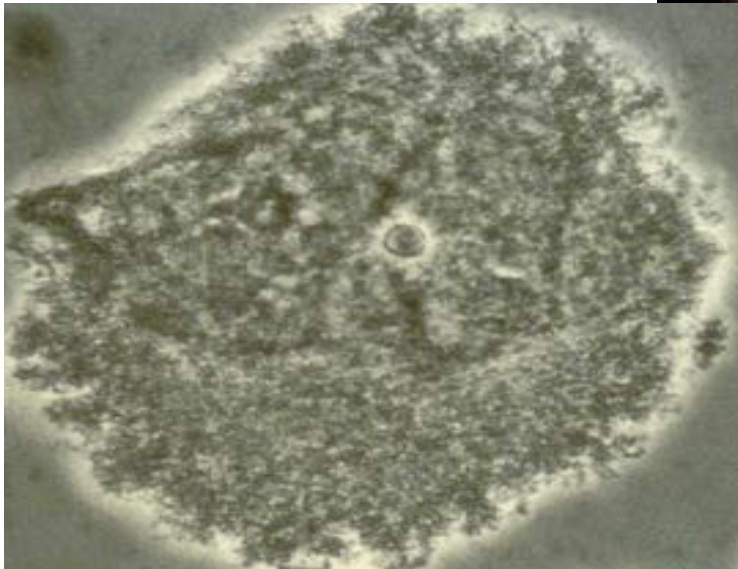
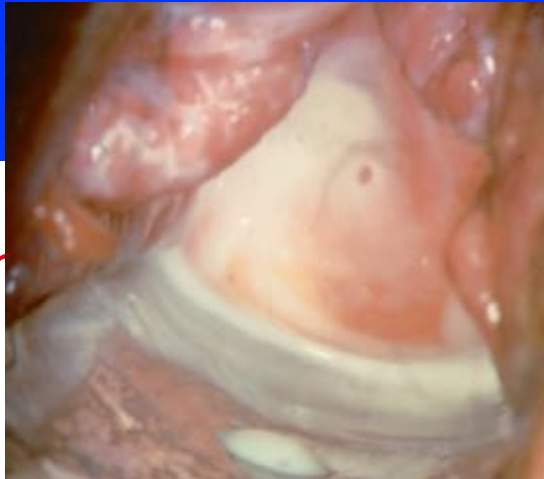


Bakteriell vaginos, en ofarlig flytning eller ett hot mot kvinnans hälsa



Amsel's kriterier för diagnostik av BV

- Typisk homogen flytning
- $\text{pH} > 4,5$
- Positiv sniff test med KOH
- Clueceller vid - nyckelceller



Molecular diagnosis Multiplex

id	Diagram			SmartArt-graphik			WordArt			
M	N	O	P	Q	R	S	T	U	V	
GeneT3	Provir33	Intake1	Npoc	Ureap	Dvag	Bvag	MU1	Avag	MU2	
555	942	EW	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
2028	1213	MH	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
5452	3700	EB	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
2829	1752	JK	NEG	POS	NEG	NEG	NEG	NEG	NEG	
4982	3287	TW	NEG	POS	NEG	NEG	NEG	NEG	NEG	
4423	2917	AK	NEG	POS	POS	NEG	NEG	POS	NEG	
4590	3043	LV	NEG	POS	POS	NEG	NEG	NEG	NEG	
6113	4154	U	NEG	POS	NEG	NEG	NEG	NEG	NEG	
4353	2874	JW	NEG	POS	NEG	NEG	NEG	NEG	NEG	
5745	3881	SB	NEG	POS	POS	NEG	NEG	POS	NEG	
3995	2572	LB	NEG	NEG	POS	NEG	NEG	NEG	NEG	
4200	2743	AB	NEG	POS	POS	NEG	NEG	NEG	NEG	
5795	3688	AS	NEG	POS	NEG	NEG	NEG	POS	NEG	
8120	4159	FA	NEG	NEG	POS	NEG	NEG	POS	NEG	
2267	1381	AD	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
3493	2210	KB	NEG	POS	POS	NEG	NEG	POS	NEG	
3239	2514	FT	NEG	NEG	POS	NEG	NEG	NEG	NEG	
2157	1348	SB	NEG	POS	POS	NEG	NEG	NEG	NEG	
5807	865	EZ	NEG	POS	POS	NEG	NEG	POS	POS	
4314	2823	CE	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
5505	3756	HR	NEG	POS	POS	NEG	POS	POS	NEG	
4313	2822	KL	NEG	POS	NEG	NEG	NEG	POS	NEG	
5349	3618	CS	NEG	NEG	POS	NEG	POS	POS	NEG	
2305	1436	MT	NEG	POS	POS	NEG	NEG	POS	NEG	
3240	2515	NN	NEG	POS	POS	NEG	NEG	NEG	NEG	
4842	3573	SO	NEG	POS	POS	NEG	NEG	NEG	NEG	
4799	3006	HA	NEG	NEG	POS	NEG	NEG	NEG	NEG	
2830	1643	AC	NEG	POS	POS	NEG	NEG	NEG	NEG	
2762	1715	VR	NEG	NEG	POS	NEG	NEG	NEG	NEG	
1408	862	RD	NEG	POS	NEG	NEG	NEG	NEG	NEG	
5617	3658	FA	NEG	POS	POS	NEG	NEG	NEG	NEG	
4199	2742	SP	NEG	NEG	NEG	NEG	NEG	NEG	NEG	
5887	4017	AA	NEG	POS	POS	NEG	POS	POS	POS	

Seeplex STI master panel 1 (STI)	Seeplex STI master panel 2 (BV)
Chlamydia trachomatis	Gardnerella vaginalis
Neisseria gonorrhoeae	Bacteroides fragilis
Mycoplasma genitalium	Mobiluncus curtisii
Mycoplasma hominis	Mobiluncus muliensis
Ureaplasma urealyticum/parvum	Atopobium vaginae
Trichomonas vaginalis	

Test på KSS Molecular diagnosis

BV * Mobiluncus Crosstabulation

Count

		BV (Gold standard)		Total
		1	0	
Multipl	1	20	3	23
ex test	0	8	80	88
Total		28	83	111

Sensitivity	0,71
Specificity	0.96
Pos. Predictive value	0.87
Neg. Predictive value	0.91

Breeding & Larsson

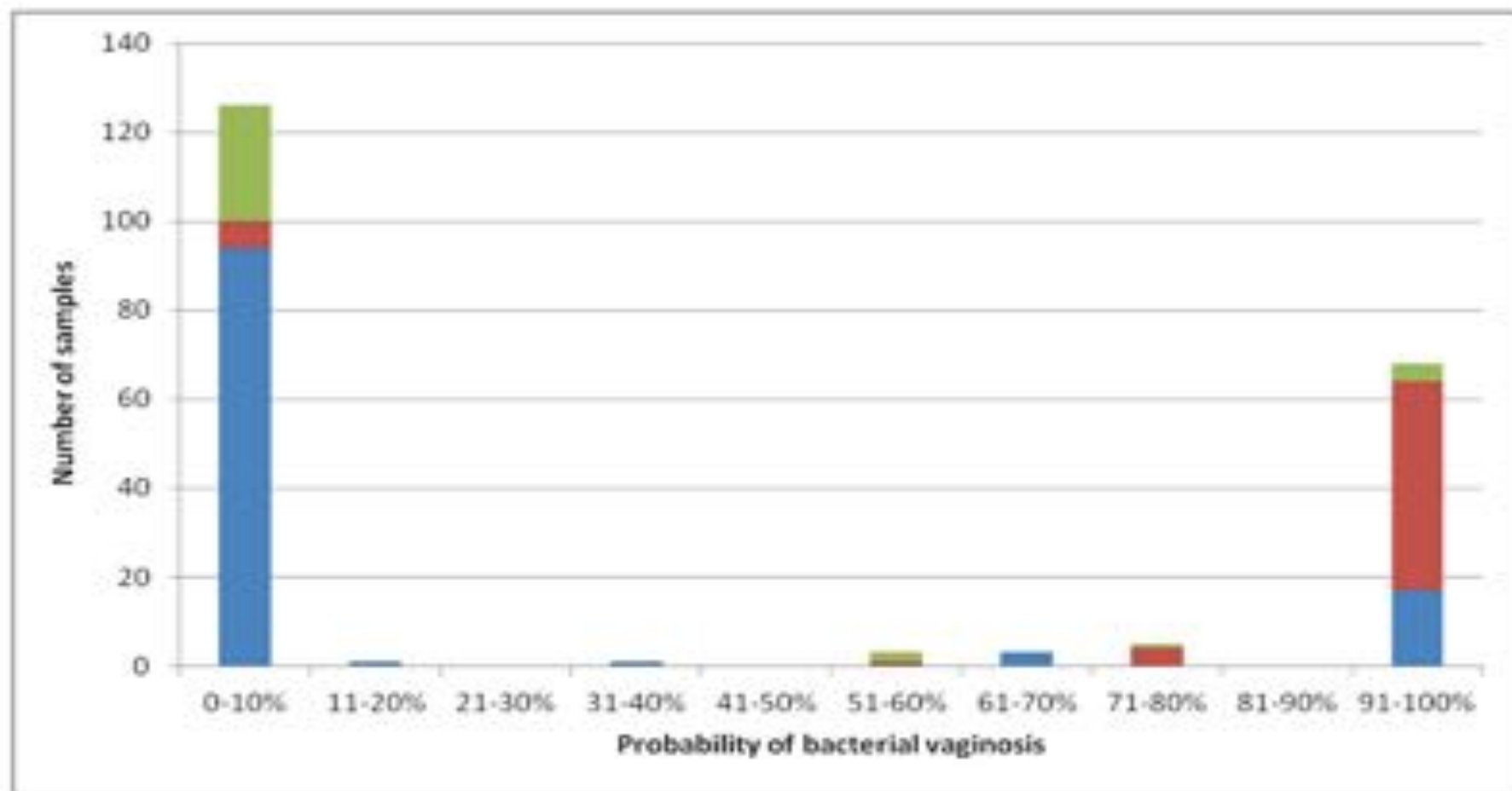
Dynamic code

- **2 smart solutions**
- **DNA is replicated until detection limit**
 - » **The smaller amount of DNA the longer it takes ie number of cycles**
 - » **Number of cycles called Ct value**
- **This is subtracted from the Ct value from lactobacilli**
- **This is called ΔCt**

Relaterat till antalet laktobaciller

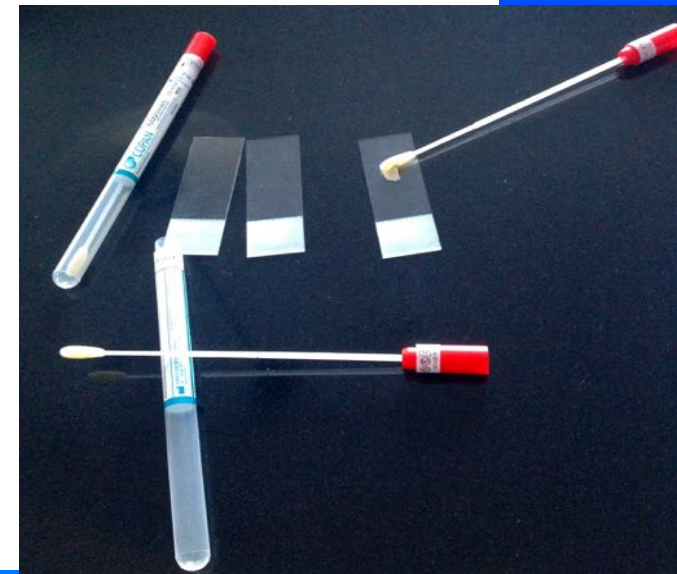
Detection rate, mean and standard deviation of ΔC_t values

Bacteria	Women in the control group,		Women with bacterial vaginosis	
	Number of samples with detected bacteria (%)	ΔC_t mean \pm SD	Number of samples with detected bacteria (%)	ΔC_t mean \pm SD
<i>Atopobium vaginae</i>	65%	12,7 \pm 9,5	100%	2,0 \pm 6,3
BVAB2	47%	9,4 \pm 9,0	81%	4,6 \pm 7,1
<i>Gardnerella vaginalis</i>	94%	8,5 \pm 8,9	98%	-1,4 \pm 5,7
<i>Leptotrichia/ Sneathia</i> spp.	10%	2,8 \pm 7,8	41%	3,2 \pm 9,5
<i>Megasphaera</i> spp.	79%	15,1 \pm 10,1	97%	1,9 \pm 7,3
<i>Mobiluncus</i> spp.	72%	17,5 \pm 6,7	83%	7,5 \pm 8,3



300 women

- Visiting for Legal abortion
- Diagnosis with air dried wet smear
 - Hay/Ison
- One extra sample for DNA



				upper	0,94
	KAPPA INDEX:		0,88		
				lower	0,82
		Molecular			
		BV	Negativ		
	BV	73	7		
Microscopy.	Negativ	7	201		
				288	

