

BCG

BCG

2000 6



.....	
.....	1
1.	1
2.	5
3.	6
.....	7
1. BCG	7
2. BCG	9
3. BCG	10
4. Tuberculins	12
5. BCG	13
.....	16
1.	16
2.	17
3.	18

.		20
1.	가	20
2.		25
3.		27
4.		29
5.	가	30
.		31
1.		31
2.		35
.		39
< >		42
< 1>	Abstraction Form	50
< 2>	Quality Assessment Form	53
ABSTRACT		56

1			22
2	가		24
3	95%		26
4		95%	28
5			29

1	95%		25
2			30

BCG

BCG

BCG

BCG

10

가

가 , protocol, ,

16

가

가

95%

BCG

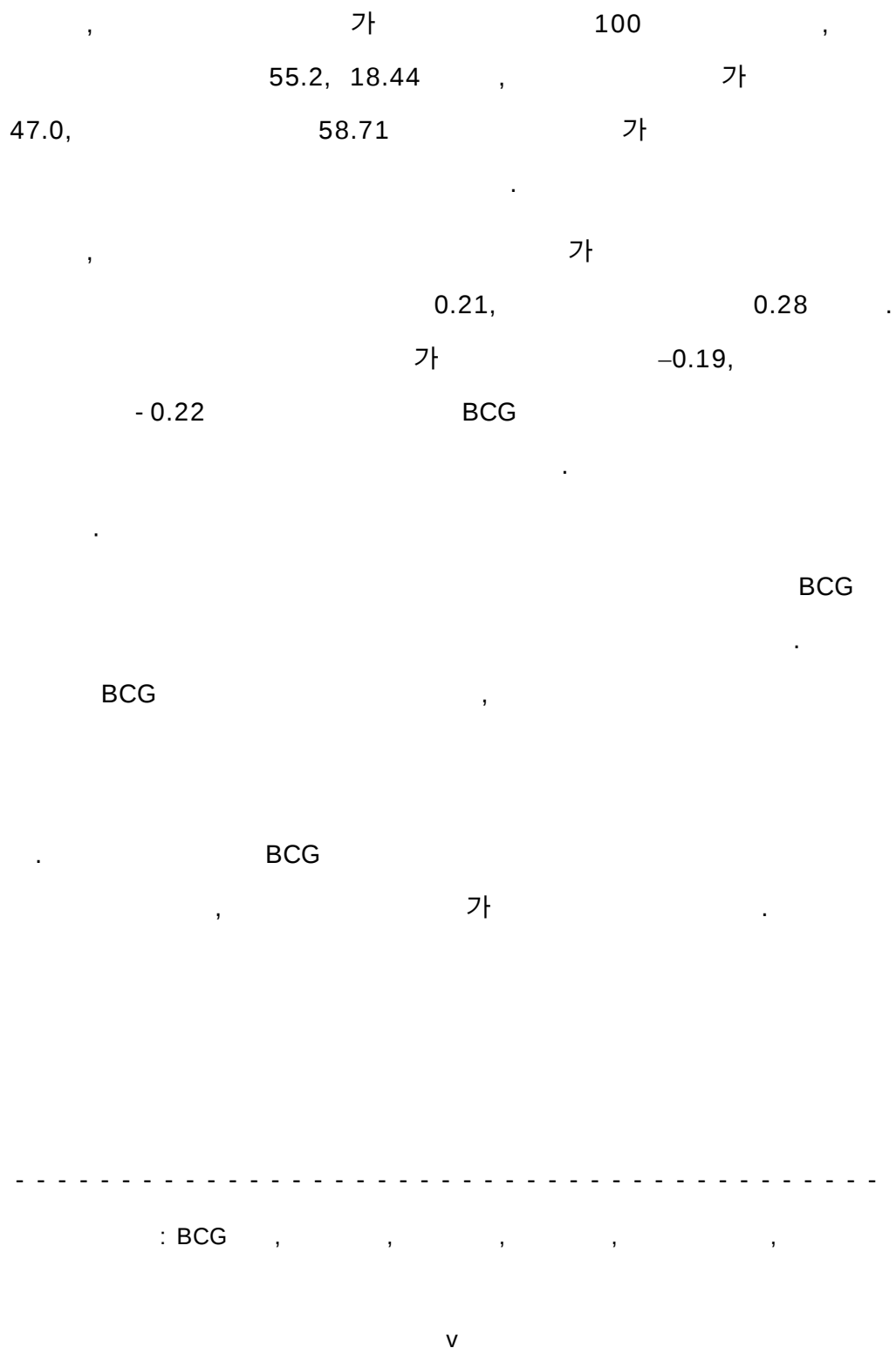
가

-0.12 (95%

: -0.14, - 0.10), - 0.07 (95% : - 0.24,

0.10)

BCG



I.

