

Asymptomatic Bacteriuria in Diabetic Women

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Asymptomatic Bacteriuria (Asymptomatic Urinary Infection)

- absence of acute symptoms referable to urinary tract
- bacteriuria: $\geq 10^5$ cfu/ml in two consecutive urine specimens

Diabetic Women

Asymptomatic Bacteriuria

	<u>Number</u>	<u>Prevalence</u>
Zhanel et al	1,072	7.9%
Sawers et al	400	9.5%
Schmitt et al	341	9.1%
Geerlings et al	636	13%

Asymptomatic Bacteriuria in Diabetic Women

Treat or Not Treat

- ? short term outcomes
 - symptomatic infection
 - metabolic control
- ? long term outcome
 - hypertension
 - renal failure
 - long term complications

Diabetic Women

Asymptomatic Bacteriuria

Patient Population

- ambulatory endocrinology referral clinics
 - tertiary care
 - private office
- aboriginal

ABU in Diabetic Women

Enrollment:	1991-1997
Screened:	1900
First positive:	268 (14.1%)
Second positive:	135/196 (69%)

Prevalence of ABU and Host Factors

Zhanel et al, CID, 1995

First culture: 156/1,099 14.2%

Second culture: 85/129 65.9%

Prevalence two cultures: 85/1,072 7.9%

Infecting Organisms

Zhanel et al, CID, 1995

Gram negative Organisms

73%

<u>Escherichia coli</u>	45	53%
<u>Klebsiella pneumoniae</u>	12	14%
<u>Enterobacter cloacae</u>	2	2.4%
<u>Klebsiella oxytoca</u>	1	1.2%
<u>Citrobacter diversus</u>	1	1.2%
<u>Citrobacter freundii</u>	1	1.2%

Infecting Organisms

Zhanel et al, CID, 1995

Gram positive Organisms			20%
<u>Streptococcus agalactia</u> (grp B)	6	7.1%	
Viridans streptococci	2	2.4%	
<u>Staphylococcus epidermidis</u>	2	2.4%	
<u>Staphylococcus aureus</u>	2	2.4%	
<u>Staphylococcus saprophyticus</u>	1	1.8%	
<u>Gardnerella vaginalis</u>	3	3.6%	
<u>Enterococcus faecalis</u>	1	1.2%	
Mixed	6	7.1%	7%

ABU in Diabetic Women: Pyuria

Zhanel et al, CID, 1995

<u>Organisms (number)</u>	<u>Mean Urine WBC/mm³</u> <u>(range)</u>
<u>E. coli</u> (45)	345 ± 935 (0-5,500)
Other Enterobacteriaceae (17)	222 ± 278 (0-930)
Streptococcus spp (8)	368 ± 814 (0-2,360)
Staphylococcus spp (5)	43.4 ± 43 (2-103)
<u>Gardnerella vaginalis</u> (3)	17 ± 12 (3- 26)
<u>Enterococcus faecalis</u> (1)	130