Sensitivity	0,91
Specificity	0,97
Pos. predictiv	0,91
Neg. predictive	0,97

tarm

Lactobacillus

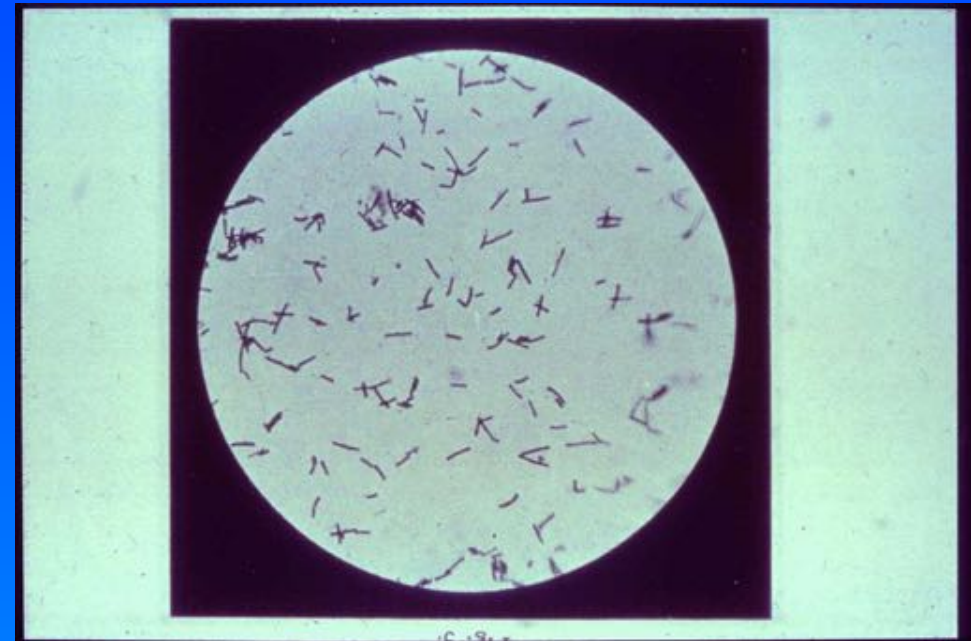
L. acidophilus
L. johnsonii
L. fermentum
L. plantarum

spp



Vagina

L. crispatus
L. jensinii
L. gasseri
L. iners
L. casei rhamnosus



Döderlein 1896

Tarm **Lactobacillus spp**

L. acidophilus
L. johnsonii
L. fermentum
L. plantarum



Vagina

L. crispatus
L. jensinii
L. gasseri
L. iners
L. casei rhamnosus

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2002, p. 2746-2749
0095-1137/02/\$04.00+0 DOI: 10.1128/JCM.40.8.2746-2749.2002
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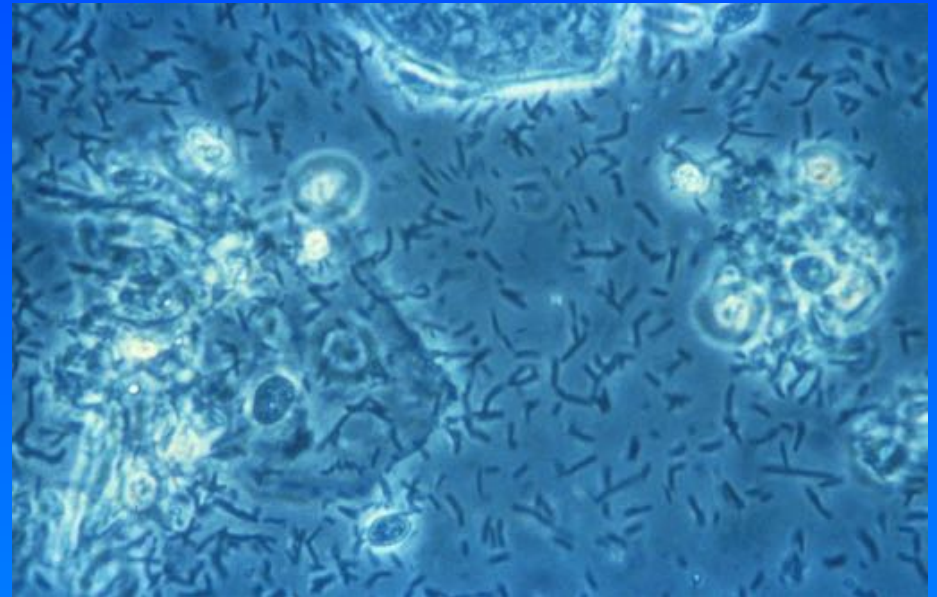
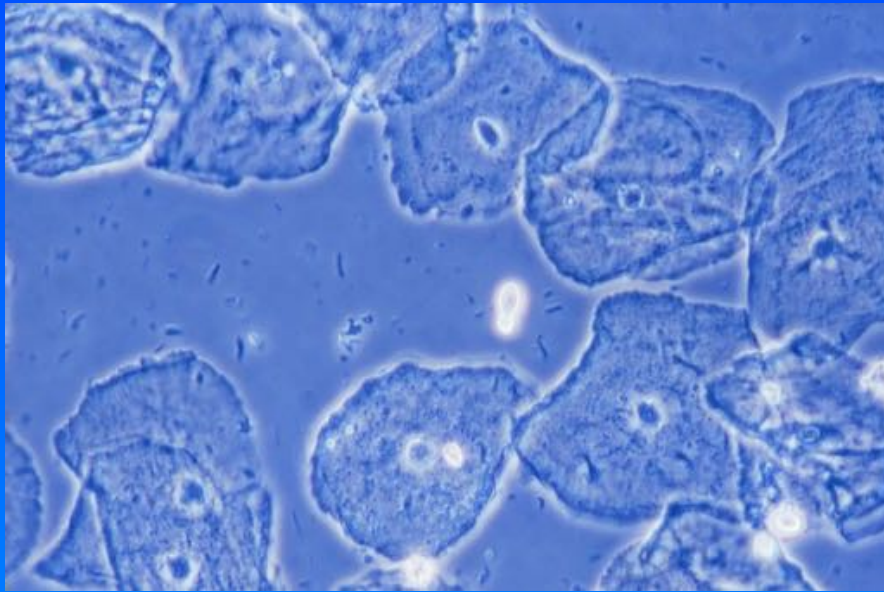
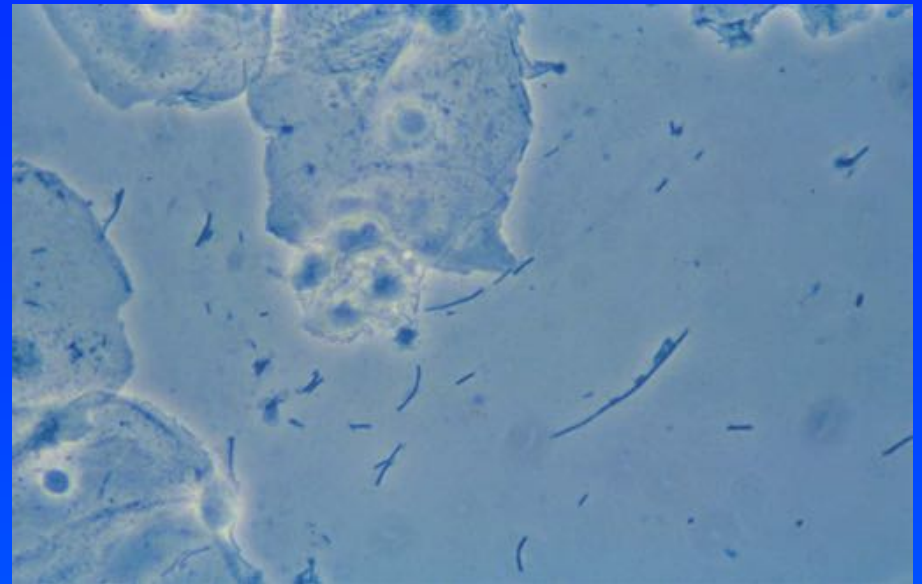
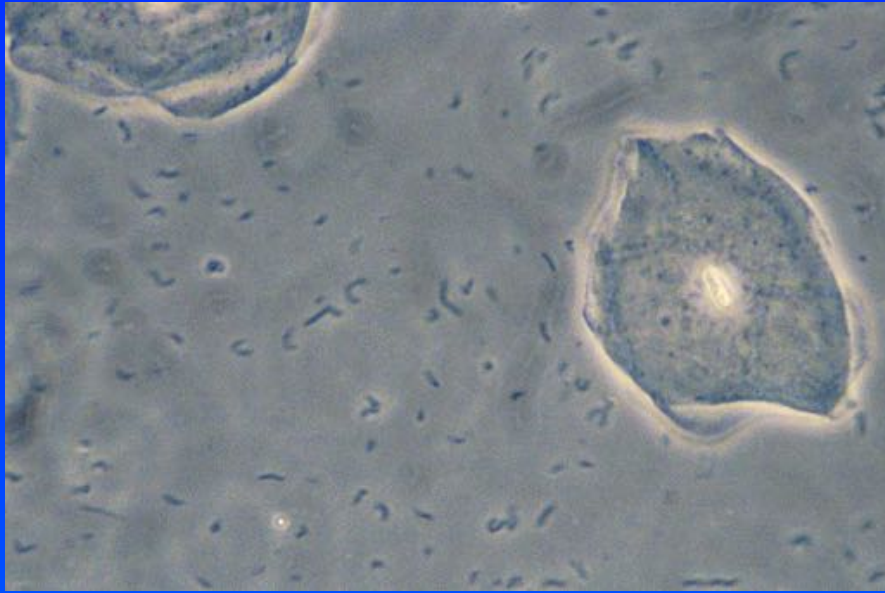
Vol. 40, N

Vaginal *Lactobacillus* Flora of Healthy Swedish Women

Alejandra Vázquez,¹ Tell Jakobsson,^{2,3} Siv Ahnmé,^{1*} Urban Forsum,²
and Göran Molin¹

Laboratory of Food Hygiene, Division of Food Technology, Lund University, SE-221 00 Lund,¹ and
Division of Clinical Microbiology² and Division of Obstetrics and Gynaecology,³ Faculty
of Health Sciences, Department of Health and Environment, SE-581 85
Linköping, Sweden

Received 26 December 2001/Returned for modification 2 March 2002/Accepted 6 May 2002





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Apotekets försäljning

- 10 milj anticandida medel
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- 8 milj Lactal och Vivag

2000

Forebyggelse og behandling af

Bakteriel vaginose



- Vivog kapsler:** En kapsel indeholder min. 10^8 springsdygtige *Lactobacillus acidophilus* og andre bakterier som i S.K.L. Hansen's undersøgelser.¹
Vægtstørrelse: Ca. 430 mg lactose pr. kapsel.
Kapsel: Oploselig gelatinekapsel uden konserver.
Holdbarhed: Mindst 24 mdr. ved stuetemperatur i ubrudt pakning.
Renhed: Ingen fremmede km.
- Indikationer:** Efter universal eller lokal antibiotika-behandling.
Cyklisk tilbagevendende fluorvaginose.
Fluorvaginose under graviditet (kan også anvendes i 1. trimester).
Candida albicans vaginitis.
- Dosering:** 1-2 kapsler daglig i op til 6 dage. Indføres i vagina.
- Priser:** 12 stk. Vivog kapsler kr. 43,00.
12 stk. Vivog kapsler med sterile engangsindføringshygiejne kr. 55,00.
- Vivog ryhed:** Som supplement anbefales Vivog Specialcreme, pH-værdi 4, uden konserver og konserveringemiddel. 250 ml kr. 29,75. 500 ml 52,50.

1) Referencer

1. Hultén, K., Axelson, C., Nilsson, C.: Treatment of bacterial vaginosis with Lactobacilli. *Sexually Transmitted Diseases*, May/June 1982, vol. 55, no. 2.
2. Nilsson, C. M. L.: *Candida albicans* vaginitis. Relieving of *Candida albicans* from *Lactobacillus acidophilus*. *Indledning til praktisk behandling*, 1987, 477-480.
3. New-Sperand, L., Sperand, L.: *Urogenitalt infektion i østrogen-påvirket livmoder*, 2002, 1982.
4. Hultén, K.: *Bakteriel vaginose og urethritis*. *Indledning til behandling*, 1987, 1987.
5. New-Sperand, L.: *Urogenitalt infektion i østrogen-påvirket livmoder*. *Indledning til behandling*, 1987, 1987.

Department of Gynecology, University Hospital, Stockholm, Sweden
Vol. 15, No. 2
P. O. Box 10000, Stockholm, S-141 86

Treatment of Bacterial Vaginosis with Lactobacilli

ANDERS HULTÉN, MD, PhD, GÖRAN AXELSON, MD, PhD, AND CARL NILSSON, MD, PhD

All women with bacterial vaginosis were treated with a double-blind, placebo-controlled treatment with with Lactobacillus acidophilus capsules. The Lactobacilli used were producing 10⁸ CFU immediately after completion of treatment. 19 out of 28 women who were treated with Lactobacilli had normal vaginal flora after 6 weeks, in comparison to none of the 29 women treated with placebo. All women harbored *Parvomonas* at inclusion. *Parvomonas* was eliminated from the vagina in 11 out of 28 healthy women after treatment. Only those of the women who received the Lactobacillus capsules were free of bacterial vaginosis after the subsequent menstruation.

From the Department of Gynecology, University Hospital, Clinical Bacteriology, and Clinical Immunology, Stockholm, Sweden.

57%

and patients who are starting to feel better

BV är ingen obalans som går att bota med laktobaciller



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Treatment of Bacterial Vaginosis with an Acid Cream: A Comparison between the Effect of Lactate-Gel and Metronidazole

Björn Andersch¹, Lars Forsman², Axel Lindvall¹, Per Färnstrand¹

¹Department of Chemistry and Center for Pharmacy, Karolinska, and

²Department of Clinical Microbiology, Sahlgrenska Hospital, Göteborg, Sweden

Key Words: Bacterial vaginosis · Lactobacilli · Vaginal pH · Amine test · Wet mount · Chloroform · Lactate-gel · Lactic acid · *Mitochondria* (Schwarz)

Abstract: Bacteriological isolation of anaerobes, *Gardnerella* and *Lactobacilli* was carried out in a group of 42 women with the diagnosis bacterial vaginosis and 42 control women. *Lactobacilli* were the predominant organisms in the control group whereas anaerobes dominated the flora in bacterial vaginosis patients. Lactate-gel (pH 5.5, 1 unit) inserted into the vagina daily for 7 days is as effective as oral metronidazole, 500 mg once daily for 7 days. The women in both groups became symptom-free and objectively improved. Anaerobes were significantly reduced ($p < 0.0001$) in both groups after 1 week treatment but *Gardnerella* was not significantly reduced. As bacterial vaginosis is generally looked upon as a mild noninflammatory condition lactate-gel seems to be an ideal treatment for this disease.

Själv-behandling med lactal gel skall aldrig rekommenderas!

study	treatment	define cure	follow up	cure rate
Andersch-86	lactal vs metronidazol	lack of one or more	1 day	100%
Andersch-90	lactal + placebo	0/4	3 month	0/20
			6 month	1/10

Kytnomedieli.se



4. 10. 1968

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Per la flora vaginale



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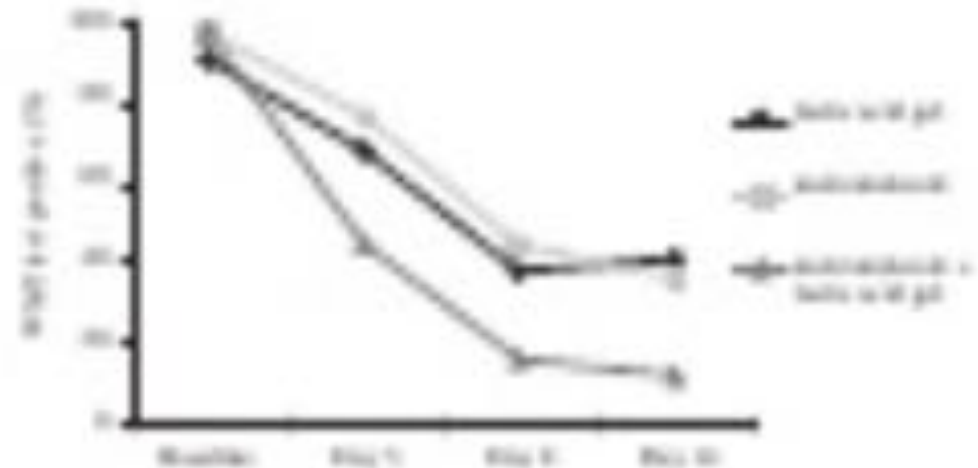
Metronidazole with Lactacyd vaginal gel in bacterial vaginosis

Ditas Cristina D. Decena¹, Jennifer T. Co², Ricardo M. Manalastas Jr³, Evelyn P. Palaypayon², Christia S. Padolina⁴, Judith M. Sison¹, Louella A. Dancel⁵ and Marievi A. Lelis⁶

¹University Santo Tomas Hospital, Manila, ²Far Eastern University-NRMF, Quezon City, ³University of the Philippines-Philippine General Hospital, Manila, ⁴Hospital ng Maynila, Manila, ⁵University of Perpetual Help Rizal-SD, Las Pilas, and ⁶University of the Philippines Statistical Society, Quezon City, Philippines

3 grupper

- Lactacyd
- Metronidazole
- Lactacyd + metronidazole
- 14 dagar utläkning
- Tele intervju efter 56 dagar



Vagi-C



Petersen EE, Genet M, Caserini M, Palmieri R. Efficacy of vitamin C vaginal tablets in the treatment of bacterial vaginosis: a randomised, double blind, placebo controlled clinical trial. *Arzneimittel-Forschung*. 2011;61(4):260-5.

