

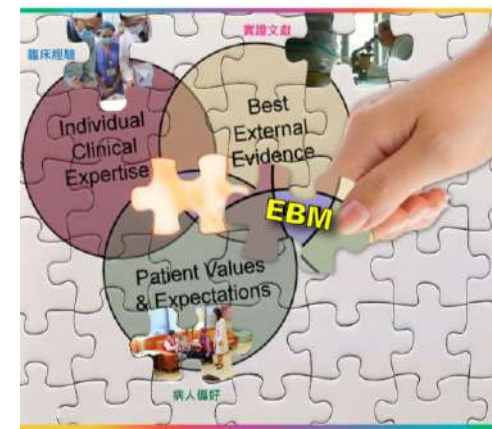
The Use of Biatain Ag in Hard-to-Heal Venous Leg Ulcers: Meta-Analysis of Randomised Controlled Trials

David Leaper¹, Christian Münter², Sylvie Meaume³, Alessandro Scalise⁴, Nacho Blanes Mompó⁵, Birte Petersen Jakobsen^{6*}, Finn Gottrup⁷

¹ Wound Healing Research Unit, Cardiff University, Cardiff, United Kingdom, ² General Practitioner, Hamburg, Germany, ³ Hôpital Rothschild, Paris, France, ⁴ Ancona Politechnical University, Faculty of Medicine, Ancona, Italy, ⁵ Hospital de Manises, Valencia, Spain, ⁶ Coloplast A/S, Humlebaek, Denmark, ⁷ Copenhagen Wound Healing Center, Bispebjerg University Hospital, Copenhagen, Denmark

PLoS One. 2013 Jul 2;8(7):e67083.
doi: 10.1371/journal.pone.0067083. Print 2013.

引言人：林芳宇
報告時間：2013年12月03日



Journal Ranking

For **2012**, the journal **PLoS One** has an Impact Factor of **3.730**.

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

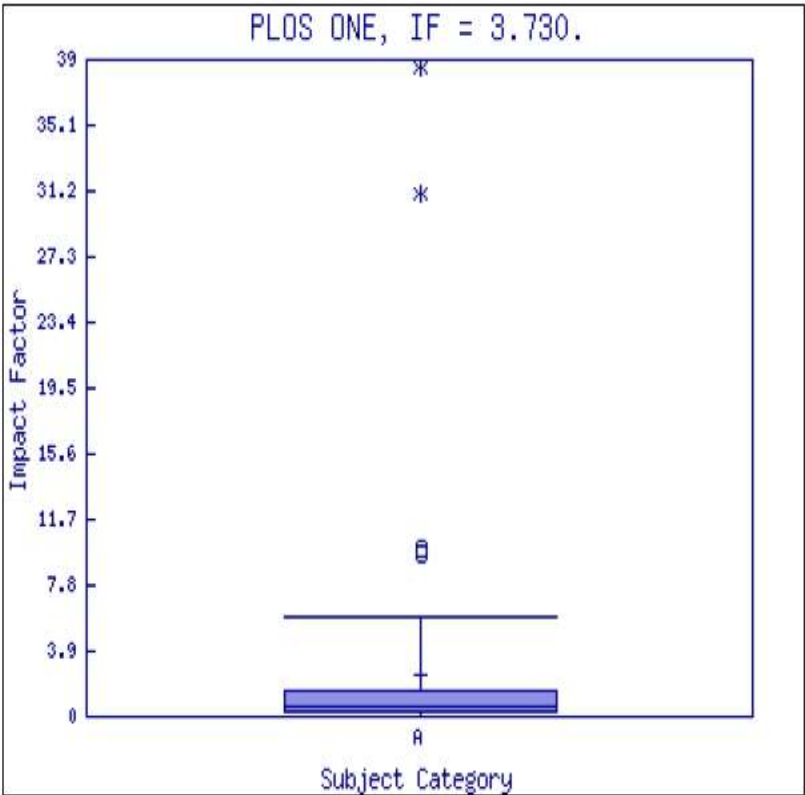
Category Name	Total Journals in Category	Journal Rank in Category	Quartile in Category
MULTIDISCIPLINARY SCIENCES	56	7	Q1

Impact factor:3.730

Category Box Plot

For **2012**, the journal **PLoS One** has an Impact Factor of **3.730**.

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.



Key
A - MULTIDISCIPLINARY SCIENCES



臨床問題 < 案例 >

- 鄒先生，50 y/o，公務員/家中主要決策者
- 診斷
 - Acute respiratory distress syndrome, severe with respiratory failure post ETT + MV, Multiple Organ Failure Status(MOFS).
 - Severe sepsis with septic shock
- 入院經過
 - 10/21因高燒不退,血壓83/45mmHg,N/S 2000ml challenge,轉ICU
 - 10/21(N)on Levophed
 - 10/22(D)SOB, acidosis→ on ETT 8.0→10/22 ARF on D/L
 - 10/23四肢大理石斑、皮膚濕冷; 10/24雙腳水泡, scortum呈深紫色
 - 10/24(D)Liver function poor → 向家屬解釋洗肝
 - 10/25 BP drop on CVVH



