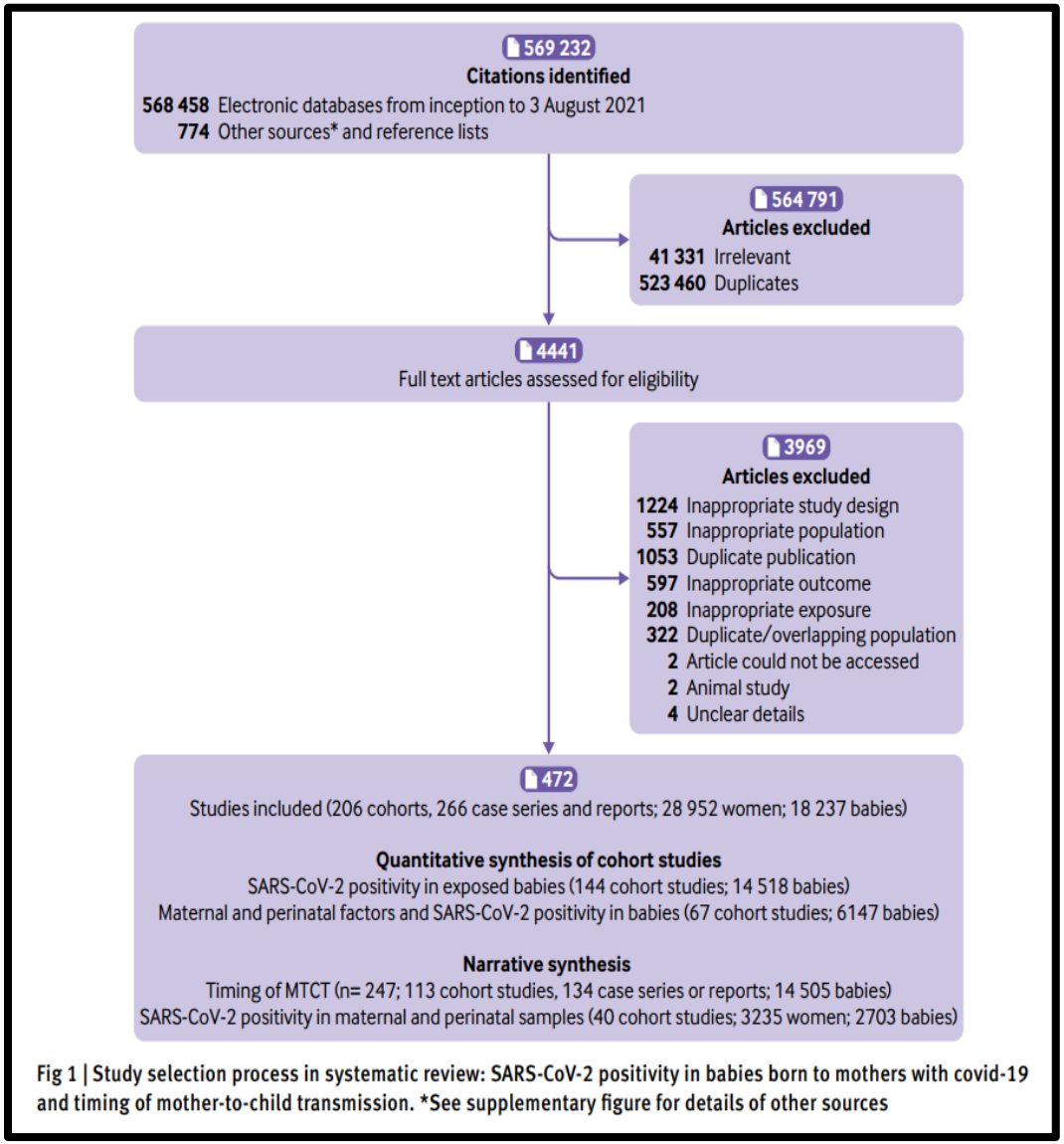
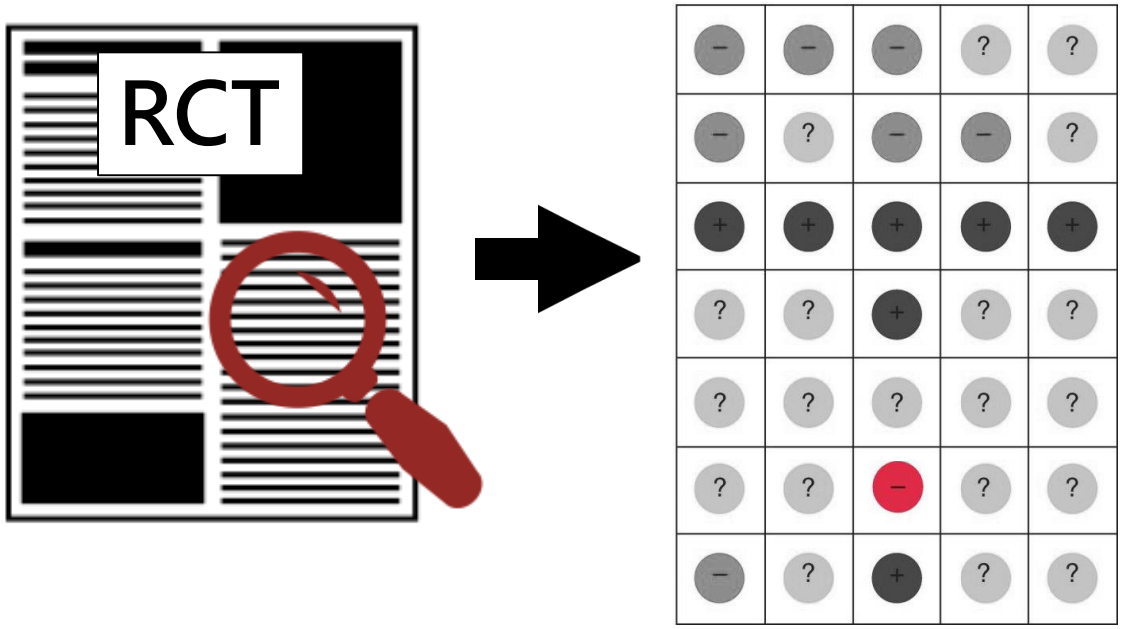