Krasnopolsky VN, Prilepskaya VN, Polatti F, Zaroquentseva NV, Bayramova GR, Caserini M, et al. Efficacy of vitamin C vaginal tablets as prophylaxis for recurrent bacterial vaginosis: a randomised, double-blind, placebo-controlled clinical trial. *Journal of clinical medicine research*. 2013;5(4):309-15.

Petersen Magnani 2004 2 v utläkning

Petersen 2011

- 277 pat double blind VIT-C vs placebo
- 6 days treatment
- 50 % cure vs 25%

- 1-2 veckor utläkning

- No clucells 65% vs 32%
- 32% hade döderlein flora vid inclusion

Vagi-C

Behandling med metronidazole eller clindamycin

De som är utläkta;

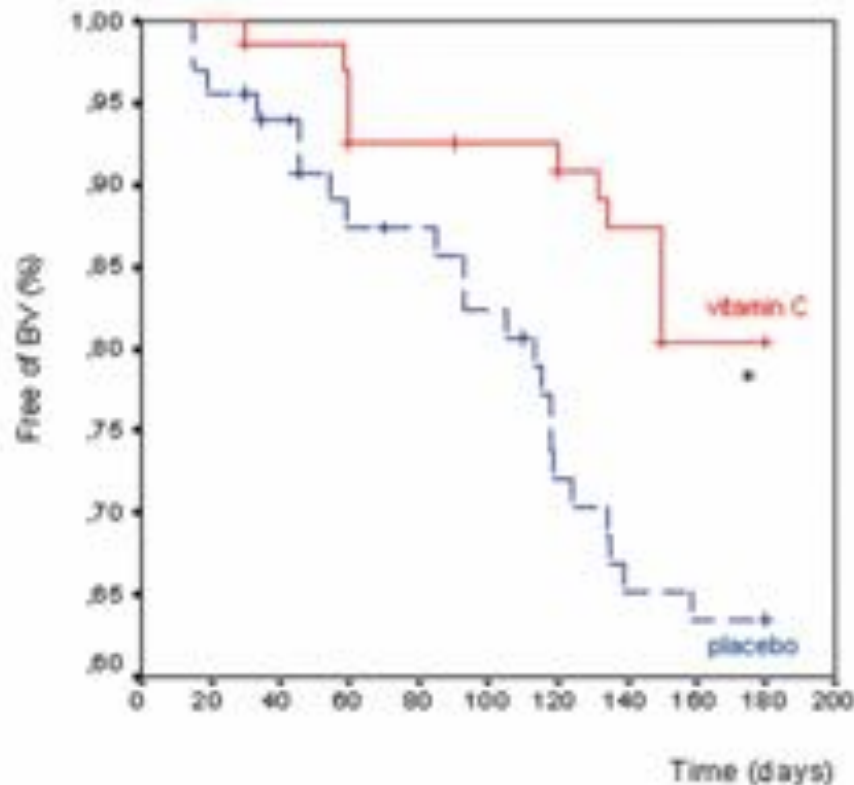
The patients applied one vaginal tablet once a day for 6 consecutive days per month after menses. n=142

Clinical visits were conducted at the end of each cycle, within 3 days of the end of the treatment, and 1 month after the end of the last cycle (final visit).

Krasnopolsky 2013

Efficacy of Vitamin C Vaginal Tablets as Prophylaxis for Recurrent Bacterial Vaginosis: A Randomised, Double-Blind, Placebo-Controlled Clinical Trial

Vladislav N. Krasnopolsky^a, Vera N. Prilepskaya^b, Franco Polatti^c, Nina V. Zarochentseva^a,
Guldana R. Bayramova^b, Maurizio Caserini^d, Renata Palmieri^{d, e}



VAGI –C

- **Metronidazole eller clindamycin utläkta efter behandling av BV**
- **Utläkning ej 3 av 4 Amsel**
- **Vit C (74) 250 mg placebo (68)**
- **6 behandlingar / mån**

- **Utläkning efter 6 månader**
- **Vit C 83%**
- **Placebo 67,6%**
- **Utvärdering månaden efter sista behandlingen**
- **Mindre än 20% cluecells**

Krasnopolsky 2013

Ny svensk studie

- En surgörande tablett som är slow realese
- 10 centra i Sverige
- Endast 2 veckors utläkning
- oligomeric lactic acid (OMLA) 700 mg lactic acid

- Laccure AB (Sweden)
-
- Anders Barth Göteborg



**Underhåll ditt
underliv med
Ellen tamponger
direkt hem i brevlådan!**

**Prova den unika, dubbelverkande
tampongen Ellen i 4 månader!
Vi bjuder på 2 paket och
ett fint partytui!**



**Värde 310:-
Du betalar 210:-**

Ja tack, jag beställer Ellen i fyra månader och får ett snyggt partytui.

Förnamn: Efternamn: Adress:

Postnr/ort: Telefon: Email:

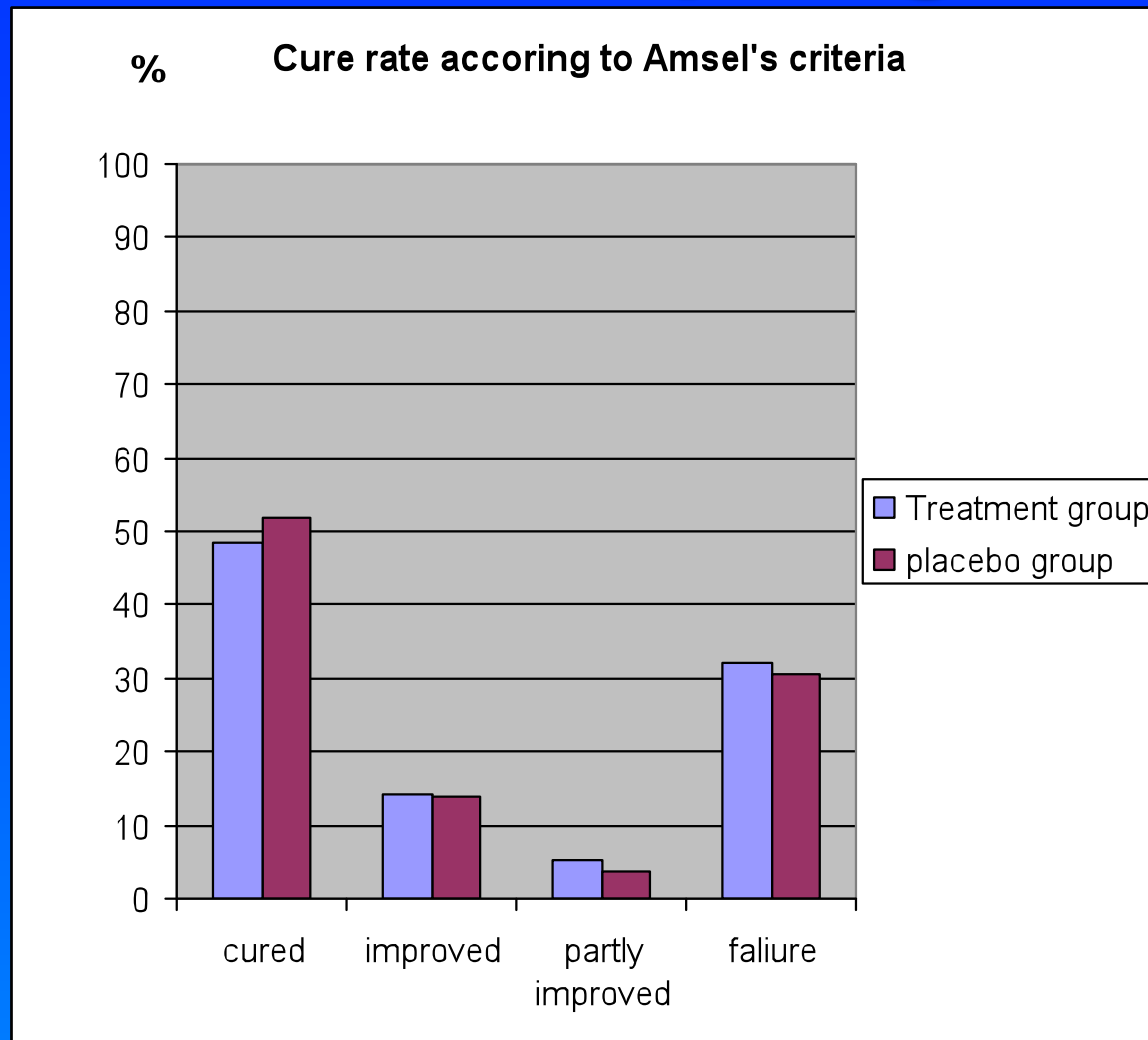
Födelsedata: dd mm åå Menscykel: 25 dagar Plus Normal Mini max 2 ifyllda fält

Mer om detta erbjudande hittar du här: [Villkor](#) [Produkten](#)

SKICKA

L fermentum
L rhamnosus
L gasseri

ELLEN tamponger fungera ej



Dalacin vag

L fermentum
L rhamnosus
L gasseri

PP 187
ITT 224

Ellen vagipills

L fermentum
L rhamnosus
L gasseri
Pediococc

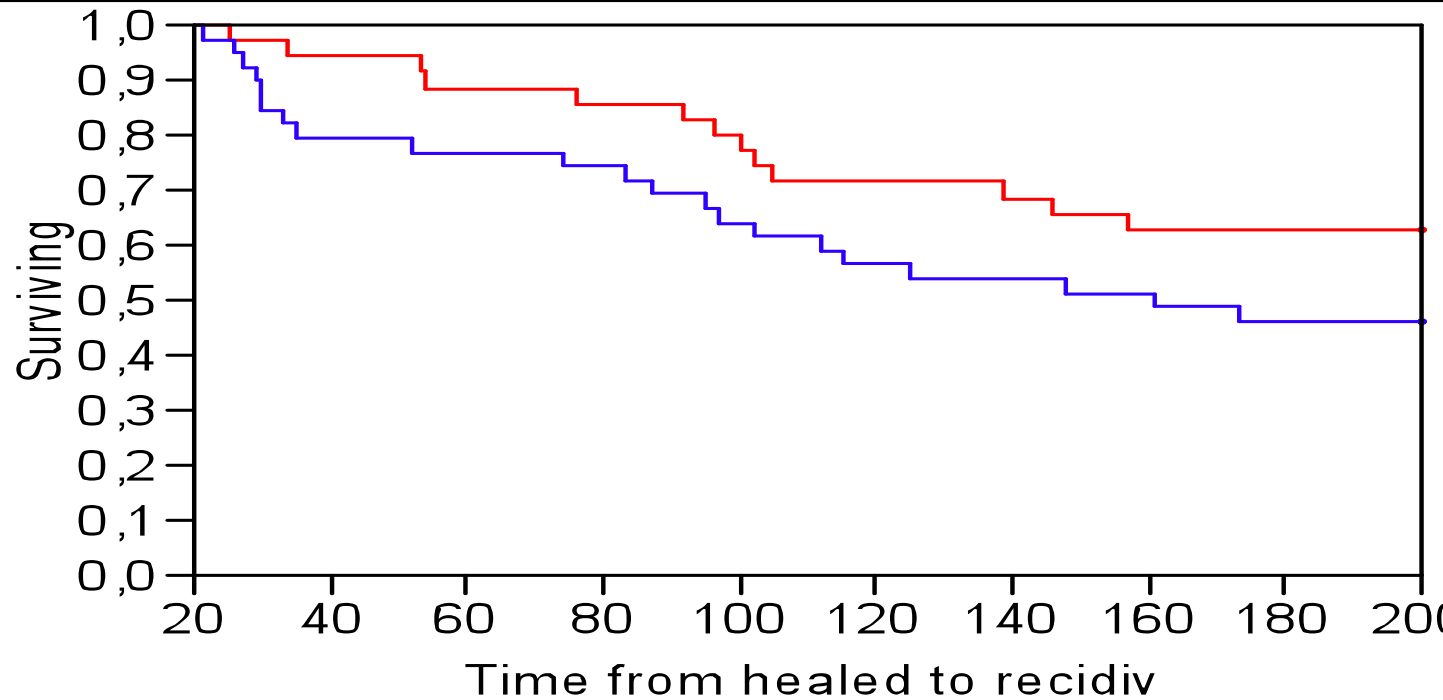
- **Koloniserings studie**
- **VVC (28-22)och BV (32-25)**
- **1 mån 53% koloniserad minst 1 LN strain.**
- **6 mån 4 st (9%).**

- **2 -3 dagar 93 % vs 83% placebo**
- **1 mån 78% vs placebo: 71%**
- **6 mån 40% vs placebo 45%**

Ehrnström et al Microbes Infect. 2010;12(10):691-9



Signifikant färre som får återfall om de får behandling med laktobaciller (EcoVag)



