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Urologic Complications of Diabetes: UroEDIC Findings

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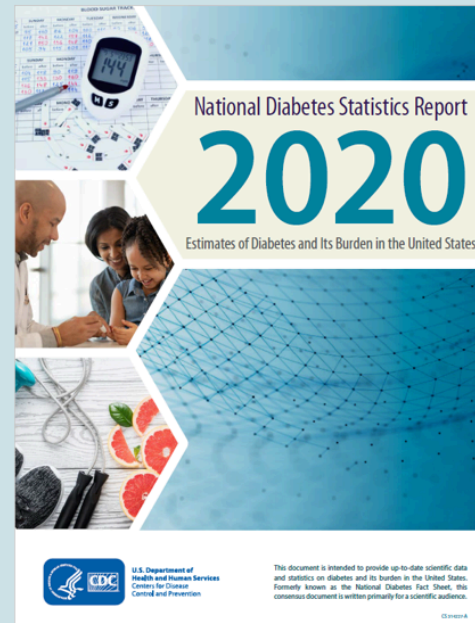


Diabetes Epidemic

Fast Facts on Diabetes

Diabetes

- **Total:** 34.2 million people have diabetes (10.5% of the US population)
- **Diagnosed:** 26.9 million people, including 26.8 million adults
- **Undiagnosed:** 7.3 million people (21.4% are undiagnosed)



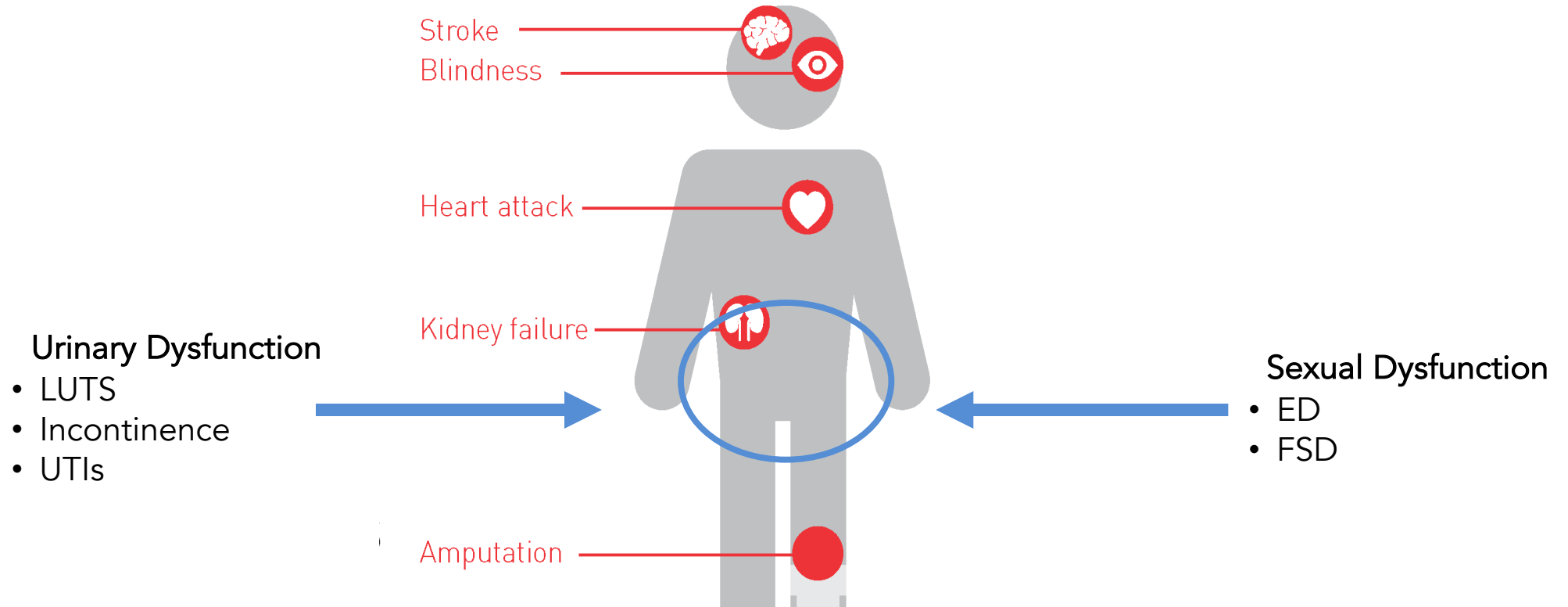
- 95% of diabetes cases in the US are associated with Type 2 diabetes (NIDDM)
- 5% associated with Type 1 DM (IDDM) – 85% living as adults



Diabetes and Urological Disorders

Consequences

Diabetes can lead to complications in many parts of the body and increase the risk of dying prematurely.





Objectives of UroEDIC

- Assemble a multidisciplinary team: urology, epidemiology, psychiatry, diabetes medicine, neuropathy, genetics
 - Determine burden of urological complications of diabetes
 - Develop risk factor models for specific urologic complications
 - Understand the impact of these conditions on quality of life
- 
- Provide information of importance to health care providers, patients and families about traditionally embarrassing health problems

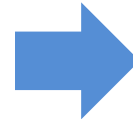


The Diabetes Control and Complications Trial (DCCT)

- multicenter, randomized clinical trial to compare *intensive* with *conventional* diabetes therapy on on early vascular and neurologic complications (1983-1993)

Epidemiology of Diabetes Interventions and Complications (EDIC)

- Observational study of the DCCT cohort to examine long term impact of initial randomization and subsequent glycemic control (1994-present)



DCCT Study Findings

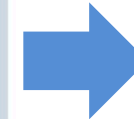
Intensive blood glucose control reduces risk of

- eye disease
76% reduced risk
- kidney disease
50% reduced risk
- nerve disease
60% reduced risk

EDIC Study Findings

Intensive blood glucose control reduces risk of

- any cardiovascular disease event
42% reduced risk
- nonfatal heart attack, stroke, or death from cardiovascular causes
57% reduced risk