1.

Mycobacterium tuberculosis

가 , 3
가 . 5 - 6%
1985 가 5
15.8%가 가 (Daniel, 1994). 1995
0.8% 1962 5.2%, 1980 2.5%, 1990
1.6% . 1997
10 57.3
(WHO, 1999; , 1995),
.

, BCG (Bacille Calmette
- Guerin)

1 BCG 1921
, 가
BCG
(Clemens , 1986; Grange , 1983), (World

Health Organization; WHO)

BCG

가

.

,

BCG

가

,

4

가

(

,

2000).

BCG

가

. BCG

가

가

(Grange , 1983), WHO

.

가

,

,

,

,

(Victoria , 1985; Lotte, 1988; Marie, 1958; Gheorchiu,

1978).

BCG

1993

가

,

(

, 1997;

,

1997; Ormerod , 1993)

BCG

가

BCG

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BCG

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5

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BCG

BCG

가가

가

BCG

(Griffith , 1961; Research Committee
of the British Tuberculosis Association, 1965, 1971)

가 .

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BCG

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BCG

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BCG

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BCG

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, 가

(Kassimi , 1995; Youmans, 1962; Raffel, 1946).

BCG

BCG

가

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가

가

(Lugosi, 1992; Landi , 1967)

BCG

가

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BCG

가

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2.

BCG

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BCG

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BCG

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, BCG

,

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, BCG

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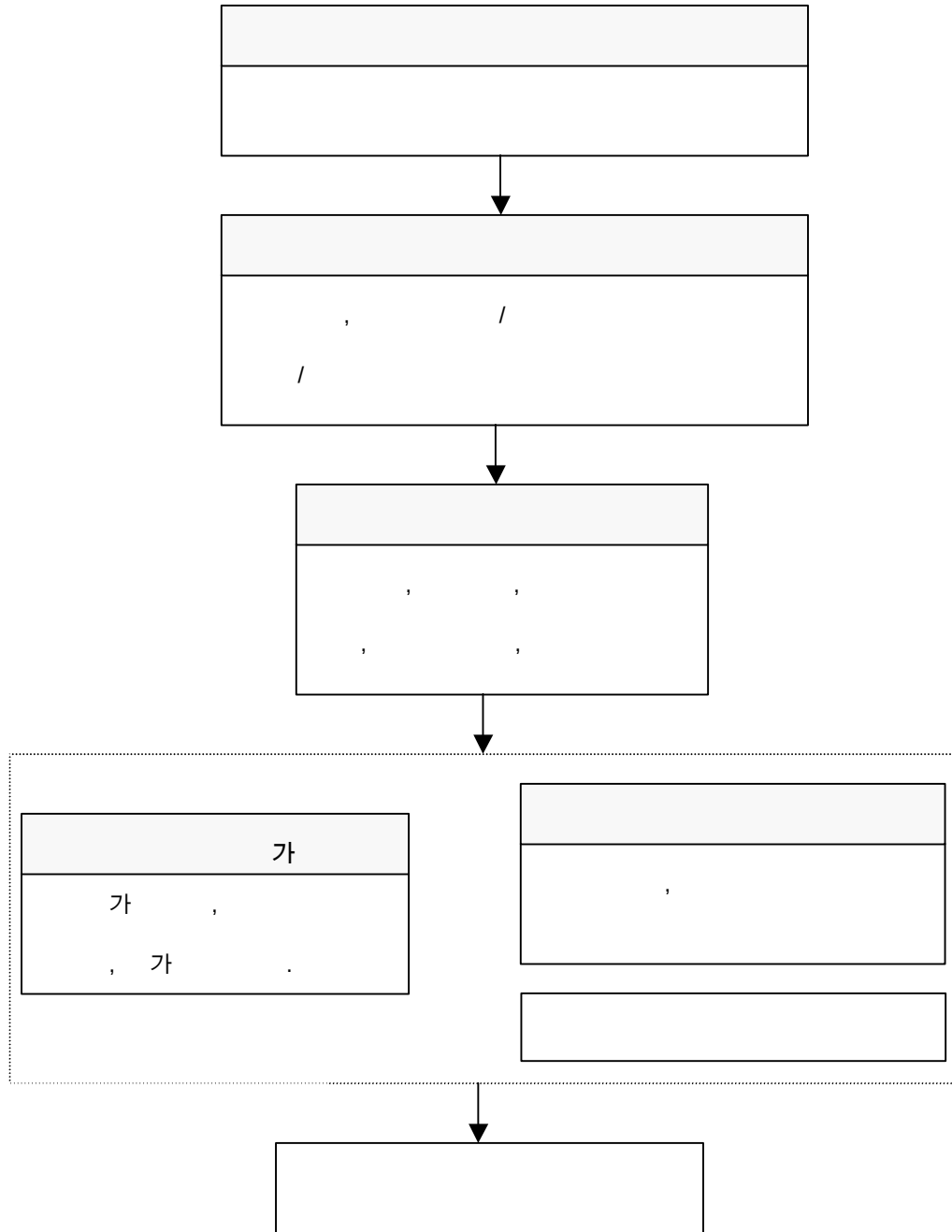
,