Research article

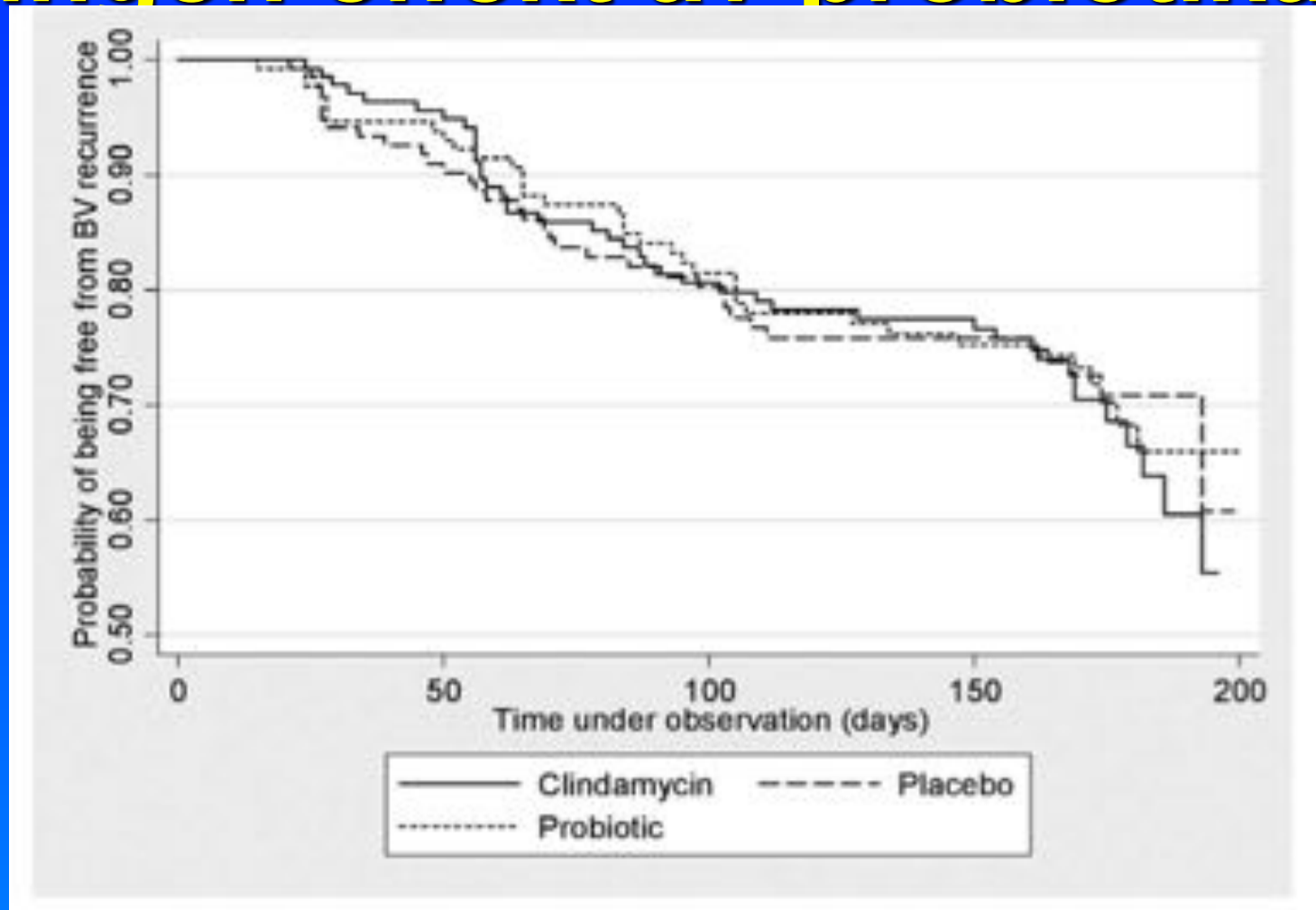
Open Access

Human lactobacilli as supplementation of clindamycin to patients with bacterial vaginosis reduce the recurrence rate; a 6-month, double-blind, randomized, placebo-controlled study

Per-Göran Larsson^{*1}, Babill Stray-Pedersen², Kjeld R Rytting³ and Stig Larsen⁴

Larsson et al 2008 BMC woman's Health

6 månader återfall ingen effekt av probiotika



Bradshaw 2012 *al PLoS ONE* 7(4)e34540

The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women (Review)

Odoye OJ, Anorho BI, Ogunola FT



The quantum theory of solids is based on the quantum theory of particles. The quantum theory of particles is based on the quantum theory of fields, which is the quantum theory of the electromagnetic field.

Quantum theory

The quantum theory of solids is based on the quantum theory of particles. The quantum theory of particles is based on the quantum theory of fields, which is the quantum theory of the electromagnetic field.

Quantum theory of fields

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Quantum theory of particles

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The quantum theory of particles is based on the quantum theory of fields. The quantum theory of fields is based on the quantum theory of the electromagnetic field. The quantum theory of the electromagnetic field is based on the quantum theory of the photon. The quantum theory of the photon is based on the quantum theory of the electromagnetic field.

The quantum theory of particles is based on the quantum theory of fields. The quantum theory of fields is based on the quantum theory of the electromagnetic field.

The quantum theory of particles is based on the quantum theory of fields. The quantum theory of fields is based on the quantum theory of the electromagnetic field.

Quantum theory of fields

**Diagnosis clinical sign +
Nugent + BV blue**

**Metronidazole gel vaginaly BID
5 days**

or

**Intravaginal lactobacilli BID for
5 days**

Test of cure at day 30.

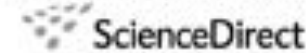
64% probiotic

55% metronidazole

Men titta på utläkning dag 6....



Available online at www.sciencedirect.com



Microbes and Infection (2006) 8, 1–5



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,
Felix Ehigiagbe^c, Andrew W. Bruce^f, Greg

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^b Bas-Gab Clinic and Maternity, 114 M.M. Way, Bessie City Military Base Hospital,

^c Department of Obstetrics and Gynaecology, University of Benin Teaching Hos

^d Clinical Medical Diagnostic Laboratories, 200 M.M. Way, Bessie

^e Department of Microbiology, Faculty of Basic and Applied Sciences, Benson Adedun Uni

^f Canadian Research & Development Centre for Products, Lawson Health Research

London, Ontario N6A 4W2, Canada

^g Department of Microbiology and Immunology, University of Western Ontario,

^h Department of Surgery, University of Western Ontario, London, Ontario, Canada

Received 27 June 2006; accepted 21 August 2006



Table 2

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

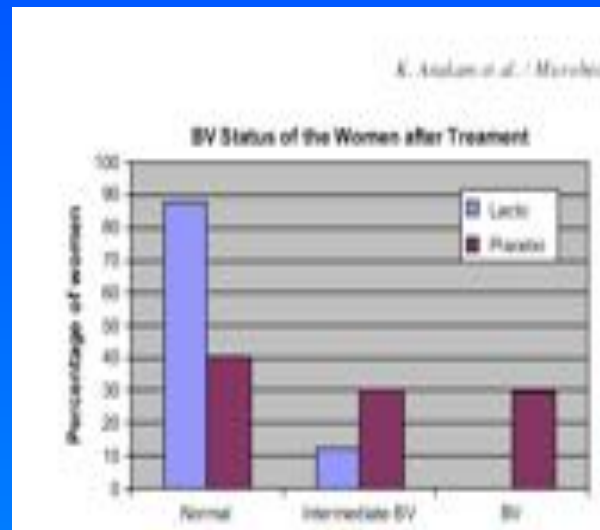
Probiotic group	Probiotic group				Metronidazole (0.75%) group			
	Day 0	Day 6	Day 15	Day 30	Day 0	Day 6	Day 15	Day 30
Signs and symptoms	20	2	2	2	20	8	8	8
Nugent score 7–10	20 (100%)	4 (20%)	3 (15%)	2 (12%)	20 (100%)	11 (55%)	11 (55%)	9 (50%)
Score 4–6	Nil	4	7	4	Nil	3	5	3
Score 0–3	Nil	12	10	11	Nil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

Diagnosis clinical sign + Nugent + BV blue

Metronidazole 500 mg BID 7 days. (57)

Treatment with oral lactobacilli for 30 days and test of cure at day 30. (49)

100% vs 70% cure according to Nugent



Hur behandlas BV bäst?

- Vad är den sanna utläkningen efter 1 behandling ?
- Vad kan patienten förvänta sig av behandlingen?
- Vad skall jag göra vid recidiv

GYNEKOLOGI

REKAMEN REVISI LAEMTON

anamnesis

- keluhan
- riwayat penyakit
- riwayat operasi

status

- pemeriksaan
- pemeriksaan

diagnosis

- pemeriksaan
- pemeriksaan

anamnesis

- keluhan
- riwayat penyakit

status

- pemeriksaan
- pemeriksaan

diagnosis

- pemeriksaan
- pemeriksaan

Saxat ur Läkemedelsboken

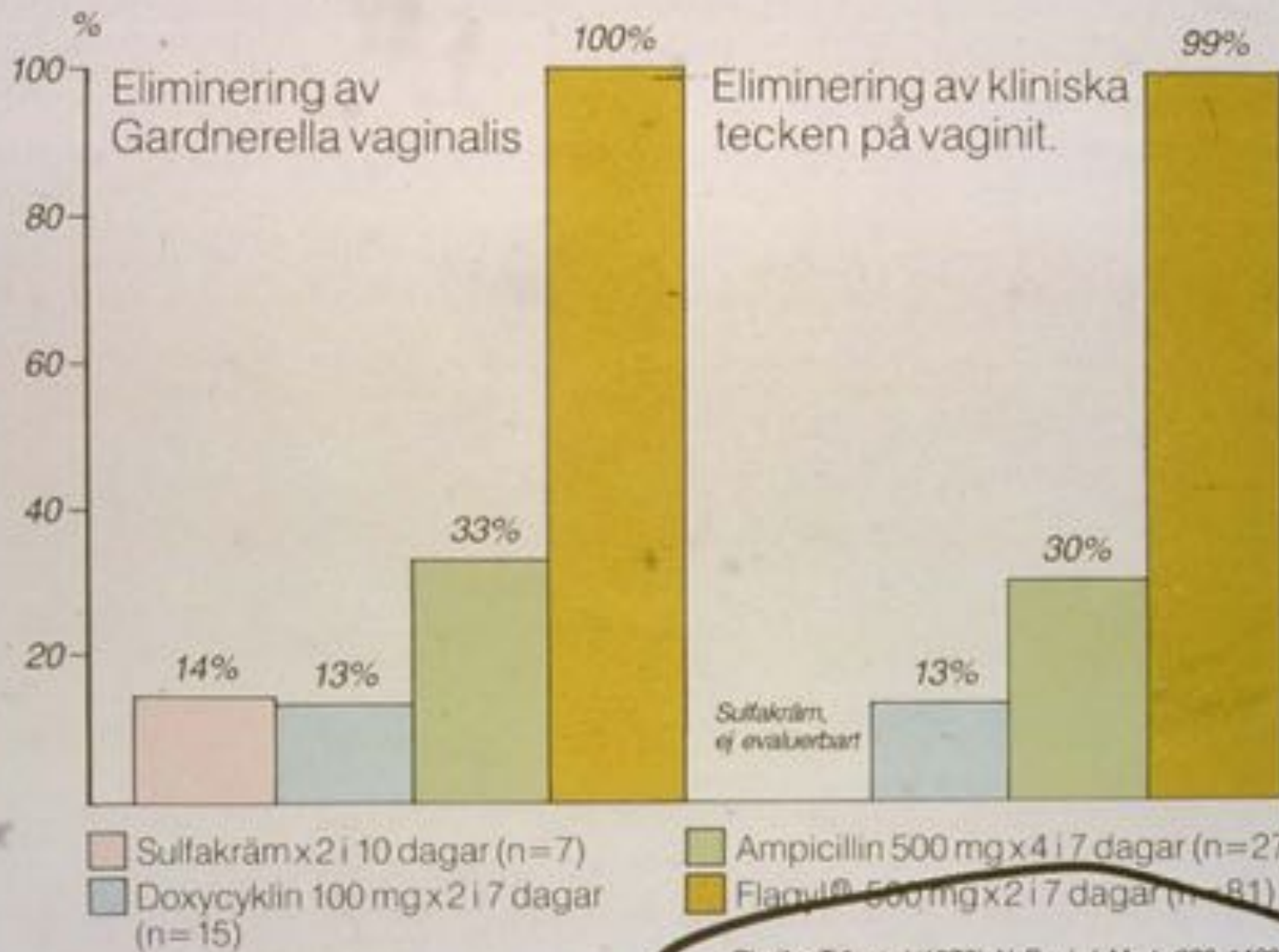
Table 1: Världens största läkemedelskoncerner 2018 (biljard dollar)

Rank	Company	Revenue	Profit	Market Share	Key Products
1	Pfizer	53.4	11.1	1.1%	Humira, Eliquis, Xarelto
2	Novartis	52.1	10.8	1.1%	Humira, Cosentyx, Opdivo
3	Roche	47.1	10.1	1.1%	Humira, Opdivo, Avastin
4	Astellas	43.1	9.1	1.1%	Imbruvica, Spravato, Tivicay
5	Amgen	42.1	8.1	1.1%	Enbry, Neulasta, Xarelto
6	AbbVie	41.1	7.1	1.1%	Humira, Skyris, Venclexta
7	Merck	40.1	6.1	1.1%	Keytruda, Gardasil, Januvia
8	Novo Nordisk	39.1	5.1	1.1%	Humalog, NovoRapid, Ozempic
9	Boehringer Ingelheim	38.1	4.1	1.1%	Plavix, Verzenio, Evion
10	Sanofi	37.1	3.1	1.1%	Humalog, Gardasil, Januvia

Key Products (highlighted in red box):

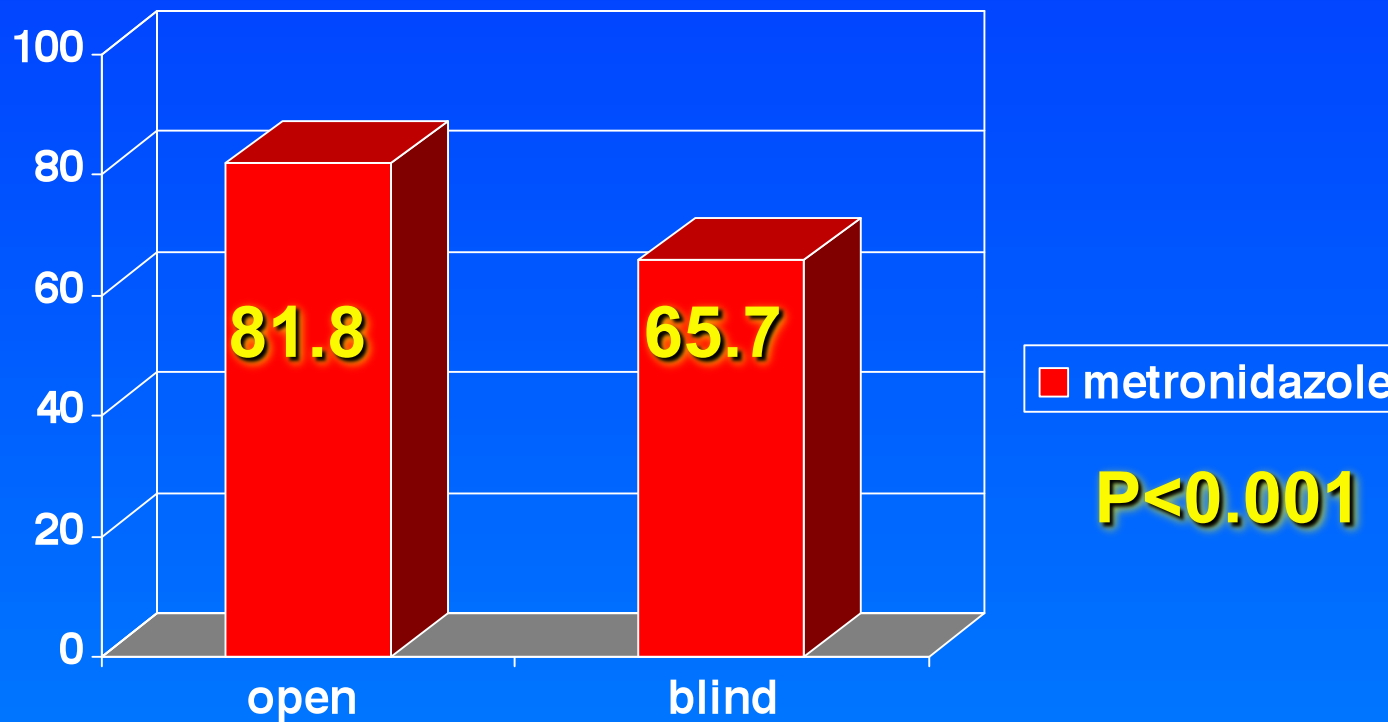
- Humira (adalimumab)
- Opdivo (nivolumab)
- Keytruda (pembrolizumab)
- Humalog (insulin lispro)
- Gardasil (HPV vaccine)
- Januvia (sitagliptin)
- NovoRapid (insulin aspart)
- Ozempic (semaglutin)
- Plavix (clopidogrel)
- Verzenio (endoxifen)
- Evion (vitamin E)

Behandlingsresultat



Phoifer, T.A. et al (1978). N. Engl. J. Med., 298, 1429.