臨床問題 < 案例 >

- 11/4 會診整外(四肢末梢發黑)
 - Wound CD with aq-BI solution or framycin
 - Consult CVS for vessel evaluation
 - Consult Ortho if amputation is indicated
- 102/11/5(D)
 - 11/05(E)on PGE1 (for 四肢發黑) → 11/14DC

Framycin 紗布用量大

自費


order



目前傷口照護方式

1. 傷口有感染用: Aquacel Ag
2. 一般傷口用(滲液多的傷口): Aquacel
3. 若是敷料沒濕可以續用
4. I-10 傷口可能與血管異常有關, 則要保持傷口乾燥
5. 其他乾淨的傷口就使用 framycin
6. 每日傷口都要拍照, 以利觀察傷口的變化



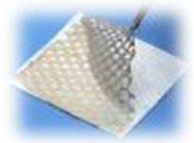


太太表示：
自費用藥都沒關係，
希望醫護團隊可以盡
全力將四肢傷口及疾
病治療好



臨床問題<疑問>

■ 病人最佳傷口照護方式是什麼？



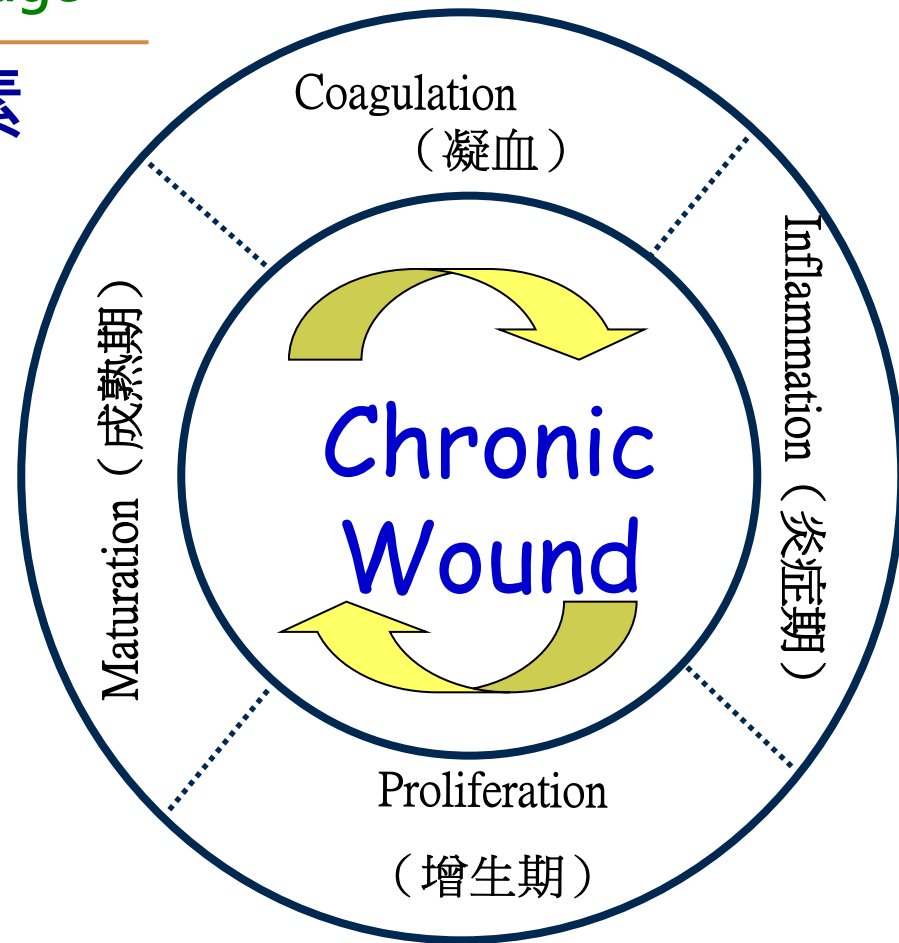
Full Line of Advanced Wound Care Supplies



背景資料 Background Knowledge

影響傷口癒合—全身性因素

- 血流供應 (Blood supply)
- 組織灌流 (Tissue perfusion)
- 營養狀況 (Nutrition status)
- 年紀大 (Old age)
- 免疫受抑制 (Immuno-suppression)
- 血液凝固障礙 (Clotting disorders)
- 肥胖 (Obesity)
- 其他疾病：惡性腫瘤 (Malignancy)
- 糖尿病 (DM) Renal/hepatic/C-V disease
- 敗血症 (Sepsis)



拖過6週以上無法癒合的傷口

前景問題 Foreground Question

P

- Hard-to-Heal Leg Ulcers

I

- Use of Hydrofiber dressing with Silver

C

- Framycin

O

- Wound inflammation
- Wound size reduction
- Wound healing rate

問題類型： ● 治療型 ○ 預後型 ○ 診斷型 ○ 傷害型

Topical silver for preventing wound infection (Review)

Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H

Level 1*



- 含銀敷料或藥膏並不能預防傷口感染或促進癒合。
- 含銀敷料或藥膏目前正被廣泛使用。它們可能促進傷口癒合或預防傷口感染，但是真相如何有待商確。

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library*

2010, Issue 3

Silver treatments and silver-impregnated dressings for the healing of leg wounds and ulcers: A systematic review and meta-analysis (2010)

Level 1*

Marissa J. Carter, PhD, MA,^a Kimberly Tingley-Kelley, MS,^a and
Robert A. Warriner III, MD, FACA, FCCP, FCCWS^b
Cody, Wyoming, and The Woodlands, Texas

Conclusions : Although our results provide some evidence that silver-impregnated dressings improve the short-term healing of wounds and ulcers, long- term effects remain unclear.

