Lifestyle Intervention Is Associated With Lower Prevalence of Urinary Incontinence

The Diabetes Prevention Program

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OBJECTIVE — Diabetes is associated with increased urinary incontinence risk. Weight loss improves incontinence, but exercise may worsen this condition. We examined whether an intensive lifestyle intervention or metformin therapy among overweight pre-diabetic women was associated with a lower prevalence of incontinence.

RESEARCH DESIGN AND METHODS — We analyzed data from the Diabetes Prevention Program, a randomized controlled trial in 27 U.S. centers. Of the 1,957 women included in this analysis, 660 (34%) were randomized to intensive lifestyle therapy, 636 (32%) to metformin, and 661 (34%) to placebo with standard lifestyle advice. The main outcome measure was incontinence symptoms by frequency and type by a validated questionnaire completed at the end-of-trial visit (mean 2.9 years).

RESULTS — The prevalence of total (stress or urge) weekly incontinence was lower among women in the intensive lifestyle group (38.3%) than those randomized to metformin (48.1%) or placebo (45.7%). This difference was most apparent among women with stress incontinence (31.3% for intensive lifestyle group vs. 39.7% for metformin vs. 36.7% for placebo, $P = 0.006$). Changes in weight accounted for most of the protective effect of the intensive lifestyle intervention on stress incontinence.

CONCLUSIONS — Less-frequent urinary incontinence may be a powerful motivator for women to choose lifestyle modification to prevent diabetes.

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Type 2 diabetes and urinary incontinence are chronic, common, and costly disorders. While ~18 million adults in the U.S. have diabetes, estimates of adults with pre-diabetes, defined as impaired glucose tolerance and/or impaired fasting glucose (1,2), range from 17 to 43 million. Recently, large randomized controlled trials have shown that diabetes can be prevented by intensive lifestyle intervention in this high-risk pre-diabetic group (3,4)

Urinary incontinence, present in nearly 50% of middle-aged and older women, results in psychological stress and social isolation and has a profound effect on quality of life (5,6). The costs of incontinence are substantial, accounting for up to $32 billion per year in the U.S., greater than the annual direct costs for breast, ovarian, cervical, and uterine cancers combined (7,8).

Type 2 diabetes is associated with a 50–70% increased risk of incontinence in women (5,9,10). There have been no studies to determine whether nondiabetic women with abnormal glucose levels (pre-diabetes) are at increased risk for incontinence. Weight reduction and increased physical activity in individuals with pre-diabetes decreases the risk of type 2 diabetes (3,4). Weight reduction in obese women with incontinence has been shown to significantly decrease incontinence in small prospective studies (11–13). However, some studies have reported that increased physical activity worsens incontinence and that incontinence may be a barrier to exercise (14,15).

We therefore examined data from 1,987 overweight women at high risk for diabetes who were enrolled in the Diabetes Prevention Program (DPP) to determine whether an intensive lifestyle intervention with improved diet and increased physical activity or metformin therapy would be associated with lower prevalence of urinary incontinence compared with a standard lifestyle intervention alone.

RESEARCH DESIGN AND METHODS

— The design, methods, baseline characteristics (16), and main findings (3) of the DPP have been published previously. Briefly, the DPP was a randomized controlled trial conducted at 27 clinical centers in the U.S. to evaluate whether intensive lifestyle intervention or treatment with metformin would prevent or delay the onset of type 2 diabetes. Eligibility criteria at baseline included age at least 25 years, BMI $\geq$24 kg/m^2, a fasting plasma glucose level 95–125 mg/dl, and a 2-h postchallenge glucose level 140–199 mg/dl. People who were taking medications that could affect glucose tolerance or who had serious medical illness were excluded. By design, approximately half of the participants were from racial/ethnic minority groups. The three interventions included an intensive lifestyle intervention, metformin at 850 mg twice daily, or placebo twice daily. All participants received standard lifestyle recommendations, including written information and an individual meeting that emphasized a

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Abbreviations: DPP, Diabetes Prevention Program.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

healthy diet, reduced weight, increased activity levels, and smoking cessation, at baseline and annually. The goals of the intensive lifestyle intervention were to lose and maintain at least 7% of initial body weight through a low-fat diet and to engage in moderate-intensity physical activity for at least 150 min each week. Details of the behavioral and educational curriculum have been published previously (17). The DPP was closed early after 2.9 years when lifestyle changes and metformin treatment had each reduced the incidence of diabetes (3).