Blinda studier har mycket sämre utläkning är öppna studier



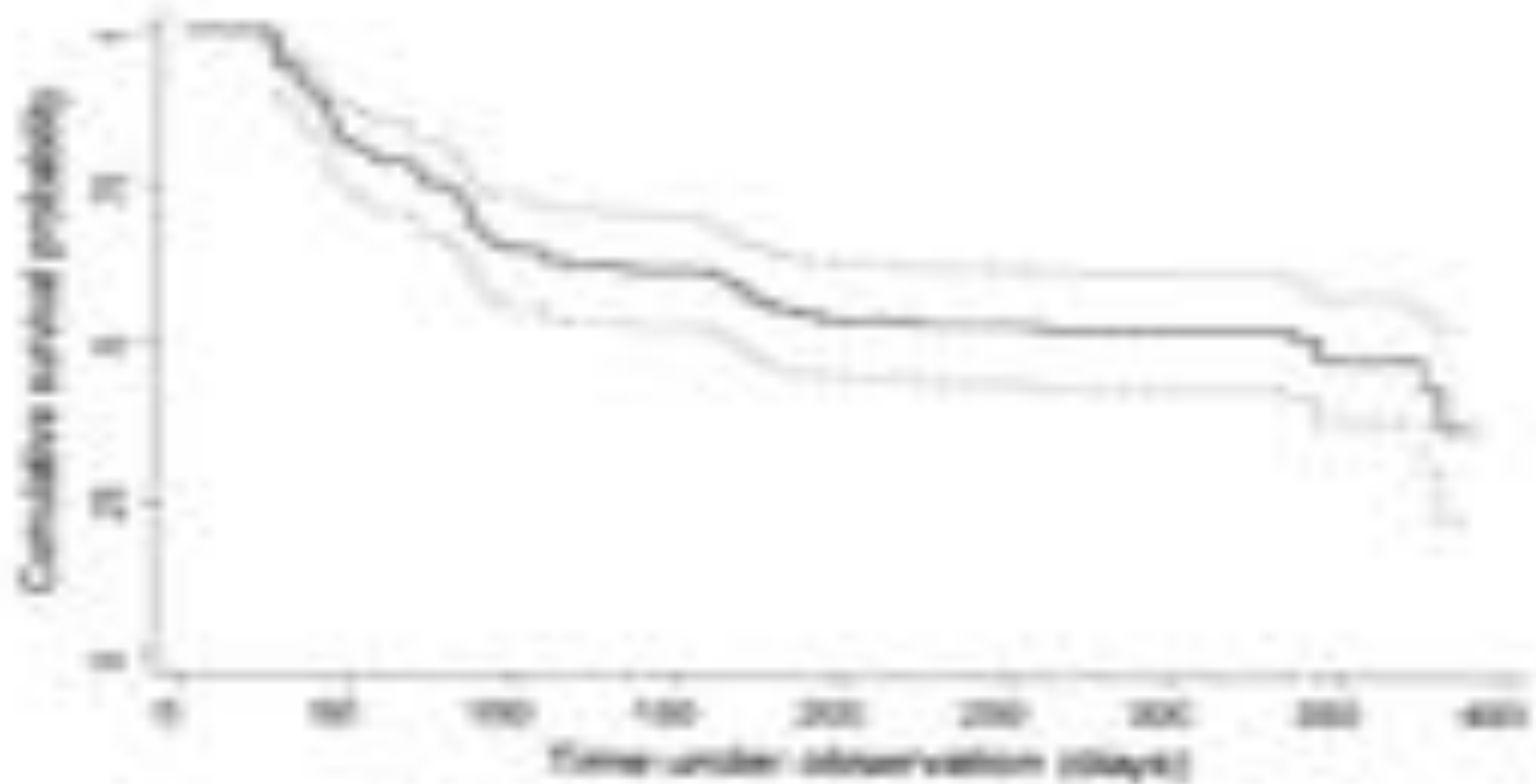


Figure 1. - Kaplan-Meier survival curve demonstrating recurrence of bacterial vaginosis over the course of 12 months after treatment for 3 days with oral metronidazole ($n = 130$). Dashed lines indicate 95% confidence intervals.

Bradshaw 2006 J Infect Dis

Bacterial vaginosis: an update on diagnosis and treatment

Expert Rev. Anti Infect. Ther. 7(9), 1109–1124 (2009)

Hans Verstraelen¹ and Rita Verhelst

¹Author for correspondence

Bacterial vaginosis is the most common cause of vaginal complaints. Bacterial vaginosis is further associated with a sizeable burden of infectious complications. Diagnosis relies on standardized clinical criteria or on scoring bacterial cell morphotypes on a Gram-stained vaginal smear. A few

Table 1. Evidence-based appraisal of the CDC treatment guidelines for bacterial vaginosis.

Comparison	Effectiveness	Comparisons	Level of evidence	Ref.
Oral metronidazole or clindamycin (500 mg)	No RCT	No RCT	No RCT	
Oral metronidazole vs oral clindamycin	Equally effective at 1 day	84 vs 90% (Grossen [1992]) 85 vs 92% (Aubert [1994])	Low-quality evidence	146 147
Intravaginal metronidazole or clindamycin or placebo	Equally effective at 4–6 weeks	Clindamycin 82 vs 85% (Lewinsohn [1996]) Metronidazole 77 vs 50% (Lewinsohn [1996])	Moderate-quality evidence	148 148
Intravaginal metronidazole vs intravaginal clindamycin	No RCT	No RCT	No RCT	
Intravaginal metronidazole or clindamycin vs oral metronidazole or clindamycin	Equally effective at 4 weeks	Paavonen (2002) Clindamycin cream (82%) Metronidazole gel (77%) Oral metronidazole (76%)	Very low-quality evidence	149

RCT, Randomized controlled trial

Bacterial Vaginosis: Treatment With Topical Intravaginal Clindamycin Phosphate

CHARLES H. LIVINGOOD III, MD, JESSICA L. THOMASOW, MD,
AND GALE B. HILL, PhD

We tested topical intravaginal clindamycin phosphate at concentrations of 0.1, 1.0, and 1.7% in the treatment of 46 women with symptomatic bacterial vaginosis in a prospective, randomized, double-blind, placebo-controlled trial, and found equal clinical treatment with 1.7% clindamycin in patients with persistent disease after 10-day treatment. Blinded intravaginal clindamycin phosphate treatment cured bacterial vaginosis in 76.1% (35/46) of all of patients 8-12 days after therapy, compared with 38.3% (18/47) of all of patients receiving placebo ($P < .001$). This study also found 88.3% (41/46) of all of patients who initially responded to clindamycin treatment showed persistent cure. There were no significant side effects. Clinical (Special 14-118) 1999

prevention are systemic antimicrobials and accept its known gastrointestinal side effects. Alternative therapy, particularly for pregnant women, is highly desirable. This study examined the safety and efficacy of topical intravaginal clindamycin at three different concentrations for treatment of bacterial vaginosis in a prospective, randomized, double-blind, placebo-controlled trial.

Materials and Methods

A total of 73 women with bacterial vaginosis were enrolled in the study from gynecology clinics at two

76% (35/46)

4 veckors utläkningen av vaginal clindamycin behandling (icke gravida) är inte bättre än 53%

	imporved (1 of 3 criteria)		cured(0 of 3 criteria)	
	number		number	
Livengood-90	14	86%	13	62%
Hillier-90	16	94%		
Schmitt-92	19	74%	19	58%
Andres-92	21	81%	21	72%
Stein-93	60	75%	60	37%
Fischbach-93	141	73%	141	55%
Dhar-94	18	78%	18	67%
Ahmed-95 (3 d)	52	65%	52	64%
Sobel-2001			180	48%
McCormack-2001	79	70%	79	49%
total	420	73,4%	583	53,4%



4 veckors utläkningen av vaginal metronidazol behandling (icke gravida) är inte bättre



	Less than 20% cluecells improved (1 of 3 criteria)		cured(0 of 3 criteria)	
	Number	%	Number	%
Hillier-93	30	73%		
Livengood-94	46	69%		
Soper-98	96	64%		
Livengood-99	178	61%		
Hanson-00	41	71%		
Schwebke-00			25	36%
	390	65.2%	25	36%

Figure 10-14

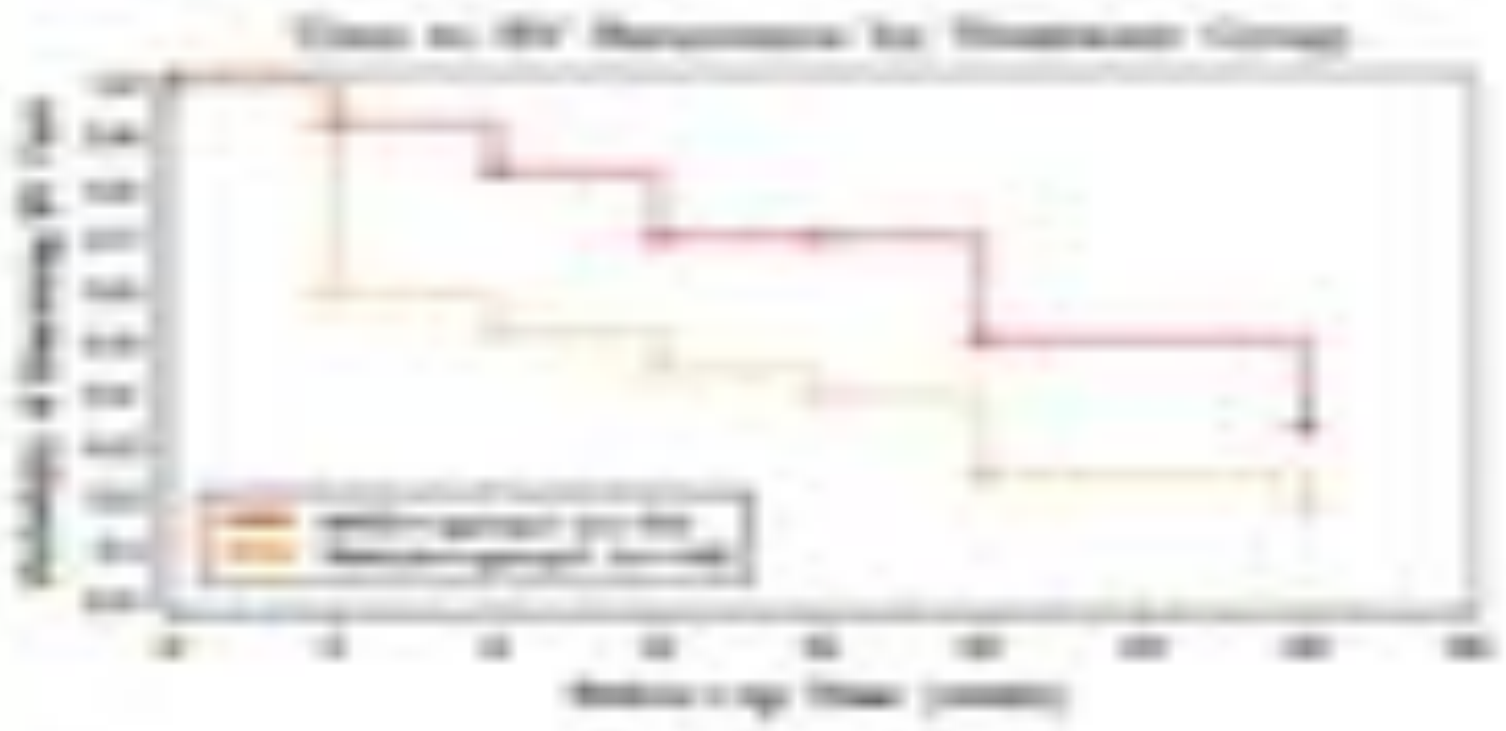
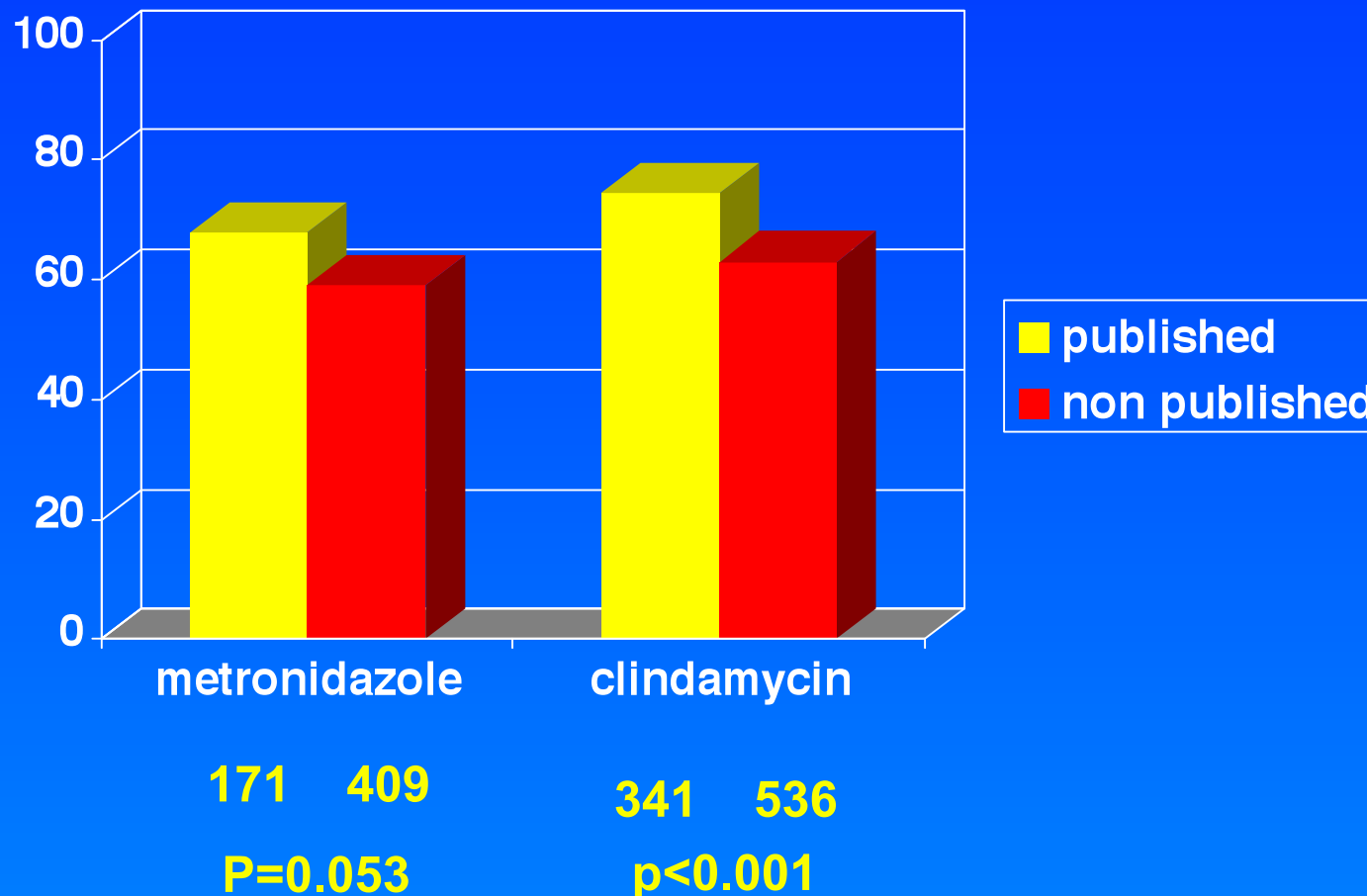


Figure 10-14. Follow-up time for development of treatment recurrence by treatment group for postoperative hysterectomy assigned to no early follow-up visits or placebo (—) or with follow-up visits as planned (---) in all early follow-up visits per protocol analysis.