UroEDIC

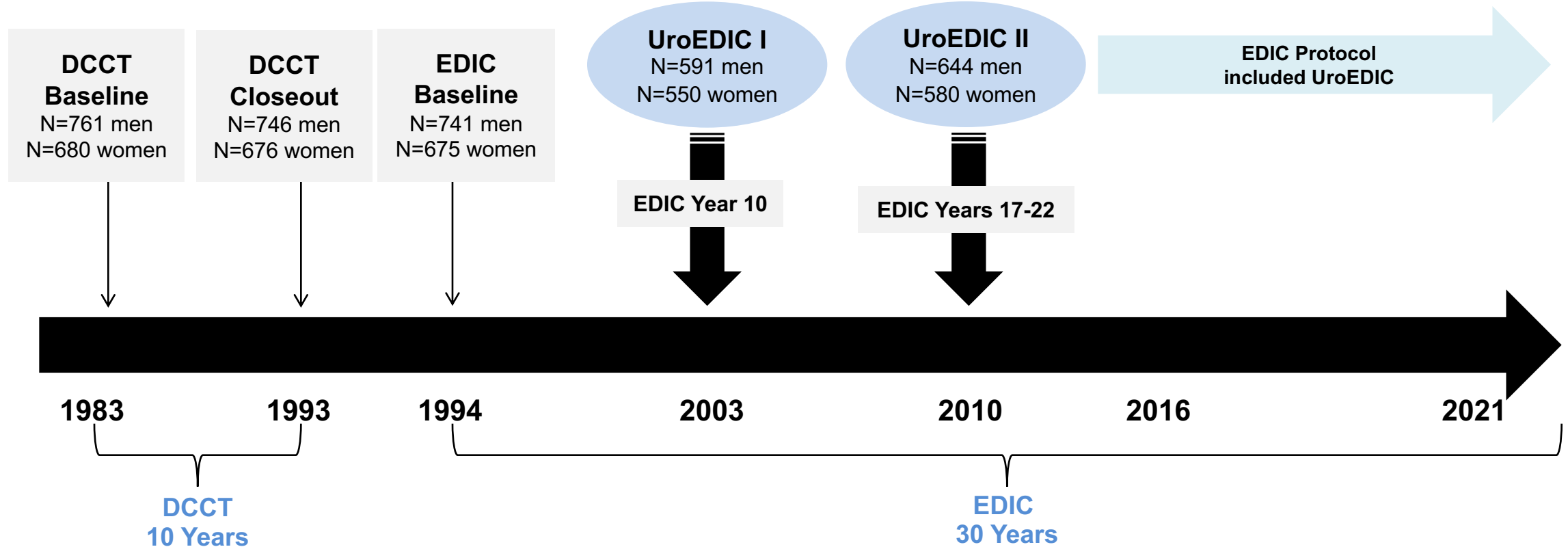
2003, 2010-current

Ancillary study to examine burden, onset and risk factors of urologic complications in T1 diabetes



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DCCT, EDIC, UroEDIC Timeline



UROEDIC I Baseline (EDIC Year 10)

- Understand the Burden of Urologic Complications in T1DM

UROEDIC II Follow-up (EDIC Years 17-current)

- Incidence, Progression, Risk factors
- Effects of hormonal status and prostate growth
- Quality of Life



Urological Disorders in UroEDIC

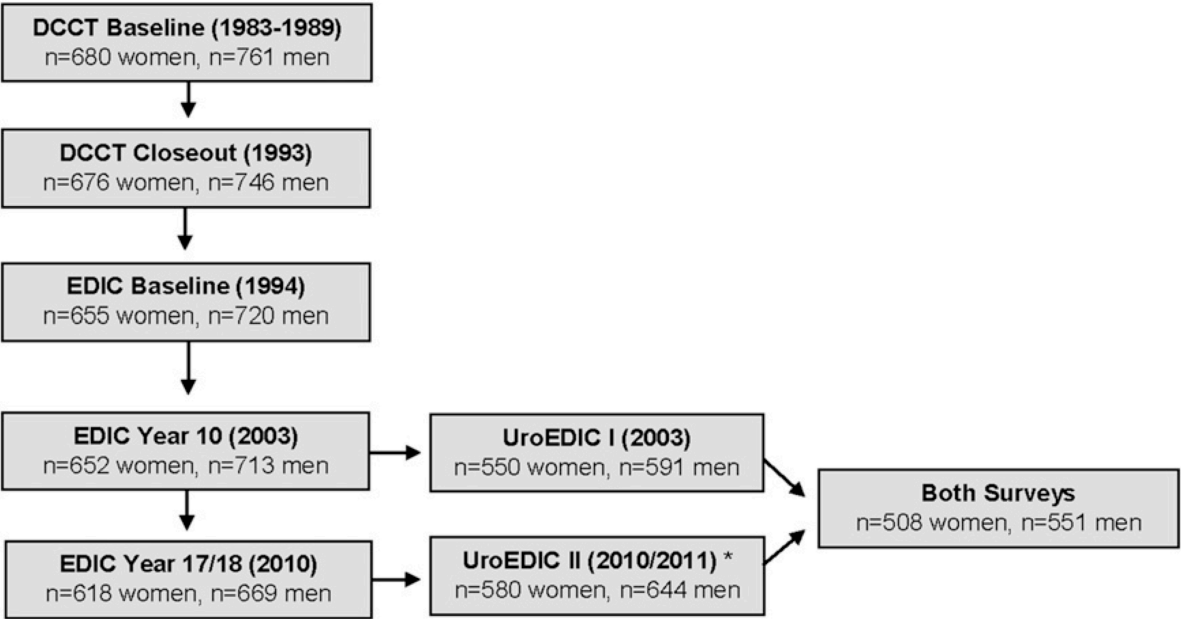


Figure 1—Study cohort diagram. Flow of participants through the study from DCCT to EDIC and UroEDIC I and II. There were a greater number of participants (1,224) in UroEDIC II compared with UroEDIC I (1,141). *Enrollees were asked to take part in UroEDIC II irrespective of participation in UroEDIC I. There was a net increase in participation from UroEDIC I to UroEDIC II.