Data collection

At the baseline examination, all participants completed a questionnaire reporting sex, age, self-identified race/ethnicity, smoking history (current, past, or never), and alcohol use (drinks per week). They answered questions regarding other physician-diagnosed medical conditions, self-rated overall health status, parity, menopausal status, hormone therapy use, and hysterectomy. All participants brought in medications they were currently using and a complete medication inventory was ascertained.

Body weight, height, waist circumference, and systolic and diastolic blood pressure were measured at designated clinical visits during the trial. Weight was measured in kilograms using a standard balance beam scale, height was measured in centimeters using the height rod attached to the standard balance beam scale or a stadiometer, and BMI (weight in kilograms divided the square of height in meters) was calculated. Waist circumference was measured using a flexible tape measure at the minimum circumference between the iliac crests and lower ribs. Physical activity was assessed at baseline and annually with the Modifiable Activity Questionnaire (18) and was calculated as the product of the duration and frequency of each activity, weighted by an estimate of the metabolic equivalent of that activity and summed for all activities, resulting in estimated average metabolic equivalent (MET) hours per week. Incident diabetes, the primary DPP outcome, was diagnosed by annual oral glucose tolerance test or a semiannual fasting plasma glucose test according to the 1997 American Diabetes Association criteria (19).

Outcome ascertainment

Urinary incontinence was determined at the end-of-trial visit using a self-administered questionnaire modified from validated questions used in previous studies (20–22). Frequency of incontinence was assessed by the question, "In the past 12 months, how often have you leaked even a small amount of urine?" (none, less than monthly, monthly, weekly, or daily). For participants with weekly or more frequent incontinence, type of incontinence was assessed by asking the question, "In the past 7 days, how many times, on average, did you leak urine. . ." ". . . during activities like coughing, sneezing, straining, laughing, or lifting?" (stress incontinence), ". . . after an urge to urinate but could not get to the bathroom fast enough?" (urge incontinence), and ". . . for other reasons (without an urge to urinate or without an activity)?" (other incontinence). Responses were recorded as times per week. The primary outcome of interest was incontinence that occurred at least weekly because it is clinically relevant.

Because urinary incontinence is a disorder primarily affecting women, we excluded all men from this analysis. Of the 2,191 women enrolled in the three arms of the DPP, we excluded 234 (11%) women with missing urinary incontinence data, leaving a total of 1,957 women for this analysis. Women missing data on urinary incontinence did not differ in incident diabetes, mean weight change, or mean change in physical activity overall or within treatment groups compared with women with completed urinary incontinence data.

Statistical analysis

Women in the three treatment groups who contributed information on incontinence were compared in terms of baseline variables using χ^2 tests, ANOVA, and Kruskal-Wallis, as appropriate. Prevalence of incontinence, both overall and by type, was compared across these three groups at the end of the trial using χ^2 tests for heterogeneity; since the overall test was statistically significant, pairwise comparisons of the lifestyle and metformin arms with placebo were conducted without adjustment of the significance level. Differences in the effects of the lifestyle intervention on incontinence across subgroups defined by baseline variables were assessed using logistic models. In these models, effects of the intensive lifestyle intervention were compared across subgroups using appropriate linear contrasts in the estimated log odds ratios (ORs) for the lifestyle versus placebo comparison; for ordinal subgroup variables including age, BMI, waist circumference, and leisure time activity, we examined trends in this parameter, while for race/ethnicity, we assessed heterogeneity across groups. The mediation of the effects of the lifestyle intervention on prevalence of weekly stress incontinence was examined using nested logistic models in which proposed mediators were added in a predetermined sequence to the basic unadjusted model comparing the lifestyle intervention to placebo. Mediation was then informally assessed by the degree of attenuation of the odds ratios for the intensive lifestyle/placebo comparison.

