

Probiotici orali in ginecologia

Pier Luigi Venturini



Dipartimento di Ginecologia
Università di Genova

Istituto Giannina Gaslini
Direttore dell'U.O di Ostetricia e Ginecologia

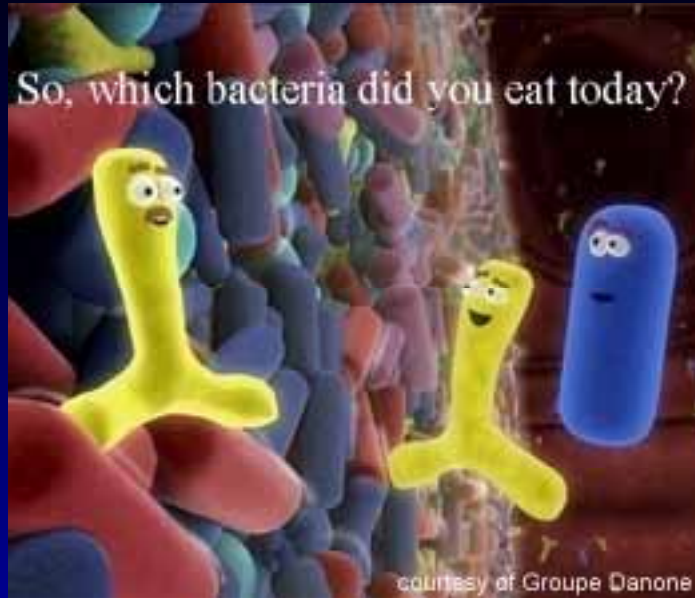


Cos'è un probiotico?

“Live microorganism which, when administered in adequate amounts, confers a health benefit on the host”

FAO/WHO

“Qualsiasi microrganismo vivo che, somministrato in quantità adeguate, ha un effetto positivo sulla salute dell'ospite”



'E' stato recentemente dimostrato che alcuni Lattobacilli possono avere un ruolo terapeutico nelle infezioni dell'apparato urogenitale femminile...'

*'...è stato inoltre dimostrato che questi batteri sono efficaci anche se somministrati **per via orale**...gli Autori hanno infatti identificato quei Lattobacilli che, isolati dalla vagina, erano in grado di **sopravvivere** al passaggio attraverso il tratto gastrointestinale, stabilendo un legame tra il tasso di sopravvivenza nell'intestino e la capacità di **colonizzare** la mucosa vaginale'*

Morelli et al., J Clin Gastroenterol 2004



FEMS Immunology and Medical Microbiology 30 (2001) 49–52

FEMS
Immunology and
Medical Microbiology

www.fems-microbiology.org

Oral probiotics can resolve urogenital infections

Gregor Reid ^{a,b,*}, Andrew W. Bruce ^a, Nicola Fraser ^a, Christine Heinemann ^a,
Janice Owen ^c, Beth Henning ^c

^a *Lawson Research Institute, 268 Grosvenor Street, London, Ont., Canada N6A 4V2*

^b *Department of Microbiology and Immunology, University of Western Ontario, London, Ont., Canada*

^c *WomensHealth of London, London, Ont., Canada*

The present study was set up to determine whether oral intake of GR-1 and RC-14 could be used to deliver the organisms to the vagina by natural colonization and ascension.

Oral probiotics can resolve urogenital infections

Gregor Reid ^{a,b,*}, Andrew W. Bruce ^a, Nicola Fraser ^a, Christine Heinemann ^a,
Janice Owen ^c, Beth Henning ^c

Obiettivo n°1: Valutare se L.RC-14 e L.GR-1, *somministrati per via orale*, sono in grado di raggiungere e colonizzare la vagina

Obiettivo n°2: Valutare se L.RC-14 e L.GR-1 possono prevenire le recidive in pazienti con infezioni urogenitali ricorrenti

Reid et al., FEMS Immunol Med Microbiol 2001

Presence of lactobacilli and identification of *L. rhamnosus* GR-1 and *L. fermentum* RC-14

