



JAMA The Journal of the
American Medical Association

Efficacy and Safety of Umbilical Cord Milking at Birth: A Systematic Review and Meta-analysis

早產兒出生時要擠壓臍帶嗎？

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日期：105年1月26日

Rank in Category: JAMA Pediatrics

Journal Ranking ⓘ

In 2014, the journal **JAMA Pediatrics** has an Impact Factor of **7.148**.

This table shows the ranking of this journal in its subject categories based on Impact Factor.

Category Name	Total Journals in Category	Journal Rank in Category	Quartile in Category
PEDIATRICS	120	2	Q1

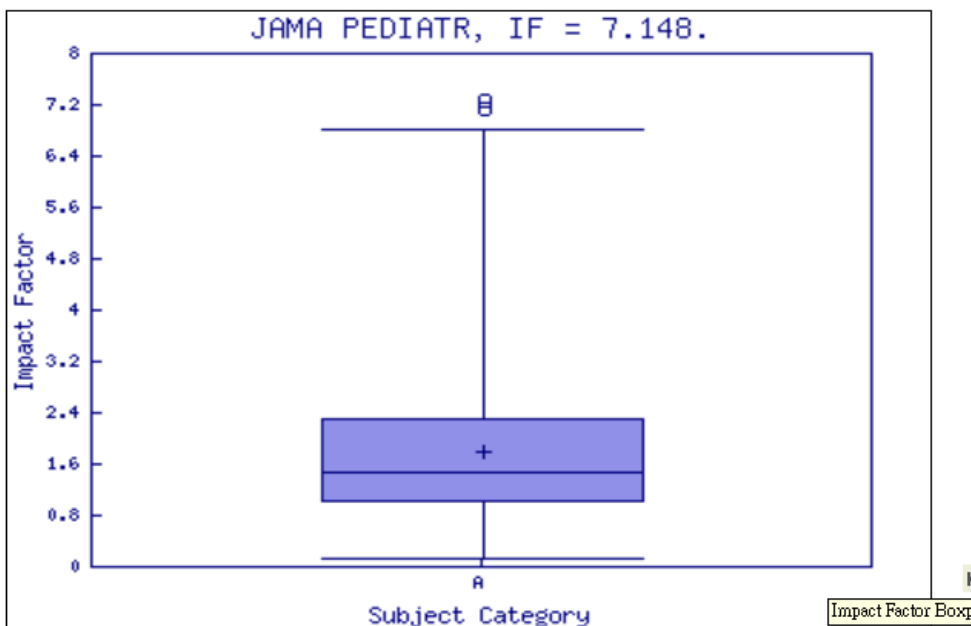
Category Box Plot ⓘ

In 2014, the journal **JAMA Pediatrics** has an Impact Factor of **7.148**.

This is a box plot of the subject category or categories to which the journal has been assigned. It provides information about the distribution of journals based on Impact Factor values. It shows median, 25th and 75th percentiles, and the extreme values of the distribution.

