

Forest plots

Paul Garner and Nathan Ford



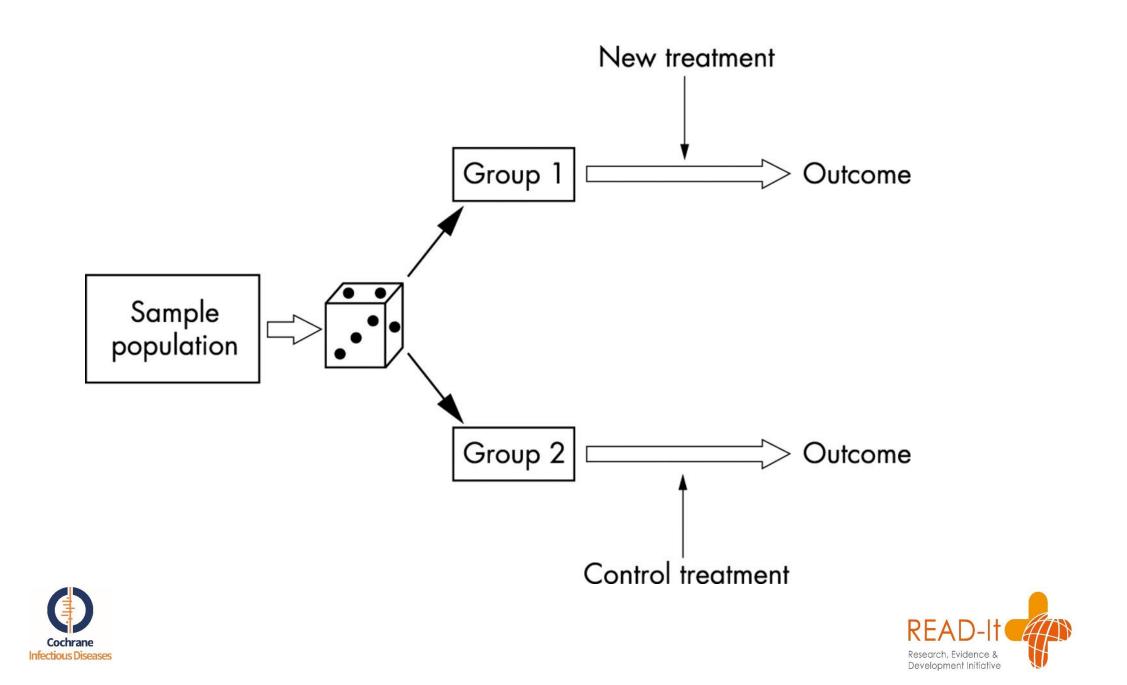


Differences between a narrative and systematic review

Narrative Review	Systematic Review	Cochrane Review
General topic	Clear question	Clear PICO
No protocol	Protocol completed before review started	Protocol refereed and published
Methods variable, not always clear	Clear methods	Standardized (Cochrane Handbook), supported by methods specialists
Vague/no inclusion criteria	Explicit inclusion criteria	Explicit inclusion criteria in protocol, and reasons for excluding studies stated in review
Risk of bias not assessed	Risk of bias and heterogeneity investigated	Systematic investigation of risk of bias and heterogeneity
Strength of evidence not assessed	Strength of evidence not usually assessed	Current reviews use GRADE methods







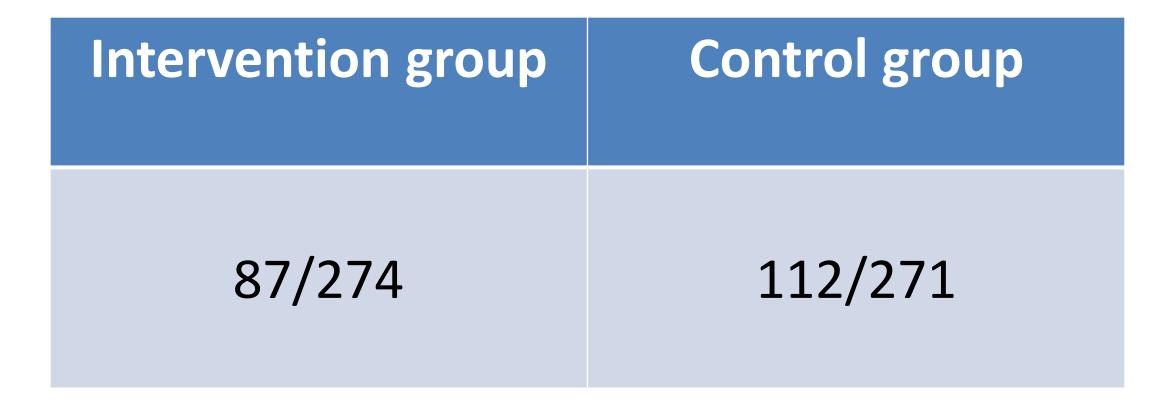
Are corticosteroids effective in TB meningitis?