Fig 1 | Study selection process in systematic review: SARS-CoV-2 positivity in babies born to mothers with covid-19 and timing of mother-to-child transmission. *See supplementary figure for details of other sources

優點

1. 搜尋了重要一級和二級資料庫
   - Pubmed
   - EMBASE
   - CENTRAL
2. 搜尋並未限制語言
3. 列出flow chart清楚說明納入、排除理由
4. 包含歐美亞洲國家文獻

☑Yes ☑No ☑Unclear

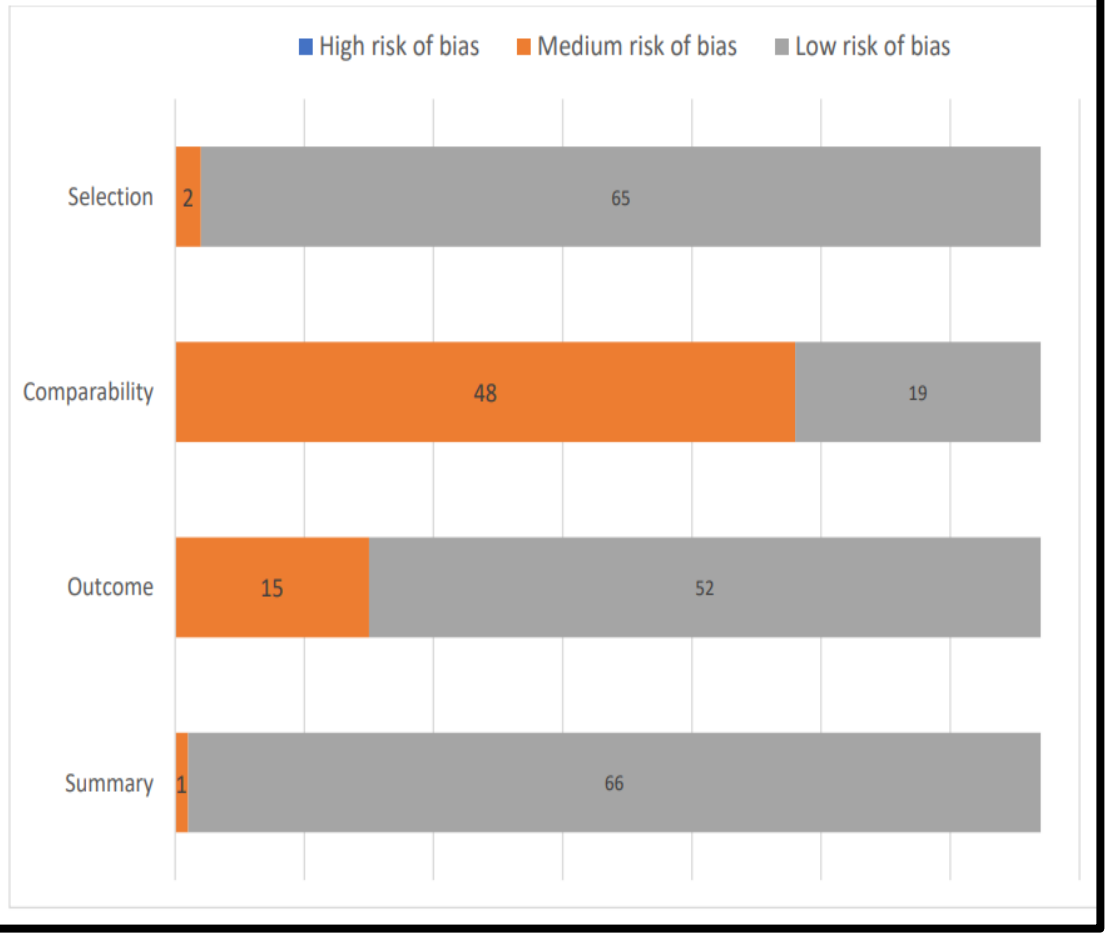


Validity

4. Did the review’ s authors do enough to assess the quality of the included studies?
作者是否有評估收納研究的品質？

評讀結果

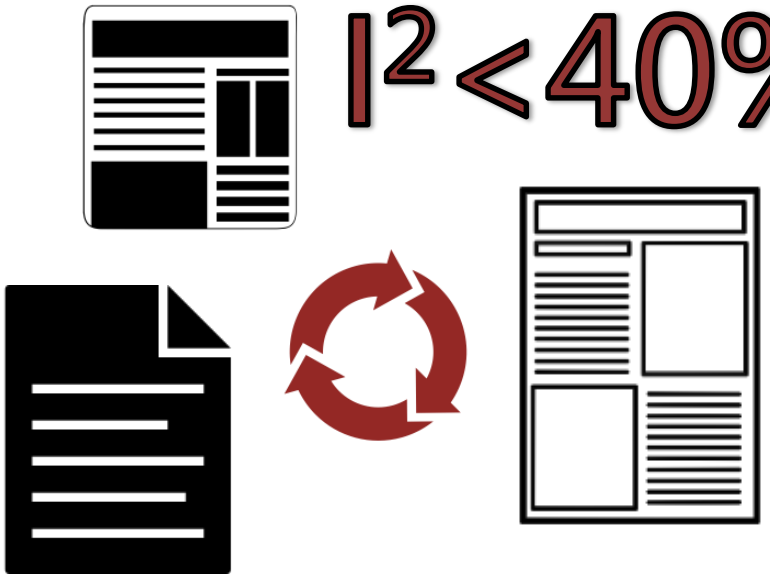
Quality assessment for risk of bias in comparative cohort studies using the Newcastle-Ottawa Scale



優點

1. 由多位作者評讀
2. 使用Newcastle-Ottawa Scale做評估cohort study之bias

☑Yes ☐ No ☐ Unclear



Validity

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？

評讀結果

Data analysis

We summarised the SARS-CoV-2 positivity rates in offspring identified by RT-PCR or anti-SARS-CoV-2 IgM assays, or both, as a proportion of all babies born to mothers with SARS-CoV-2 infection in cohort