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介紹

Background

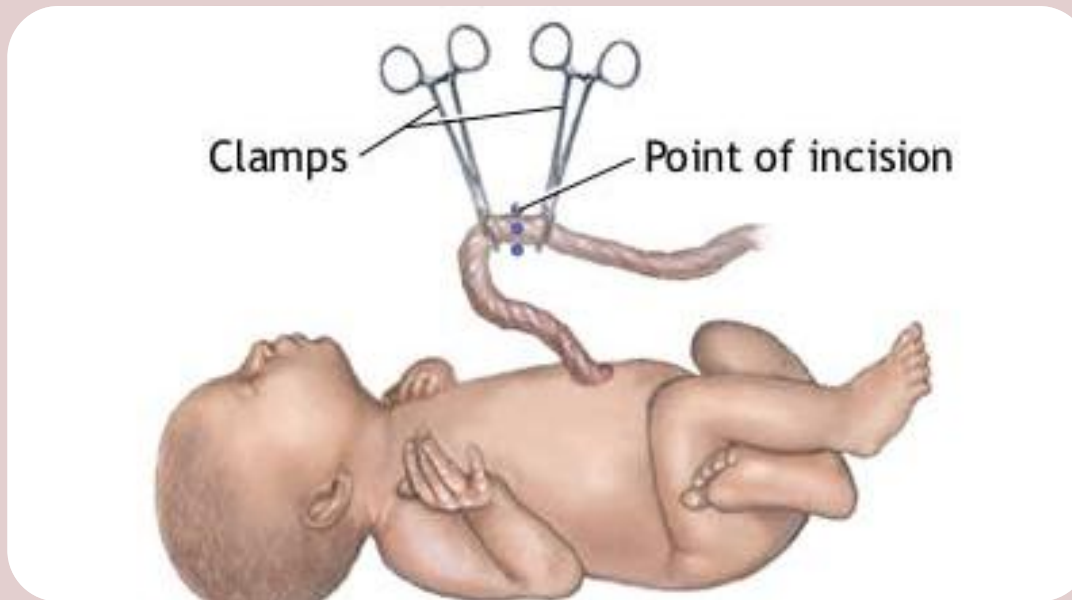
- Umbilical cord milking (UCM) is suspected to improve neonatal outcomes.
- Methodological limitations of older studies hindered the adoption of UCM as a standard of care.
- Difference between delayed cord clamping (DCC) and UCM:
 - DCC: passive transfer of additional blood volume occurs at a slow rate.
 - UCM: an active transfer of additional blood at a rapid rate and within a short time.

Study Objective

- To perform a systematic review and meta-analysis of the efficacy and safety of UCM in full-term and preterm neonates.

步驟 1: 系統性文獻回顧探討的問題為何? -1

p	2 populations (gestational age <33 and $\geq$ 33 weeks, full-term and preterm infants) handling the umbilical cord at birth
i	umbilical cord milking (UCM)
C	including immediate cord clamping (ICC), delayed cord clamping (DCC), or no intervention



步驟 1: 系統性文獻回顧探討的問題為何? -2

Primary and Secondary outcome

- 出生時狀況
 - 臍動脈pH值、1分鐘及5分鐘Apgar Score
- 血液系統
 - 出生48小時內血比容和血紅素值
 - 出院前需要輸血PPRBC
 - 出院前最高血清膽紅素值
 - 高膽紅素血症需要照光、紅血球增多症
 - 3至6個月的血紅素和血鐵蛋白
- 短期併發症
 - 呼吸窘迫徵候群
 - 出生24小時低血壓requiring volume or inotrope support.
 - 所有等級的腦室出血
 - 28天至36週 (矯正週數) 氧氣依賴程度
 - stage II or III 壞死性小腸結腸炎
 - 晚發性敗血症、動脈導管未關閉、早產兒視網膜病變
- 18至24個月神經發育結果

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？

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)。

- Published RCTs were identified using manual and electronic search strategies.
- This search was applied to **MEDLINE** (1946 to April 2014), **EMBASE** (1980 to April 17, 2014), **CINAHL** (1982 to April 2014), and the **Cochrane** Central Register of **Controlled Trials** (April 2014) (eMethods in the Supplement).
- We also searched the **online meta-register** of Current Controlled Trials for relevant ongoing clinical trials (April 2014).
- Additional citations were sought by **hand searching** the reference list of the retrieved articles.

步驟 2: 系統性文獻回顧的品質如何? (FAITH)