- What study design
- What is in the intervention group?
- What is in the control group?
- What is the outcome?





Thwaites 2004

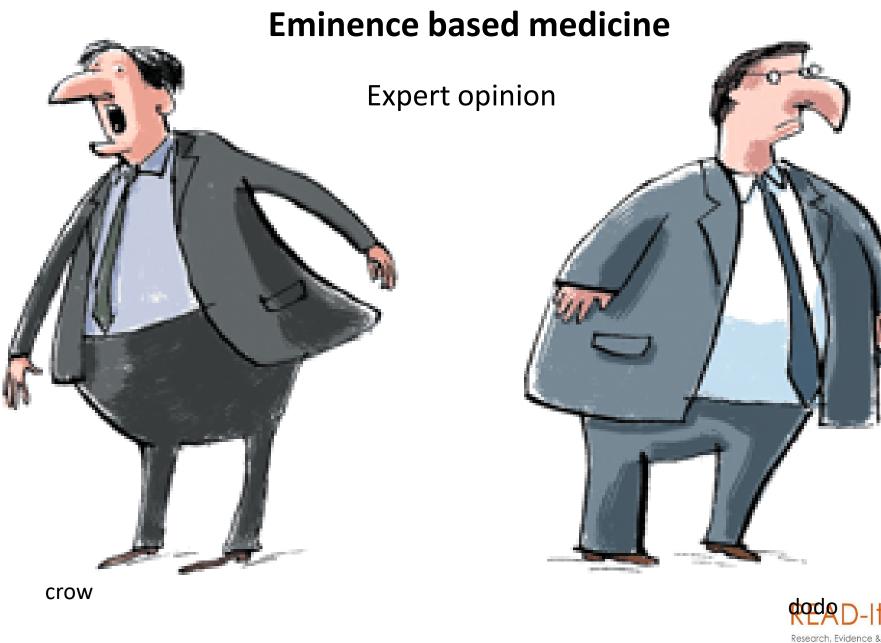


Relative risk is 0.77 (95%CI 0.61 to 0.96)

Why are systematic reviews and meta-analyses needed?







Development Initiative



Meta-analysis and Forest Plots

- A way of combining results from a number of individual trials to produce a summary result
- A forest plot displays the summary result of a meta-analysis and the results of the individual studies