	Respondents	Prevalence
	N (%)	%
Women	508	
LUTS	506 (99)	22
FSD	297 (58)	42
UI	493 (97)	31
Men	551	
LUTS	550 (99)	24
ED	525 (95)	45
Low desire	506 (92)	40



Glycemic control and Erectile Dysfunction

Table 1. Multivariable logistic regression model of the difference between DCCT intensive vs conventional glycemic therapy in the prevalence of ED

	OR (95% CI)	p Value (likelihood ratio chi-square test)
DCCT intervention (intensive vs conventional glycemic therapy)*		
Primary prevention cohort	1.24 (0.68, 2.28)	0.49
Secondary intervention cohort	0.33 (0.18, 0.60)	<0.001
HbA1c at eligibility (per HbA1c%)	1.36 (1.19, 1.56)	<0.001
Diabetes duration (per mo)	1.00 (0.99, 1.01)	0.87
Age (per yr)	1.13 (1.09, 1.17)	<0.001

- HbA1c at trial baseline associated with 36% increased odds of ED onset 20 years later
- Early glycemic control important for future risk of ED - *"Metabolic memory"*

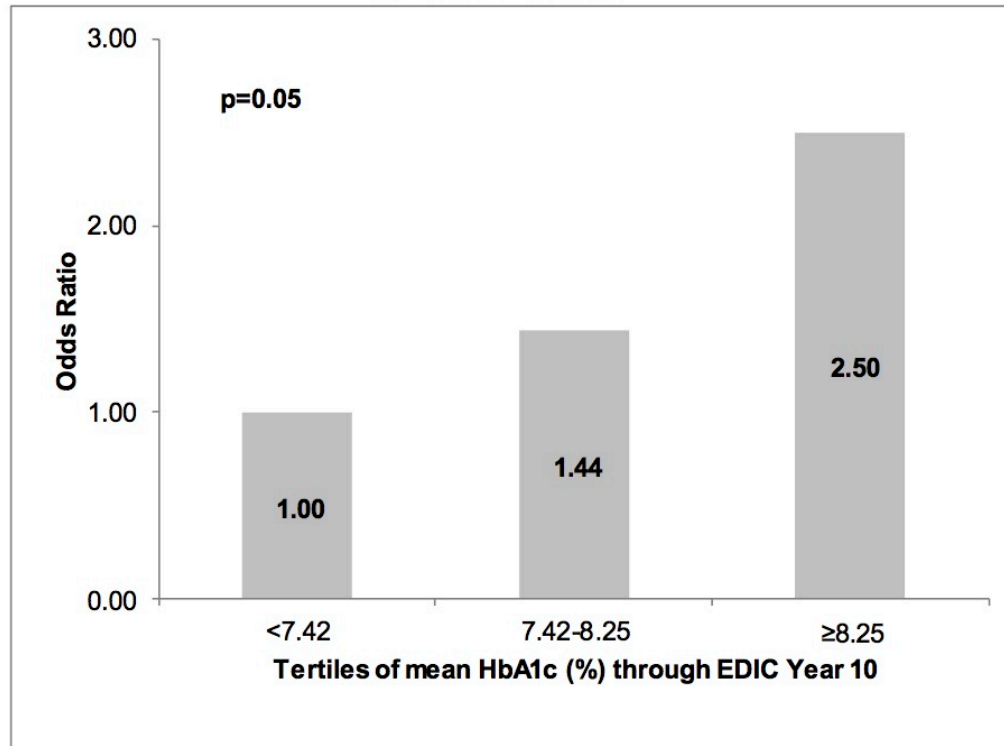


Glycemic control and Urinary Dysfunction

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Urinary Incontinence

Figure 2. Multivariable adjusted odds ratios* of incident weekly UI at EDIC year 17 by tertiles of HbA1c[†]



Note: p-value based on overall Wald chi square test for parameter estimate of HbA1c in multivariable logistic regression model.

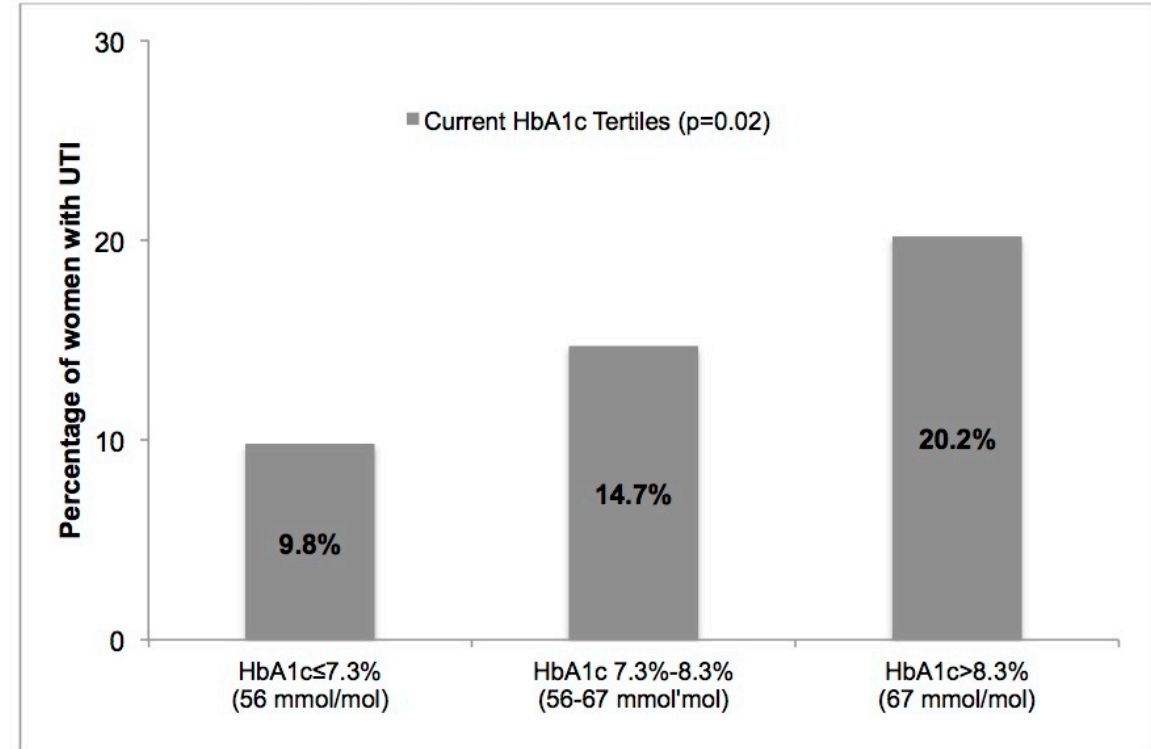
* Odds of incident weekly UI adjusted for attained age, DCCT cohort assignment, DCCT treatment group, EDIC mean daily insulin dose, BMI, parity, hysterectomy, autonomic neuropathy, and UTI during EDIC.