ABU in Diabetic Women

Urinary Leukocyte Counts

Zhanel, CID, 1995

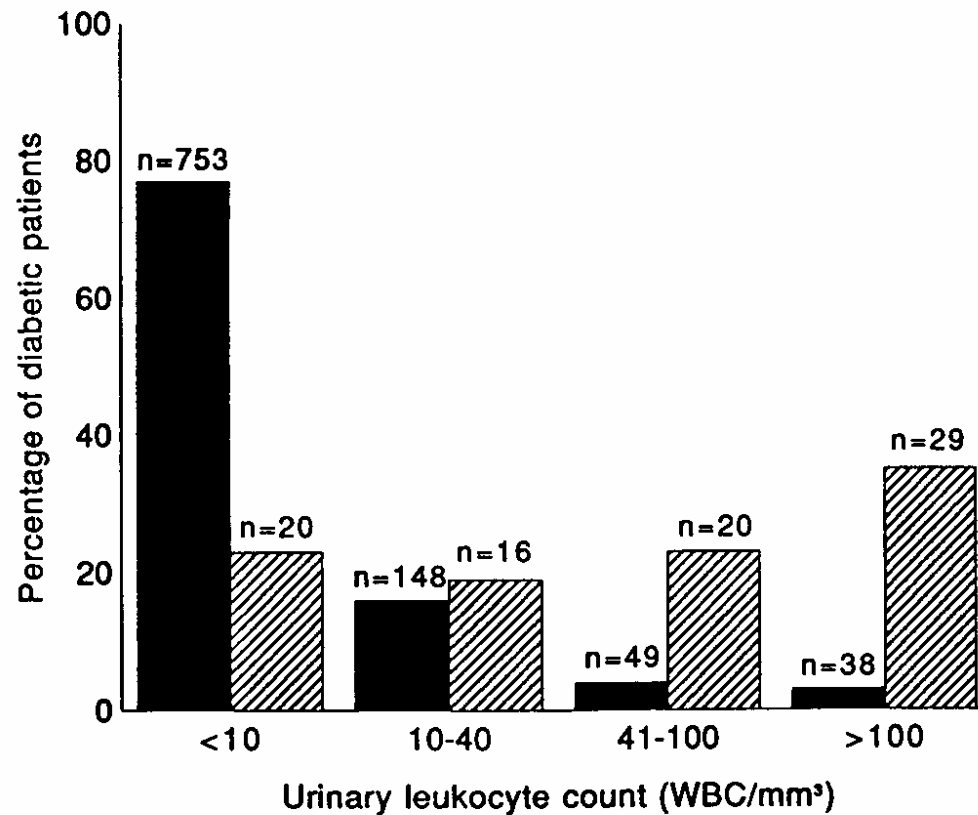


Figure 1. Frequency distribution of urinary leukocyte counts in bacteriuric and nonbacteriuric diabetic women (■ = nonbacteriuric; ▨ = bacteriuric; WBC = white blood cells).

Pyuria and Persistence of ABU in Diabetic Women

Zhanel et al, CID, 1991

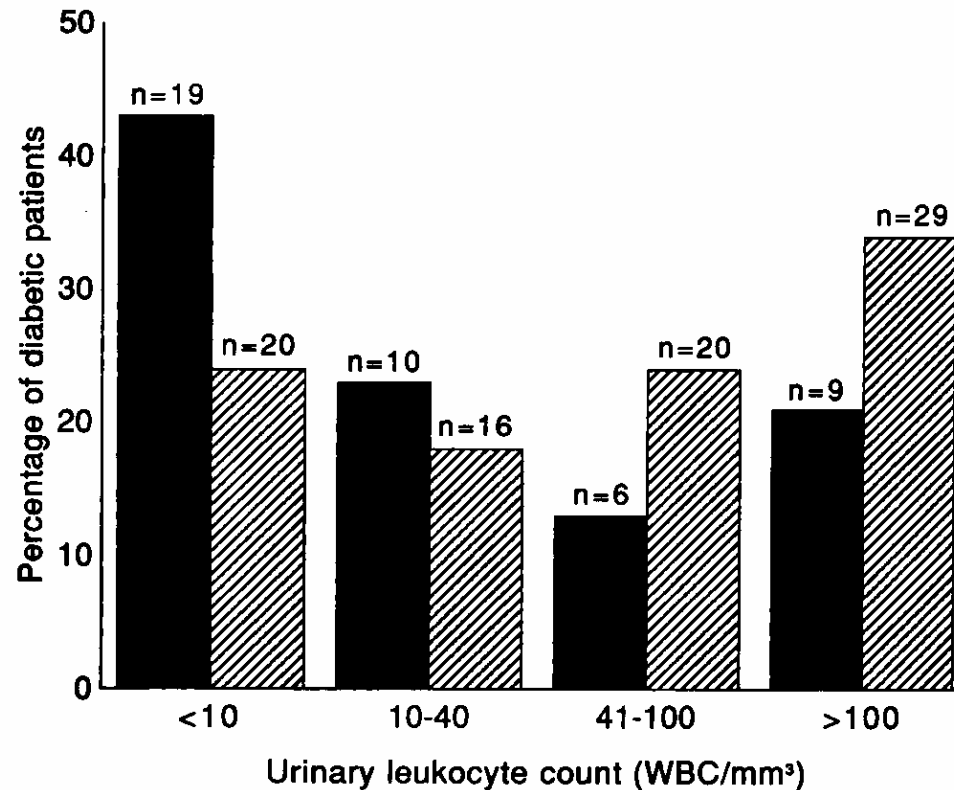


Figure 2. Comparison of urinary leukocyte counts in persistently bacteriuric subjects and subjects whose initial bacteriuria spontaneously cleared (■ = cleared bacteriuria; ▨ = persistent bacteriuria; WBC = white blood cells).