studies. After transforming data using Freeman-Tukey double arcsine transformation, we used DerSimonian and Laird random effects meta-analysis to calculate rates and corresponding 95% confidence intervals. Heterogeneity was reported as I^2 and τ^2 estimates. Sensitivity analysis for SARS-CoV-2 positivity rates in babies was done by restricting the analysis to studies at low risk of bias, babies tested at less than 24 hours after birth, and babies born to women with SARS-CoV-2 infection diagnosed antenatally. The rates of SARS-CoV-2 positivity were also evaluated by subgroups of studies involving babies and mothers from various World Bank regions.

優點

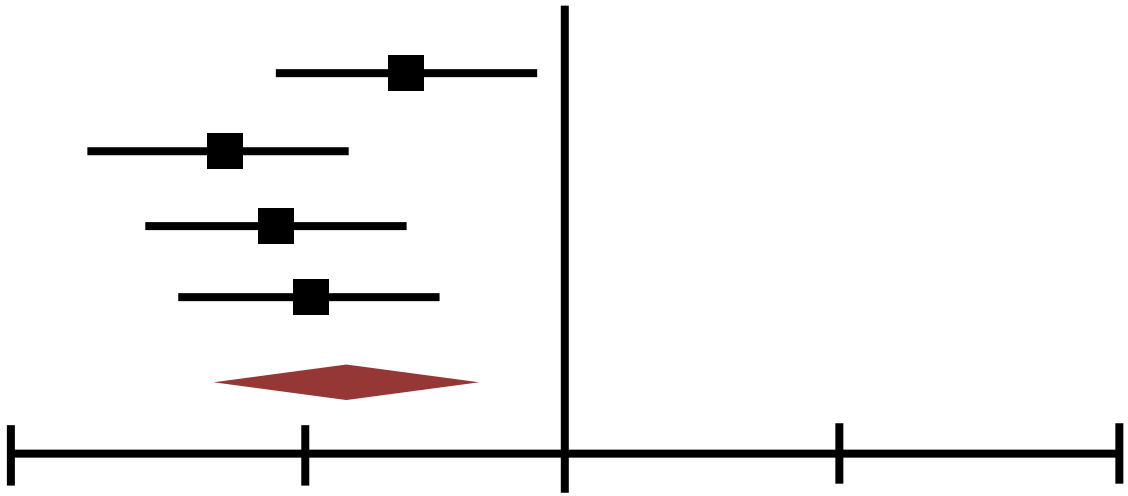
1. 有明確的定義感染時間
2. 合併時也使用random effect以及I^2來評估異質性
3. 選擇的文章亦都屬於low risk of bias文獻

☑Yes ☐ No ☐ Unclear

Appendix 3. Summary of time of sample collection, type of samples and test for categorization of timing of vertical transmission for live-born infants (a) and fetal demise (b) in women with documented SARS-CoV-2 infection

(a)