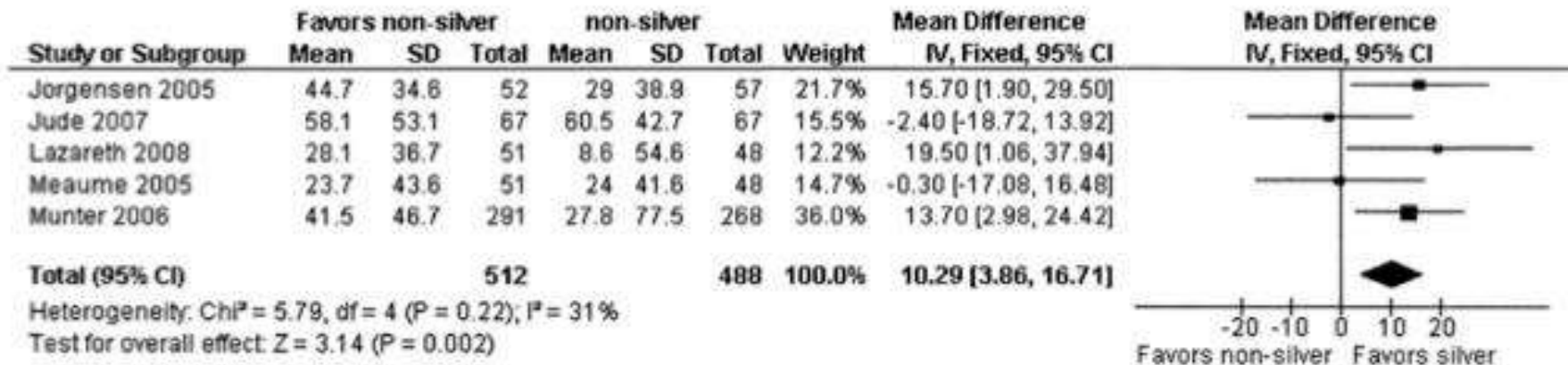


Fig 3. Forest plot of wound size reduction (%) meta-analysis for silver-impregnated dressing studies using data from Lazareth et al³⁸ for 4 weeks. *CI*, Confidence interval; *df*, degrees of freedom; *IV*, inverse variance.

有更新的文獻嗎？

re·search

/rɪ'sɜːtʃ/

[plural]

1 serious st-

discover new facts

research into

student

lab

interested in or need
doing some research

I've done some research

★符合PICO ★年代最新 ★符合研究設計 ★ Impact Factor:3.730

OPEN ACCESS Freely available online

PLOS ONE

The Use of Biatain Ag in Hard-to-Heal Venous Leg Ulcers: Meta-Analysis of Randomised Controlled Trials

David Leaper¹, Christian Münter², Sylvie Meaume³, Alessandro Scalise⁴, Nacho Blanes Mompó⁵, Birte Petersen Jakobsen^{6*}, Finn Gottrup⁷

Abstract

Background: Venous leg ulcers are common, troublesome, and their failure to heal is often related to a heavy burden. Ionized silver has both anti-inflammatory and antimicrobial properties. The ulcer healing properties of a new dressing foam dressing Biatain Ag has been examined in 4 randomized controlled trials (RCTs).

Aim: To evaluate ulcer healing with a meta-analytic approach after treatment with either Biatain Ag or a non-active dressing.

Patients and Methods: 685 subjects with pure or mixed hard-to-heal venous leg ulcers were included in the meta-analysis.

Results: Biatain Ag showed a significant treatment effect ($p < 0.0001$), responder rate ($p < 0.001$), and healing rate ($p = 0.002$).

Conclusion: The meta-analysis of the 4 RCTs provided statistical significant evidence to support the use of Biatain Ag dressing in treatment of hard-to-heal venous leg ulcers.

Received November 28, 2012; Accepted May 15, 2013;

Published July 2, 2013

選用文獻之PICO，研究對象基本資料

Table 1. Data sources considered for inclusion in the meta-analysis.