ABU in Diabetic Women

Univariate Analysis: Host Factors

Zhanel, CID 1995

No difference: age, weight, previous UTI (p=0.06)

Hgb A₁C

reintopathy, neuropathy , renal function

Significant duration diabetes

Type II, oral hypoglycemia

heart disease

aboriginal

Asymptomatic Bacteriuria Diabetic Women (Multivariate)

Zhanel et al, CID 1995

Host factor	Number (%)		<i>P</i> value)	OR (95% CI)
	Nonbacteriuric (<i>n</i> =987)	Bacteriuric (<i>n</i> =85)		
Years of diabetes				
<1	251 (25.4)	7 (8.2)	...	1.0
1-5	197 (20)	16 (18.8)	.066	2.4 (09.-6.2)
5-10	168 (17)	20 (23.5)	.004	3.7 (1.5-9.3)
10-20	227 (23)	30 (35.3)	.001	4.3 (1.8-10.1)
>20	144 (14.6)	12 (14.1)	.015	3.3 (1.3-8.7)
Current treatment				
Diet	264 (26.7)	14 (16.5)	...	1.0
Insulin	499 (50.6)	38 (44.7)	...	1.0
Oral hypoglycemic (OH)	203 (20.6)	29 (34.1)	.08	1.6-(0.9-2.6)
Insulin & OH	31 (3.1)	4 (4.7)	...	1.0
Aboriginal origin	61 (6.2)	15 (17.6)	<.0001	3.8(2.0-7.4)

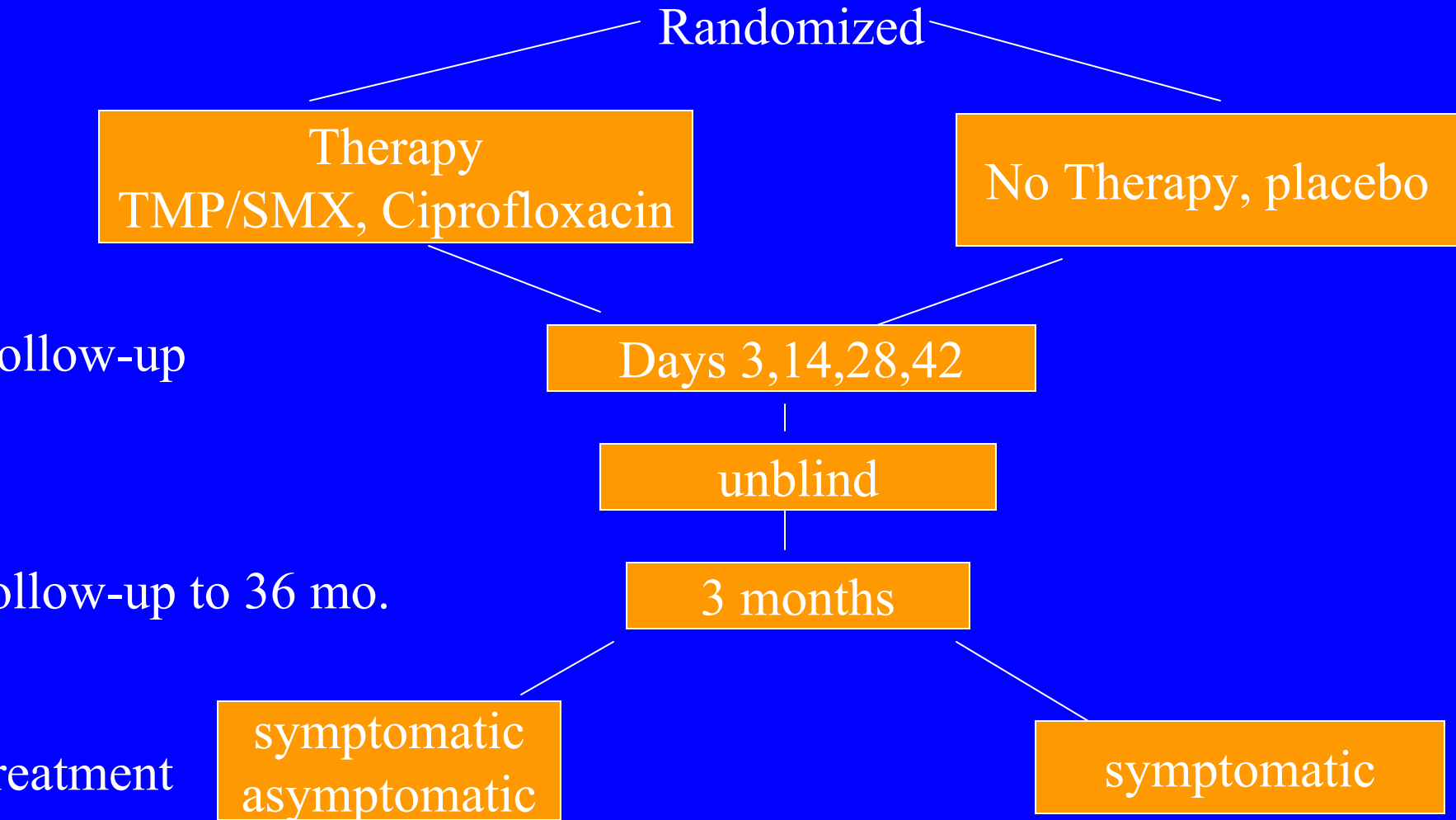
Antibiotic Treatment of ASB in Diabetic Women