† EDIC mean HbA1c through Year 10 (HbA1c reference <7.42%).

41% increase in odds of UI per HbA1c% increase over the long term - *sustained glycemic control*

Urinary Tract Infections

Figure 2. Percentage of women with UTI* at EDIC Year 17 per tertile of current EDIC Year 16 HbA1c



Note: p-values based on Mantel-Haenszel chi square test

* UTI defined as ≥1 episode in past 12 months.

21% increase in UTI count per HbA1c% increase contemporaneously - *glucotoxic event*



Not all about glycemic control

Erectile Dysfunction

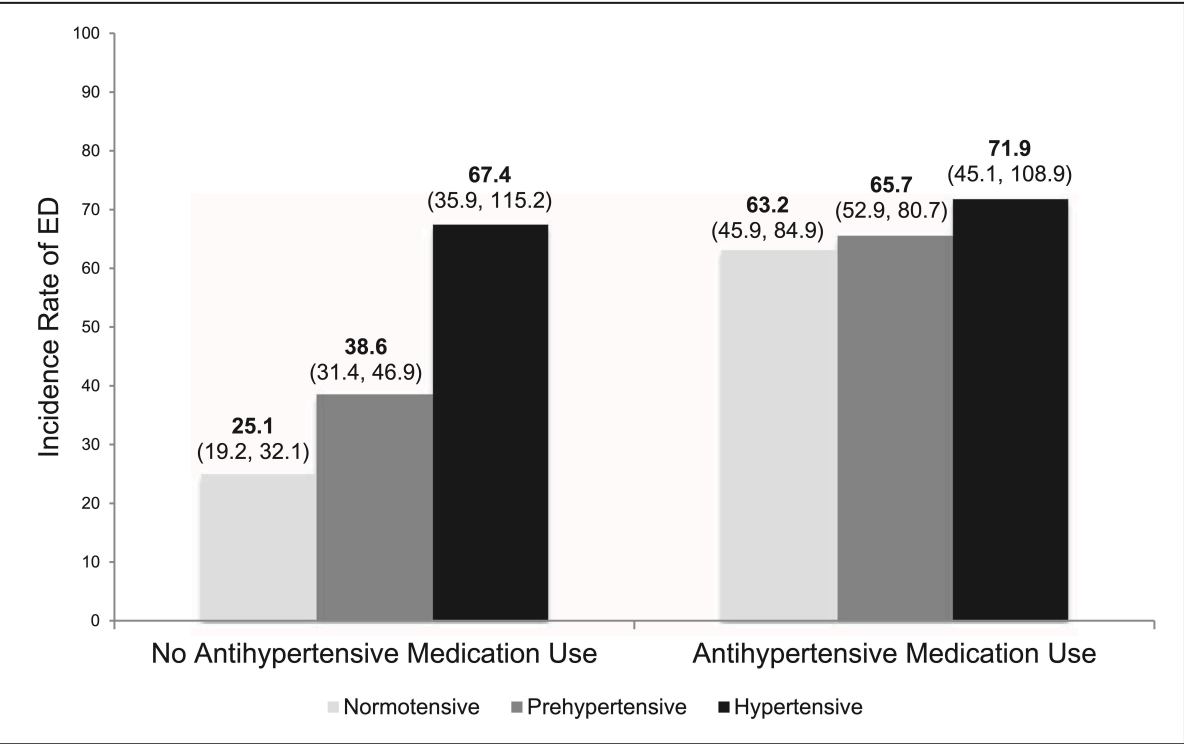


Table 3. Multivariable Adjusted Hazard Ratios (95%CI)* for Risk of ED by Preceding 3 Year Mean Systolic, Diastolic and Pulse Pressure

Characteristic	No Antihypertensive Use
Systolic Blood Pressure (per 10mmHg increase)	1.21 (1.04, 1.41)
Diastolic Blood Pressure (per 10mmHg increase)	1.25 (0.99, 1.59)
Pulse Pressure (SBP-DBP) (per 10mmHg increase)	1.17 (0.96, 1.42)

*Adjusted for time-dependent versions of Age, Cigarette Smoking and time-weighted HbA1c
Note: Separate Cox proportional hazards models built for each blood pressure variable

Note: Incidence rates of ED are per 1000-person years.