가

,

.

3.



II.

1. BCG

(Live attenuated vaccine)

(inactivated vaccine)

(
, 2000). BCG(Bacillus Calmette - Guerin) 1902 Nocard가
Calmette Guerin 13 231
BCG Macrophage

(Lymphokine)

Macrophage

BCG 1921 25

, 2

(Scandinavian Red Cross Societies) UNICEF BCG

BCG

WHO EPI(Expanded Program of Immunization)

85% (戸井田, 1996).

BCG 1952 , 1960
 Pasteur - 1173P2 BCG
 , 1979
 . 1987
 BCG 가
 .
 BCG (Mycobacterium bovis)
 ,
 .(Behr MA, 1999; Grange, 1986; Nyboe, 1966). BCG
 .
 Glaxo - 1077, Tokyo - 172, Pasteur - 1173P2, Copenhagen - 1331
 BCG 90%
 Pasteur - 1173P2 ,
 Pasteur - 1173P2 BCG 가
 Copenhagen - 1331 Tokyo - 172
 (,2000).

2. BCG

BCG .

BCG 0 - 84%

, 1980 BCG

Chingleput Trial BCG 7.5

BCG 가

BCG 가 (戸井田, 1996).

Colditz BCG BCG

50%, 70%

(Colditz , 1994), BCG

가 87%

(Batieha , 1998). BCG

6 가 가 (Romanas,

1987) BCG BCG

1975 7 - 1977 7 , BCG

0

33 가 , BCG BCG

1986 - 1992

가 3 1994

.

7 - 12% , 27%

Thilothammal BCG

77% 가 (Thilothammal , 1996), Guler BCG , , X , CT 가 (Guler , 1998), Mittal BCG (Mittal , 1996) BCG . Mariana 1990 - BCG (Marianna , 1998).

3. BCG

BCG 1921 Weil - Halle . BCG . , 가 BCG 1923 Weil - Halle , BCG

. Wallgren 1928
 . , ,
 가
 BCG WHO
 Rosenthal
 1967
 .
 .
 가
 가 0.04 - 0.05mg
 80mg/ml
 가 (Sawada, 1971), Ormed
 BCG
 가 80%
 가 (Ormed , 1993).
 12 0.05ml, 1
 0.1ml BCG
 , .

4. Tuberculins

Tuberculin

가 ,
(Old Tuberculin) 1890 Koch
가
가 ,
가가 가 Old tuberculin ,
가
Purified protein derivative of tuberculin(PPD) (, 1999).
tuberculoprotein ,
(Mantoux test) (Heaf test, tine test)
old tuberculin PPD
가
가 Mantoux test , PPD
0.1ml(10unit) 48 - 72
5 - 10mm
(5TU)
tubercule bacillus

Heaf test 1ml PPD 10
 multiple - puncture gun 2 1mm, 2
 2mm . 3 - 10
 grade 1, 2, 3, 4 , grade 2
 (Mantoux test 5 - 14mm) tuberculoprotein
 (Martindale 32nd.
 1999). BCG
 ,
 . BCG
 (, 1999).

5. BCG

1)

BCG

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BCG

가

,

.

BCG

(CDC, 1996).

1951 (26) 3

BCG BCG

가 BCG 가 .

1952 BCG ,

BCG

BCG , 1965

BCG . 1967

BCG 가 , 26 646

BCG 79.3%,

0.3% . 1967 4

BCG

(室橋豊穂, 1995).

BCG 1981 64

118 ,

10 BCG (Grange ,

1983). BCG WHO EPI(Expanded Program of Immunization)

85% (戸井田, 1996).

2)

BCG
BCG
BCG
WHO
1997
0 - 29
1965 25.3%, 1975 58.4%, 1985 80.3%, 1995 91.7%
가 (, 1995).