Timing of transmission and categories	Early *in utero* exposure testing							PLUS	Later exposure testing									
Time of sample collection	Birth to age <24 hours								24-48 hr	≥48 hr	24-48 hr	≥48 hr	Repeated within 10 d	24 hr-7 d	7-14 d	Repeated within 10 d	>14 d	Repeated within 10 d
Type of sample and test	Sterile sample			Non-sterile sample			Serology (IgM/IgA)		Sterile[4] sample		Non-sterile[5] sample			Serology (IgM/IgA)				
	Neonatal blood	Amniotic fluid	Lower respiratory tract[1]/CSF	Placenta RT-PCR /ISH	Placenta IHC/ microscopy	Upper respiratory tract[2]/other[3]												
***In Utero* (live birth)** (maternal infection anytime during pregnancy)																		
Confirmed	+	+	+	+		+	+		+									
Possible	+	+	+	+	+	+	+				+			+				
Unlikely	+	+	+	+	+	+	+		NEG		NEG			NEG				
	NEG	NEG	NEG	NEG	NEG	NEG	NEG		+		+			+				
Indeterminate	+	+	+	+	+	+	+		ND		ND			ND				
	ND	ND	ND	ND	ND	ND	ND				+			+				
Intrapartum (maternal infection near the time of birth)																		
Confirmed	NEG	NEG	NEG	NEG	NEG	NEG	NEG		+		+	+ to 7 d			+	+		
Possible	ND	ND	ND	ND	ND	ND	ND		+		+	+ to 7 d			+	+		
Unlikely	ND	ND	ND	ND	ND	ND	ND		+	NEG	+	NEG			+	NEG		
Early Postnatal (maternal infection near the time of birth)																		
Confirmed	NEG	NEG	NEG	NEG	NEG	NEG	NEG		NEG	+	NEG	+	+	NEG	NEG		+	+
Possible	ND	ND	ND	ND	ND	ND	ND		ND	+	ND	+	+	ND	ND		+	+
Unlikely	ND	ND	ND	ND	ND	ND	ND		ND		ND	+	NEG	ND	ND		+	NEG
Indeterminate	ND	ND	ND	ND	ND	ND	ND		ND		ND	+	ND	ND	ND		+	ND



Importance

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

主要結果- rates of sars-cov-2 positivity in babies

Test	No of studies	No of events/ No in group	Proportion (95% CI)	Proportion (95% CI)	τ^2	I^2 (%)
All babies						
RT-PCR only	140	501/14 271		1.80 (1.18 to 2.51)	0.03	77
Anti-SARS-CoV-2 IgM antibody	15	25/583		2.55 (0.52 to 5.55)	0.03	53
RT-PCR or anti-SARS-CoV-2 IgM antibody, or both	144	519/14 518		1.94 (1.31 to 2.66)	0.04	77
Timing of exposure and test						
Maternal antenatal SARS-CoV-2 infection	69	115/4643		1.34 (0.62 to 2.23)	0.02	61
Neonatal testing <24 hrs of birth	32	47/2640		0.93 (0.15 to 2.12)	0.03	66
Study quality						
High quality studies	114	253/8457		1.73 (1.07 to 2.50)	0.03	71

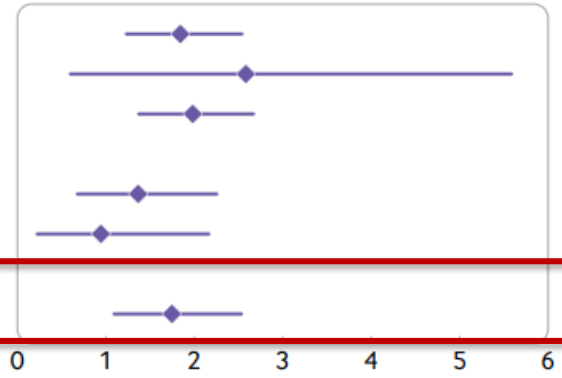


Fig 2 | Rates of SARS-CoV-2 positivity in babies (including fetuses) born to mothers seeking hospital care for any reason and having active or recently diagnosed SARS-CoV-2 infection. RT-PCR=reverse transcriptase polymerase chain reaction

評讀結果

Heterogeneity	I2=71%，屬於高異質性
Outcome	the SARS-CoV-2 RT-PCR positivity rate limited to high quality studies was 1.7% (1.1% to 2.5)
Conclusion	確診產婦之胎兒確診機率約為1.7%

次要結果

Table 3 | Maternal and perinatal factors associated with SARS-CoV-2 positivity in offspring