Steroids versus placebo in TB meningitis Outcome is DEATH

Corticosteroid Control			Risk Ratio	Risk Ratio		
Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
o 24 month	s					
5	29	2	30	0.7%	2.59 [0.54, 12.29]	
72	145	79	135	30.7%	0.85 [0.68, 1.05]	-
5	24	7	23	2.7%	0.68 [0.25, 1.85]	
4	29	6	29	2.3%	0.67 [0.21, 2.12]	
17	65	13	32	6.5%	0.64 [0.36, 1.16]	
6	11	9	12	3.2%	0.73 [0.39, 1.37]	
9	41	19	46	6.7%	0.53 [0.27, 1.04]	
4	70	13	71	4.8%	0.31 [0.11, 0.91]	
87	274	112	271	42.3%	0.77 [0.61, 0.96]	-
	688		649	100.0%	0.75 [0.65, 0.87]	•
209		260				
7.59, df = 8	(P = 0.4)	47); I ² = 0	%			
Z = 3.90 (P	< 0.000)1)				
	Events 5 72 5 4 17 6 9 4 87 209 7.59, df = 8	EventsTotal 5 29 72 145 5 24 4 29 17 65 6 11 9 41 4 70 87 274 688 209 7.59 , df = 8 (P = 0.4)	EventsTotalEvents52927214579524742961765136119941194701387274112688209260	EventsTotalEventsTotal 24 months 52923072145791355247234296291765133261191294119464701371872741122716886492092607.59, df = 8 (P = 0.47); I ² = 0%	EventsTotalEventsTotalWeight 24 months 529230 0.7% 7214579135 30.7% 524723 2.7% 429629 2.3% 17651332 6.5% 611912 3.2% 9411946 6.7% 4701371 4.8% 87274112271 42.3% 688649100.0%2092607.59, df = 8 (P = 0.47); I ² = 0%	EventsTotalEventsTotalWeightM-H, Fixed, 95% Cl 24 months 529230 0.7% $2.59 [0.54, 12.29]$ 72 14579135 30.7% $0.85 [0.68, 1.05]$ 5 24723 2.7% $0.68 [0.25, 1.85]$ 4 29629 2.3% $0.67 [0.21, 2.12]$ 17 651332 6.5% $0.64 [0.36, 1.16]$ 6 11912 3.2% $0.73 [0.39, 1.37]$ 9 411946 6.7% $0.53 [0.27, 1.04]$ 4 701371 4.8% $0.31 [0.11, 0.91]$ 87 274112271 42.3% $0.77 [0.61, 0.96]$ 688 649100.0\% $0.75 [0.65, 0.87]$ 209 260 $7.59, df = 8 (P = 0.47); P = 0\%$ $P = 0.47$

Neurological disability

	Corticost	eroid	Contr	ol		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	ABCDEFG
1.2.1 Follow-up 2 to 2	24 months							
Kumarvelu 1994	0	24	1	23	1.6%	0.32 [0.01, 7.48] 👘		•••?
Girgis 1991	14	145	27	135	29.1%	0.48 [0.26, 0.88]		•??••??
Lardizabal 1998	10	29	14	29	14.6%	0.71 [0.38, 1.34]		???••••
Schoeman 1997	14	70	19	71	19.7%	0.75 [0.41, 1.37]		???••?•
Malhotra 2009	11	65	5	32	7.0%	1.08 [0.41, 2.85]		• ? ? • • • •
Thwaites 2004	34	274	22	271	23.0%	1.53 [0.92, 2.54]	⊢∎	
Prasad 2006	5	41	3	46	2.9%	1.87 [0.48, 7.34]		•••••??
Chotmongkol 1996 Subtotal (95% CI)	4	29 677	2	30 637	2.0% 100.0 %	2.07 [0.41, 10.44] 0.92 [0.71, 1.20]	•	? • • • ? ? ? ?
Total events	92		93					
Heterogeneity: Chi ² =	: 11.85, df =	7 (P = 0	.11); I ² =	41%				
Test for overall effect:		•						





Any corticosteroid compared to control for tuberculous meningitis

Participant or population: adults or children with tuberculous meningitis on tuberculosis (TB) chemotherapy Settings: hospital care Intervention: any corticosteroid Comparison: placebo or no corticosteroid

Outcomes		comparative risks 95% Cl)	Relative effect (95% Cl)	Number of participants (trials)	Quality of the evidence (GRADE)
	Assumed risk*	Corresponding risk			
	Control	Corticosteroid			
Follow-up to 2 to 24 mont	hs				
Death	41 per 100	31 per 100 (27 to 36)	RR 0.75 (0.65 to 0.87)	1337 (9 trials)	⊕⊕⊕⊕ high ^{1,2,3,4,5}
Disabling neurological deficit	8 per 100	7 per 100 (6 to 10)	RR 0.92 (0.71 to 1.20)	1314 (8 trials)	⊕⊕⊜⊜ ^{6,7,8} low

a small but nevertheless a real difference in age incidence in the two sexes.