Autonomic neuropathy

Urinary Incontinence in Women

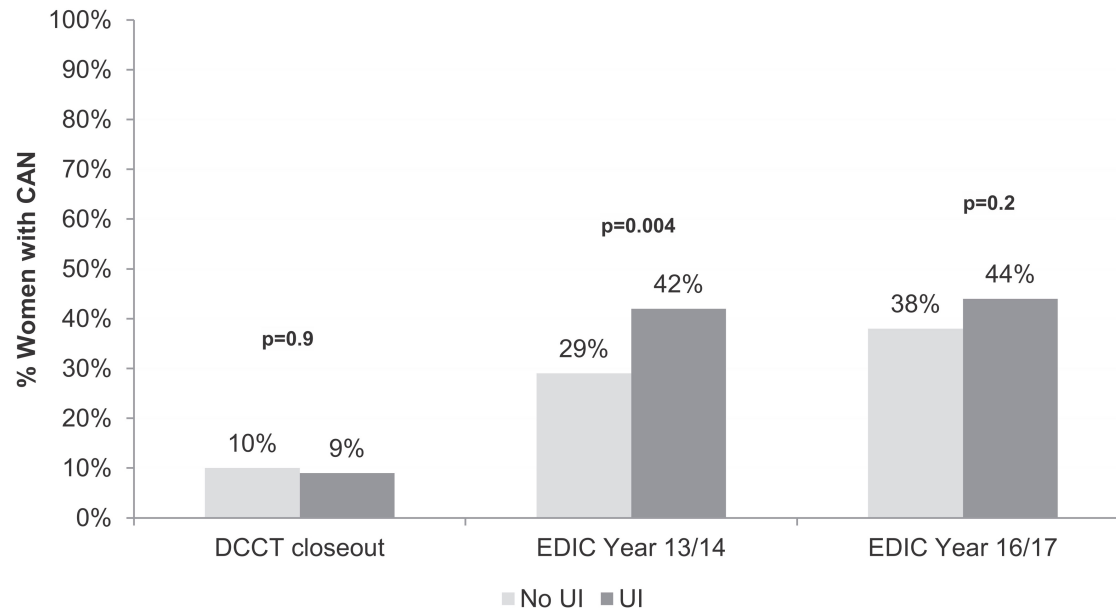


Figure 2—Prevalence of CAN among women with FSD and UI in DCCT/EDIC. CAN defined as an R-R variation <15 or R-R variation between 15 and 19.9 