

# UTI in Postmenopausal Women

- UTI common among postmenopausal women
- Most earlier studies involved reproductive-age, sexually active women or elderly, institutionalized women. Risk factors:
  - Young women: sexual activity, spermicides, prior UTI
  - Elderly women: chronic illness, debility, dementia
- What factors influence susceptibility in relatively healthy postmenopausal women?

# Diabetes and UTI

- Diabetes well known risk factor for bacteriuria (and probably pyelonephritis)
- Role in symptomatic UTI?
- Relationship to glycemic control?
- Characteristics of infections in diabetics
- Relationship to other potential predisposing/protective factors
  - Sexual activity
  - Post-void residual
  - Hormone use

# Overview of Studies

- Sequential case-control & prospective cohort studies to ascertain the risk of UTI associated with diabetes and identify modifying factors.
- Both studies were population-based, enrolling women aged 55–75, who were members of Group Health Cooperative of Puget Sound (GHC), a staff-model HMO with >400,000 members

# Case-Control Study

- **Cases:** women who had acute cystitis in prior month
  - Lab files: cultures yielding  $\geq 10^5$  cfu of uropathogen
  - Medical records to confirm acute urinary symptoms
  - Exclusions: institutionalized, wheelchair dependent, dementia, catheter, ESRD, chronic antibiotics, active cancer
- **Controls:** randomly selected from enrollment files
  - Lab files, records reviewed to exclude recent UTI
  - Frequency matched to cases by age within 2 years
- **Exposures:** ascertainment by interview, exam
  - Self-report of diabetes confirmed using diabetes registry

Boyko, Fihn, Scholes, et al. Diabetes Care 2002;25:1778–1783.

Hu, Boyko, Scholes, et al. Arch Intern Med (in press).

# Other Exposures & Covariates

- **Interview**
  - Family history
  - Sexual activity
  - Habits/hygiene
  - Hormone use
  - Previous UTI
  - Continence
- **Laboratory files:** HbA1c (available for 89% diabetic pts)
- **Examination** (conducted >4-6 wks after acute UTI)
  - Performed on a subsample of volunteers
  - Urine culture
  - PVR (n=748)
  - Vag. culture (n=454)

# Prospective Cohort Study

- **Subjects:** Randomly selected women aged 55-75 with no UTI during the preceding 90 days.
  - Exclusions: same as case-control study
- **Outcomes:** UTI and asymptomatic bacteriuria (ASB)
- **Follow-up:** Baseline and 2 annual follow-up exams:
  - HbA1c                      – PVR                      – Urine culture
  - Ongoing surveillance for UTI included self-report confirmed by culture (dipslide) and medical record review.
  - Diaries: hormone use, incontinence
- **Other exposures & covariates:** similar to case-control study

# Results: Case-Control Study

## Characteristics of Patients

	<u>Case (n=901)</u>	<u>Control (n=913)</u>
Mean age	66.1 yrs	66.2 yrs
Married	64%	63%
Caucasian	93%	92%
>12 yrs education	58%	59%
Income <\$25K	37%	37%

# Results: Case-Control Study

## Overall Risk Factors

<u>Exposure</u>	<u>OR (95% CI)</u>	<u>p value</u>
Age	1.0 (1.0-1.0)	0.14
Past history of UTI	4.2 (3.3-5.4)	<0.001
Sexual Activity $\geq 1$ /wk	4.2 (3.3-5.4)	<0.001
Diabetes-oral/insulin Rx	2.8 (1.8-4.4)	<0.001
Incontinence >Monthly	1.4 (1.0-1.8)	0.03
Avg. oral estrogen >0.625/d	1.6 (1.0-2.6)	0.06



# Results: Case-Control Study

## Effect of Diabetes

- 13.1% of cases and 6.8% of controls were diabetic.
- Age-adjusted OR for UTI 2.2 (95% CI 1.6 –3.0)
  - little change after adjusting for sexual activity & past UTIs.
- OR for UTI higher in diabetic women using oral hypoglycemics (OR 2.9, 95% CI 1.7–5.1) or insulin (2.6, 1.5– 4.6) but not those treated with lifestyle changes (1.3, 0.7–2.3).

# Results: Case-Control Study

<u>Diabetic Exposure</u>	<u>Age-Adj. OR</u>	<u>Multivariate OR*</u>
Diabetes Present	2.2 (1.6-3.0)	2.2 (1.5-3.1)
Treatment		
None/lifestyle	1.3 (0.7–2.3)	1.4 (0.8–2.5)
Oral agents	2.9 (1.7–5.1)	2.8 (1.6–5.1)
Insulin	2.6 (1.5–4.6)	2.7 (1.4–4.9)
Duration		
<10yrs	1.9 (1.2–2.9)	2.0 (1.2–3.2)
≥10yrs	2.6 (1.6–4.3)	2.4 (1.5–4.0)
HBA1c		
≤8.0%	2.5 (1.4–4.5)	2.4 (1.3–4.5)
>8.0%	2.7 (1.6–4.7)	2.7 (1.5–4.9)