Studies ¹	Ulcer types ²	Comparison
Jørgensen et al. (2005)	Venous/arterial ulcers	Foam dressing (Biatain)
Münter et al. (2006)	Venous, mixed, arterial, diabetic and pressure ulcers	Local best practice
Humbert et al. (2006)	Venous, mixed	Local best practice
Senet et al. (2013)	Venous	Foam dressing (Biatain)

本研究的傷口類型：
Venous/arterial/diabetic/pressure ulcer, mixed

¹All studies were multinational except Humbert et al. which was a French study. ²Only subjects with venous or mixed ulcer aetiologies were selected for the meta-analysis. ³Local Best Practice included foams/alginate (53%), hydrocolloids (12%), gauze (3%), silver dressings (17%), other microbial dressings (9%) and other active dressings (6%).

doi:10.1371/journal.pone.0067083.t001

Table 2. Numbers and baseline characteristics of patients included in the meta-analysis.

Studies	Subjects in trial	Subjects included in analysis (%)	Reason for exclusion	Gender ¹ , female (%)	Age ² , mean (SD)	Baseline ulcer area ³ (cm ²), mean (SD)	Baseline ulcer age ⁴ (years), mean (SD)
Jørgensen et al. (2005)	129	129 (100)	No exclusions	82 (63.6)	71.6 (12.4)	10.1 (9.8)	2.7 (4.2)
Münter et al. (2006)	619	315 (51)	Ulcer types other than venous or mixed. Active comparators or gauze	226 (71.7)	70.9 (12.5)	38.3 (69.6)	2.7 (5.0)
Humbert et al. (2006)	80	60 (75)	Ulcer type other than venous or mixed	41 (68.3)	74.4 (10.5)	13.2 (11.1)	1.9 (3.5)
Senet et al. (2013)	181	181 (100)	No exclusions	97 (53.6)	73.5 (12.2)	15.0 (13.7)	2.8 (4.7)
Total subjects	1009	685 (68)	–	446 (65.1)	–	–	–

Baseline differences across the studies: ¹($p=0.001$), the fraction of females in the study by Senet et al. is substantially smaller. ²($p=0.07$) no significant difference of patient age, ³($p<0.0001$), significant larger ulcers were included in the study by Münter et al., ⁴($p=0.002$), the study by Humbert et al. included somewhat younger ulcers.

doi:10.1371/journal.pone.0067083.t002

The Use of Biatain Ag in Hard-to-Heal Venous Leg Ulcers: Meta-Analysis of Randomised Controlled Trials

David Leaper¹, Christian Münter², Sylvie Meaume³, Alessandro Scalise⁴, Nacho Blanes Mompó⁵, Birte Petersen Jakobsen^{6*}, Finn Gottrup⁷

FAITH Systematic review Checklist

快速評讀 [系統性文獻回顧Systematic Review]

- 步驟1: 系統性文獻回顧探討的問題為何？
- 步驟2: 系統性文獻回顧的品質如何？
- 步驟3: 結果為何？

Section A: Valid?

步驟1:系統性文獻回顧探討的問題為何？

YES

P

- Hard-to-Heal Leg Ulcers

I

- Use of Hydrofiber dressing with Silver

C

- Framycin

O

- Wound inflammation
- Wound size reduction
- Wound healing rate

Abstract

Background: Venous leg ulcers are common, troublesome, and their failure to heal is often related to a heavy bio-burden. Ionized silver has both anti-inflammatory and antimicrobial properties. The ulcer healing properties of the silver releasing foam dressing Biatain Ag has been examined in 4 randomized controlled trials (RCTs).

Aim: To evaluate ulcer healing through a meta-analytic approach after treatment with either Biatain Ag or a non-active dressing.

Patients and Methods: 685 subjects with pure or mixed hard-to-heal venous leg ulcers were included in the meta-analysis.

Result: Biatain Ag showed a significant treatment effect ($p < 0.0001$), responder rate ($p < 0.001$), and healing rate ($p = 0.002$).

Conclusion: The meta-analysis of the 4 RCTs provided statistical significant evidence to support the use of Biatain Ag dressing in treatment of hard-to-heal venous leg ulcers.

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?

YES

Methods

至少2個資料庫

Data Sources

Pubmed and the Cochrane Library were searched using the term 'Biatain Ag' or 'Biatain Argent' or 'Biatain Plata' or 'Contreet' without date restriction (Figure 1). An 'in-house' literature and knowledge' database was also searched in using the same terms. For the present meta-analysis it was decided to include only data from RCTs. Of the studies found in which Biatain Ag dressings were used for the treatment of chronic leg ulcers; only four were RCTs [24;27;35;36]. In two of the RCTs [24;27] the dressings were Contreet® (a previous version of Biatain Ag with the same active ingredients). In the two remaining RCTs [35;36] the dressings were Biatain Ag, which is the currently used dressing. The included data sets were overlapping.

文獻搜尋不只限於英文
同時使用MeSH字串及一般檢索詞彙(Text words)

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?