RESULTS — Equal proportions of the 1,957 women were randomized to each intervention group. Women were on average 50 years of age (±10 years, range 26–84), with a BMI of 35 kg/m^2 and a waist circumference of 104 cm (Table 1). The treatment groups were balanced with regard to all demographic, ethnic, behavioral, body composition, reproductive, and metabolic characteristics. The only baseline variables that differed significantly by treatment assignment were prevalence of hormone therapy and self-rated general health status. More women in the metformin intervention were using hormone therapy than those in the intensive lifestyle intervention or placebo groups ($P = 0.01$), and a higher proportion of women assigned to intensive lifestyle therapy reported excellent or very good general health than those in the other two groups ($P = 0.02$).

The average change in weight for women in the intensive lifestyle group was −3.4 ± 8.2 kg vs. −1.5 ± 7.6 kg in the metformin group vs. +0.5 ± 6.7 kg in the placebo group ($P < 0.001$). The average change in leisure-time physical activity was highest in the intensive lifestyle group (5.2 ± 19.9 MET h/week vs. 0.8 ± 18.0 in the metformin group and −0.3 ± 20.7 in the placebo group, $P < 0.001$). Women in the intensive lifestyle group had the lowest incidence of diabetes over the mean 2.9 years of follow-up (14.9% vs. 23.9% in the metformin group and 30.9% in the placebo group, $P < 0.001$ comparing three groups).

At the end-of-trial visit, the overall prevalence of weekly incontinence differed significantly by treatment. Fewer women in the intensive lifestyle intervention had weekly incontinence compared with women in the metformin or placebo groups (38.3% vs. 48.1% vs. 45.7%, respectively, $P = 0.001$). After adjusting for

Table 1—*Baseline characteristics of women in the DPP by treatment group*

	Overall	Lifestyle	Metformin	Placebo	*P**
n	1,957	660	636	661	
Age (years)	49.6 ± 10.0	49.3 ± 10.6	49.9 ± 9.6	49.5 ± 9.7	0.51
Race/ethnicity					0.71
White	1,031 (52.7)	343 (52.0)	333 (52.4)	355 (53.7)	
African American	430 (22.0)	138 (20.9)	148 (23.3)	144 (21.8)	
Hispanic	294 (15.0)	103 (15.6)	97 (15.3)	94 (14.2)	
Native American	147 (7.5)	51 (7.7)	45 (7.1)	51 (7.7)	
Asian	55 (2.8)	25 (3.8)	13 (2.0)	17 (2.6)	
Weekly alcohol use	319 (16.3)	105 (15.9)	97 (15.3)	117 (17.7)	0.46
Current smoking	126 (6.4)	36 (5.5)	38 (6.0)	52 (7.9)	0.17
General health (%)					
Excellent/very good	1,039 (53.1)	385 (58.3)	324 (50.9)	330 (49.9)	0.02
Good	744 (38.0)	227 (34.4)	251 (39.5)	266 (40.2)	
Fair/poor	174 (8.9)	48 (7.3)	61 (9.6)	65 (9.8)	
Weight (kg)	92.0 ± 20.3	91.8 ± 20.5	92.0 ± 19.9	92.2 ± 20.5	0.92
BMI (kg/m^{2-})	34.9 ± 6.9	34.7 ± 6.9	34.8 ± 6.9	35.1 ± 7.0	0.66
Waist circumference (cm)	103.6 ± 14.8	103.5 ± 15.0	103.2 ± 14.9	103.9 ± 14.6	0.68
Number of live births (%)					0.97
None	89 (5.3)	30 (5.4)	28 (5.2)	31 (5.4)	
One	292 (17.5)	100 (18.0)	95 (17.5)	97 (17.0)	
Two	588 (35.3)	188 (33.8)	190 (35.1)	210 (36.9)	
Three or more	698 (41.9)	238 (42.8)	229 (42.3)	231 (40.6)	
Hysterectomy	493 (25.2)	164 (24.8)	165 (25.9)	164 (24.8)	0.87
Menopause	990 (50.6)	336 (50.9)	309 (48.9)	345 (52.2)	0.78
Current hormone therapy use	489 (25.0)	168 (25.5)	180 (28.3)	141 (21.3)	0.01
Years of estrogen use	5.9 ± 7.0	6.3 ± 6.9	6.2 ± 7.8	5.2 ± 6.2	0.18
Fasting glucose (mg/dl)	105.5 ± 8.1	105.1 ± 7.8	105.7 ± 8.3	105.6 ± 8.2	0.35
2-h postchallenge glucose (mg/dl)	164.8 ± 17.2	164.1 ± 16.9	166.1 ± 17.6	164.3 ± 17.2	0.07
HbA_{1c} (%)	5.9 ± 0.5	5.9 ± 0.5	5.9 ± 0.5	5.9 ± 0.5	0.52
Fasting insulin (μU/ml)	26.5 ± 14.2	26.6 ± 14.5	26.9 ± 14.2	26.1 ± 13.9	0.59