Adjusted for age, history of UTI and avg. frequency sexual intercourse past

# Results: Case-Control Study

## Organisms Isolated

<u>Uropathogen</u>	<u>All cases</u>	<u>Diabetic patients</u>
E. Coli	75%	83%
Enterococcus	5%	2%
Proteus spp.	4%	4%
Grp B strep.	4%	2%
Klebsiella spp.	7%	5%
Other organism	5%	4%

## Results: Case-Control Study

- No significant differences PVR between diabetic and nondiabetic women.
- Higher prevalence of *E. coli* colonization in women with insulin-treated diabetes (62%) vs. women without diabetes or with diabetes not treated with insulin (38%). Presence of diabetes unassociated with the presence of lactobacilli.

Pabich, Fihn, Stamm, et al. J Infect Dis 2003;188:1054-8.

# Characteristics of Cohort Study Participants

	<u>Diabetes Present (n=799)</u>	<u>Diabetes Absent (n=218)</u>
Age 55-64	54%	49%
Age 65-75	46%	51%
White	91%	77%
Other ethnicity	9.5%	23%
Married	63%	62%
No sexual activity past mon.	57%	68%
No Previous UTI	35%	31%

# Results – Prospective Cohort Study

- 218 diabetic and 799 non-diabetic women accrued 1773 person-yrs and experienced 138 acute UTIs (7/100 person-yrs). 81% completed full 2-yr F/U.
- Major predictors of UTI and ASB:
  - Lifetime history of UTI :  $\geq 6$  UTIs vs. 0 - RR 6.9 (3.5-13.6)
  - Diabetes

	<u>Incidence UTI</u>	<u>Incidence ASB</u>
Diabetes	12.2	6.7
No diabetes	6.7	3.0
Rel. Risk (95% CI)	1.8, 1.2-2.7	2.3, 1.3-3.9

# Control, Treatment & Duration of Diabetes\*

	UTI			ASB		
	N	Incid	RR	N	Incid	RR
HbA1c $\leq 7.5$	26	11.4	1.7 (1.1-2.7)	15	6.8	2.3 (1.3-3.9)
7.6 – 8.5	10	15.3	2.3 (1.1-4.4)	5	8.0	2.7 (0.8-6.9)
>8.5	7	14.3	2.1 (0.8-4.6)	2	4.1	1.4 (0.2-5.3)
No meds	5	4.3	0.7 (0.2-1.6)	7	6.3	2.1 (0.8-4.8)
Oral meds	17	10.1	1.5 (0.9-2.6)	10	6.1	2.1 (0.9-4.2)
Insulin	21	31.1	4.7 (2.8-7.5)	6	9.0	3.0 (1.1-7.2)
Dur. <10yr	19	7.9	1.2 (0.7-2.0)	13	5.6	1.9 (0.9-3.6)
$\geq 10$ yr	24	21.4	3.2 (2.0-5.1)	10	9.0	3.0 (1.4-6.2)

\*Referent to women without diabetes

# Cox Proportional Hazards Model

	Hazard Ratio for 1 <sup>st</sup> Episode ASB	Hazard Ratio for All UTI
Diab. present	2.1 (1.2-3.5)	1.4 (0.9-2.3)
HbA1c $\leq 7.5$	2.0 (1.0-3.6)	1.3 (0.7-2.3)
7.6 – 8.5	2.2 (0.8-6.1)	1.8 (0.9-3.3)
>8.5	2.7 (1.0-7.2)	1.9 (0.7-4.8)
No meds	1.8 (0.2-1.6)	0.5 (0.2-1.2)
Oral meds	2.1 (0.9-2.6)	1.3 (0.7-2.3)
Insulin	2.7 (2.8-7.5)	3.7 (1.8-7.3)
Dur. <10yr	1.8 (0.9-3.3)	0.9 (0.5-1.6)
$\geq 10$ yr	2.8 (1.4-5.7)	2.6 (1.3-5.1)

Adjusted for age, past UTI, sexual activity past yr, PVR, ASB at baseline and ethnicity.



# Not Significant (barely)

- Incontinence
- Sexual activity
- Estrogen use

# Limitations

- Limited to single HMO
- Definition of UTI  $\geq 10^5$ cfu/ml (missed low-count infxs.)
- Generally good glycemic control
- Case control study:
  - Possible recall bias
  - Cultures, PVR performed on subset of patients a mean of  $\sim 3$  months after “reference date”
- Cohort Study
  - Participation
  - Losses to follow-up

# Conclusions

- Among community-dwelling post-menopausal women, the presence of diabetes and a past history of UTI appear to the strongest risk factors for acute UTI and ASB.
- Longer duration and insulin treatment confer highest risk, probably reflecting the effects of severe disease.
- Recent glucose control not strongly associated with risk.
- The distribution of infecting organisms, alterations in vaginal flora, PVR are similar to those found in women without diabetes suggesting a similar mechanisms
  - ? Increased adherence
  - Other defects

# Collaborators

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