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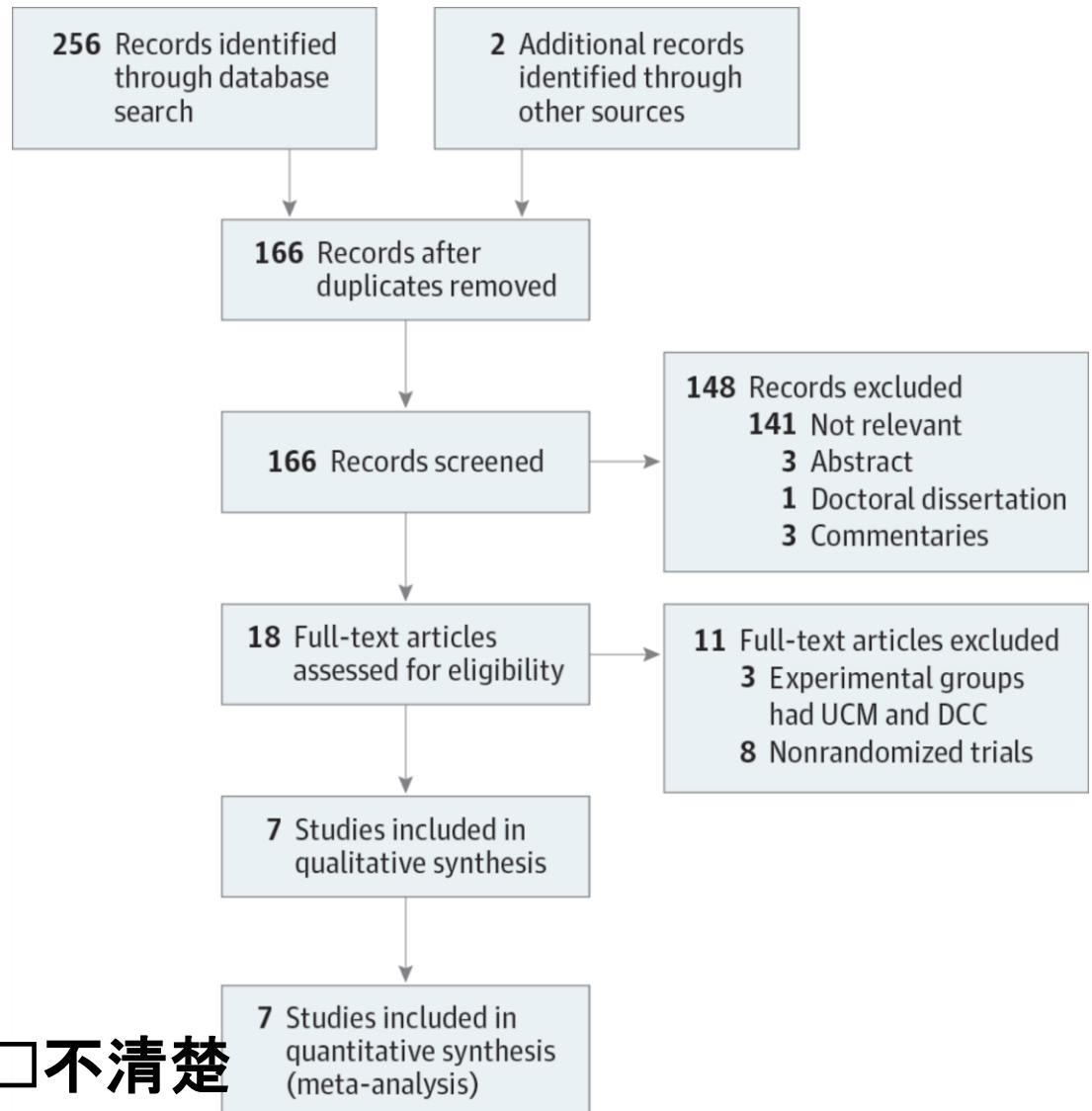
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Search strategy

- A combination of text words and exploded medical subject headings were used to maximize the volume of literature retrieved.
- To identify the intervention of interest, we used the **Boolean search term** “or” to explode (search by subject heading) and map (search by keyword) the medical subject headings “**stripping**” or “**milking**” or “**squeezing**”.
- The same Boolean search term was used to explode and map the medical subject headings “**umbilicus**” or “**umbilical cord**” or “**cord**”.
- The 2 Boolean searches were then combined using the Boolean term “and”. Searches were **limited to human infants** but were **not limited by language** or type of study to maximize our results.
- Outcome was not specified in our search to capture all potential studies that evaluated the strategy of umbilical cord milking.