(To be concluded in next week's issue)

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EPISIOTOMY

BY

J. D. S. FLEW, M.D., M.R.C.O.G.

During the training of the medical student and pupil midwife in the labour ward much stress is laid upon the prevention of \mathbf{ar} perineal tears, and to a great extent their skill at delivery is st, judged on the results obtained by them in this direction. Whilst agreeing that, in general, an intact perineum is better than a torn one, this statement needs qualification and consideration ra Tl before it can pass unchallenged. Lubin (1932) has stated: " It is presupposed that a patient without a lacerated perineum at fares better than her more unfortunate sister in so far as puerperal morbidity, comfort, future pathology, and disability ff (are concerned." The damage incurred by the patient in order OI. to maintain the integrity of her perineum must be considered.

Disadvantages of a Torn Perineum

of What are the possible disadvantages of a torn perineum? tis. The apparent in a computer tree through the orbination and

620 Nov. 11, 1944

Results

In 135 consecutive primigravid private patients delivered per vaginam I find the following results:

Normal delivery without episiotomy, 63 cases	46.7%
Episiotomy performed in 72 cases	53.3%
Of the episiotomy cases 52 had a normal delivery, and there-	
fore the total normal delivery rate (115 cases in 135) is	81.1%
Among the remainder, all of which had episiotomy performed,	
there were 17 forceps deliveries	12.6%
The remaining 3 cases comprised 2 extended breech and 1	
perforation of a hydrocephalic head	

The relatively low forceps rate for primigravidae in private practice I attribute almost entirely to the episiotomy rate of

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BRITISH 623 MEDICAL JOURNAL

Summary

The disadvantages of a torn perineum are discussed and compared with the disadvantages of unseen damage that may occur as a result of keeping the perineum intact.

In order to minimize all these disadvantages early episiotomy is advocated, and the cases in which episiotomy should be performed are stated.

The relation of injury sustained during labour to prolapse and vaginal hernia is discussed.

Certain perineal anatomical points of practical importance in performing episiotomy are mentioned.

The methods of performing episiotomy are described.

Figures are given which indicate that patients on whom early episiotomy is carried out are less prone to pelvic damage than those in whom the perineum remains intact. Jiang H et al.. Selective versus routine use of episiotomy for vaginal birth. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD000081. DOI: 10.1002/14651858.CD000081.pub3.

In women where no instrumental delivery is intended, selective episiotomy policies result in fewer women with severe perineal/vaginal trauma. Other findings, both in the short or long term, provide no clear evidence that selective episiotomy policies results in harm to mother or baby.





Patient or population: Women in labour where operative delivery was not anticipated. (Women were above 16 years old and between 28 gestational weeks and full term, with a live singleton fetus, without severe medical or psychiatric conditions, and had vaginal birth.)

Setting: Hospitals in high-, middle- and low-income countries. (Studies were carried out between July 1982 and October 2009, in Argentina, Canada, Columbia, Germany, Ireland, Malaysia, Pakistan, Saudi Arabia, Spain, and the UK. Five studies were carried out in university teaching hospitals, and one of these five studies recruited some participants from a mid-complexity level hospital. The other six studies were conducted in maternity units with inadequate information to judge the institution's level.)

Intervention: Selective episiotomy (episiotomy rates in the selective group ranged from 8% to 59%).

Comparison: Routine episiotomy (episiotomy rates in the routine group ranged from 61% to 100%; episiotomy rate differences between the groups within trials varied from 21% to 91%).

Outcomes	Anticipated abs (95% CI)	solute effects*	Relative ef- № of partici- fect pants (95% CI) (studies)		Certainty of the evidence (GRADE)	Comments
	Risk with routine epi- siotomy	Risk with se- lective epi- siotomy	(,	,,		
Severe perineal/vagi- nal trauma	3.6 per 100	2.5 per 100 (1.9 to 3.4)	RR 0.70 (0.52 to 0.94)	5375 (8 RCTs)	⊕⊕©© low ^{1,2,3}	Selective episiotomy compared to routine may reduce severe perineal/vaginal trauma
					due to imprecision and incon- sistency	
Blood loss at delivery	The mean	lood loss at (95% CI from elivery was 75 mL less to		336	000	We do not know if selective episiotomy
	delivery was			(2 RCTs)	very low ^{4,5,6}	compared to routine affects blood loss at delivery
	278 mL	20 mL more)	due to risk of bia		due to risk of bias, impreci- sion and inconsistency	
Babies with newborn 0 per 100		0 per 100	no events	501 (2 PCTs)	###©	Both selective episiotomy and routine prob-
Apgar score < 7 at 5 minutes				(2 RCTs)	moderate ^{7,8}	ably has little or no effect on Apgar < 7 at 5 minutes
	Due to imprecision		Due to imprecision			