Patient	One year history	Preswab	Week of swab collection post start of therapy on day 1					
			1	2	3	4	8	12
CK	YV	no lacto	++ GR-1	++ GR-1	++ GR-1	++ GR-1,RC-14	++ GR-1	++ GR-1
TR	YV, UTI	low lacto	+ GR-1	++ GR-1	NS	++ RC-14	++ GR-1	++ GR-1,RC-14
SH	YV	no lacto	+ GR-1	+++ GR-1,RC-14	++ RC-14	++ Ant RC-14		
BC	BV	low lacto	+ RC-14	++ GR-1	++ RC-14	+ RC-14		
AD	YV	lacto	+ GR-1	+ GR-1	+ GR-1	++ GR-1		
AC	YV	lacto	+ RC-14	+ RC-14	NS	++ RC-14		
SB	BV,YV	low lacto	+ RC-14	+ RC-14	+ RC-14			
SO	YV	lacto	++ GR-1	++ GR-1	++ GR-1,RC-14	++ GR-1,RC-14		
JA	UTI,YV	low lacto	++	++	++	++	++	++
AL	UTI,YV	lacto	GR-1 and RC-14 both recovered at each sampling time					
			+ RC-14	NS	NS	NS		

The results showed that *L. rhamnosus* GR-1 and/or *L. fermentum* RC-14 were recovered from the vagina within one week in all 10 patients

RISULTATI

Nessuna delle pazienti ha avuto effetti collaterali e tutte hanno riferito un miglioramento delle condizioni generali di salute

Presenza di LRC-14 e LGR-1 dopo 7 giorni	100%
Presenza di LRC-14 e LGR-1 dopo 3 mesi	33%
Recidive delle infezioni urogenitali dopo 3 mesi	0%
Normalizzazione del Nugent score* dopo 7 giorni	100%
*Nugent score: 0-3 = normale; 4-6 = intermedio; 7-10 = BV	



FEMS Immunology and Medical Microbiology 32 (2001) 37–41

FEMS
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Medical Microbiology

www.fems-microbiology.org

Probiotic *Lactobacillus* dose required to restore and maintain a normal vaginal flora

Gregor Reid ^{a,b,c,*}, Dee Beuerman ^a, Christine Heinemann ^a, Andrew W. Bruce ^a

^a H414, Lawson Health Research Institute, University of Western Ontario, 268 Grosvenor Street, London, ON, Canada N6A 4V2

^b Department of Microbiology and Immunology, University of Western Ontario, London, ON, Canada

^c Department of Surgery, University of Western Ontario, London, ON, Canada

Obiettivo :

Determinare la dose di lattobacilli in grado di modificare la microflora vaginale

Nugent scoring outcomes of patients in Group 4 given once daily 10^{10} *L. rhamnosus* GG control

Patient #	History	Day 0	Day 7	Day 14	Day 21	Day 28	Day 35	Day 42
134	UTI/YV	Normal	Int.	Int.	Normal	Int.	Int.	Int.
135	YV	BV	BV	N/A	N/A	Int.	Int.	Int.
136	BV/YV	Normal	Normal	Normal	Normal	Normal	Normal	Normal
137	UTI/YV	Int.	Int.	Int.	Normal	Int.	Int.	BV
138	YV	BV	BV	BV	Normal	Normal	Normal	Normal
140	UTI/YV	Int.	Int.	Int.	Int.	Int.	Int.	Int.
141	None	BV	BV	BV	N/A	N/A	N/A	BV
142	YV/BV	Normal	Int.	Normal	Normal	Normal	Normal	Normal
144	YV	Normal	Normal	Normal	Int.	Int.	Int.	Int.