III.

1.

1)

1 Medline(1960 - 2000)
, BCG vaccine, PPD, Tuberculin, Intradermal,
Percutaneous, Multiple puncture .
KoreaMed, NACSIS Webcat

2)

BCG
BCG
(crossover)
. BCG , BCG
가 가

BCG가

.

2.

, , ,
,
, , , ,
(1) .

10 - 13

,

.

가 (2)

가 . 가 ,

protocol, , , 16

Ronchon, Moher 가 (check list)

(Moher , 1998; Moher , 1995; Ronchon , 1994).

3 , 0 . ,

(induration)

5 . 가 가

50 , 가

3.

가 Khan, Oxman, Jenicek
 , 가 L ' abbeka, Lau
 Pharmacoepidemiology (Khan
 , 1996; Oxman , 1994; Jenicek, 1988; Einarson, 1998; L ' abbeka
 , 1987; Lau, 1997).

BCG
 (RD: Rate Difference)^a 95% (confidence
 interval)
 BCG
 가 (weight; W_i) 가 (weighted
 overall effect size)^b 95%
 (inverse variance method)
 (DerSimonian , 1986).

^a RD (Rate difference) :

^b (weighted overall effect size)= $\sum W_i RD_i / \sum W_i$

(homogeneity)

c , 가

DerSimonian (random effect

model) d 95% (fixed effect

model)

가, , 가

(subgroup)

95%

가 (publication bias) x

y (funnel plots)

가 .

$$^c Q = \sum W_i (RD_i - RD)^2$$

$$^d RD^* = \sum W_i^* RD_i / \sum W_i, \quad W_i^* = 1 / (1/W_i + \tau^2),$$

$$\tau^2 = \{Q - (k - 1)\} / \{\sum W_i - (\sum W_i^2) / \sum W_i\}$$

IV.

1. 가

1)

BCG

13

10

. (Research Committee of the British
Tuberculosis Association, 1965) 1971 4

, Sawada

가 ,

(Sawada, 1972). Griffith 가

(Crossover design)

(Griffith , 1961, 1963).

가 3 , , ,

가 7 . (comparative

clinical trial)

BCG

(randomization)

Jarad

4

. 가 0 - 5

4 3
 BCG
 6 - 60 Kemp
 2 3 2
 8 - 13 , 1 , 2 , 3
 . Landi
 BCG 1 22
 (1).

표 1. 연구대상 논문의 일반적 특성

저자, 연도	연구설계방법	출판국	대상자연령	대상자수 (MTP+IDT ²)	Pre -test ³	Post-test ⁴	test 시기 ⁵
김우성 등, 1997	Comparative	Korea	neonate	371	no	5TU PPD	10-16주
김정희 등, 1999	Comparative	Korea	3-15month	143	no	5TU PPD	8-60주
김상재 등, 1983	Comparative	Korea	1-2yr	651	no	1TU PPD	9-10주
Jarad 등, 1999	Comparative (Randomized)	England	10-14yr	169	yes	Heaf	8주
Kemp 등, 1996	Comparative (Randomized)	USA	18-45yr	59	yes	10TU PPD	8주
Research committee of the British Tuberculosis association, 1971	Comparative	Scotland	11-12yr	805	yes	10TU PPD	8-13주
Landi 등, 1967	Comparative	Canada	High school, student nurse	708	yes	5-10TU PPD	6-8주
S Afr. Tuberculosis Study group 1973	Comparative (Randomized)	South Africa	7-15yr	3706	yes	2TU PPD	10주
Rahaju 등, 1970	Comparative	Indonesia	0-5yr	191	no	5TU PPD	12주
Vaughan 등, 1973	Comparative (Randomized)	Tanzania	7-10yr	238	yes	2TU PPD	10-12주