步驟 2: 系統性文獻回顧的品質如何? (FAITH)



評讀結果: ☒ 是 ☐ 否 ☐ 不清楚

步驟 2: 系統性文獻回顧的品質如何? (FAITH)

A—文獻是否經過嚴格評讀 (Appraisal) ?

最好的狀況是？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)

- Both reviewers independently assessed the risk for bias in each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.
- Any disagreements were resolved by discussion and consensus.
- The risk for bias was assessed using the following key criteria: sequence generation, allocation concealment, blinding of assessors, and attrition bias.
- We assessed each criterion as having a low, high, or unclear risk for bias.
- An overall risk for bias was determined for each study according to the criteria suggested by Higgins and Green.

評讀結果: ☒是 ☐否 ☐不清楚

步驟 2: 系統性文獻回顧的品質如何? (FAITH)

eTable. Risk for bias in included studies

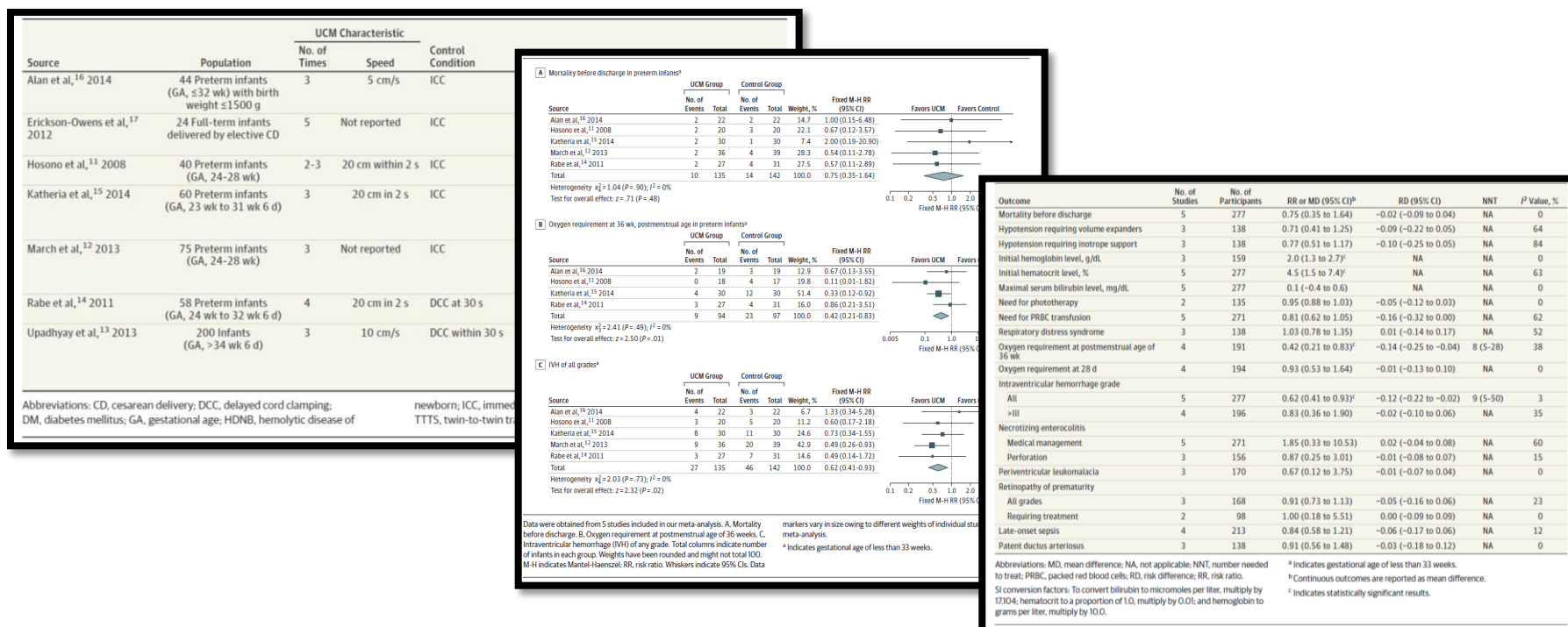
	Random Sequence Generation	Allocation Concealment	Blinding	Incomplete Outcome Data	Selective Reporting	Other Biases
Alan et al, ¹ 2014	Unclear	Low	Low	Low	Low	Low
Erickson-Owens et al, ² 2012	Unclear	Unclear	Low	Low	Low	Unclear
Hosono et al, ³ 2008	Low	Low	Low	Low	Low	Low
Katheria et al, ⁴ 2014	Unclear	Low	Low	Low	Low	Low
March et al, ⁵ 2013	Low	Low	Low	Low	Low	Low
Rabe et al, ⁶ 2011	Low	Low	Low	Low	Low	Low
Upadhyay et al, ⁷ 2013	Low	Low	Low	Low	Low	Low