Sobel 2005 Am J Obstet Gynecol

I icke publicerade studier är det lägre utläkning!!



FLAGYL®

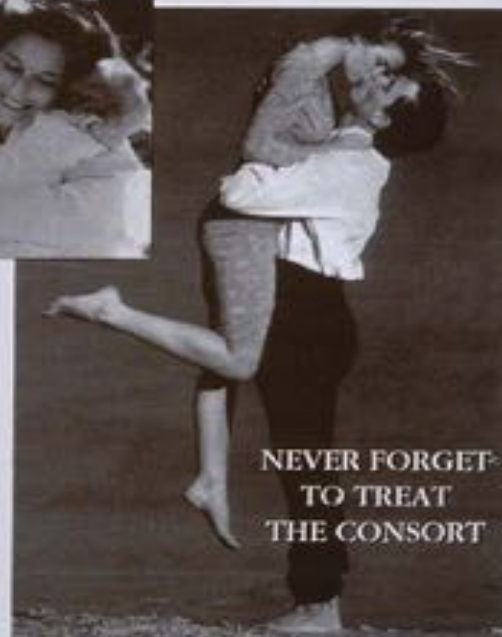
metronidazole

The most successful treatment
whatever the dosage regimen (17).



TREATMENT:

- two 2g doses at a 48 h interval (D1 and D3) (22,38).
- "single-dose" treatment; 2g on retiring (30,31,44).
- local treatment; with FLAGYL inserts with or without oral treatment (5,32).




NEVER FORGET
TO TREAT
THE CONSORT

References

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For further information see local medical catalogue text

 **RHÔNE-POULENC RORER**

Grini Næringspark 17, Postboks 33, 1345 Østerås, Tel.: 67 14 99 92, Fax.: 67 14 85 66

Behandling av partner lönar sig inte!

	def cured	partner treated		partner not treated	
		n	%	n	%
Heikkinen-89	symptoms	15/24	63%	12/21	57%
Mengel-89	Gram-stain		80%		65%
Swedberg-85	no cl on Gram	17/25	68%	25/39	64%
Veitorp-88	3 of 4	40/55	72%	37/52	71%
Moi-89	3 of 4	93/116	80%	92/108	85%
Colli-97	12 week	38/43	88%	32/41	78%
	total		77%		75%

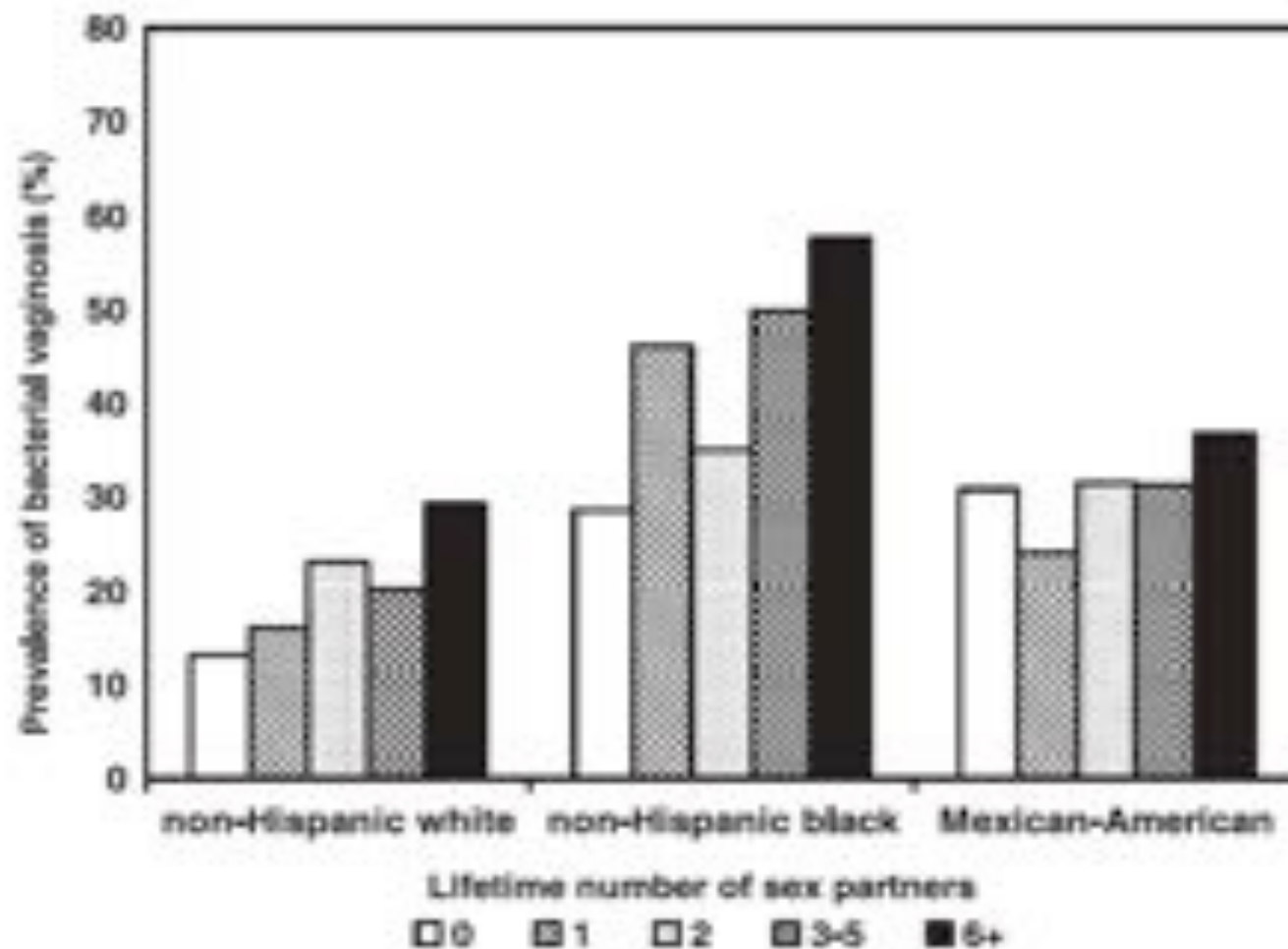


Fig. 1. Prevalence of bacterial vaginosis (Nugent's Gram stain score 7-10) by race/ethnicity and lifetime number of sex partners. χ^2 for trend for non-Hispanic whites $P = 0.0003$, for non-Hispanic blacks $P < 0.0001$, for Mexican Americans $P = 0.19$.

Antalet sex partners och BV

Koumans Sex Transm dis 2007

Recurrence of BV

- 404 kvinnor 6 månader 28% recurrence
- Samma sex partner HR 1.9
- Ej condom HR 1.9
- Östrogen p-piller HR 0.5

Extended antimicrobial treatment of bacterial vaginosis combined with human lactobacilli to find the best treatment and minimize the risk of relapses

Per-Göran Larsson^{1*}, Erik Brandborg¹, Urban Forsum², Sonal Pendharkar³, Kasper Krogh Andersen⁴, Salmir Nasic⁵, Lennart Hammarström⁶ and Harold Marcotte⁷

Abstract

Background: The primary objective of this study was to investigate if extended antibiotic treatment against bacterial vaginosis (BV) together with adjunct lactobacilli treatment could cure BV and, furthermore, to investigate factors that could cause relapse.

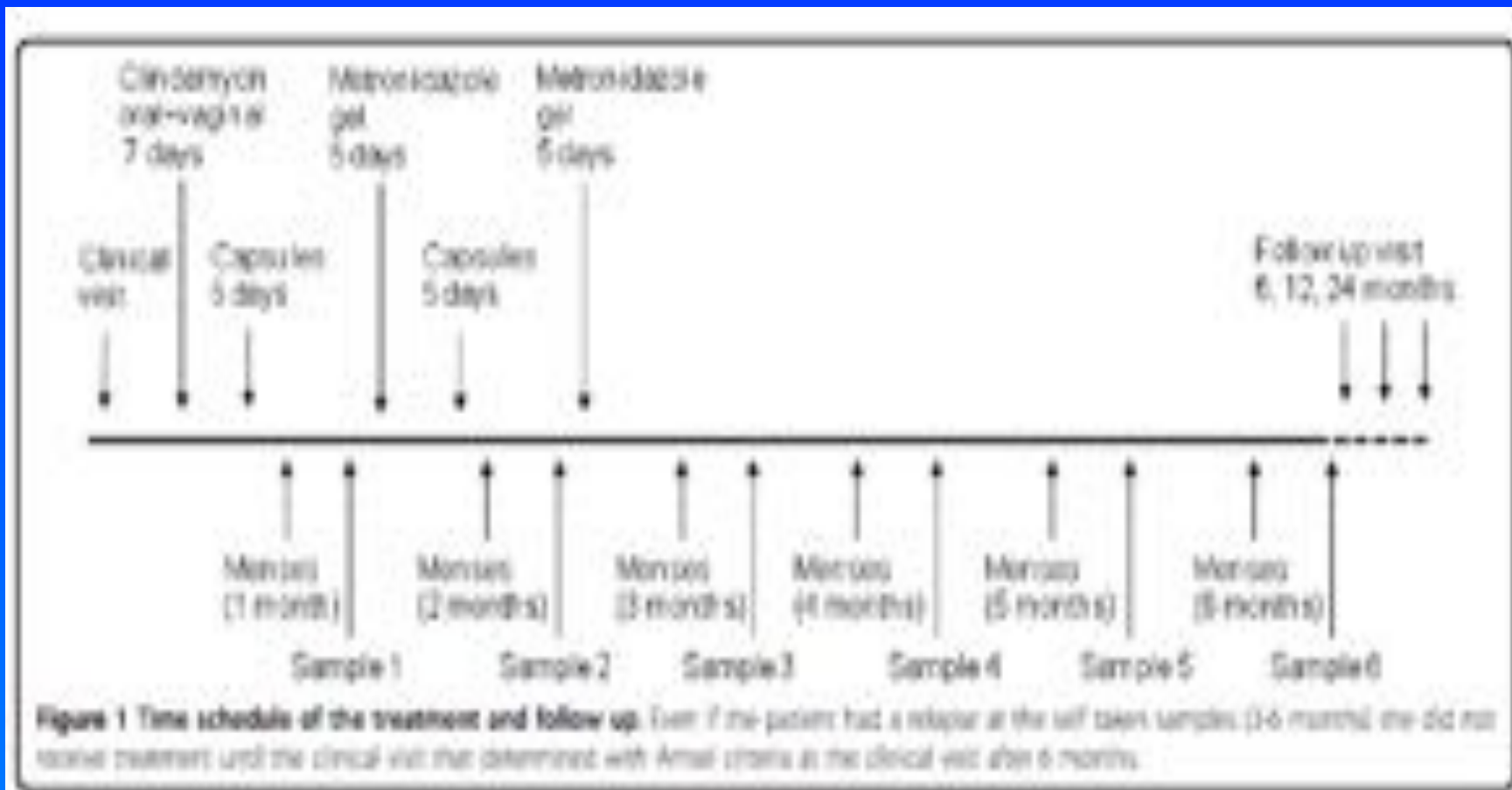
Methods: In all, 60 consecutive women with bacterial vaginosis diagnosed by Amsel criteria were offered a much more aggressive treatment of BV than used in normal clinical practice with repeated antibiotic treatment with clindamycin and metronidazole together with vaginal gelatine capsules containing different strains of lactobacilli both newly characterised and a commercial one (10^7 freeze-dried bacteria per capsule). Oral clindamycin treatment was also given to the patient's sexual partner.

Results: The cure rate was 34.5% after 6 months. The patients were then followed as long as possible or until a relapse. The cure rate was 65.1% at 12 months and 53.0% after 24 months. There was no significant difference in cure rate depending on which *Lactobacillus* strains were given to the women or if the women were colonised by lactobacilli. The most striking factor was a new sex partner during the follow up period where the Odds Ratio of having a relapse was 9.3 (2.8-31.2) if the patients had a new sex partner during the observation period.