MTP¹: Multiple-puncture group, IDT²: Intradermal Technique group

Pre-test³: BCG백신 투여 전 결핵반응 검사, Post-test⁴: BCG백신 투여 후 결핵반응 검사

test 시기⁵: BCG백신 투여 후 결핵반응 검사 시기

2) 가

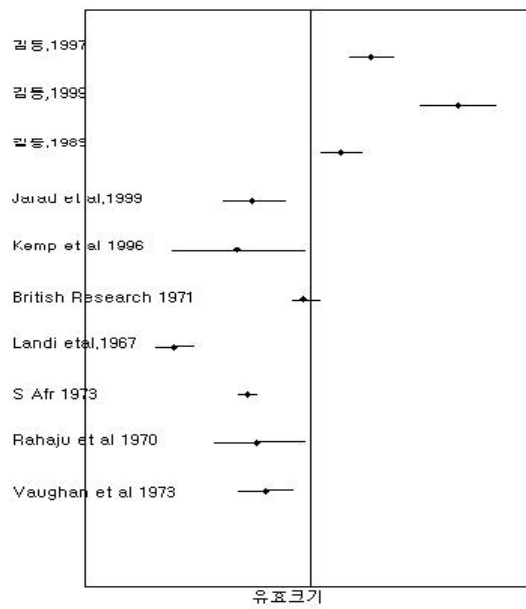
가 가
가 100
32 , 85 , 55.2, 18.44 .
가 47.0, 12.12, 가
58.71, 0.64 가
($p>0.05$). 가
가 13 가
6 가 ,
4 12 30 가
(2).

표 2. 연구대상 논문의 질평가 결과

문항내용	대상논문										합계	평균
	김등, 1997	김등, 1999	김등, 1983	Jarad 1999	Kemp 1996	Research Committee 1971	Landi 1967	S Afr 1970	Rahaju 1970	Vaughan 1973		
Center status	0	1.5	0	0	1	3	3	3	1	1	13.5	1.35
Compatibility of study objects	3	1.5	1.5	3	3	3	3	1.5	1.5	3	24	2.4
Selection description	3	3	0	3	3	1.5	0	3	0	3	19.5	1.95
No. of subjects seen and reject log	3	3	3	3	3	3	3	3	3	3	30	3.0
Withdrawals	3	3	1.5	3	3	1.5	1.5	1.5	3	1.5	22.5	2.25
Therapeutic regimen definition	3	3	3	3	1.5	3	3	3	3	3	28.5	2.85
Randomization	0	0	0	3	3	1.5	0	3	0	3	13.5	1.35
Observer blinding	0	0	0	5	3	0	0	5	0	5	18	1.8
Administrator Control	0	0	0	3	0	1.5	0	3	0	0	7.5	0.75
Reviewer control	0	0	0	3	0	1.5	0	3	0	0	7.5	0.75
Strain&Batch control	0	0	3	1.5	0	0	0	3	0	0	7.5	0.75
Outcome description	3	3	3	3	3	3	3	3	3	3	30	3.0
Criteria objective	0	0	0	3	1.5	1.5	0	0	0	0	6	0.6
Statistical analysis	3	3	0	3	3	0	0	3	0	0	15	1.5
Major endpoint	3	3	1.5	3	3	1.5	1.5	3	1.5	3	24	2.4
Starting&stopping date	3	3	0	0	0	3	0	0	0	0	9	0.9
합계	27	27	16.5	42.5	31	28.5	18	41	16	28.5	276	27.6
총점(%)	54	54	33	85	62	57	36	82	32	57	552	55.2
각 논문별 질평가 총점(%)의 평균: 55.2. 표준편차: 18.44												

2.

10 (effect size)
 95% (3). 10
 3 BCG
 97.67%, 97.53%, 73.81%
 95% 0
 , 7
 95%
 0
 .
 (1).



(1)

표 3. 유효크기와 95%신뢰구간

저자,연도	MTP ¹	IDT ²	RD ³	95%CI ⁴
김우성 등, 1997	0.9767	0.7632	0.2135	0.13 0.29
김정희 등, 1999	0.9753	0.4516	0.5237	0.40 0.65
김상재 등, 1983	0.7381	0.6316	0.1065	0.03 0.18
Jarad 등, 1999	0.7284	0.9318	-0.2034	-0.31 -0.09
Kemp 등, 1996	0.5000	0.7586	-0.2586	-0.50 -0.02
Research committee of the British T&T association.1971	0.8957	0.9204	-0.0247	-0.07 0.02
Landi 등, 1967	0.5047	0.9858	-0.4812	-0.55 -0.41
South Afr. Tuberculosis Study group, 1973	0.4892	0.7102	-0.2209	-0.25 -0.19
Rahaju 등, 1970	0.4407	0.6288	-0.1881	-0.34 -0.04
Vaughan 등, 1973	0.7845	0.9426	-0.1581	-0.24 -0.07

MTP¹: multiple puncture group conversion rate,
RD³: Rate Difference (MTP¹-IDT²) ,
IDT²: Intradermal group conversion rate
95%CI⁴: 95% Confidence Interval

3.

(homogeneity)

Q 368.42 (p<0.05).

가

BCG

95%

BCG

가

- 0.12, 95%

(- 0.14,

- 0.10)

BCG

τ^2 0.0716,

- 0.07, 95%

(- 0.24, 0.10) (4).