評讀結果: ☒是 ☐否 ☐不清楚

步驟 2: 系統性文獻回顧的品質如何? (FAITH)

T一作者是否以表格和圖表「總結」(total up) 試驗結果?

最好的狀況是? 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。



評讀結果: ■是 □否 不清楚

步驟 2: 系統性文獻回顧的品質如何? (FAITH)

H—試驗的結果是否相近—異質性 (Heterogeneity) ?

最好的狀況是？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。

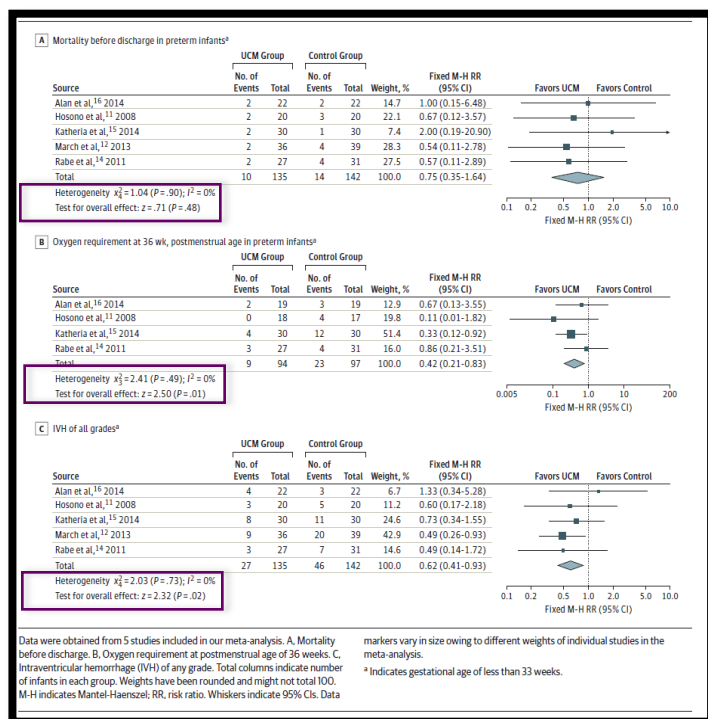


Table 2. Comparison of Umbilical Cord Milking vs Control Intervention in Preterm Infants^a