Summary of women with a healthy Nugent score for their vaginal flora before treatment and at days 28 and 42 following treatment with *L. rhamnosus* GR-1 and *L. fermentum* RC-14 (Groups 1–3) or *L. rhamnosus* GG

	Percentage of women with healthy ^a vaginal flora			
	Group 1 (8×10^8)	Group 2 (1.6×10^9)	Group 3 (6×10^9)	Group 4 (10^{10} GG)
Before treatment	40	50	27	44
At end of treatment	60	82	45	38
Two weeks after treatment	56	90	30	33



Oral use of *Lactobacillus rhamnosus* GR-1 and
L. fermentum RC-14 significantly alters vaginal flora:
randomized, placebo-controlled trial in 64 healthy women

Gregor Reid ^{a-c,*}, Duane Charbonneau ^d, Julie Erb ^d, Barbara Kochanowski ^d,
Dee Beuerman ^a, Russ Poehner ^d, Andrew W. Bruce ^a

^a Lawson Health Research Institute, Canadian Research and Development Center for Probiotics, 268 Grosvenor Street, London, ON, Canada N6A 4V2

^b Department of Microbiology and Immunology, Canadian Research and Development Center for Probiotics, 268 Grosvenor Street, London, ON,
Canada N6A 4V2

^c Department of Surgery, Canadian Research and Development Center for Probiotics, 268 Grosvenor Street, London, ON, Canada N6A 4V2

^d Procter and Gamble Healthcare Research, Mason, OH, USA

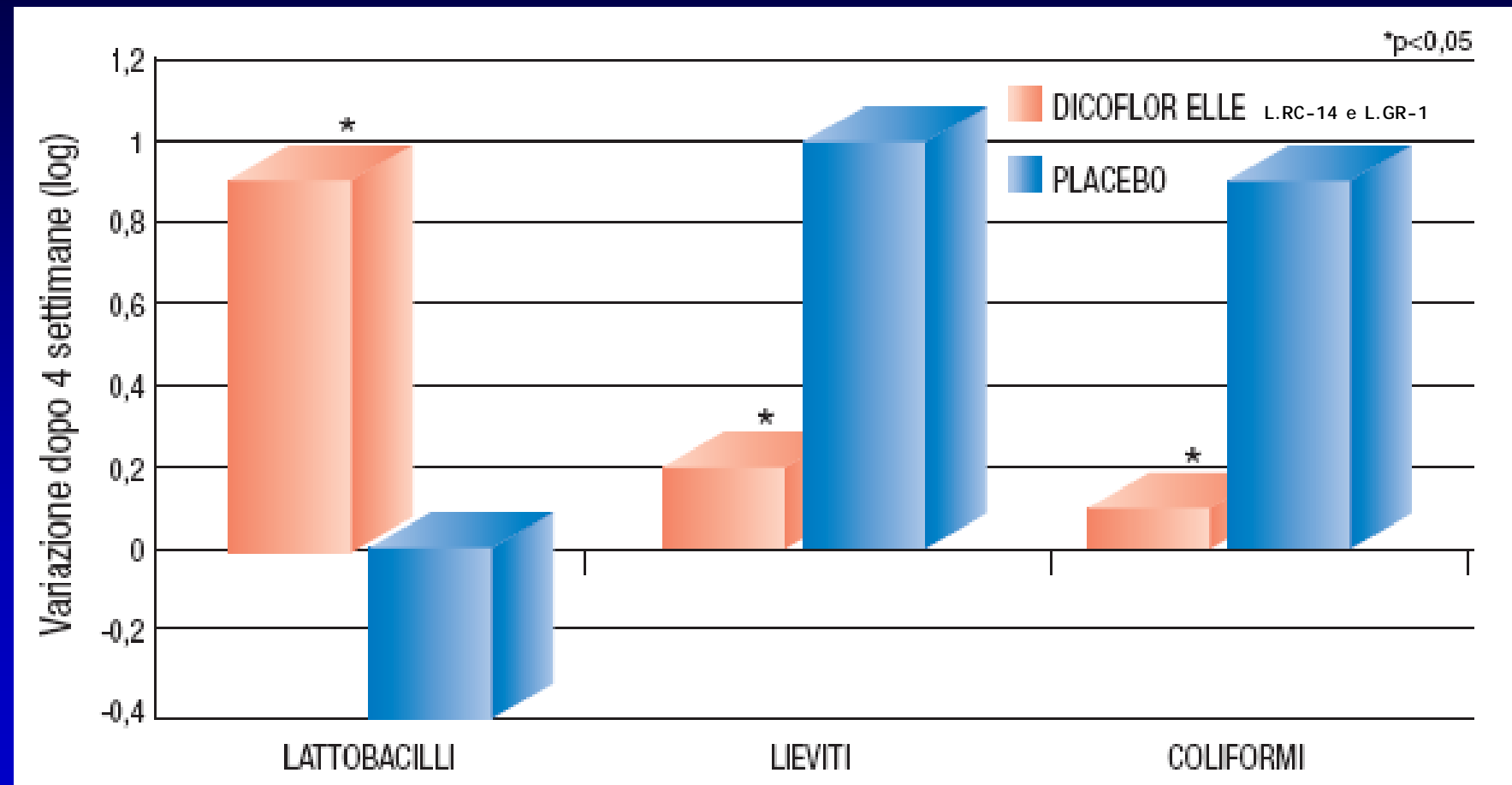
Obiettivo n°1: Valutare la sicurezza della somministrazione per via orale di L.RC-14 e L.GR-1 a donne sane