YES

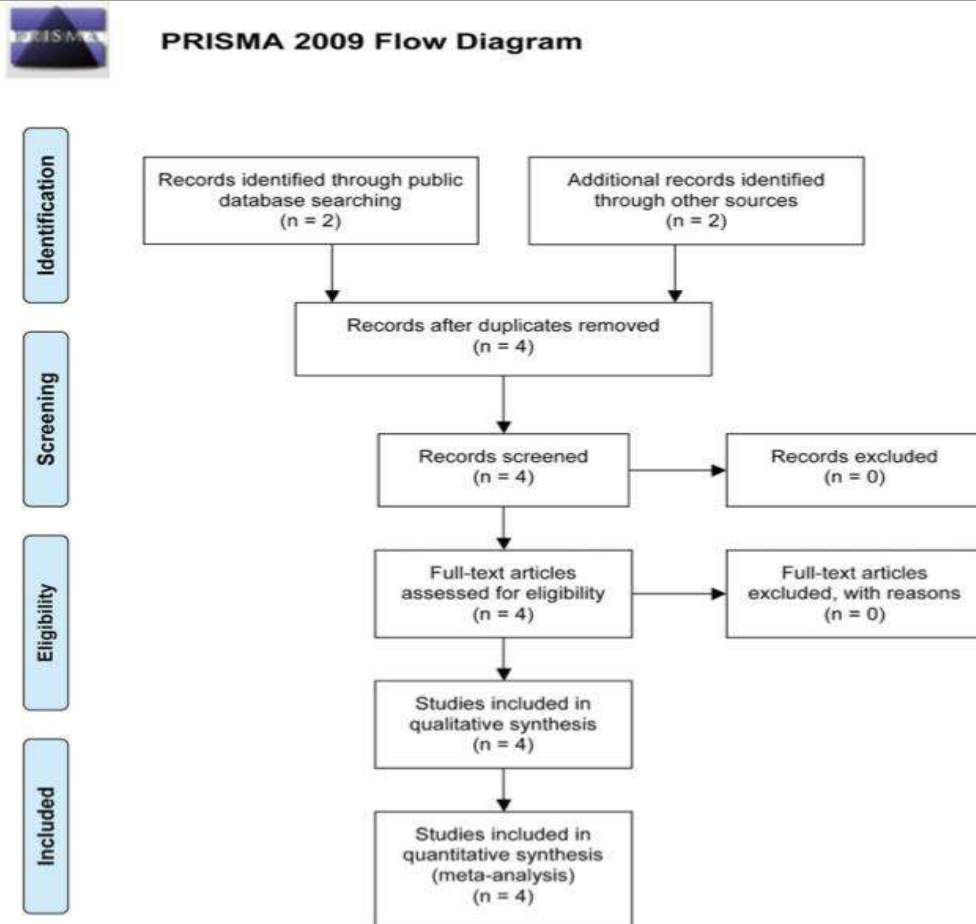


Figure 1. Flow chart of literature search.
doi:10.1371/journal.pone.0067083.g001

以PRISMA
流程圖呈現

步驟2:系統性文獻回顧的品質如何?(FAITH)



unclear

A-文獻是否經過嚴格評讀 (Appraisal) ?

Methods

Data Sources

Pubmed and the Cochrane Library term 'Biatain Ag' or 'Biatain Argon' 'Contreet' without date restriction (I literature and knowledge' database was an the same terms. For the present meta-analysis it was decided to include only data from RCTs. Of the studies found in which Biatain Ag dressings were used for the treatment of chronic leg ulcers; only four were RCTs [24;27;35;36]. In two of the RCTs [24;27] the dressing was Contreet® (a previous version of Biatain Ag with identical silver content and release), and in the two remaining studies the dressing was Biatain Ag, which is the currently used name for the product. None of the included data sets were overlapping.

只提到選擇RCT文章，沒有提及是以何種標準進行嚴格評讀

步驟2:系統性文獻回顧的品質如何?(FAITH)

I-是否只納入(included) 具有良好效度的文章?

unclear

Data Sources

Pubmed and the Cochrane Library were searched using the term 'Biatain Ag' or 'Biatain Argent' or 'Biatain Plata' or 'Contreet' without date restriction (Figure 1). An 'in-house literature and knowledge' database was also searched in using the same terms. For the present meta-analysis it was decided to include only data from RCTs. Of the studies found in which Biatain Ag dressings were used for the treatment of leg ulcers; only four were RCTs [24;27;35;36]. In two of the RCTs [24;27] the dressing was Contreet® (a previous version of Biatain Ag with identical properties). The results of the remaining studies currently used in the meta-analysis were overlaid on the data sets were overlaid.

- 只提到選擇RCT文章，無清楚描述如何隨機分配、盲法、完整追蹤...等內容
- 無法確定是否具良好效度

Meta-analysis (Statistical Pooling) and Statistical Methods

The baseline characteristics and measurement of ulcer area, at four weeks, were available in all included data sets and were selected as primary evaluation points in the meta-analysis. The meta-analysis was carried out on the 4 RCTs with the following outcomes:

- (i) relative reduction of ulcer area over 4 weeks
- (ii) response rate; defined as the proportion of subjects with a relative ulcer area reduction of $\geq 40\%$ at 4 weeks (indicative of a favorable healing prognosis [37])
- (iii) complete healing (healers), defined as the proportion of subjects with a healed ulcer at 4 weeks.

步驟2:系統性文獻回顧的品質如何?(FAITH)

T - 作者是否以表格和圖表『總結』 (total up) 試驗結果?

Yes

Table 3. Percent relative reduction of ulcer area at week 4 for each study and the whole data set.