Outcome	No. of Studies	No. of Participants	RR or MD (95% CI) ^b	RD (95% CI)	NNT	I ² Value, %
Mortality before discharge	5	277	0.75 (0.35 to 1.64)	-0.02 (-0.09 to 0.04)	NA	0
Hypotension requiring volume expanders	3	138	0.71 (0.41 to 1.25)	-0.09 (-0.22 to 0.05)	NA	64
Hypotension requiring inotrope support	3	138	0.77 (0.51 to 1.17)	-0.10 (-0.25 to 0.05)	NA	84
Initial hemoglobin level, g/dL	3	159	2.0 (1.3 to 2.7) ^c	NA	NA	0
Initial hematocrit level, %	5	277	4.5 (1.5 to 7.4) ^c	NA	NA	63
Maximal serum bilirubin level, mg/dL	5	277	0.1 (-0.4 to 0.6)	NA	NA	0
Need for phototherapy	2	135	0.95 (0.88 to 1.03)	-0.05 (-0.12 to 0.03)	NA	0
Need for PRBC transfusion	5	271	0.81 (0.62 to 1.05)	-0.16 (-0.32 to 0.00)	NA	62
Respiratory distress syndrome	3	138	1.03 (0.78 to 1.35)	0.01 (-0.14 to 0.17)	NA	52
Oxygen requirement at postmenstrual age of 36 wk	4	191	0.42 (0.21 to 0.83) ^c	-0.14 (-0.25 to -0.04)	8 (5-28)	38
Oxygen requirement at 28 d	4	194	0.93 (0.53 to 1.64)	-0.01 (-0.13 to 0.10)	NA	0
Intraventricular hemorrhage grade						
All	5	277	0.62 (0.41 to 0.93) ^c	-0.12 (-0.22 to -0.02)	9 (5-50)	3
>III	4	196	0.83 (0.36 to 1.90)	-0.02 (-0.10 to 0.06)	NA	35
Necrotizing enterocolitis						
Medical management	5	271	1.85 (0.33 to 10.53)	0.02 (-0.04 to 0.08)	NA	60
Perforation	3	156	0.87 (0.25 to 3.01)	-0.01 (-0.08 to 0.07)	NA	15
Periventricular leukomalacia	3	170	0.67 (0.12 to 3.75)	-0.01 (-0.07 to 0.04)	NA	0
Retinopathy of prematurity						
All grades	3	168	0.91 (0.73 to 1.13)	-0.05 (-0.16 to 0.06)	NA	23
Requiring treatment	2	98	1.00 (0.18 to 5.51)	0.00 (-0.09 to 0.09)	NA	0
Late-onset sepsis	4	213	0.84 (0.58 to 1.21)	-0.06 (-0.17 to 0.06)	NA	12
Patent ductus arteriosus	3	138	0.91 (0.56 to 1.48)	-0.03 (-0.18 to 0.12)	NA	0

評讀結果: ■是 □否 不清楚

研究結果

Table 1. Characteristics of the Included Studies

Source	Population	UCM Characteristic		Control Condition	Exclusion Criteria
		No. of Times	Speed		
Alan et al, ¹⁶ 2014	44 Preterm infants (GA, ≤ 32 wk) with birth weight ≤ 1500 g	3	5 cm/s	ICC	Suspected TTTS or discordant twin, major congenital and chromosomal anomalies, vaginal bleeding, HDNB or hydrops fetalis, IUGR, maternal DM treated with insulin
Erickson-Owens et al, ¹⁷ 2012	24 Full-term infants delivered by elective CD	5	Not reported	ICC	Maternal medical or obstetric complications, maternal severe anemia or clotting disorders, suspected IUGR, smoking, congenital anomalies
Hosono et al, ¹¹ 2008	40 Preterm infants (GA, 24-28 wk)	2-3	20 cm within 2 s	ICC	Multiple births, major congenital anomalies, hydrops fetalis
Katheria et al, ¹⁵ 2014	60 Preterm infants (GA, 23 wk to 31 wk 6 d)	3	20 cm in 2 s	ICC	Pregnant women with imminent delivery, monochorionic multiple births, incarcerated mothers, placenta previa, concerns of abruption, refusal by obstetrician
March et al, ¹² 2013	75 Preterm infants (GA, 24-28 wk)	3	Not reported	ICC	Major congenital anomalies, Rh sensitization, hydrops fetalis, maternal recent exposure to parvovirus, elevated peak systolic velocity of the fetal middle cerebral artery, suspected placental abruption
Rabe et al, ¹⁴ 2011	58 Preterm infants (GA, 24 wk to 32 wk 6 d)	4	20 cm in 2 s	DCC at 30 s	Multiple pregnancy, hydrops fetalis, Rh sensitization, major congenital anomalies
Upadhyay et al, ¹³ 2013	200 Infants (GA, >34 wk 6 d)	3	10 cm/s	DCC within 30 s	Umbilical cord length <25 cm, nonvigorous, meconium-stained amniotic fluid, CD for fetal compromise, multiple births, Rh-negative mothers, major congenital anomalies, cord prolapse, placenta previa or abruption, cord abnormalities (true knots), hydrops fetalis