Data are means ± SD or *n* (%). **P* value by χ^2 tests, ANOVA, and Kruskal-Wallis tests, as appropriate.

baseline hormone therapy use, general health status, and 2-h postchallenge glucose categories, women randomized to intensive lifestyle therapy had significantly lower odds of weekly urinary incontinence compared with women assigned to placebo (OR 0.76 [95% CI 0.61–0.95]). The prevalence of weekly incontinence by type (stress or urge) by treatment group is shown in Table 2. While estimates were similar for urge incontinence in each of the three groups, weekly stress incontinence was significantly lower in women assigned to intensive lifestyle therapy compared with the other two groups ($P = 0.006$). The apparent beneficial effect of lifestyle intervention on weekly stress incontinence did not differ by age categories, race/ethnicity, BMI, waist circumference, or physical activity at baseline (Table 3). Metformin therapy had no effect on the prevalence or odds of total weekly urinary incontinence (1.09[0.87–1.36]) or on the odds of weekly stress incontinence (1.13 [0.90–1.42]) or weekly urge incontinence (1.15 [0.90–1.48]).

Intensive lifestyle intervention was associated with a 20% reduction in the odds (OR 0.80 [95% CI 0.64–1.01]) of weekly stress incontinence compared with placebo after adjusting for baseline covariates. We performed sequential models adjusting for possible mediators of this association. In combination, incident diabetes, percent changes in physical activity, and weight explained 35% of the treatment effect (Fig. 1). Percent change in weight accounted for almost all of the treatment effect explained, with change in exercise and incident diabetes each explaining ~5%. Similar results were obtained when absolute change or end-of-study values rather than percent change in the mediators were added to the models.

CONCLUSIONS — After ~3 years, overweight women at risk for diabetes who were assigned to intensive lifestyle

Table 2—*Prevalence of weekly urinary incontinence by type at the end-of-trial visit*

	Placebo	Intensive lifestyle intervention	*P**	Metformin	*P**	*P*†
n	660	659		635		
Stress UI	242 (36.7)	206 (31.3)	0.04	252 (39.7)	0.26	0.006
Urge UI	169 (25.6)	156 (23.7)	0.41	182 (28.7)	0.22	0.12

Data are *n* (%). **P* for comparison between intensive lifestyle intervention and placebo and between metformin therapy and placebo. †*P* for overall comparison. UI, urinary incontinence.