Outcomes	Anticipated absolute effects* (95% CI) Risk with routine epi- siotomy Risk with siotomy Risk with siotomy		Relative ef- fect (95% CI)	№ of partici- pants (studies)	Certainty of the evidence (GRADE)	Comments	
Perineal infection	2 per 100	2 per 100 (0.9 to 3.6)	RR 0.90 (0.45 to 1.82)	1467 (3 RCTs)	000 9 9	Selective episiotomy compared to routine may result in little or no difference in per- ineal infection	
					Due to imprecision	meatimection	
Women with mod- erate or severe pain	45.1 per 100	32 per 100 (21.6 to 47.3)	RR 0.71 (0.48 to 1.05)	165 (1 RCT)	⊕©©© very low ^{10,11,12}	We do not know if selective episioto- my compared to routine results in fewer	
(measured by visual analogue scale)					Due to imprecision and indi- rectness	women with moderate or severe perineal pain	
Women with long- term dyspareunia (≥	12.9 per 100	14.8 per 100 (10.9 to 19.8)	RR 1.14 (0.84 to 1.53)	1107 (3 RCTs)	⊕⊕⊕⊝ moderate ¹³	Selective episiotomy compared to routine probably results in little or no difference in	
6 months)					Due to imprecision	women with dyspareunia at > 6 months	
Women with long- term urinary inconti-	32.2 per 100	31 per 100 (21.5 to 46.3)	RR 0.98 (0.67 to 1.44)	1107 (3 RCTs)	⊕⊕©© low ^{13,14}	Selective episiotomy compared to routine results may have little or no difference in	
nence (≥ 6 months)					Due to risk of bias and impre- cision	the number of women with urinary inconti- nence > 6 months	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI)

CI: Confidence interval; RR: Risk ratio





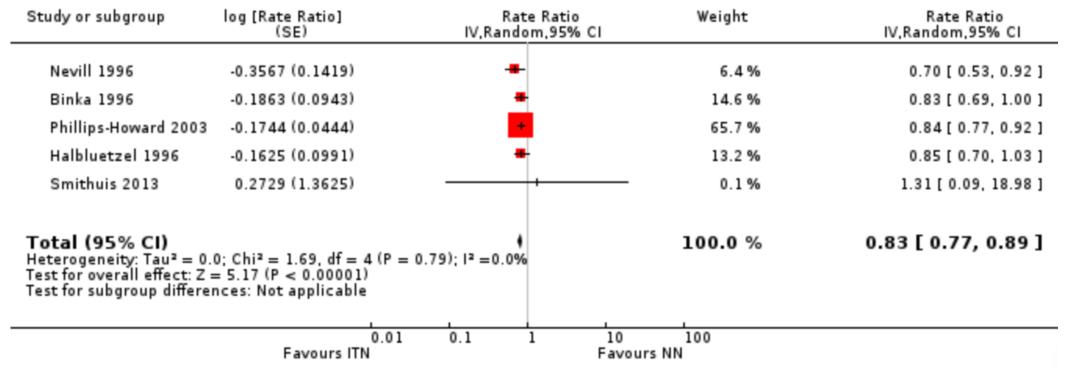
1. Insecticide-treated nets for malaria Reduce child mortality by 17% (high certainty evidence)

Review: Insecticide-treated nets for preventing malaria Comparison: 1 Insecticide-treated nets versus no nets Outcome: 1 Child mortality from all causes



Cochrane

Infectious Diseases



1. Insecticide-treated bednets for malaria

Editions: 1998, 2004 and 2018

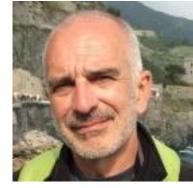
Impact on mortality underpinned the investment