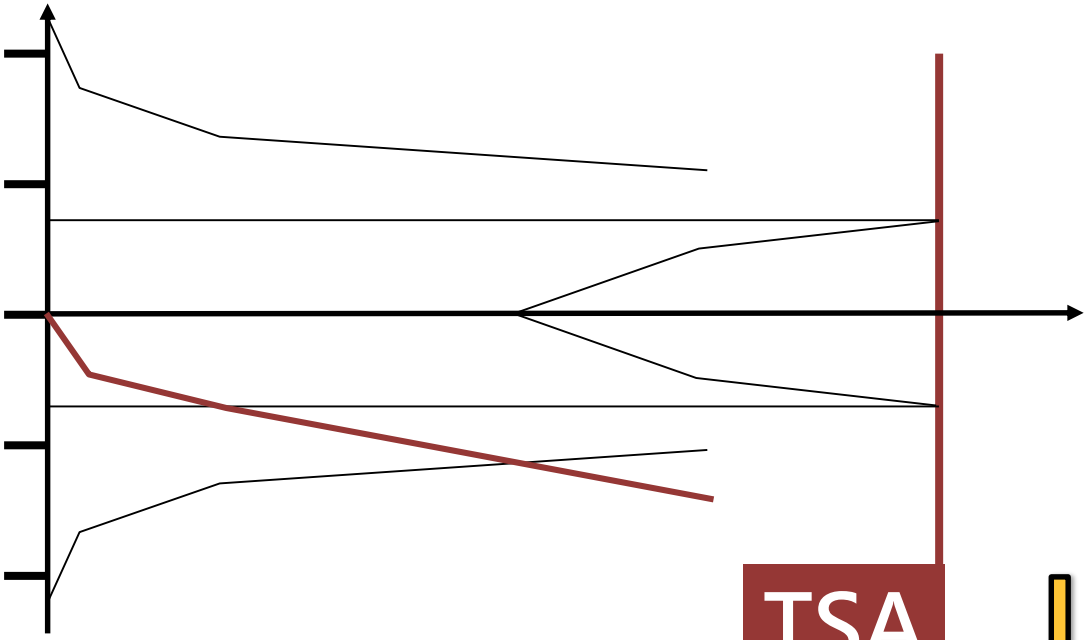
Risk factors	No of studies	No of mother-baby dyads	No of test positive babies*/ No with risk factors	No of test positive babies*/ No without risk factors	Odds ratio (95% CI)	I^2 (%)
Maternal factors						
Severe covid-19	22	2842	18/331	125/2511	2.36 (1.28 to 4.36)	10
Maternal death	7	725	6/15	28/710	14.09 (4.14 to 47.97)	0
Admission to ICU	19	2851	7/92	123/2759	3.46 (1.74 to 6.91)	0
Timing of maternal infection						
Postnatal *v* antenatal	12	750	19/122	54/628	4.99 (1.24 to 20.13)	65
3rd *v* 1st or 2nd trimester	13	1422	104/1403	2/19	0.29 (0.08 to 1.10)	0
Intrapartum factors						
Preterm *v* term	40	4126	55/618	203/3508	1.47 (0.99 to 2.17)	2
Mode of delivery	49	4814	159/2429	99/2385	1.38 (0.97 to 1.95)	18
Postnatal care						
Not separated at birth *v* separated	11	1617	42/658	48/959	1.37 (0.47 to 3.98)	64
Breastfed *v* not breastfed	13	1545	43/783	39/762	0.74 (0.34 to 1.62)	29

ICU=intensive care unit; CI=confidence interval.
*Reverse transcriptase polymerase chain reaction.

評讀結果

1. 以哺餵母乳跟感染有無關係來看，並無影響胎兒確診機率
2. 增加胎兒感染風險的risk factor為severe COVID-19, maternal death, ICU admission

☑Yes ☐ No ☐ Unclear



Importance

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

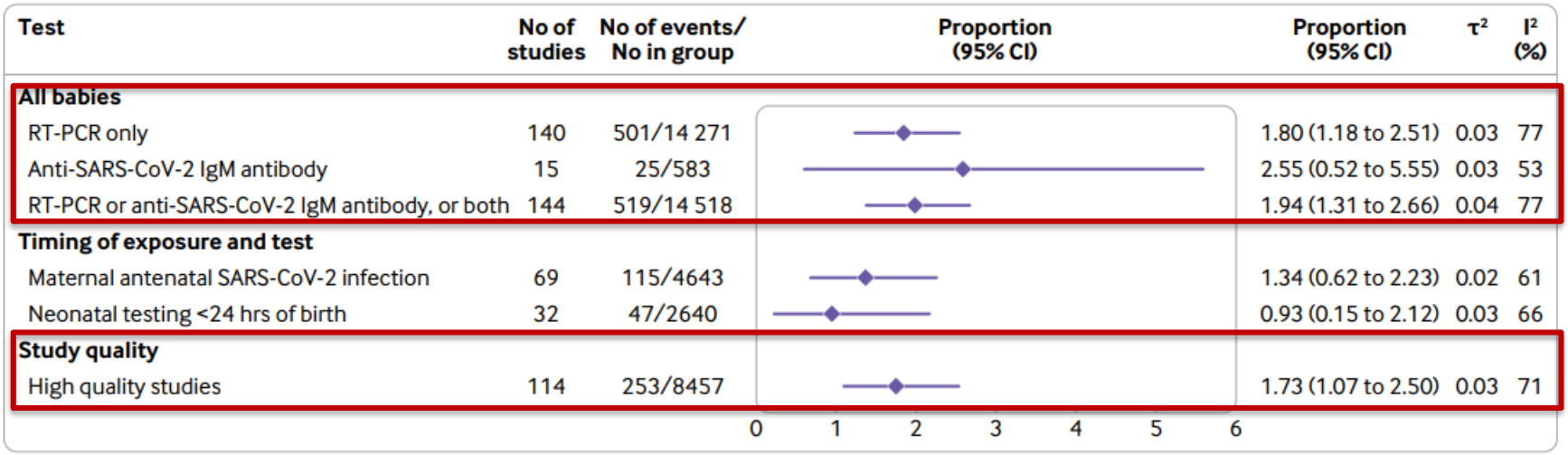


Fig 2 | Rates of SARS-CoV-2 positivity in babies (including fetuses) born to mothers seeking hospital care for any reason and having active or recently diagnosed SARS-CoV-2 infection. RT-PCR=reverse transcriptase polymerase chain reaction