NEJM, 2002

Screened	1900
First positive	268 (14%)
Second positive	135/196 (69%)
Enrolled: no treatment	50
treatment	55

Antibiotic Treatment of ABU in Diabetic Women

Harding, NEJM, 2002



Antimicrobial Treatment of ASB in Diabetic Women

NEJM, 2002

	<u>Not treated</u> (N=50)	<u>Treated</u> (N=55)
Age	57 ± 11 yr	54 ± 12 yr
Followed (mo)	26.2 ± 11	27.6 ± 11
Organisms:		
<u>E. coli</u>	31 (62%)	33 (60%)
Other gram-negative	6 (12%)	12 (22%)
Pyuria: median (range)	40.5 (0-3360)	44 (0-1600)

Asymptomatic Bacteriuria in Diabetic Women

Placebo/Treatment

Harding, NEJM, 2002

Similar: sexual activity

history UTI

history GU surgery

diabetes type (80% Type II)

duration

complications

blood glucose, Hgb A₁C

glycosuria, proteinuria

Antimicrobial Treatment of ASB in Diabetic Women

Short Term Microbiologic Outcome

NEJM, 2002

	<u>Placebo</u>	<u>Antimicrobial</u>
Day 3	4 (8%)	46 (94%)
Day 14	9 (18%)	48 (98%)
Day 28	10 (20%)	42 (86%)
Day 42	11 (22%)	39 (80%)