Studies	Comparator (SD)	Experimental (SD)	All (SD)
Jørgensen et al. (2005)	30.9 (41.5)	39.9 (37.7)	35.5 (39.7)
Münter et al. (2006)	26.6 (50.7)	40.8 (26.7)	41.3 (43.5)

以表及森林圖(Forest plot)
總結試驗結果

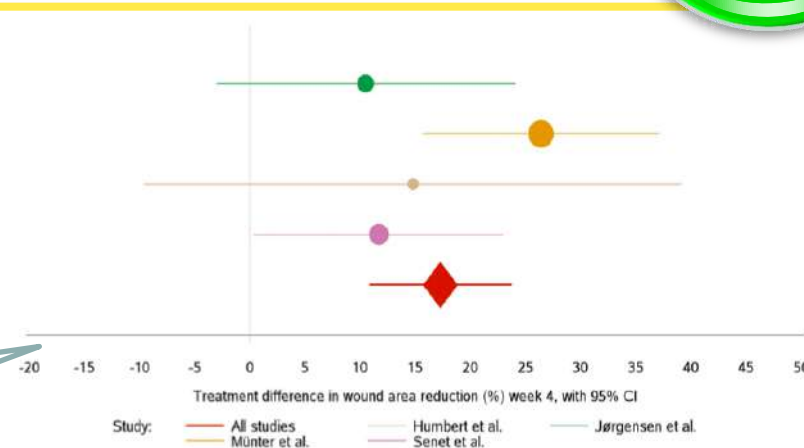


Figure 2. Forest plot showing the estimated treatment differences defined by percentage relative reduction. The solid vertical line represents a treatment difference of zero. The confidence intervals (95%) are illustrated by the length of the horizontal lines. The sizes of the filled circles are adjusted to the size of the corresponding study. doi:10.1371/journal.pone.0067083.g002

Table 4. Total and study wise treatment effects.

Studies	Control		Experimental		Treatment diff. CI	p-value
	n	LSMeans	n	LSMeans		
Jørgensen et al. (2005)	61	34.16	64	44.61	10.45 [-3.07; 23.96]	0.1285
Münter et al. (2006)	115	27.15	200	53.54	26.39 [15.70; 37.08]	<0.0001
Humbert et al. (2006)	30	11.24	28	26.03	14.79 [-9.55; 39.13]	0.2283
Senet et al. (2013)	84	29.27	77	40.92	11.65 [0.38; 22.92]	0.0428
All	290	25.46	369	42.78	17.31 [10.90; 23.73]	<0.0001

Treatment effects are estimated by least square means (extracted from the ANCOVA model) with confidence intervals and p-values for each study and the whole data set.

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) ?

No

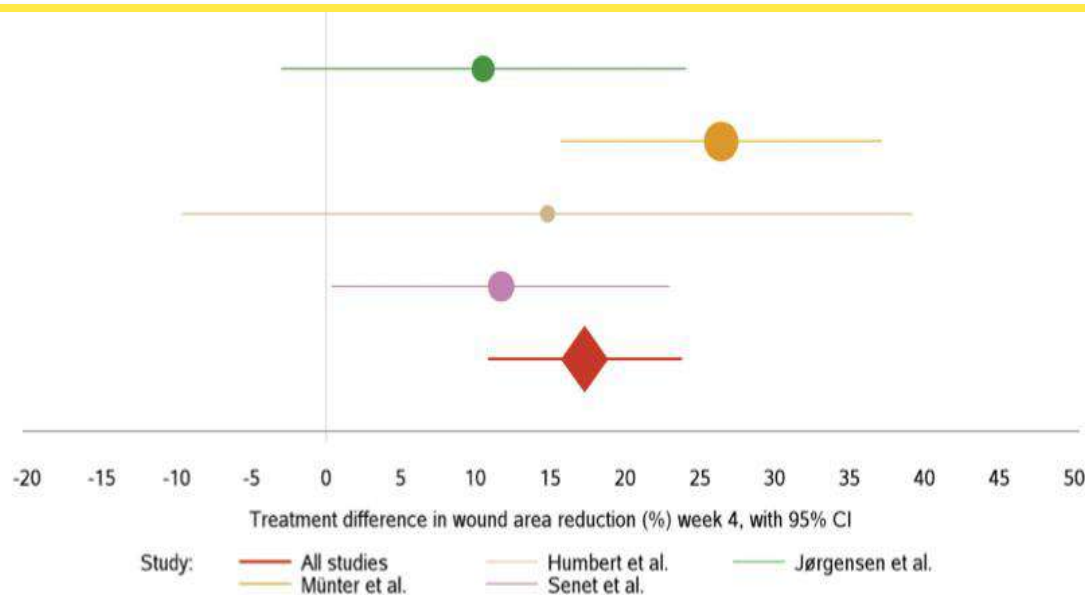


Figure 2. Forest plot showing the estimated treatment differences defined by percentage relative reduction. The solid vertical line represents a treatment difference of zero. The confidence intervals (95%) are illustrated by the length of the horizontal lines. The sizes of the filled circles are adjusted to the size of the corresponding study.
doi:10.1371/journal.pone.0067083.g002

- 欠缺呈現異質性分析 (Heterogeneity)
- 作者可增加評估差異是否顯著 (χ^2, I^2)

研究結果為何¹?