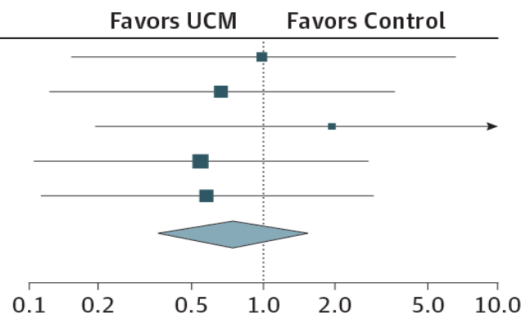
Abbreviations: CD, cesarean delivery; DCC, delayed cord clamping; DM, diabetes mellitus; GA, gestational age; HDNB, hemolytic disease of newborn;

ICC, immediate cord clamping; IUGR, intrauterine growth restriction; TTTS, twin-to-twin transfusion syndrome; UCM, umbilical cord milking.

A Mortality before discharge in preterm infants^a

5 studies, 277 preterm infants [RR] 0.75, 95% CI 0.35–1.64, p=0.48

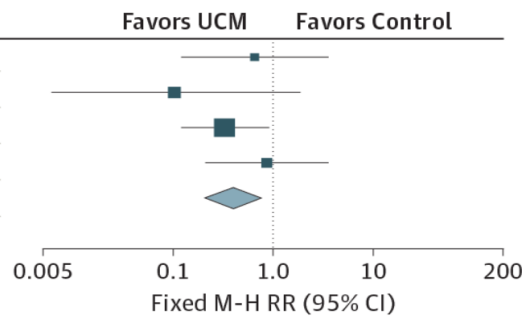
Source	UCM Group		Control Group		Weight, %	Fixed M-H RR (95% CI)
	No. of Events	Total	No. of Events	Total		
Alan et al, ¹⁶ 2014	2	22	2	22	14.7	1.00 (0.15-6.48)
Hosono et al, ¹¹ 2008	2	20	3	20	22.1	0.67 (0.12-3.57)
Katheria et al, ¹⁵ 2014	2	30	1	30	7.4	2.00 (0.19-20.90)
March et al, ¹² 2013	2	36	4	39	28.3	0.54 (0.11-2.78)
Rabe et al, ¹⁴ 2011	2	27	4	31	27.5	0.57 (0.11-2.89)
Total	10	135	14	142	100.0	0.75 (0.35-1.64)
Heterogeneity $\chi^2_4 = 1.04$ ($P = .90$); $I^2 = 0\%$						
Test for overall effect: $z = .71$ ($P = .48$)						



B Oxygen requirement at 36 wk, postmenstrual age in preterm infants^a

4 studies, 191 preterm infants [RR] 0.42, 95% CI 0.21–0.83, p=0.01

Source	UCM Group		Control Group		Weight, %	Fixed M-H RR (95% CI)
	No. of Events	Total	No. of Events	Total		
Alan et al, ¹⁶ 2014	2	19	3	19	12.9	0.67 (0.13-3.55)
Hosono et al, ¹¹ 2008	0	18	4	17	19.8	0.11 (0.01-1.82)
Katheria et al, ¹⁵ 2014	4	30	12	30	51.4	0.33 (0.12-0.92)
Rabe et al, ¹⁴ 2011	3	27	4	31	16.0	0.86 (0.21-3.51)
Total	9	94	23	97	100.0	0.42 (0.21-0.83)
Heterogeneity $\chi^2_3 = 2.41$ ($P = .49$); $I^2 = 0\%$						
Test for overall effect: $z = 2.50$ ($P = .01$)						