ABU in Diabetic Women

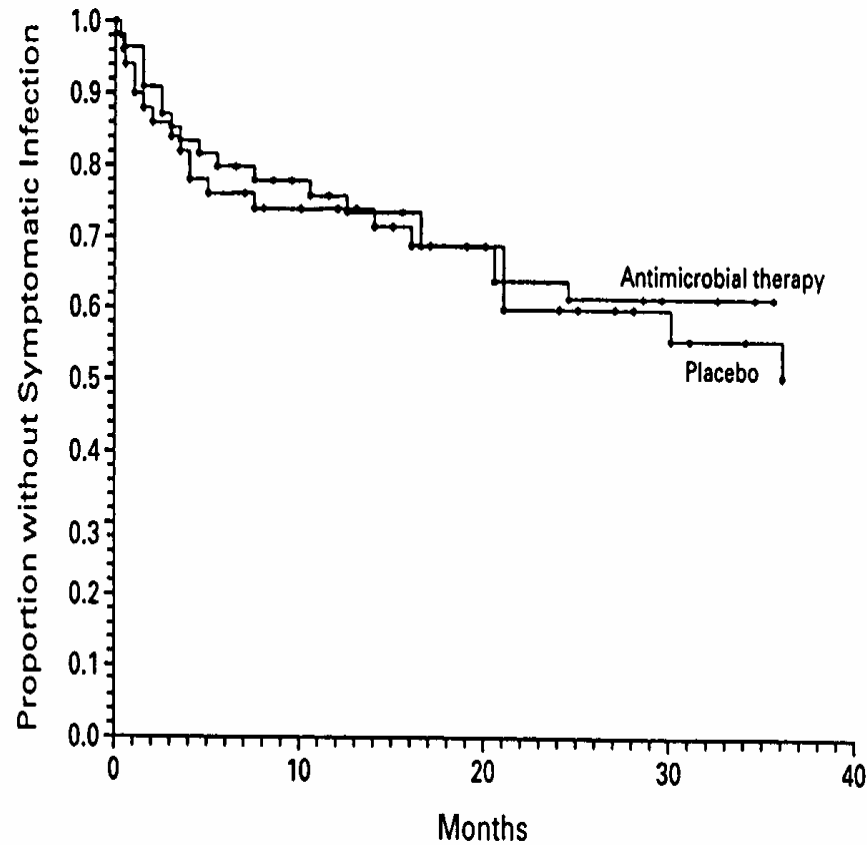
Duration of Therapy

	<u>Cure</u>	<u>Relapse</u>
Randomized 14 days	39/49 (80%)	4 (8.2%)
3 days	1/7 (14%)	6 (86%)
Treatment 3d: Asx	32/47 (68%)	13 (28%)
Sx	17/24 (71%)	7 (29%)

Treatment of ASB in Diabetic Women

Time to Symptomatic Infection

NEJM, 2002



Treatment of ASB in Diabetic Women Long Term Outcome

NEJM, 2000

Number (/1000 days)

	<u>Not</u> <u>treated</u>	<u>Treated</u>	<u>RR</u>	<u>p</u>
Symptomatic UTI	44(1.1)	43(0.93)	1.19(.28,1.81)	0.42
Cystitis	33(0.83)	37(0.80)	1.03(.65,1.65)	0.89
Pyelonephritis	11(0.28)	6(0.13)	2.13(.81,5.62)	0.13

Treatment of ASB in Diabetic Women Long Term Outcome

NEJM, 2000

	Episodes/1000 days (Number)		<u>RR</u>	<u>p</u>
	<u>Not treated</u>	<u>Treated</u>		
Other outcomes				
Asymptomatic UTI	0.53(23)	1.43(66)	0.37(.23,.59)	<0.001
Hospitalization UTI	0.10(5)	0.06(3)	1.93(.47,7.89)	0.36
Hospitalization other	0.38(15)	0.37(17)	1.02(.51,2.05)	0.95