plus a Valsalva ratio ≤ 1.5 or a supine-to-standing drop of 10 mmHg in DBP (20).

Erectile Dysfunction / LUTS in Men

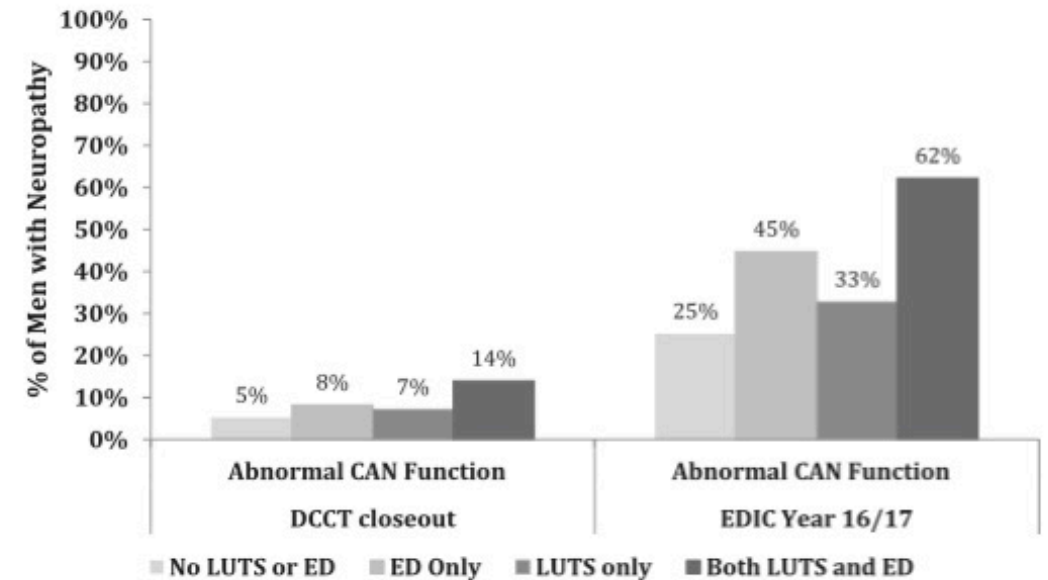
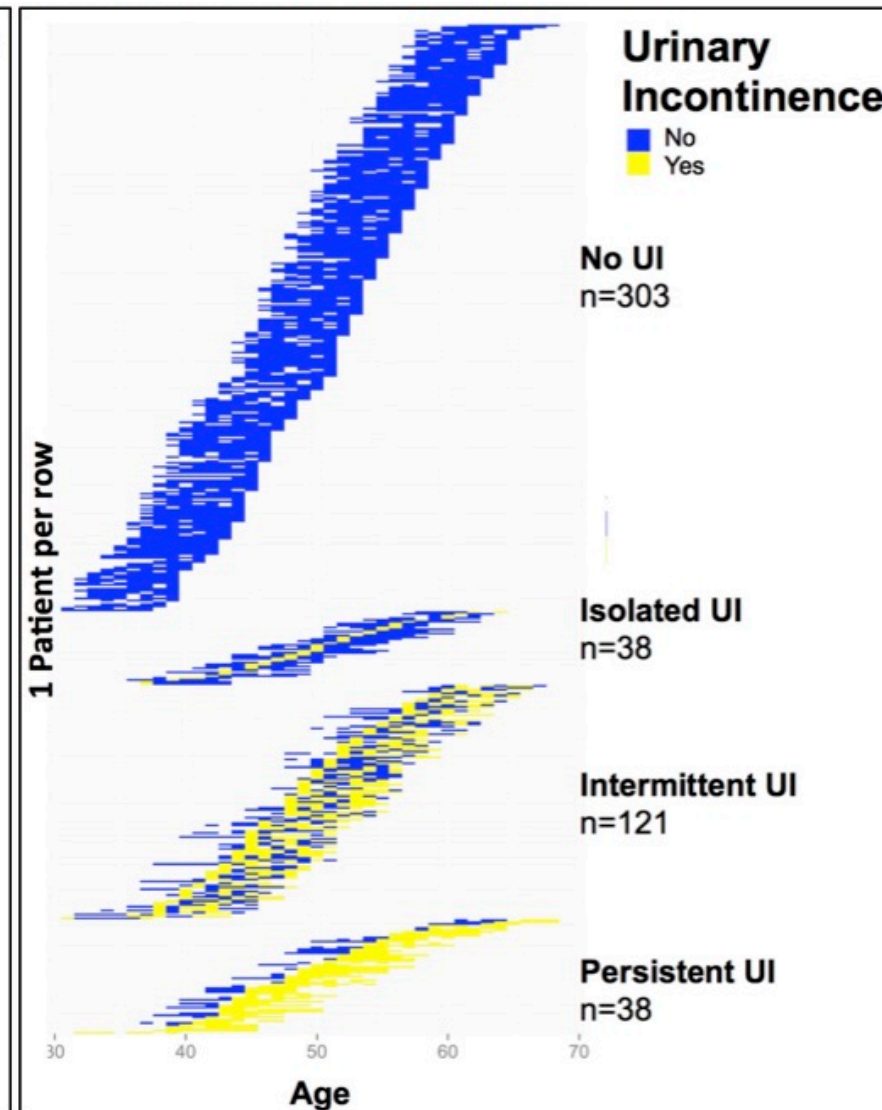
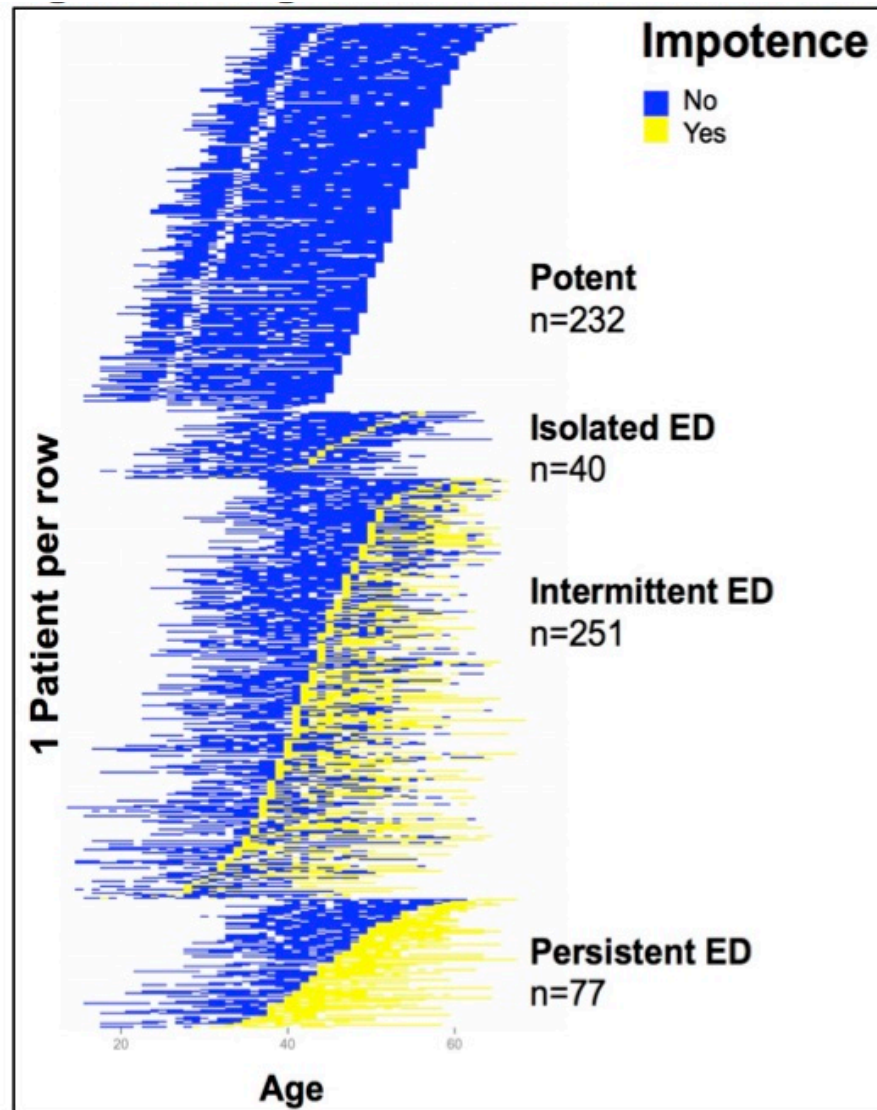