Table 3. Percent relative reduction of ulcer area at week 4 for each study and the whole data set.

Studies	Comparator (SD)	Experimental (SD)	All (SD)
Jørgensen et al. (2005)	30.9 (41.5)	39.9 (37.7)	35.5 (39.7)
Münter et al. (2006)	26.6 (50.7)	49.8 (36.2)	41.3 (43.5)
Humbert et al. (2006)	12.9 (48.7)	29.8 (38.7)	21.1 (44.6)
Senet et al. (2013)	27.5 (37.0)	35.4 (35.2)	31.3 (36.3)
All	26.3 (45.0)	43.5 (37.0)	36.0 (41.6)

doi:10.1371/journal.pone.0067083.t003



Table 4. Total and study wise treatment effects.

Studies	Control		Experimental		Treatment diff. CI	p-value
	n	LSMeans	n	LSMeans		
Jørgensen et al. (2005)	61	34.16	64	44.61	10.45 [−3.07; 23.96]	0.1285
Münter et al. (2006)	115	27.15	200	53.54	26.39 [15.70; 37.08]	<0.0001
Humbert et al. (2006)	30	11.24	28	26.03	14.79 [−9.55; 39.13]	0.2283
Senet et al. (2013)	84	29.27	77	40.92	11.65 [0.38; 22.92]	0.0428
All	290	25.46	369	42.78	17.31 [10.90; 23.73]	<0.0001

Treatment effects are estimated by least square means (extracted from the ANCOVA model) with confidence intervals and p-values for each study and the whole data set.

doi:10.1371/journal.pone.0067083.t004

研究結果為何²?