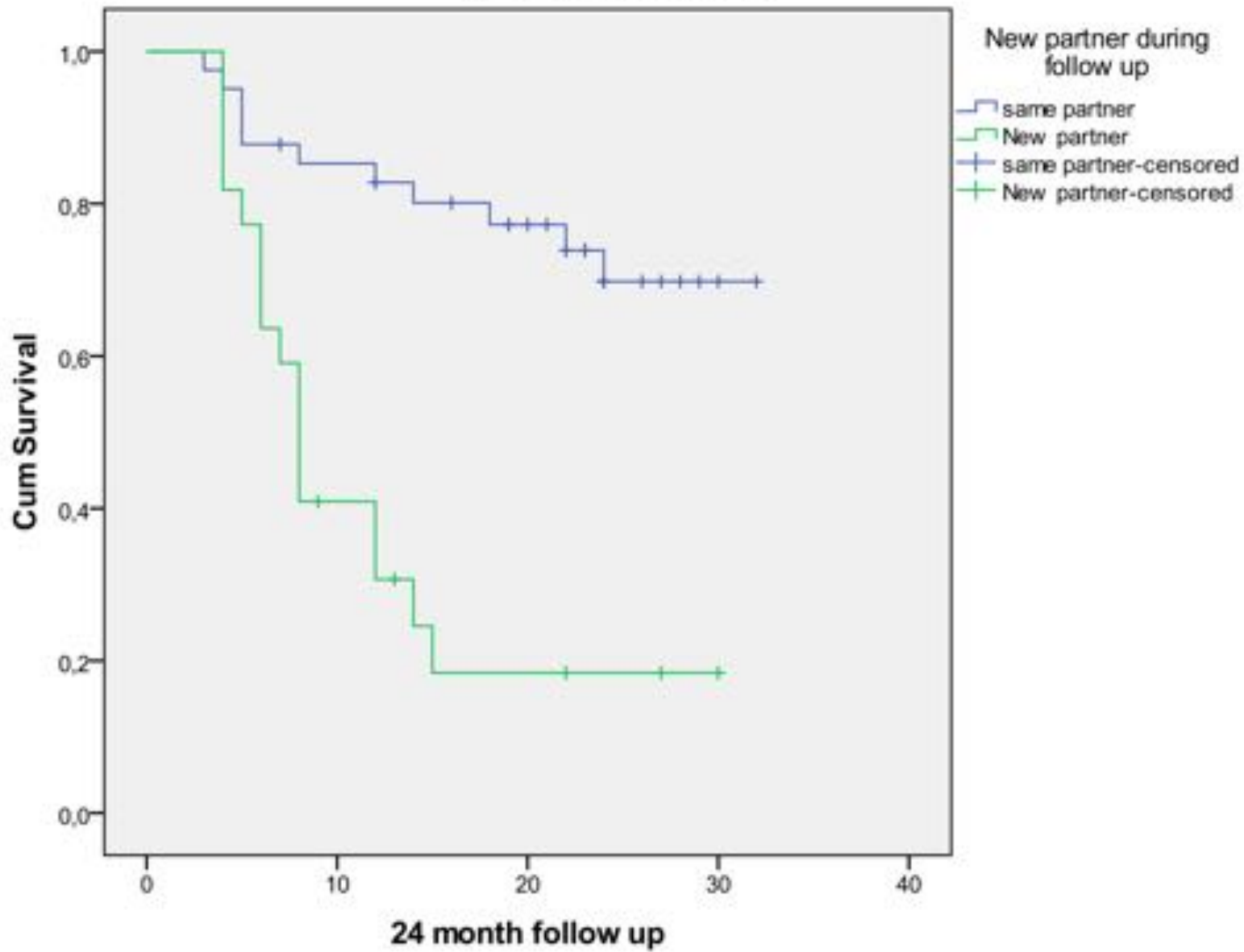
Conclusions: The study shows that aggressive treatment of the patient with antibiotics combined with specific *Lactobacillus* strain administration and partner treatment can provide long lasting cure. A striking result of our study is that change of partner is strongly associated with relapse of BV.

Trial registration: ClinicalTrials.gov, NCT01240322

Aggressiv behandling av BV



Survival Functions



Inkubations tiden går det att räkna ut?

median time was 2 months with a range of 1-22 months
and a mean time of 3.8 months.

Table 7 Study results of suppressive treatment of BV

Study	Treatment	Cure rate after			
		>1 month	3 months	6 months	12 months
Sobel 1993 [50]	Oral metronidazole 7 days		25%		
	Topical clindamycin 7 days		38%		
Boris 1997* [28]	Oral metronidazole 10 days (for some 3 times)				63%
Eriksson 2005** [23]	Topical clindamycin 3 days + lactobacilli tampons	57%			
	Topical clindamycin 3 days + placebo tampons	60%			
Sobel 2006 [7]	10 days vaginal metronidazole + twice weekly for 4 months		43%		
	10 days vaginal metronidazole + placebo		19%		
Bradshaw 2006 [6]	Oral metronidazole 7 days		46%	36%	31%
Schwebke 2007 [51]	Metronidazole gel twice weekly for 6 months			33%	
Marcone 2008 [29]	Oral metronidazole 7 days		71%	67%	
	Oral metronidazole 7 days + Lactobacillus rhomnosus for 2 months		88%	83%	
Lanson 2008 [13]	Topical clindamycin 7 days + lactobacilli			53%	
	Topical clindamycin 7 days + placebo			39%	
Reichman 2009 [52]	Triple treatment with oral nitroimidazole		63%	50%	
	21 days boric acid intravaginal and Metronidazole gel 20 weeks (6 month treatment)				
Ehnstrom 2010 [37]	Vaginal clindamycin + 5 types of lactobacilli			50%	
Marcone 2010 [30]	Oral metronidazole 7 days			74%	69%
	Oral metronidazole 7 days + Lactobacillus rhomnosus for 6 months			96%	91%
This study	Oral and vaginal clindamycin + vaginal metronidazole + lactobacilli			74.6%	65.1%

*Only cured patients were followed and some were treated 3 times.

**minimum 2 menstruations periods.

PM för behandling

Behandlingsstege – menscykel 1

Steg	Dag	Ordination	Kostnad*	Utläkningschans
1	1–7	Vaginalgel Clindamycin, till kvällen	171 kr	45–50 %
2	1–7	Kapsel Clindamycin, morgon och kväll	122 kr	+10 %
3	1–7	Partnerbehandling enligt 2		+10 %
4	8–13	Vagitorium EcoVag, 1 st till kvällen	163 kr	+10 %

Behandlingstillägg – menscykel 2 + 3 (+ 4)

Steg	Dag	Ordination	Kostnad 2 cykler
5	1–5	Vaginalgel Metronidazol (Zidoval), till kvällen	152 kr
6	6–10	Vagitorium EcoVag, 1 st till kvällen	109 kr
7		Kan upprepas efter ytterligare en menstruation	

Utläkningsgraden vid 12 mån ökar sålunda successivt. Total utläkningsgrad för hela regimen är cirka 70–75 %.

Recept stöd

Läkemedel

<i>Ordinerat Typ</i>	<i>Form</i>	<i>Namn</i>	<i>Mängd</i>	<i>Effekt</i>
<input type="radio"/> Recept	Gel	Clindamycin (Dalacin) 2 %	40 g	Antibiotika
<input type="radio"/> Recept	Kapsel	Clindamycin (Dalacin) 300 mg	32 st	Antibiotika
<input type="radio"/> Recept	Gel	Metronidazol (Zidoval)	40 g	Antibiotika
<input type="radio"/> Recept	Gel	Metronidazol (Zidoval)	40 g	Antibiotika
<input type="radio"/> Receptfritt	Vaginalkapsel	EcoVag	10 st	Mjölksyrebakterier

Slutsatser om BV

- **BV diagnosen är svår.**
- **BV behandlingen är urusel. I Inte bättre än 50% utläkta efter 4 veckor.**
- **BV är ett hot mot kvinnans hälsa och graviditeten**
- **Partner behandling är troligen viktig.**
- **Oseriösa företag luras med meningslös behandling.**
- **Var går gränsen mellan forskningsfusk och dålig forskning?**
- **Läs mer än abstraktet i en artikel. Och bara för den är publicerad betyder inte att det är sant.**
- **Lita inte alltid på metaanalyser.**

Donaxyl

- Registrerat sedan 2014
- Godkänt av TLV och är rabatterat



Start

Läkemedel

Medicinteknik

Tandvård

Apotek

Beslut

Press

Start / Beslut / Beslut läkemedel / Generell subvention / Donaxyl vaginaltablett ingår i hög

Beslut

Sök i databasen

Beslut läkemedel

Generell subvention

Begränsad subvention

Avslag och utslutningar

Uppföljningsbeslut

Prishöjningar

Överklagade beslut

Takpris i utbytesgrupper

Begärda utträden ur
läkemedelsförmånerna

Beslut förbrukningsartiklar

Beslut tillsyn

Donaxyl vaginaltablett ingår i högkostnadsskyddet

1) Lyssna

Donaxyl vaginaltablett (dekvaliniumklorid) för behandling av bakteriell vaginos ingår i högkostnadsskyddet från och med den 25 oktober 2014.

Donaxyl vaginaltablett används för behandling av bakteriell vaginos. Bakteriell vaginos innebär att bakteriesammansättningen i slidan är förändrad och att andra bakterier än de skyddande mjölksyrebakterierna har ökat. Tillståndet ökar risken för infektioner och prematur (för tidig) förlösning.

Donaxyl vaginaltablett innehåller den aktiva substansen dekvaliniumklorid och är ett antiseptiskt medel. De övriga behandlingsalternativen mot bakteriell vaginos består alla av antibiotika. Svårighetsgraden av bakteriell vaginos bedöms vanligtvis vara låg, men kan i vissa fall vara medelhög, till exempel hos gravida kvinnor eller vid infektion efter vaginala ingrepp.

TLV bedömer att effekten av Donaxyl är likvärdig övriga behandlingsalternativ. Det begärda priset för Donaxyl är högre än priset för det mest relevanta jämförelsealternativet, men är det samma som priset för det dyraste och mest förskrivna behandlingsalternativet.

Swidsinski Biofilm

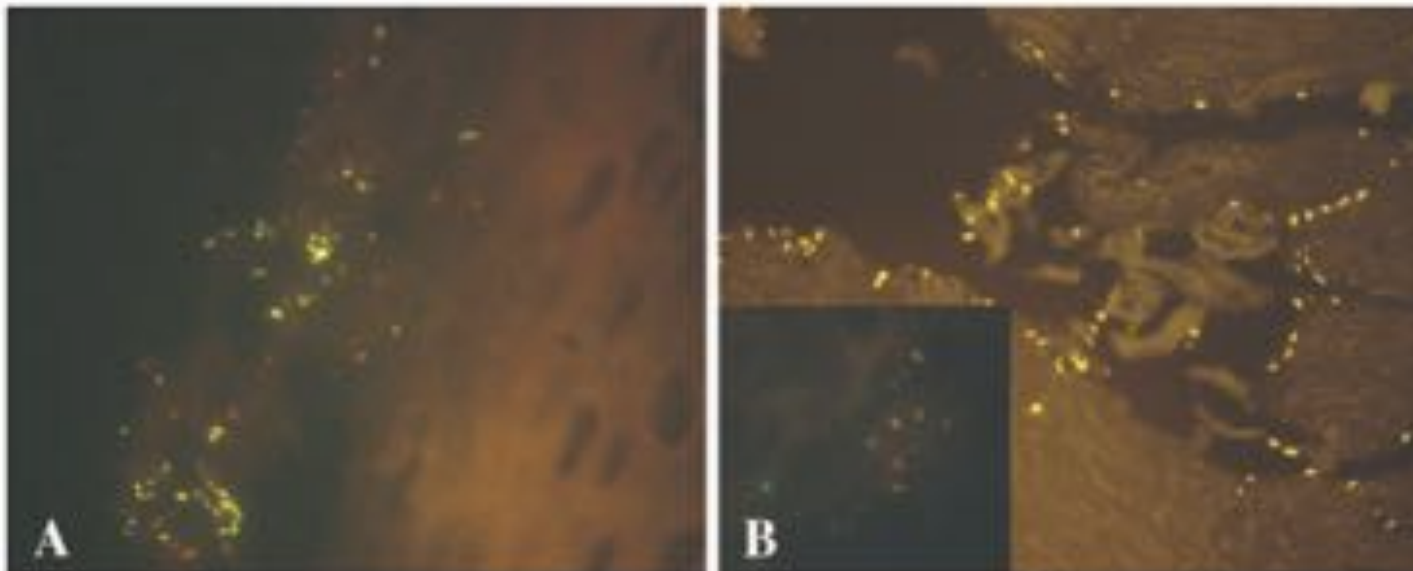


Fig. 2. Vaginal epithelium from healthy postmenopausal woman with unstructured biofilm. A triple contrasted hybridization with Lab-Cy3 (orange), Eub-fluorescein isothiocyanate (green), and GardV-Cy5 (red) probes is shown on the left (A), x1000

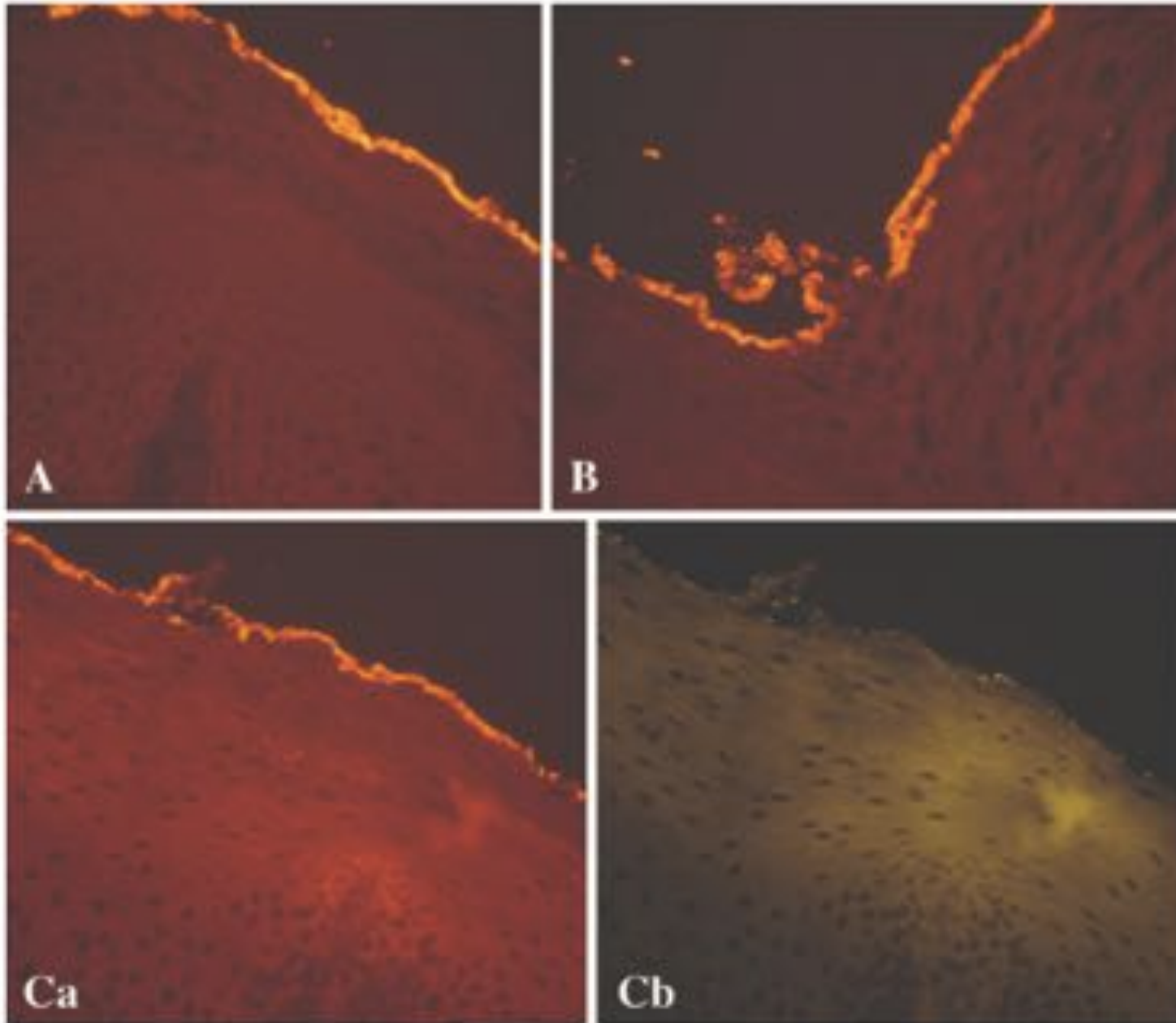
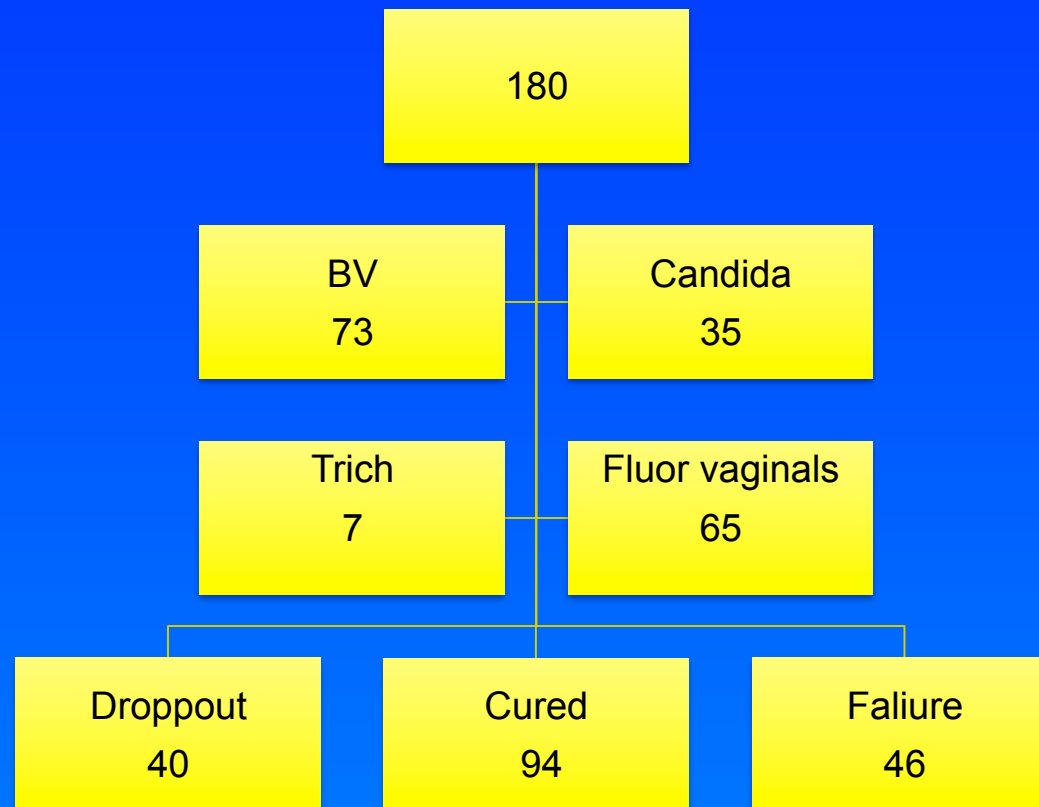