Figure 3. Prevalence of CAN at DCCT closeout and EDIC year 16/17 by ED and LUTS status at EDIC year 17.



Longitudinal ED and UI Phenotypes

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Intermittent Phenotype:

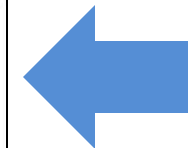
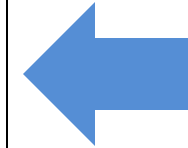
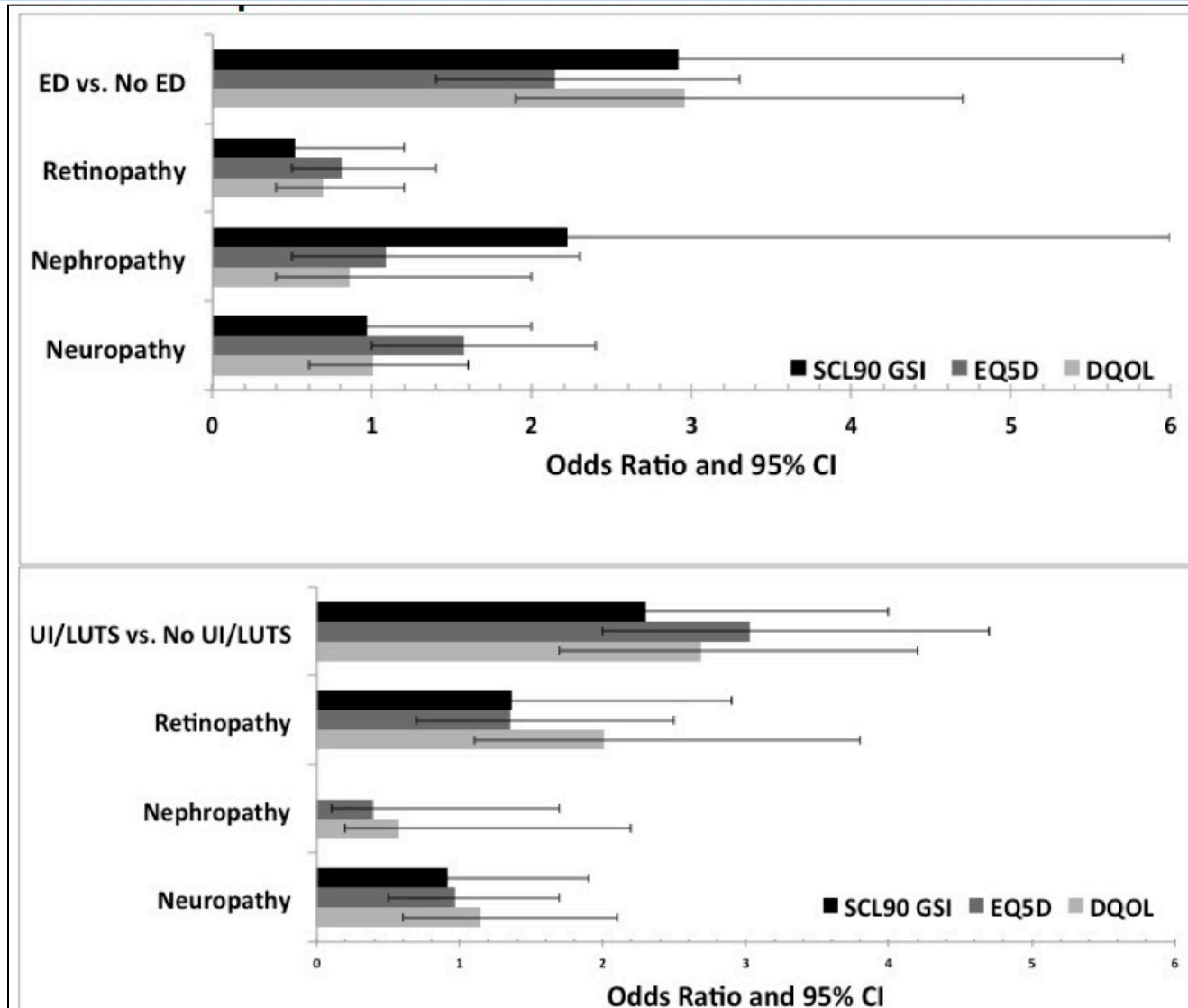
- Traditional Risk Factors (BMI, hysterectomy)
- HbA1c

Persistent Phenotype:

- Autonomic Dysfunction



Urologic Complications and Quality of Life



- Odds of poor QOL defined by lowest quartile of QOL scores
- Effect of ED/UI on poor QOL higher than those observed for other complications
- Participants significantly impacted by urologic disorders



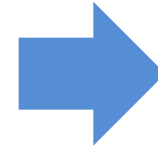
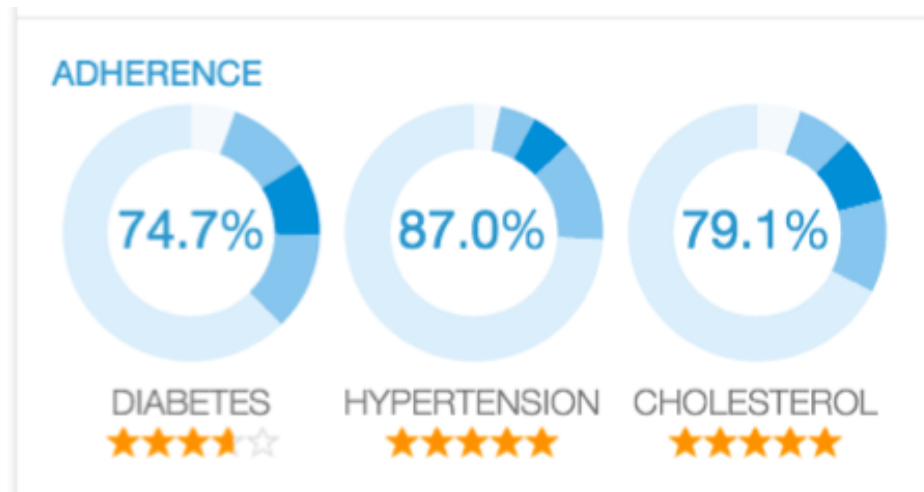
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Impact

Medication Adherence

Scope of the Problem

For every 100 prescriptions written...



Fringe Benefit of Weight Loss Surgery: Bye, Bye Incontinence?

Written by [Kathleen Doherty](#)



Bariatric surgery often produces a welcome fringe benefit for women affected by urinary incontinence (UI). As weight declines, women notice an improvement of the symptoms, or are even cured, according to new research.