U^e 0.6130

$$^e U = (\sum W_i \times RD)^2 / \sum W_i$$

4.		95%	
RD [†]	95% CI [‡]	RD [†]	95% CI [‡]
- 0.12	(- 0.14, - 0.10)	- 0.07	(- 0.24, 0.10)

[†] RD ; Rate Difference

[‡] 95% CI ; 95% Confidence Interval

4.

10 가, 가 ,
 , 가
 (5).
 가 .
 3 가 0.28, 95%
 (- 0.36, 0.92) , 7 가
 -0.22, 95% (- 0.43, - 0.01) . ,
 U 0.74(p> 0.05), 4.04(p<0.05)

5.

		RD [*]		P [†]	‡
		3	0.28	0.22	0.04
		7	- 0.22	0.14	- 0.22
가	>55	5	0.03	0.09	0.30
	≤ 55	5	- 0.17	0.38	-
		≤ 5	0.16	0.29	0.03
		≥ 6	- 0.22	0.15	- 0.22

^{*} RD ; Rate Difference

[†] P ; t - test

[‡] ; 가 (p<0.05)

가 55 가 가 55

55 t - test 가

가

가

5

가

0.17, 95% (-0.05, 0.38) , 6

가 -0.22, 95% (- 0.36, - 0.09)

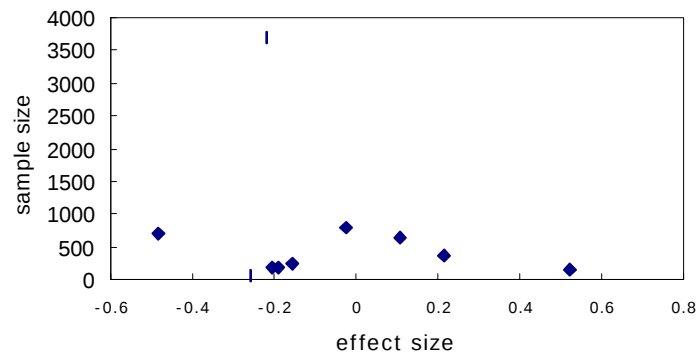
U 2.34(p= 0.13), 10.40(p=0.001)

6

5. 가

y , x
(2). 10

.



2.

V.

1.

10 57.3 .

(WHO, 1999;

, 1995),

BCG

가 , 4 가
(, 2000).

WHO

Tokyo 172

BCG

1993 가

BCG

가 BCG .

BCG 5

, BCG BCG

가가 가 BCG

(Griffith , 1961; Research Committee of the British
Tuberculosis Association, 1965, 1971) BCG

가 .