Treatment of ASB in Diabetic Women Long Term Outcome

NEJM, 2000

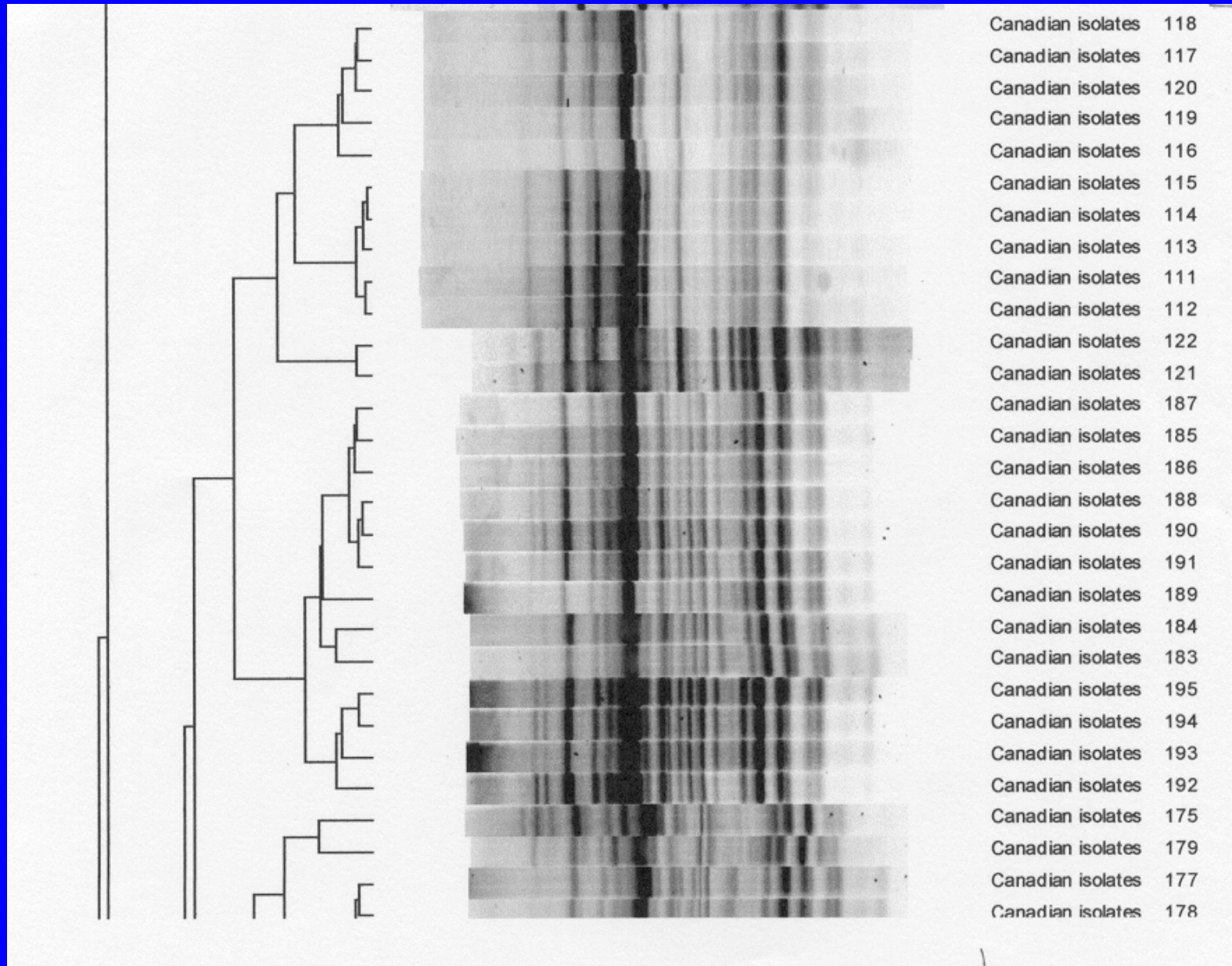
	<u>Antibiotic days/1000</u>		<u>RR</u>	<u>p</u>
	<u>Not treated</u>	<u>Treated</u>		
All UTI	33.7	158.2	0.21(.2,.22)	<0.001
Symptomatic UTI	10.9	8.26	1.31(1.14,1.51)	<0.001
Asymptomatic UTI	0	30.1	-	
Prophylactic/suppressive	22.9	119.9	0.19(.18,.20)	<0.001
Other infections	28.1	23.2	1.21(1.11,1.31)	<0.001