Obiettivo n°2: Valutare se la somministrazione di L.RC-14 e L.GR-1 può modificare la concentrazione di batteri patogeni nella vagina

Summary of culture results pooled from all 64 subjects

Organisms tested	Mean log difference from day 0 values				
	Subjects	Day 7	Day 28	Day 60	Day 90
Lactobacillus counts	Lactobacilli	0.2	0.9*	0.5*	0
Lactobacillus counts	Placebo	-0.3	-0.4	0.1	-0.4
Yeast counts	Lactobacilli	0	0.2*	1.1	0.5
Yeast counts	Placebo	0.4	1.0	1.7	0.9
Coliform counts	Lactobacilli	-0.2	0.1*	-0.1*	0.3*
Coliform counts	Placebo	0	0.9	0.5	1.1

RISULTATI



Reid et al., FEMS Immunol Med Microbiol 2003

CONCLUSIONI

1. L.GR-1 e L.RC-14 possono essere assunti quotidianamente per 2 mesi senza effetti collaterali
2. L.GR-1 e L.RC-14 migliorano, già dopo 4 settimane, la composizione della microflora vaginale
3. L'effetto protettivo di L.GR-1 e L.RC-14 è ancora visibile dopo 1 mese dalla fine del trattamento



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Original article

Clinical study comparing probiotic *Lactobacillus* GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis

Kingsley C. Anukam^{a,d,e}, Emmanuel Osazuwa^a, Gibson I. Osemene^b,
Felix Ehigiagbe^c, Andrew W. Bruce^f, Gregor Reid^{f,g,h,*}

Two dried capsules containing *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 each night for 5 days, or 0.75% metronidazole gel, applied vaginally twice a day (in the morning and evening).

Results of the BV status (based on Nugent score and BV Blue test) of patients treated with vaginal probiotics GR-1/RC-14 and Metronidazole (0.75%) vaginal gel at day 0, 6, 15 and 30

BV status	Probiotic group				Metronidazole (0.75%) group			
	Day 0	Day 6	Day 15	Day 30	Day 0	Day 6	Day 15	Day 30
Signs and symptoms	20	2	2	2	20	8	8	8
Nugent score 7–10	20 (100%)	4 (20%)	3 (15%)	2 (12%)	20 (100%)	11 (55%)	11 (55%)	9 (50%)
Score 4–6	Nil	4	7	4	Nil	3	5	3
Score 0–3	Nil	12	10	11	Nil	6	4	6
Positive BV Blue test	20 (100%)	6 (30%)	3 (15%)	2 (12%)	20 (100%)	15 (75%)	13 (65%)	10 (56%)

Responses to lifestyle questionnaires after the treatment for the two groups at day 30