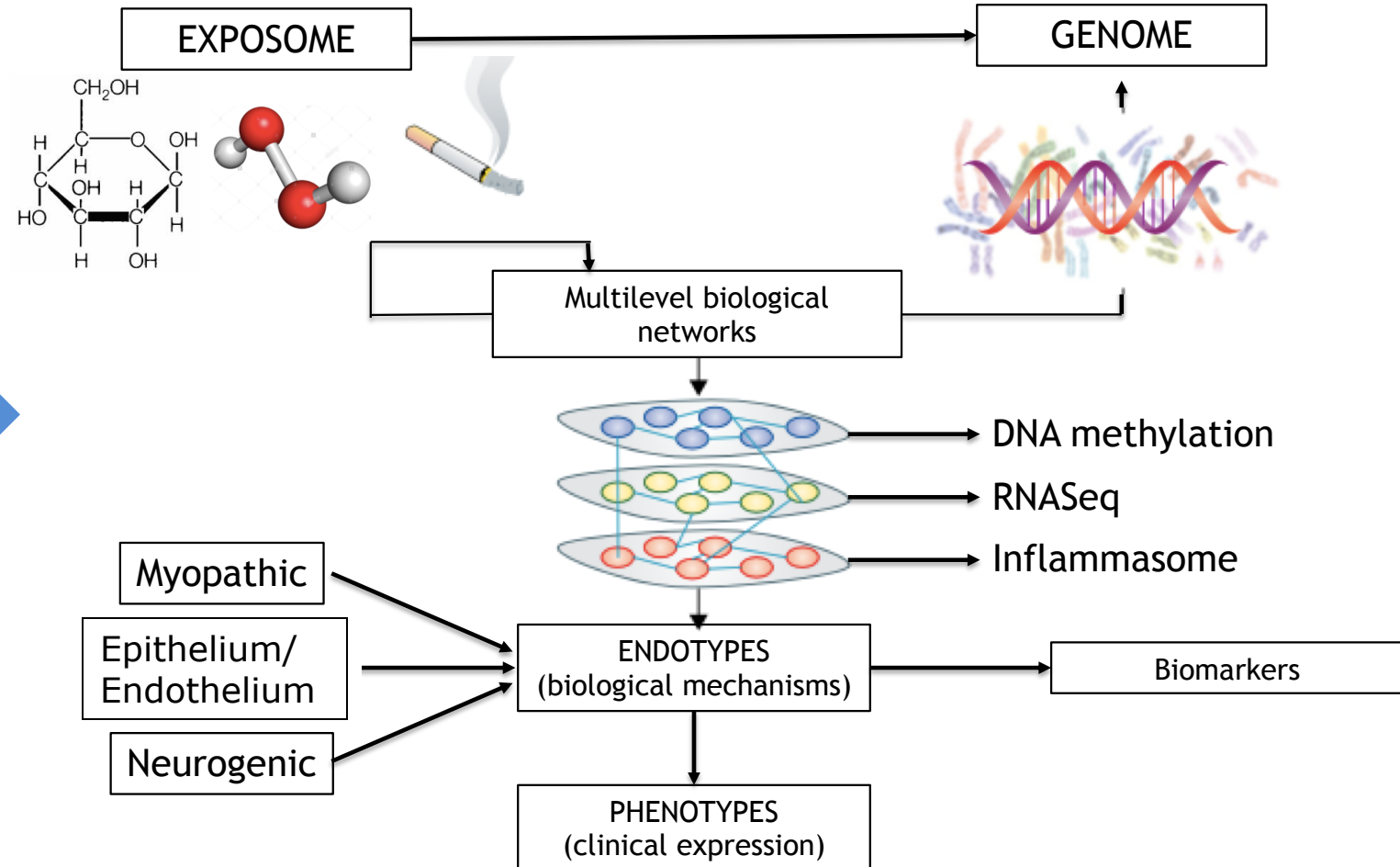
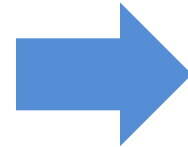




Systems Biology Approach

Can we do a better job of identifying high risk individuals and can we prevent/treat them?

- Comprehensive study of natural history
- Validate subphenotypes
- Understand mechanisms





Acknowledgements



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- NIDDK R01 DK55017
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UroEDIC I Team

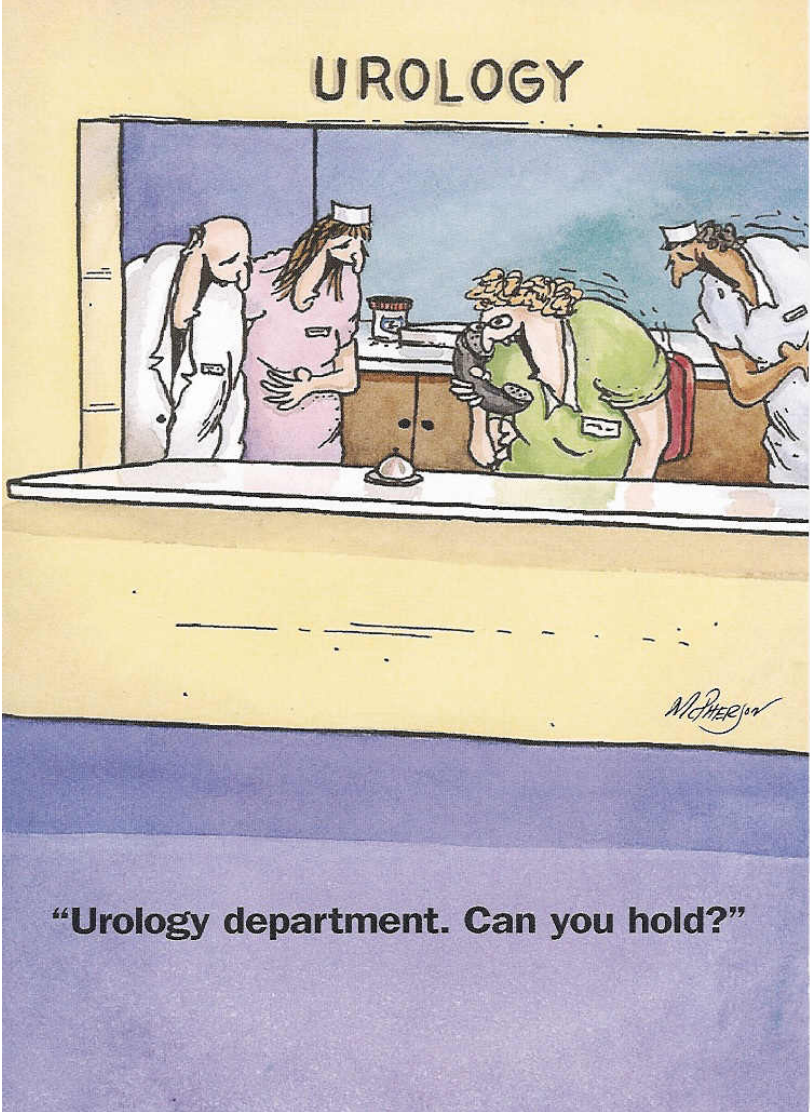
- Jeanette Brown
- Patricia Cleary
- Leroy Nyberg

UroEDIC II Team

- Hunter Wessells (CoPI)
- William Herman
- Rodica Pop-Busui
- Barbara Braffett
- James Hotaling
- Patty Gatcomb
- Cathy Martin
- Andrew Paterson
- Mike Steffes
- Catherine Kowie
- John Kusek/Ziya Kirkali



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“Urology department. Can you hold?”