Natural History of Bacteriuria Diabetic Women

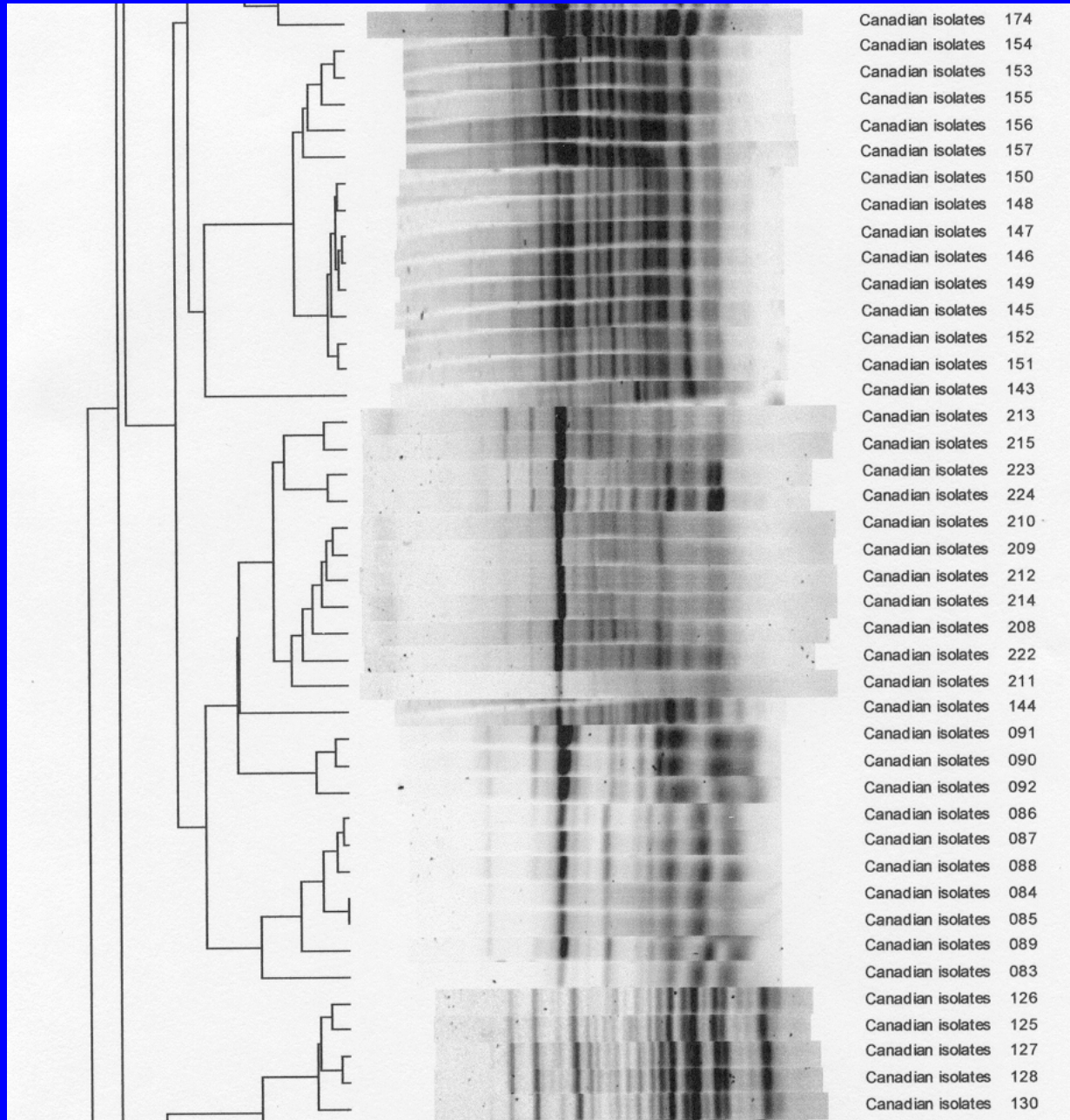
50 women

			<u>Mean time</u>	<u>Reinfected</u>
→	Symptomatic UTI	11 (22%)	2.9 mo	73%
→	Cleared, other antibiotics	15 (30%)	7.8 mo	47%
→	Resolved spontaneously	13 (26%)	3.3 mo	31%
→	Remained bacteriuric	11 (22%)	31.8 mo	

ABU in Diabetic Women: *E. coli* typing



ABU in Diabetic Women: E. coli typing



ABU in Diabetic Women

Symptomatic UTI

NEJM, 2002

	NT (N=50)	T (N=55)
None	30 (50%)	32 (58%)
One episode	6 (12%)	8 (15%)
>One episodes proportion	14 (28%) 86%	15 (27%) 82%

ABU in Diabetic Women

Symptomatic UTI

NEJM, 2002

Associations >1 episode:

No therapy: sexually active
neuropathy

Therapy: none

All subjects: previous UTI
glycosuria

ABU in Diabetic Women

End of Study

	<u>NT</u>	<u>T</u>
Hgb A1C	10.4±3% (30)	10.1±3% (37)
Serum creatinine	0.93±.35 (36)	1.03±.41 (43)
Urinary protein	0.98±1.32 (50)	0.8±1.24 (55)

Conclusions

Asymptomatic bacteriuria in women with diabetes

- not harmful
- no benefits with treatment
- no indication for screening