Changes in condition since treatment	Probiotics group (<i>N</i> = 17)	Metronidazole group (<i>N</i> = 18)
I got relief		
Within 1 day	Nil	Nil
2 days	Nil	Nil
3 days	9	3
4 days	5	5
5 days	3	10
I did not get relief	Nil	Nil
Problem was completely resolved		
Within 1 day	Nil	Nil
2 days	Nil	Nil
3 days	5	2
4 days	2	4
5 days	8	6
Did not resolve	2	6
Any side effect?		
Yes	2	11
No	15	7
Number of sex partners for this one month		
0	9	7
1	8	11
2	Nil	Nil
More than 2	Nil	Nil

Effect of Lactobacilli Oral Supplement on the Vaginal Microflora of Antibiotic Treated Patients: Randomized, Placebo-Controlled Study

Gregor Reid^{*,**,*†}, Jo-Anne Hammond^{*,****} and Andrew W. Bruce^{*}**

**Canadian Research and Development Centre for Probiotics, Lawson Health Research Institute,*

***Department of Microbiology and Immunology,*

****Department of Surgery,*

*****Department of Family Medicine, University of Western Ontario, London, Canada*

A double-blind, randomized, placebo-controlled study was undertaken on female patients to determine how many yeast infections occurred following 10 days antibiotic use. In addition, the study was designed to examine whether oral use of probiotic lactobacilli can reduce the risk of vaginal infection.

Lactobacillus treated				Placebo treated			
Nugent scores				Nugent scores			
Patient	Antibiotic	Day 0	Day 30	Patient	Antibiotic	Day 0	Day 30
1	clarithromycin	1	2	2	amoxicillin	0	0
4	clarithromycin	0	3	7	azithromycin	1	1
5	azithromycin	1	1	8	penicillin V	4	3
6	clarithromycin	3	3	10	cefuroxime	1	8
9	azithromycin	5	5	13	clarithromycin	7	6
11	amoxicillin	1	0	21x	clarithromycin	1	2
29	amoxicillin	1	1	27	amoxicillin	5	2
40	amoxicillin	5	2	37	azithromycin	5	5
43	clarithromycin	3	2	39	penicillin V	5	2
44	clarithromycin	6	5	41	clarithromycin	1	0
47	tetracycline	1	4	42	clarithromycin	2	10
58	clarithromycin	1*	1	57	cefuroxime	0	10
		2.4	2.4			2.7	4.1

daily use of probiotics was safe and could potentially reduce the risk of patients developing bacterial vaginosis after antibiotic use.



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Original article

Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14: randomized, double-blind, placebo controlled trial