Table 3 | Maternal and perinatal factors associated with SARS-CoV-2 positivity in offspring

Risk factors	No of studies	No of mother-baby dyads	No of test positive babies*/ No with risk factors	No of test positive babies*/ No without risk factors	Odds ratio (95% CI)	I^2 (%)
Maternal factors						
Severe covid-19	22	2842	18/331	125/2511	2.36 (1.28 to 4.36)	10
Maternal death	7	725	6/15	28/710	14.09 (4.14 to 47.97)	0
Admission to ICU	19	2851	7/92	123/2759	3.46 (1.74 to 6.91)	0
Timing of maternal infection						
Postnatal *v* antenatal	12	750	19/122	54/628	4.99 (1.24 to 20.13)	65
3rd *v* 1st or 2nd trimester	13	1422	104/1403	2/19	0.29 (0.08 to 1.10)	0
Intrapartum factors						
Preterm *v* term	40	4126	55/618	203/3508	1.47 (0.99 to 2.17)	2
Mode of delivery	49	4814	159/2429	99/2385	1.38 (0.97 to 1.95)	18
Postnatal care						
Not separated at birth *v* separated	11	1617	42/658	48/959	1.37 (0.47 to 3.98)	64
Breastfed *v* not breastfed	13	1545	43/783	39/762	0.74 (0.34 to 1.62)	29

ICU=intensive care unit; CI=confidence interval.
*Reverse transcriptase polymerase chain reaction.

☑ Yes ☐ No ☐ Unclear

Practice

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

Table 1 | Maternal and perinatal characteristics of babies (including fetuses) with confirmed in utero, intrapartum, and early postnatal transmission of SARS-CoV-2

	Maternal characteristics	Mode of delivery	Measures to prevent SARS-CoV-2 MTCT	Tests for SARS-CoV-2 MTCT		Fetal and neonatal characteristics
				Initial test	Further tests	
Confirmed in utero MTCT						
Live births:						
Behling 2020	Age 36 years; asymptomatic for covid-19; SARS-CoV-2 IgG positive on postnatal day 10	Operative vaginal delivery	None reported	Placenta RT-PCR positive	At autopsy, SARS-CoV-2 found in neonatal organs by nested RT-PCR	Gestational age 39 weeks; body weight 2600 g; admitted to neonatal intensive care unit owing to symptoms; died on day 4 after birth
Correia 2020	Age 40 years; pre-eclampsia and previous risk of preterm delivery; symptoms of covid-19; RT-PCR positive on nasopharyngeal swab at 34 weeks before delivery; stool RT-PCR positive	Caesarean section	Delivery in negative pressure room; no skin-to-skin contact	Blood sample and nasopharyngeal swab RT-PCR positive at 30 minutes	Deep tracheal aspirate RT-PCR positive at 48 hours, and days 9, 15, and 19; blood IgM and IgG initially negative on days 3, 7, and 11, and then positive on day 15; stool PCR positive on day 7	Gestational age 34 weeks; body weight 1510 g; Apgar score 1 and 5 minutes: 8 and 9; required positive airway pressure ventilation, admitted to neonatal intensive care unit; alive
Lima 2020*	Age 27 years, gravida 2 (para not reported); no comorbidities; flu-like symptoms at 29 weeks; rapid serological test IgM positive and IgG positive at 32 weeks	Caesarean section	Mother wore N95 mask during delivery in isolated operative room; immediate mother-baby separation; breastfed from day 7	Blood sample and nasopharyngeal swab RT-PCR positive at one hour; cord blood IgM negative but IgG positive; peripheral blood at birth IgM negative but IgG positive; placenta and amniotic fluid RT-PCR negative; chorion RT-PCR inconclusive	Blood sample and nasopharyngeal swab RT-PCR positive on day 5; nasopharyngeal swab negative on days 13 and 14	Gestational age 33 weeks; body weight 2400 g; Apgar score 1 and 5 minutes: 7 and 9; fetal echocardiogram at 32 weeks showed high risk of cardiac tamponade, leading to emergency caesarean section; prophylactic steroids given for fetal lung maturation; bag mask ventilation at birth, then transferred to neonatal intensive care unit; computed tomography scan showed some lung changes; became unstable on day 3 and was intubated; pericardial drain inserted; extubated on day 7; alive on discharge
NG DCE 2021	Age 39 years; primigravida; fever and cough; signs of pneumonia on chest radiograph; nasopharyngeal swab RT-PCR positive at 29 gestational weeks	Preterm labour, spontaneous vaginal delivery	Mother wore surgical mask during delivery; mother-baby separation at birth	Nasopharyngeal swab RT-PCR positive at 2 hours; blood sample IgM and IgG negative at birth	Tracheal aspirate RT-PCR positive at 26 hours; blood sample IgM and IgG positive on day 14	Gestational age 29 weeks; body weight 1100 g; Apgar score 1 and 5 minutes: 9 and 9; symptoms present; respiratory distress, required non-invasive continuous positive airway pressure ventilation; bilateral ground glass opacities on computed tomography scan; alive
Fetal death:						
Rodrigues 2020	Age 19 years; no medical history; nasopharyngeal swab RT-PCR positive just before delivery; asymptomatic	Vaginal delivery (stillbirth)	None	Fetal tissues RT-PCR positive at autopsy		No fetal heartbeat at 34 weeks; small for gestational age (third centile); body weight 1460 g
Valdespino-Vazquez 2020 (twins)	Age 28 years; gravida 4 para 3; fever, headache, arthralgia, fatigue at 13 weeks, and also dark vaginal bleeding; nasopharyngeal swab initially RT-PCR negative but became positive	Vaginal delivery (miscarriage)	None reported	Fetal organs RT-PCR and immunofluorescence positive in both fetuses; fetus 1 electron microscopy positive in lung	Placenta RT-PCR positive; electron microscopy positive; immunofluorescence positive in both placentas	Gestational age 13 weeks; diamniotic twin pregnancy, no heartbeat in both at 13 weeks. Twin 1: length 12, body weight 37 g. Twin 2: severely macerated
Confirmed intrapartum MTCT						
Zeng 2020 (baby 1; baby 2)	Nasopharyngeal swab RT-PCR positive just before delivery; fever and pneumonia (computed tomography scan); not admitted to intensive care unit; no information on maternal characteristics	Caesarean section	Mother-baby separation at birth; not breastfed	Amniotic fluid and cord blood RT-PCR negative	Nasopharyngeal swab RT-PCR positive on days 2 and 4	Gestational age 40 weeks. Baby 1: body weight 3250 g; lethargy, fever; pneumonia on chest radiograph; admitted to neonatal intensive care unit; alive. Baby 2: body weight 3360 g; lethargy, vomiting, fever; pneumonia on chest radiograph; alive