BCG

BCG

BCG

(Tuberculin

) 100%

, BCG

. BCG BCG

, , ,

, 가 가

가 BCG

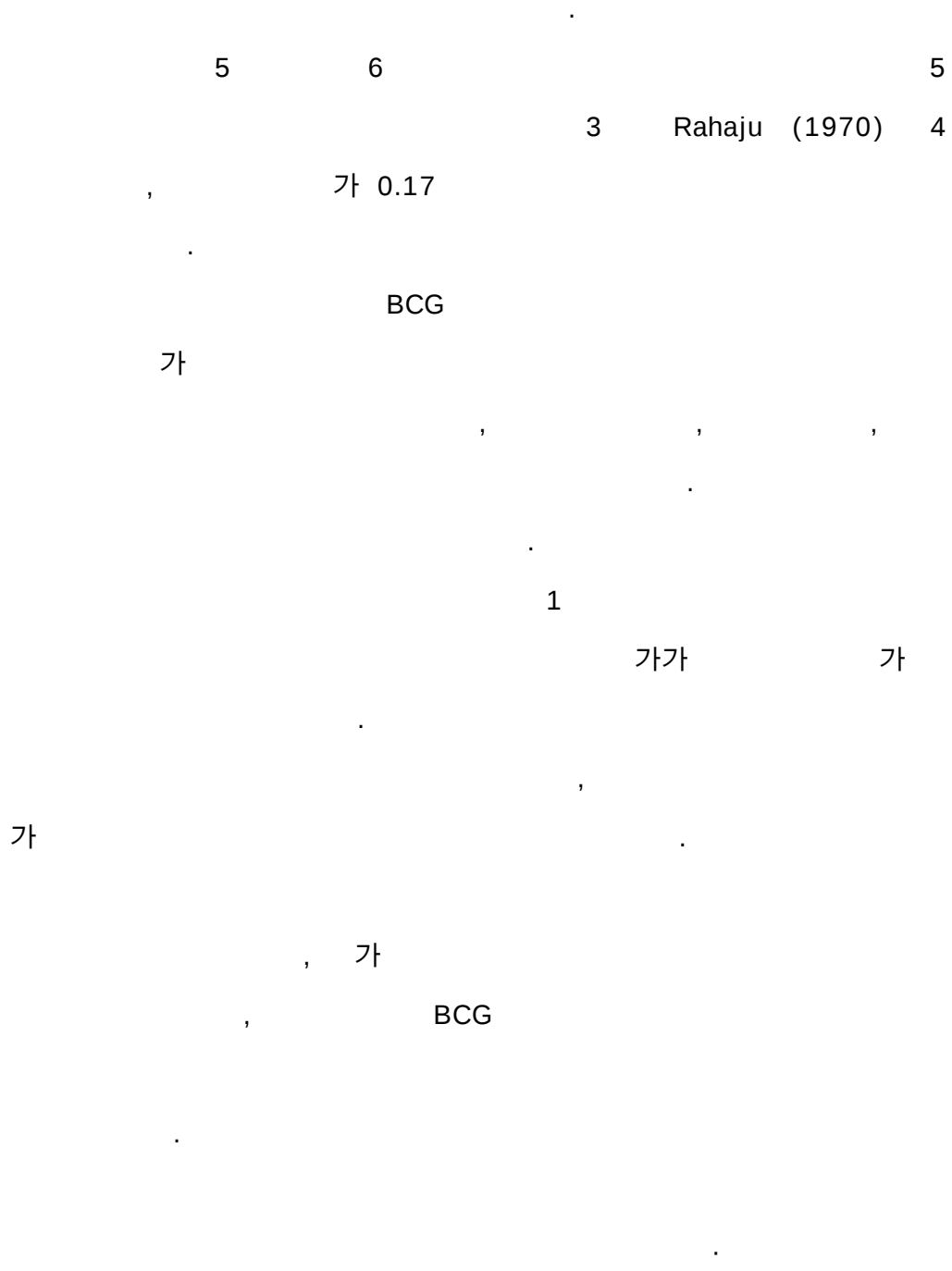
가

가 Moher (1998, 1995), Ronchon
(1994) 가 가 (check list)
16 0 - 3 ,
가
5
가 가
10
(1999) (1971)
가
, (1983)
(1973)
Glaxo - 1077, Tokyo - 172, Pasteur - 1173P2,
Copenhagen - 1331
가
가
가
BCG

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1930 Birge Cochrane
가
. 가
DerSimonian
95%
(, 1998).
가 가
, 가 .
가 가
,
가,
가,
가,
1 가
가,
.

2.

가 3 , , 가 가 7
(Comparative Clinical trial) ,
4 .
(7 - 15) , (18 - 45) , 가
1960 - 70 5 , 1990 4
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3 ,
BCG
(1983) 2 1990
.
BCG
1993 BCG 4
.
가 10
100 55.2, 18.44 . 가
47.0, 12.12 , 가
58.71, 0.64 가
($p>0.05$). 가
가 13 가 6
가 , 4



BCG

.

BCG

가

, 가

BCG

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, ,

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가 .

BCG

가

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VI

BCG , 가
(, 2000). BCG
BCG
BCG
BCG
10 , 3
7 ,
가 10 55.2, 18.44 ,
가 47.0, 12.12, 가
58.71, 0.64 가
BCG
가 0.07

BCG

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가,

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가

가

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0.28,

0.22

BCG

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5

6

5

4

0.17

BCG

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가

가

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BCG

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가

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BCG

가

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가

BCG

가

. , 2000
 , . BCG
 . 1997; 40: 489 - 496
 , . BCG . 1985 ;
 32(2): 75 - 85
 , , . BCG
 (II). 1983; 1 - 18
 , , . BCG
 . 1999; 42: 1507
 . BCG .
 , 1992
 , , . BCG
 . 1993; 36: 1300 - 1307
 . 7 , 1995
 . , 1998
 , , . BCG
 . 1997; 40: 1120 - 1130
 . 2 . , 1999
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< 1>

Abstraction Form

Authors _____ Resources _____

Country _____ Year Publication _____

Title _____

Study Design _____

Randomized Yes No Unknown _____

Placebo Yes No

Subjects

Total Number of eligible subjects: _____

Subjects enrolled : _____

Subjects state: _____

Age range: _____ Gender (No. of male): _____

Number of subjects completed trial: _____

MTP No. _____ IDT No. _____

Bias Control

Administrator : Yes No Unknown

Reviewer : Yes No Unknown

Intervention

- Prevaccination tuberculin test : Yes No Unknown

- Dosage and method :