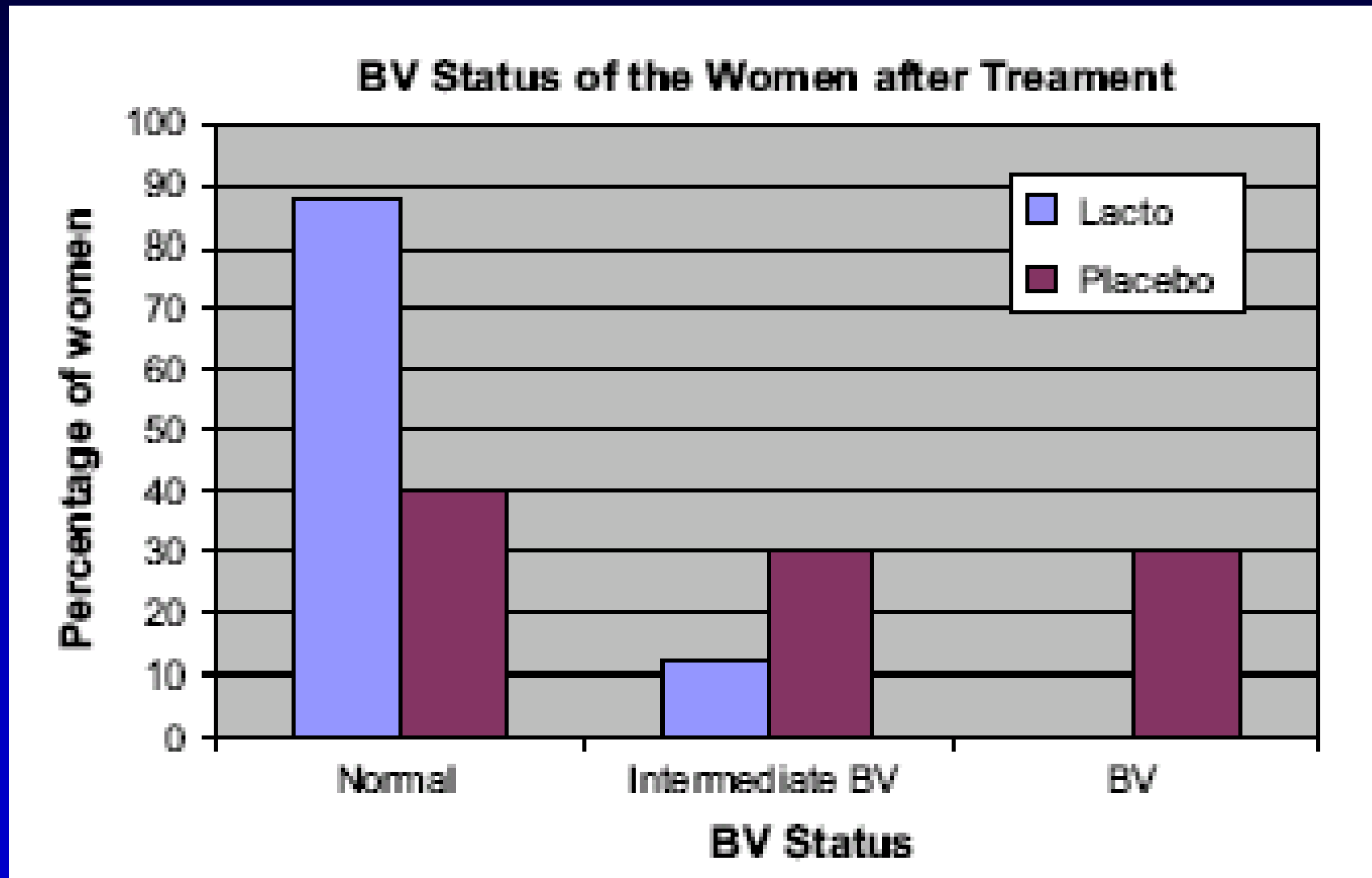
Kingsley Anukam^{a,d,1}, Emmanuel Osazuwa^a, Ijeoma Ahonkhai^a, Michael Ngwu^e,
Gibson Osemene^{f,g}, Andrew W. Bruce^b, Gregor Reid^{b,c,*}

Obiettivo: Valutare se L.RC-14 e L.GR-1 sono in grado di aumentare l'efficacia della terapia convenzionale della vaginosi batterica

Results of clinical study

Criteria	Metronidazole (1 g, days 1–7) plus <i>Lactobacillus</i> (days 1–30)		Metronidazole (1 g, days 1–7) plus placebo (days 1–30)	
	Day 0	Day 30	Day 0	Day 30
Positive clinically (discharge and 'fishy' odor)	65	5 ^a $p = 0.005$ compared to placebo	60	19
Positive BVBlue test (sialidase)	65	6 ^b $p = 0.035$ compared to placebo	60	17
Positive Nugent score (7–10 representative of BV)	65	0 $P = 0.003$ compared to placebo	60	17

RISULTATI



Anukam et al., Microbes Infect 2006

Linee Guida per i probiotici

(FAO/WHO)

Identificazione
del ceppo
(fenotipo e
genotipo)

Deposito del
ceppo presso
una ceppoteca
internazionale

Determinazione
della sicurezza
d'uso (studi su
animali e
sull'uomo)

**VERO
PROBIOTICO**

Determinazione
dell'efficacia
(studi clinici)