Table 1 | Continued

	Maternal characteristics	Mode of delivery	Measures to prevent SARS-CoV-2 MTCT	Tests for SARS-CoV-2 MTCT		Fetal and neonatal characteristics
				Initial test	Further tests	
Confirmed early postpartum MTCT						
Bastug 2020	Age 20 years; gravida 2 para 2, covid-19 diagnosed at 39 weeks, asymptomatic; nasopharyngeal swab RT-PCR positive just before delivery; breast milk RT-PCR positive	Vaginal delivery	Mother wore mask during delivery and when expressing breast milk; neonate separated from mother after birth and given expressed breast milk	Nasopharyngeal swab RT-PCR negative on day 1	Peripheral blood RT-PCR positive on day 4	Gestational age 39 weeks; body weight 2980 g; admitted to neonatal intensive care unit; asymptomatic; alive
Demirjian 2020	Age 34 years; gravida 3 para 2, covid-19 diagnosed at 38 weeks; severe symptoms of increasing dyspnoea requiring intubation in intensive care unit; sputum RT-PCR positive just before delivery; maternal blood RT-PCR positive	Caesarean section	Mother-baby separation at birth; formula fed exclusively	Nasopharyngeal swab and rectal, peripheral blood, and cerebrospinal fluid samples RT-PCR negative on day 1	Nasopharyngeal swab RT-PCR positive on days 4 and 8; rectal and peripheral blood samples RT-PCR positive on day 7 (rectal sample RT-PCR negative on day 4 and peripheral blood sample RT-PCR negative on day 5	Gestational age 39 weeks; body weight 4170 g; Apgar score 1, 5, and 10 minutes: 5, 9, and 9; fever, coryza, and mild tachypnoea; alive
Gordon 2020	Age 36 years; gravida 3 para 0; covid-19 diagnosed at 32 weeks; cough, high fever, and lymphopenia; nasopharyngeal swab RT-PCR positive just before delivery	Caesarean section	Mother wore mask during delivery; neonate separated from mother after birth	Nasopharyngeal swab RT-PCR negative on day 1	Nasopharyngeal swab RT-PCR positive on days 4 and 14 (with further positive test results on days 21 and 29)	Gestational age 32 weeks; body weight 2150 g; alive; radiography findings consistent with surfactant deficiency lung disease
Komiazyk 2020	Age 28 years; asymptomatic; nasopharyngeal swab RT-PCR positive just before delivery (results known after delivery)	Vaginal delivery	Skin-to-skin contact; mother-baby separation later when maternal RT-PCR result was known	Nasopharyngeal swab RT-PCR negative on day 1	Nasopharyngeal swab RT-PCR positive on days 5 and 10	Gestational age 40 weeks; Apgar score 10; asymptomatic; alive
Yu 2020	Gravida 1 para 0, symptomatic, covid-19 diagnosed at 38 weeks; nasopharyngeal swab RT-PCR positive on postnatal day 1	Caesarean section	Neonate in room with mother; not breastfed	Cord blood sample RT-PCR negative	Nasopharyngeal swab RT-PCR positive on days 7 and 15	Gestational age 38 weeks; body weight 3600 g; Apgar score "normal"; fever; chest radiograph showed diffuse consolidation; alive

MTCT=mother-to-child-transmission (according to World Health Organization classification); RT-PCR=reverse transcriptase polymerase chain reaction.
*Classified as "confirmed" in utero as tests were repeated <24 hours, despite not meeting WHO criteria of positive test result at 24-48 hours.