Citations: 2231

2 billion mosquito nets delivered worldwide since 2004







2. Amodiaquine for uncomplicated malaria

40 trials included

17 were unpublished20 were in French

Amodiaquine higher cure rates than chloroquine

Amodiaquine reintroduced in Africa

Comparison: Outcome:		uine vs chloroc logic success	luine in sympto	omatic patie	nts		
Study		Expt n/N	Ctrl n/N	Weight	Peto OR	(95%CI)	
day 7							
Brazil 1983-84		15 / 36	13 / 30	4.2	•		0.94 [0.35,2.47]
Cameroun-Kumb	a 92	7/7	8/9	0.3			→ 5.92 [0.11,307.59]
Cameroun-South	88	82 / 119	39 / 117	15.4			4.13 [2.48,6.87]
CamerounBanga	ngt92	15 / 22	9 / 18	2.5	_	_	2.09 [0.60,7.35]
CamerounYaoun	de 92	19 / 19	15 / 18	0.7	-		- 8.82 [0.86,90.57]
Congo 92		22 / 26	9 / 23	3.0			6.80 [2.15,21.52]
Congo P-Noire 8	6	9 / 18	9 / 17	2.3			0.89 [0.24,3.30]
EquatorialGuinea		41 / 42	25 / 43	3.9			9.47 [3.43,26.11]
Gambia 94		82 / 100	64 / 100	10.3			2.48 [1.33,4.62]
Ivory Coast 93		51 / 62	41 / 59	5.8	-		2.00 [0.87,4.60]
Kenya 1989		59 / 73	29 / 85	10.2			6.56 [3.50,12.29]
Kenya-Entosopia	91	49 / 60	19 / 54	7.2			6.78 [3.22,14.30]
Kenya-Kilifi 1993		29 / 40	17 / 43	5.4			3.74 [1.58,8.84]
Kenya-Malindi 19	84	60 / 60	61 / 69	2.0			7.23 [1.73,30.16]
Kenya-Migori 199	90	27 / 30	20 / 35	3.4		- _	5.03 [1.71,14.84]
Kenya-Ortum 199		21 / 22	14 / 29	2.9			8.57 [2.63,27.96]
Kenya-Turiani 19	91	51 / 52	10 / 49	6.4			24.90 [11.26,55.09]
Kenya-Turiani 19	92	50 / 51	34 / 42	2.1		+	6.92 [1.75,27.32]
Kenya-West 1987		9 / 27	5 / 56	2.7			5.58 [1.65,18.89]
Madagascar 83/8	4	54 / 56	44 / 59	3.8			5.58 [2.00,15.57]
Madagascar 85/8		57 / 62	50 / 60	3.5	_	_	2.21 [0.75,6.47]
Nigeria-Ibadan 84		22 / 22	22 / 22	0.0			1.00 [0.00,0.00]
Nigeria-Ibadan 90		52 / 52	43 / 46	0.8	4		- 8.80 [0.89,87.05]
Philippines 84/85		7 / 13	14 / 14	1.3	-		0.08 [0.01,0.45]
Subtotal (99%CI)		890 / 1071	614 / 1097	100.0		•	4.29 [3.30,5.58]
Chi-square 203.4							

3. Oral rehydration salt solution for diarrhoea



Fewer children put on intravenous drips with the new ORS formula

Seokyung Hahn et al. BMJ 2001

Study	Intervention n/N	Control n/N	Odds ratio (95% Cl fixed)	Weight %	Odds ratio (95% CI fixed)
Bangladesh 1995a ¹¹	4/19	5/19		3.0	0.75 (0.17 to 3.36)
Bangladesh 1996a ¹³ *	0/18	0/18		0.0	Not estimable
CHOICE 200114	34/341	50/334	-8-	34.5	0.63 (0.40 to 1.00)
Colombia 2000 ¹⁵	7/71	16/69		11.1	0.36 (0.14 to 0.95)
Egypt 1996a ¹⁷	6/45	5/44		3.3	1.20 (0.34 to 4.26)
Egypt 1996b ¹⁸	1/94	8/96		5.9	0.12 (0.01 to 0.97)
India 1984a ¹⁹ *	0/22	0/22		0.0	Not estimable
India 2000b ²¹	11/88	12/82		8.2	0.83 (0.35 to 2.01)
Mexico 1990a ²²	2/82	7/84		5.1	0.28 (0.06 to 1.37)
Panama 1982 ²³ *	0/33	0/30		0.0	Not estimable
USA 1982 ²³	0/15	1/20		1.0	0.42 (0.02 to 11.03
WH0 1995 ²⁴	33/221	43/218		27.9	0.71 (0.43 to 1.18)
Total (95% CI) χ^2 =6.52, (df=8), z=3.5	98/1049	147/1036	•	100.0	0.61 (0.47 to 0.81)
$\chi = 0.52$, (ui=0), $z = 5.5$	iU	0.0)1 0.1 1 10 1	00	
		Favol	rs treatment Favours cor	itroi	