	BCG strain	Dosage	method
MTP			
IDT			

Other:

- Post - vaccination tuberculin test

Dosage & _____

Administraion Method_____

Vaccination test _____

Test _____

Conversion _____

Outcome and Results

	Conversion No	Induration size	Conversion rate
MTP			
IDT			

Other: _____

Adverse Reaction or Local Reaction

	Adverse Reactions	Local Reactions
MTP		
IDT		

Other: _____

< 2>

Quality Assessment Form

ID _____

Title _____

Type of Trial _____

Resources _____

Country Year Publication _____

Basic Descriptive Material

1) Center status

3 Cooperative study >3 group 1.5 Cooperative study <3 groups

0 Single center/Unknown

Study protocol

2) Compatibility of Study Object

3 Exactly Compatible 1.5 Partial 0 No

3) Selection Description

3 Adequate 1.5 Fair 0 Inadequate

4) Number of subjects seen and reject log

3 Yes 1.5 Partial 0 Unknown

5) Withdrawals

3	No withdrawals	1.5	List given	0	No list
---	----------------	-----	------------	---	---------

6) Therapeutic regimen definition

3	Adequate	1.5	Fair	0	Inadequate
---	----------	-----	------	---	------------

7) Randomization

3	Yes	1.5	Partial	0	No/Unknown
---	-----	-----	---------	---	------------

8) Blinding - Observer to results

5	Yes	2.5	Partial	0	No/unknown
---	-----	-----	---------	---	------------

9) Bias Control - Administrator

3	Yes	1.5	Partial	0	No/unknown
---	-----	-----	---------	---	------------

10) Bias Control - Reviewer

3	Yes	1.5	artial	0	No/unknown
---	-----	-----	--------	---	------------

11) Bias Control - Strain and Batch

3	Yes	1.5	Partial	0	No/Unknown
---	-----	-----	---------	---	------------

12) Description of the criteria for measuring outcomes

3	Yes	1.5	Partial	0	No/unknown
---	-----	-----	---------	---	------------

13) The objective of criteria

3	Yes	1.5	Partial	0	No
---	-----	-----	---------	---	----

Data Analysis

14) Appropriate Statistical Analyses

3	Good	1.5	Poor	0	Inadequate
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15) Major Endpoint

3 Test & P 1.5 P, No test, Test, No P 0 Neither

Presentation of Results

16) Dates of Starting and Sopping accession

3 Yes 0 No

(total)

ABSTRACT

Tuberculin Conversion Rate Difference by Administration Methods of BCG Vaccine : A Meta - Analysis

Yun - Hee, Jang
Graduate School of
Health Science and Management
Yonsei University

(Directed by Prof. Chung Mo Nam, Ph. D)

The aim of this study was to provide basic information that can be useful in selecting more effective administration method of BCG vaccine by reviewing current trends and results of studies which compare multiple puncture BCG vaccination method with conventional intradermal method, and by quantitative meta - analysis combining conversion rate difference of tuberculin test.

A total of 10 articles were eligible for the inclusion criteria. The quality assessment form consisting of 4 parts – basic descriptive material, study protocol, data analysis, presentation of results and 16 check lists were used as an instrument of quality assessment. For quantitative meta - analysis, the weighted overall effect size was estimated by fixed effect model and random effect model.

The results of this study are as follows.

First, the weighted overall effect size of tuberculin conversion rate difference following multiple puncture and intradermal BCG vaccination were -0.12 and -0.07 by fixed effect model and random effect model respectively. This means that Intradermal method of BCG vaccination have shown the higher conversion rate of tuberculin test than that of Multiple puncture method.

Second, in quality assessment of total 10 studies the average score is 58.71, standard deviation(SD) is 18.44, providing 100 as maximum score. In 3 domestic studies average quality score is 47.0 and 58.71 in 7 foreign countries. Domestic studies' average score is lower than others but statistically insignificant.

Third, classifying studies into two groups by study publication countries, estimated weighted overall effect size by random effect model is 0.28 in domestic studies, -0.22 in foreign countries. In domestic studies, conversion rate following multiple puncture BCG vaccination is higher than intradermal method.

The Results obtained by quantitative meta-analysis, tuberculin conversion rate following conventional interdermal BCG vaccination is higher than that of multiple puncture method. But there are many advantages to the multiple puncture method. It is easy to use, requires less skill and training, occurs few local adverse reaction and less administration site pain. Therefore further well-designed systemic studies to ascertain the more effective administration method of BCG vaccination should be performed.