Fig. 3. Three adjacent microscopic fields (A, B, C) show a continuous *Gardnerella vaginalis* biofilm covering the vaginal

Studien 1993-1995

- Beh 6 dagar kontroll 5-7 dagar efter
- 3-4 veckor efter första besök
- BV enl Amsel + confirmed by culutre G vag and bacteroides/petrovella
- Candida enl Wet smear or culture
- Trichomonas enl wet smear
- Fluor vaginalis signs of vaginitis and LBG II or III

BV behandling Fluomycin mot povidone iodine



Petersen 2002

Table 2: Development of efficacy criteria upon therapy in the entire population.

Criteria	Test group			Reference group		
	Entry	Control 1	Control 2	Entry	Control 1	Control 2
Patients evaluated	121	118	94	59	59	46
Total symptoms score (mean \pm SD) ^{a)}	5.1 \pm 2.3	1.8 \pm 1.6	1.3 \pm 1.4	5.1 \pm 2.0	1.5 \pm 1.2	1.0 \pm 1.2
Vaginal pH (mean \pm SD) ^{a)}	5.2 \pm 0.7	4.6 \pm 0.6	4.6 \pm 0.6	5.1 \pm 0.6	4.7 \pm 0.6	4.5 \pm 0.5
Degree of purity (%)						
grade I	0.8	25.0	51.0	0.0	21.4	54.4
grade II	43.0	64.7	37.3	43.9	60.7	32.6
grade III	56.2	9.5	9.6	54.4	17.9	13.0
grade IV	0.0	0.9	2.1	1.7	0.0	0.0
Leukocytes ^{b)} (%)						
> 10	63.6	29.3	22.3	58.6	28.1	21.7
Lactobacilli ^{c)} (%)						
None	44.6	12.9	11.7	43.1	28.1	10.9
1-50	50.4	59.5	39.4	48.3	49.1	43.5
> 50	5	27.6	48.9	8.6	22.8	45.6

^{a)} SD = standard deviation. ^{b)} Per field of view (400 \times). ^{c)} Per field of view (1000 \times).

Table 3: Evaluation of therapeutic efficacy (global assessment by the investigator).

	Test preparation		Reference preparation	
	Control 1	Control 2	Control 1	Control 2
Entire population				
Patients evaluated	115	93	59	44
Complete or considerable improvement	69.6 %	78.5 %	66.1 %	72.7 %
Bacterial vaginosis				
Patients evaluated	45	36	25	20
Complete or considerable improvement	82.2 %	75.0 %	76.0 %	75.0 %
Fluor vaginalis				
Patients evaluated	43	35	20	14
Complete or considerable improvement	53.5 %	77.1 %	60.0 %	64.3 %
Candidiasis				
Patients evaluated	23	19	12	9
Complete or considerable improvement	78.3 %	84.2 %	67.7 %	88.9 %

36 / 73

Table 4: Development of efficacy criteria upon therapy in the subgroup bacterial vaginosis.

Criteria	Test group			Reference group		
	Entry	Control 1	Control 2	Entry	Control 1	Control 2
Patients evaluated	48	46	37	25	23	20
Total symptoms score (mean \pm SD)	4.3 \pm 2.3	1.3 \pm 1.3	1.6 \pm 1.5	4.6 \pm 1.8	1.4 \pm 0.9	0.8 \pm 1.1
Vaginal pH (mean \pm SD)	5.3 \pm 0.4	4.5 \pm 0.5	4.5 \pm 0.4	5.3 \pm 0.6	4.7 \pm 0.6	4.5 \pm 0.4
Whiff test positive (%)	89.6	4.3	22.2	92.0	25.0	5.9
Degree of purity						
Grade I/II (%)	12.5	87.0	78.3	12.5	72.7	80.0
Lactobacilli ^{a)}						
> 50 (%)	2.1	41.3	62.2	4.2	21.7	65.0
Clue cells ^{b)} (%)	81.3	8.7	24.3	96.0	30.4	10.0
<i>Gardnerella vaginalis</i> ^{c)} (%)	60.4	6.5	24.3	68.0	28.0	5.0
<i>Bacteroides/Prevotella</i> ^{c)} (%)	37.5	15.2	16.2	36.0	4.0	5.0
<i>Mycoplasma hominis</i> ^{c)} (%)	18.8	6.5	5.4	12.0	8.0	10.0

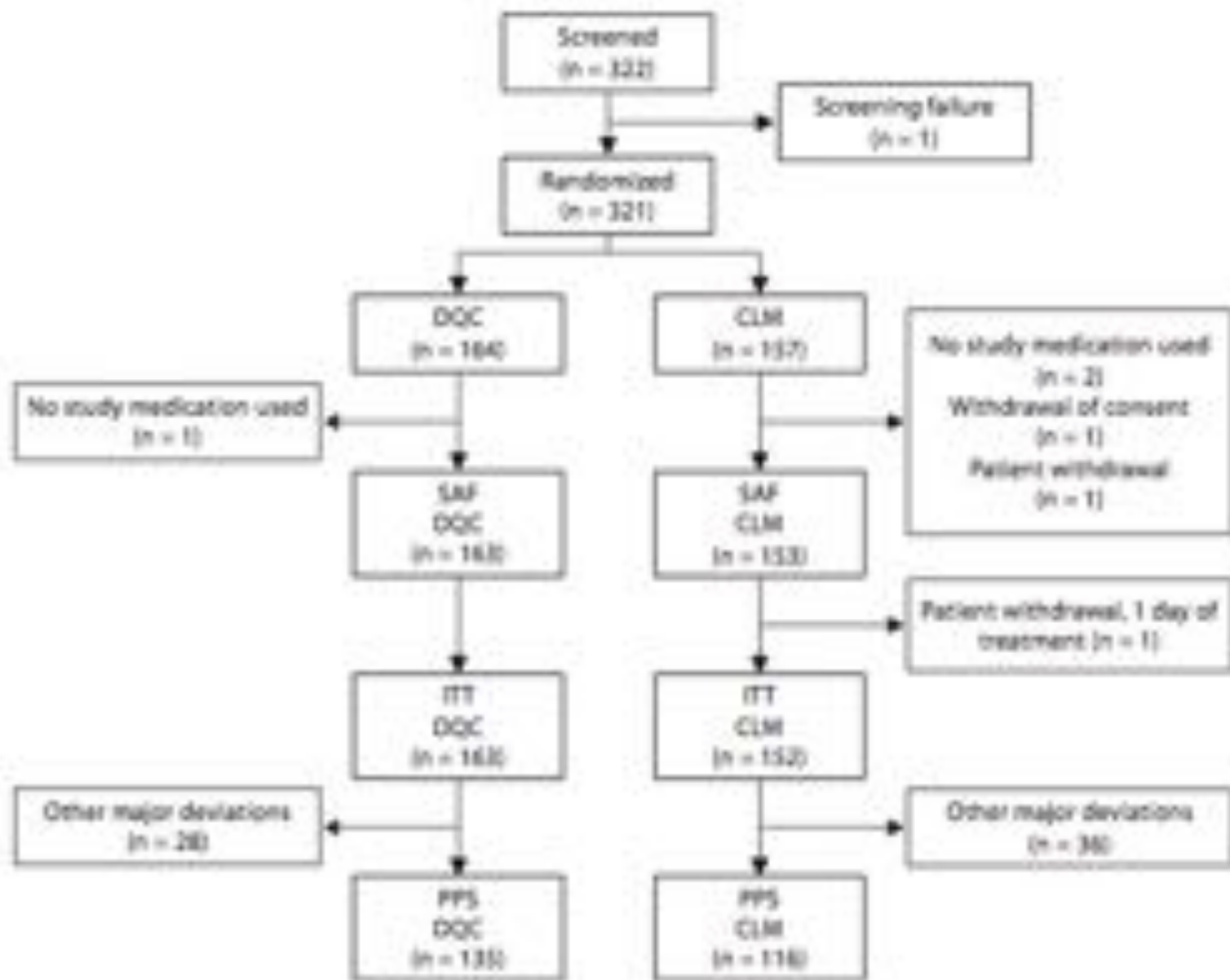
^{a)} Per field of view (1000x). ^{b)} Presence in wet smear. ^{c)} Microbiological cultures grown from samples of the vaginal secretion.

Det var 73 BV av 180 (40%)

A Comparison of Dequalinium Chloride Vaginal Tablets (Fluomizin®) and Clindamycin Vaginal Cream in the Treatment of Bacterial Vaginosis: A Single-Blind, Randomized Clinical Trial of Efficacy and Safety

Ernst Rainer Weissenbacher^a Gilbert Donders^{b, c} Vit Unzeitig^f
Begoña Martinez de Tejada^d Stefan Gerber^e Michael Halaška^g
Jiří Špaček^h Fluomizin Study Group

2011



drug they were using despite the blinded boxes, as one drug's formulation was a cream, while the other was a tablet. To overcome possible bias in the efficacy assessment by the investigator, two physicians were involved during the visits: the 'treating' physician dispensed the study medication according to randomization code and assessed compliance and side effects, and the 'evaluating' physician assessed the efficacy while blinded to

2007-2008

parents. To be included in the study, women had to be diagnosed with BV, for which all 4 Amsel criteria [21] had to be present: (1) characteristic grey, homogeneous, malodorous discharge, (2) pH > 4.5, (3) a positive KOH test for amines, and (4) clue cells (positive if $\geq 20\%$ of the epithelial cells of the wet mount were clue cells). Women were required to use effective contraception, but

Test of cure

- **Absence of < 20% cluecells + neg 2 Amsel**
- **LBC scoring to Donders**

Donders et al. [22] as normal, grade-I flora (LBG I), intermediate, grade-II flora (LBG II), and abnormal, grade-III flora (LBG III).

- **This clinical trial was registered at EudraCT (2006-004398-89) and at ClinicalTrial.gov (Med380104, NCT01125410). The study was conducted in 15 centers in five countries in accordance with the Declaration of Helsinki and the GCP guidelines, and approved by all local Ethics Committees. All women gave written informed consent and were enrolled into the study from January 2007 to July 2008. This report complies with the CONSORT guidelines.**

	Total, n	Missing, n	Cured, n	Cure rate, %
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Follow-up visit C2

PPS

DQC	135	3	105	79.5
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CLM	116	–	90	77.6
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ITT

DQC	163	8	116	74.8
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CLM	152	9	107	74.8
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LBG, n (%)	DQC (n = 163)	CLM (n = 152)	P-value
Entry			
LBG I	1 (0.6)	1 (0.7)	
LBG II	37 (22.7)	38 (25.0)	
LBG III	125 (76.7)	113 (74.3)	0.89
C1			
LBG I	90 (57.0)	79 (55.2)	
LBG II	49 (31.0)	38 (26.6)	
LBG III	19 (12.0)	24 (16.8)	0.42
C2			
LBG I	101 (67.3)	80 (58.4)	
LBG II	33 (22.0)	40 (29.2)	
LBG III	16 (10.7)	16 (11.7)	0.30

Non-responders and recurrences, n (%)

Non-responders	17 (10.4)	23 (15.2)	0.21
BV recurrence	22 (13.5)	14 (9.2)	0.23
Total failures	39 (23.9)	37 (24.3)	0.93

Då blir utläkningen 71 respektive 73%

	Total, n	Missing, n	Cured, n	Cure rate, %
<i>Follow-up visit C2</i>				
PPS				
DQC	135	3	105	79.5
CLM	116	-	90	77.6
ITT				
DQC	163	8	116	74.8
CLM	152	9	107	74.8

Table 6. Cure rate comparison (ITT, n = 315)

	Follow-up visit C1			Follow-up visit C2		
	DQC (n = 163)	CLM (n = 152)	p value*	DQC (n = 163)	CLM (n = 152)	p value*
Based on all 4 Amsel criteria						
Cured ^a – no clue cells and ≥2 others negative	79.7%	78.7%	0.83	74.8%	74.8%	1.00
Cured – all 4 negative	52.9%	41.8%	0.06	56.7%	50.4%	0.29
Improved – ≥3 of 4 negative	80.4%	79.4%	0.84	79.3%	80.0%	0.89
Based on 3 Amsel criteria ^b						
Cured – all 3 negative	58.2%	44.0%	0.01	60.0%	53.3%	0.26
Improved – ≥2 of 3 negative	84.2%	83.7%	0.91	80.7%	83.8%	0.49

* χ^2 test. ^a Primary efficacy variable of this study. ^b pH >4.5, clue cells, KOH test.

Donaxyl

- **Registrerat**
- **Godkänt av TLV och är rabatterat**
- **Bygger på EN studie. Tveksam sådan**
- **Ansökt om etikprövning att testa 50 pat med 6 mån utläkning**