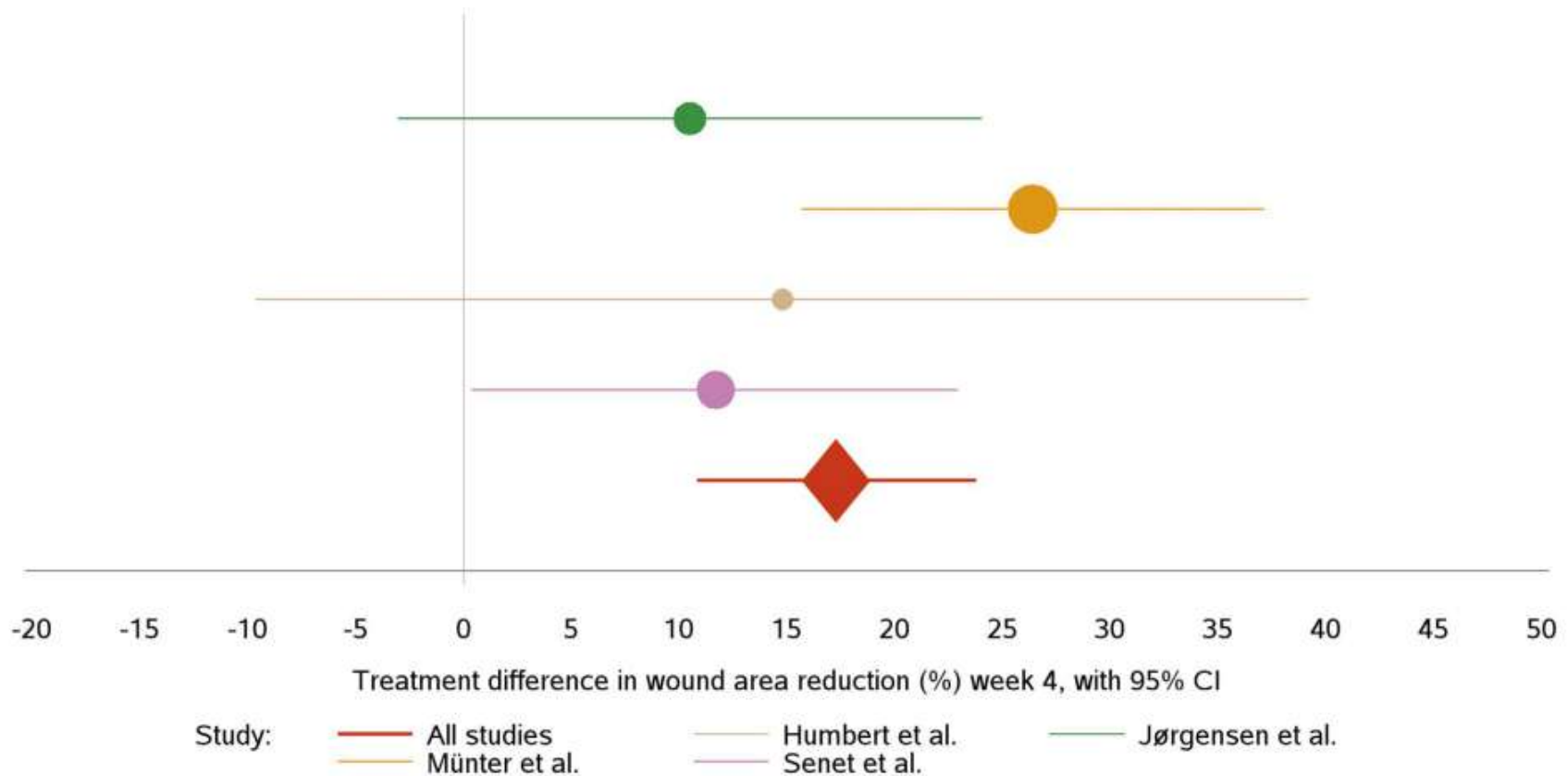


Figure 2. Forest plot showing the estimated treatment differences defined by percentage relative reduction. The solid vertical line represents a treatment difference of zero. The confidence intervals (95%) are illustrated by the length of the horizontal lines. The sizes of the filled circles are adjusted to the size of the corresponding study.
doi:10.1371/journal.pone.0067083.g002



Table: Steps in finding evidence ("Levels") for different types of question

Developed by: Iain Chalmers (James Lind Library), Paul Glasziou (OCEBM), Trish Greenhalgh (UCL), Carl Heneghan (OCEBM), Jeremy Howick (OCEBM), A. Moschetti, Bob Phillips, and Hazel Thornton

Level 2*

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is it? (E.g., Pre-test probabilities)	Most relevant local and current random sample survey (or censuses)	Systematic review of current surveys	Systematic review of local non-random sample	Systematic review of case-series	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms
Is this test accurate? (Diagnostic accuracy)	Systematic review of cross sectional studies	Systematic review of cross sectional studies With consistently applied reference standard and blinding	Systematic review of non-consecutive studies, or studies without consistently applied reference standards.	Systematic review of case-control study, or cross-sectional study with non-independent reference standard	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms
What will happen if we do nothing? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort or control arm of randomized trial	Systematic review of case-series	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms
Does this treatment help? (Treatment Benefits)	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational studies with dramatic effect	Non-randomized controlled cohort/follow-up study	Systematic review of case-control studies, historically controlled studies	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials or n-of-1 trial	Systematic review of nested case-control or dramatic effect	Non-randomized controlled cohort/follow-up study	Case-control studies, historically controlled studies	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms
What are the RARE harms? (Treatment Harms)	Systematic review of case-control studies, or studies revealing dramatic effects	Randomized trial or (exceptionally) observational study with dramatic effect			
Is early detection worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study	Case-control studies, historically controlled studies	Opinion without explicit critical appraisal, based on limited/undocumented experience, or based on mechanisms

* 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.

臨床抉擇




Step 1 Ask

Step 2: Acquire

Step 3: Appraisal

Step 4 : Apply

不同臨床決策對醫療品質的影響

治療方案	優勢	缺點	敷料
Framycin Gauze Dressing	<ol style="list-style-type: none"> 1.便宜(13元/片) 2.臨床較能被醫師接受 	<ol style="list-style-type: none"> 1.無法吸附滲液 2.增加換藥次數及時間 3.護理人力耗費 	
Hydrofiber Wound Dressing [Aquacel]	<ol style="list-style-type: none"> 1.吸附滲液 2.較能減少疼痛 3.換藥次數減少 4.減省護理人力 	<p>自費 (10*10cm) 136/片</p>	
Hydrofiber Dressing with Silver [Aquacel Ag]	<ol style="list-style-type: none"> 1.吸附滲液 2.適用於感染性傷口 3.增加病人換藥之滿意度 4.減省護理人力 	<p>自費 (10*10cm) 251/片</p>	

討論

- Cochrane Review (2007, 2010)顯示，接受含銀離子敷料治療感染性傷口，對傷口癒合速度無明顯增加，但可改善換藥的舒適程度，目前院內已有Aquacel® Hydrofiber Dressing with silver及Aquacel® Hydrofiber Dressing等敷料，您會建議使用嗎？
- Discussion Point
 - ✓ 本篇文獻只納入4篇 RCT，且過程嚴謹度呈現不慎清楚
 - ✓ 如果要將實證文獻運用於臨床病人，需考慮族群是否符合
 - ✓ 臨床照護經驗分享：
 - 銀(Ag)有局部抗發炎及抗菌效果，但對於傷口癒合無顯著的療效
 - Hydrofiber Dressing內含高纖維材質，具300倍吸收傷口滲液的功效
 - ✓ 本敷料需自費，長期使用需考慮病人的經濟負擔

臨床應用

以病人可了解的語言進行說明、共同決策

決策1: 是否建議本病人使用**不含銀的親水性纖維敷料**?
(AQUACEL Hydrofiber Dressing)



- 同意 : 16
- 懷疑 : 5
- 不同意 : 0



決策2: 是否建議病人使用**含銀的親水性纖維敷料**?
(AQUACEL Hydrofiber Dressing with silver) ?



- 同意 : 7
- 懷疑 : 14
- 不同意 : 0





Thank you!