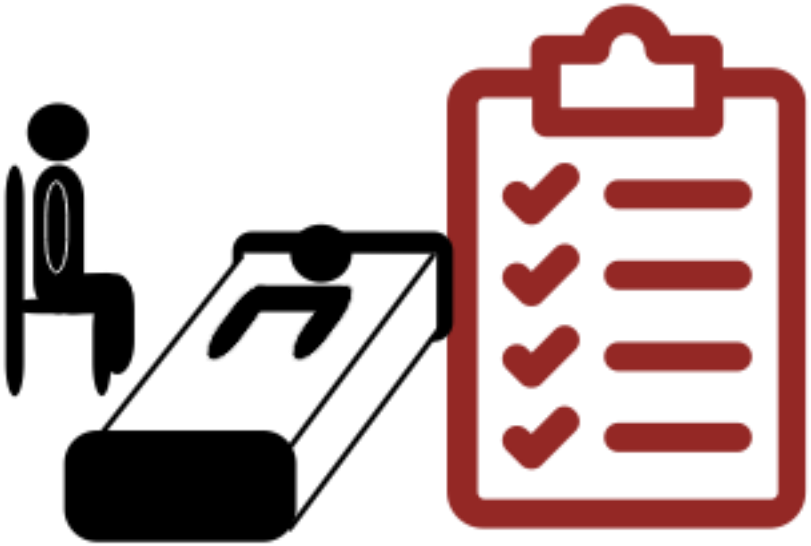
included studies were from the World Bank regions of Europe and Central Asia (145/472, 31%) and North America (87/472, 18%), followed by East Asia and Pacific (73/472, 15%), Middle East and North Africa (60/472, 13%), Latin America and the Caribbean (51/472, 11%), and South Asia (51/472, 11%), and five studies were from Sub-Saharan Africa (5/472, 1%).

評估適用性-比較評讀文獻及臨床情境

	評讀文獻	臨床情境
P	• Neonate	• Neonate
I	• Mother with Covid-19 infection	• Mother(39weeks) with Covid-19 infection
C	• Mother with no exposure	• Mother with no exposure
O	• Neonate with COVID PCR positive rate	• Neonate with COVID PCR positive rate

1. 我們的病患與文獻研究是否相似？ ☑年齡 ☑性別 ☑種族 ☑共病 ☑同時服用其他治療藥物 ☑疾病嚴重度	**是**
2. 這項暴露跟檢測在台灣是否可行？	**可**

☑Yes ☐ No ☐ Unclear



Practice

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

	重要臨床結果	評讀之文獻
傳播途徑	In utero transmission	✓
傳播途徑	Intrapartum exposure	✓
傳播途徑	Early postnatal exposure	✓
傳播時間點	Postnatal v antenatal	✓
傳播時間點	3rd v 1st or 2nd trimester	✓
Postnatal care	Not separated at birth *v* separated	✓
Postnatal care	Breastfed *v* not breastfed	✓

	重要臨床結果	評讀之文獻
Maternal factors	Severe covid-19	✓
Maternal factors	Maternal death	✓
Maternal factors	Admission to ICU	✓
intrapartum factors	Preterm v term	✓
intrapartum factors	Mode of delivery	✓

☑Yes ☐ No ☐ Unclear

Practice

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 ☑ Unclear

評定證據等級-OCEBM Level of Evidence, 2011

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	nception 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	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided	Case-series, case-control, or historically controlled	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Rando or (ex			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Rando			

【預後型問題】

cohort之系統性回顧文章

證據等級為 **Level 1**

※經嚴格評讀，無其他需要考慮降階理由

考慮降階之理由

- ☐研究品質差
- ☐絕對效果小
- ☐PICO和臨床情境不相符
- ☐證據間沒有一致性
- ☐研究不精確(95%CI過大)

評定證據等級-GRADEpro online

● 不嚴重　● 嚴重　● 很嚴重

臨床問題:

		『主要』結果	『次要』結果
		SMD(95%CI) 1.8[1.2,2.5]	OR(95%CI) 0.74 %[0.34,1.62]
研究設計		Observational study	Observational study
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	●	●
升階	1. 效果顯著		
	2. 降低干擾因素		
	3. 具劑量-反應效果		
證據等級		⊕⊕⊕⊕ HIGH	⊕⊕⊕⊕ HIGH

Reference: GRADEpro GDT

臨床應用-回覆病人問題

您好，經過我們專業團隊的實證查證結果，目前有2022年的系統性回顧文獻支持。確診的媽媽還是會有機會傳染給寶寶，而哺乳則不會提高確診的風險。因此建議如果需要哺乳仍能在做好保護措施的情況下哺育母乳。

感謝各位評審聆聽！