* No patients required intravenous infusion



Reduced osmolarity : oral rehydration salts (ORS) formulation : a report from a meeting of experts jointly organised by UNICEF and WHO : UNICEF house, New York, USA, 18 July 2001

Directly observed therapy for TB

Hiroshi Nakajima Director General of WHO



"DOTS is the greatest invention since the discovery of penicillin"

WHO Press Release November 1997

Jimmy Volmink Cochrane Author



"DOTS is conspicuous in its absence among the trials we reviewed...(research) evaluating the independent effects are awaited"

BMJ systematic review November 1997

Five trials, no difference between self treatment and DOTS for cure

Review: Directly observed therapy for treating tuberculosis Comparison: 1 Directly observed versus self-administered

Outcome: 1 Cure (negative sputum smear in last month of Rx in patients +ve initially)

Study or subgroup	Directly	Observed T n/N	Shelnfaqqofministered therapy n/N		sk Ratio lom,95% Cl	Weight	Risk Ratio M-H,Random,95% Cl
Zwarenstein 2000 Z	AF (1)	31/54	9/22	_		7.2 %	1.40 [0.81, 2.44]
Zwarenstein 1998 Z	AF (2)	42/111	31/61	-	+	14.0 %	0.74 [0.53, 1.05]
Kamolratanakul 199	9 THA (3)	315/414	283/422		➡	32.1 %	1.13 [1.04, 1.24]
Walley 2001 PAK (4)		199/335	100/162	-	-	27.3 %	0.96 [0.83, 1.12]
Hsieh 2008 TWN (5)		30/32	22/32			19.5 %	1.36 [1.06, 1.75]
Total (95% CI) Total events: 617 (Dire Heterogeneity: Tau ² = Test for overall effect: 2 Test for subgroup differ	0.02; Chi² Z = 0.87 (= 12.44, df P = 0.38)	699 y), 445 (Self administered t = 4 (P = 0.01); I ² =68% e	therapy)	•	100.0 %	1.08 [0.91, 1.27]
		Favours	0.2 self administered	0.5 Favo	1 2 ours directly o	5 bserved	

(1) Directly observed patients visited nurses at a clinic or lay health workers at their home

- (2) Directly observed patients had to visit a clinic
- (3) Directly Observed patients chose observer. In the initial 2 months, DO had more intense contact.

(4) Directly observed patients observed by healthworkers at clinic, or community health workers or family members at home.

(5) Directly observed patients observed by case manager for first two months only

nfectious Diseases



	Relative risk	: (95% CI)	Relative risk (95% CI)	Weight (%)
Wohl et al (2006) ²²			1-00 (0-75-1-33)	11-27%
Macalino et al (2007) ²³			1-63 (1-01-2-64)	6-01%
Sarna et al (2008) ³⁵			0-90 (0-73-1-12)	13-83%
Taiwo et al (2008)26			1-23 (1-05-1-44)	16-46%
Maru et al (2009) ²⁷		_	1-02 (0-76-1-38)	10-83%
Nachega et al (2009) ¹³			0-89 (0-71-1-12)	13-38%
Gross et al (2009) ²⁸			072 (0-51-1-02)	9-31%
Naidoo et al (2009) ²⁹			0-95 (0-68-1-33)	9-62%
Bangsberg et al (2009) ³⁰		-	1-44 (0-72-2-89)	3-41%
Amsten et al (2009) ³²			1-60 (0-98-2-62)	5-86%
Overall		—	1.04 (0.91-1.20)	100-00%
	T			
	0.5 1.0	2-0 3-0		
	4	2.0 3.0		
	Self-administered	DOT better		

treatment better

DOT DEL