C IVH of all grades^a

5 studies, 277 preterm infants [RR] 0.62, 95% CI 0.41–0.93, p=0.02

Source	UCM Group		Control Group		Weight, %	Fixed M-H RR (95% CI)
	No. of Events	Total	No. of Events	Total		
Alan et al, ¹⁶ 2014	4	22	3	22	6.7	1.33 (0.34-5.28)
Hosono et al, ¹¹ 2008	3	20	5	20	11.2	0.60 (0.17-2.18)
Katheria et al, ¹⁵ 2014	8	30	11	30	24.6	0.73 (0.34-1.55)
March et al, ¹² 2013	9	36	20	39	42.9	0.49 (0.26-0.93)
Rabe et al, ¹⁴ 2011	3	27	7	31	14.6	0.49 (0.14-1.72)
Total	27	135	46	142	100.0	0.62 (0.41-0.93)
Heterogeneity $\chi^2_4 = 2.03$ ($P = .73$); $I^2 = 0\%$						
Test for overall effect: $z = 2.32$ ($P = .02$)						

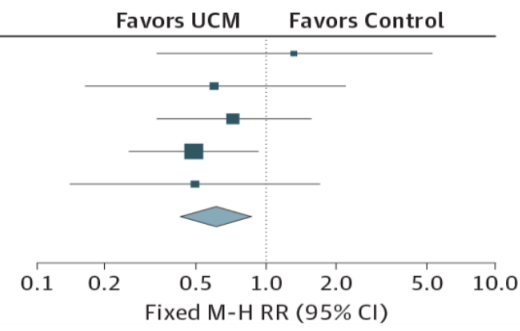


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Abbreviations: MD, mean difference; NA, not applicable; NNT, number needed to treat; PRBC, packed red blood cells; RD, risk difference; RR, risk ratio.

SI conversion factors: To convert bilirubin to micromoles per liter, multiply by 17.104; hematocrit to a proportion of 1.0, multiply by 0.01; and hemoglobin to grams per liter, multiply by 10.0.

^a Indicates gestational age of less than 33 weeks.

^b Continuous outcomes are reported as mean difference.

^c Indicates statistically significant results.

結果

Comparison of Full-Term Infants

Primary Outcome

- None of the included studies reported on mortality.

Secondary Outcomes

- In the first 48 hours after birth, the UCM group had significantly higher hematocrit values (mean difference [MD], 7.5% [95% CI, 0.7%-1.5%]; to convert to a proportion of 1.0, multiply by 0.01) and higher hemoglobin values (MD, 1.2 [95% CI, 0.8-1.5] g/dL; to convert to grams per liter, multiply by 10.0).
- No significant difference between the 2 groups in peak bilirubin level and in the need for phototherapy.
- At 6 weeks of age, the UCM group had significantly higher levels of hemoglobin (MD, 1.1 [95% CI, 0.7-1.5] g/dL) and ferritin (MD, 79 [95% CI, 58-101] ng/mL; to convert to micrograms per liter, multiply by 2.247).

結論

- In infants born at **GA $\leq$ 33 weeks**, UCM was associated with higher initial hemoglobin values, a lower risk for oxygen requirement at 36 weeks, and a lower risk of IVH of all grades.
- There was no difference in the need for blood transfusion or in the risk for severe IVH or periventricular brain injury.
- In infants with a **GA >33 weeks**, UCM was associated with higher hemoglobin values in the first 48 hours of life and at 6 weeks of age without an increase in the risk of hyperbilirubinemia.
- None of the studies evaluated long-term neurodevelopmental outcomes.

≤33週早產兒生產時，是否建議醫師進行umbilical cord milking(UCM)？

同意13人

不同意0人

需討論8人



- 由婦兒科醫師帶回科會討論，若要執行，建議早產兒生產時可預留臍帶約10公分，由兒科醫師進行UCM，詳細方法須再討論

Benefits of Cord Milking

Pregnancyexercise.co.nz



**THANK
YOU!**