Table 3—*Effects of intensive lifestyle intervention versus standard lifestyle on weekly stress incontinence by baseline covariates*

	Total	Intensive lifestyle group	Placebo group	OR (95% CI)	*P* for treatment	*P* for interaction*
Age (years)						
25–44	441 (33.4)	67 (28.4)	77 (37.7)	0.65 (0.44–0.98)	0.04	0.23
45–59	671 (50.8)	104 (33.7)	136 (37.7)	0.84 (0.61–1.15)	0.28	
≥60	209 (15.8)	35 (30.7)	29 (30.5)	1.00 (0.56–1.82)	0.98	
Race/ethnicity						
Caucasian	698 (52.8)	114 (33.2)	146 (41.2)	0.71 (0.52–0.97)	0.03	0.66
African American	282 (21.3)	33 (24.1)	40 (27.8)	0.82 (0.48–1.41)	0.48	
Hispanic	197 (14.9)	33 (32.0)	29 (30.9)	1.05 (0.58–1.93)	0.86	
Native American	102 (7.7)	20 (39.2)	20 (39.2)	1.00 (0.45–2.21)	1.00	
Asian	42 (3.2)	6 (24.0)	7 (41.2)	0.45 (0.12–1.71)	0.24	
BMI (kg/m^2)						
22 to <25	36 (2.7)	4 (20.0)	4 (25.0)	0.75 (0.15–3.62)	0.72	0.25
25 to <30	323 (24.5)	41 (25.5)	56 (34.6)	0.65 (0.40–1.04)	0.07	
30 to <35	386 (29.2)	55 (27.2)	69 (37.7)	0.62 (0.40–0.95)	0.03	
35 to <40	299 (22.6)	54 (37.0)	59 (38.8)	0.92 (0.58–1.48)	0.74	
≥40	277 (21.0)	52 (40.0)	54 (36.7)	1.15 (0.71–1.86)	0.58	
Waist circumference (cm)						
<80	28 (2.1)	5 (31.3)	5 (41.7)	0.64 (0.13–3.03)	0.57	0.79
80 to <88	160 (12.1)	19 (25.3)	27 (31.8)	0.73 (0.36–1.46)	0.37	
≥88	1131 (85.7)	181 (31.9)	209 (37.2)	0.79 (0.62–1.01)	0.06	
Leisure-time activity (MET)						
<3.12	348 (26.4)	59 (35.3)	57 (31.8)	1.17 (0.75–1.83)	0.49	0.24
3.12 to <8.08	327 (24.8)	51 (30.0)	65 (41.4)	0.61 (0.38–0.96)	0.03	
8.08 to <16.88	320 (24.2)	50 (29.2)	54 (36.2)	0.73 (0.45–1.16)	0.18	
≥16.88	325 (24.6)	46 (30.7)	66 (37.7)	0.73 (0.46–1.16)	0.18	
Fasting glucose (mg/dl)						
95–109	939 (73.2)	142 (30.0)	178 (38.4)	0.68 (0.52–0.90)	0.006	0.09
110–125	344 (26.8)	59 (34.9)	58 (33.1)	1.08 (0.69–1.69)	0.73	
2-h postchallenge glucose (mg/dl)						
140–153	444 (33.6)	62 (27.8)	81 (36.7)	0.66 (0.45–0.99)	0.05	0.20
154–172	438 (33.2)	70 (32.4)	86 (38.7)	0.76 (0.51–1.12)	0.17	
173–199	439 (33.2)	74 (33.6)	75 (34.6)	0.96 (0.65–1.42)	0.84	

Data are *n* (%) unless otherwise indicated. *Test for trend for treatment effects across the categories; for race, we performed a test for heterogeneity.

modification had significantly lower prevalence of total (stress or urge) weekly urinary incontinence compared with women assigned to metformin or placebo. This result appeared to be due to differences in weekly stress incontinence. The beneficial effect was comparable across subgroups.

Weight loss was the most important mediator of the beneficial effect of the intensive lifestyle change program on stress incontinence. Weight reduction has been shown to improve incontinence in morbidly obese women undergoing bariatric surgery and in moderately obese women in weight-reduction programs (11–13). Presumably, increasing body weight causes increased abdominal weight, increased intra-abdominal pressure, and increased intravesicular pressure and urethral mobility, resulting in incontinence (12). Studies have shown that a

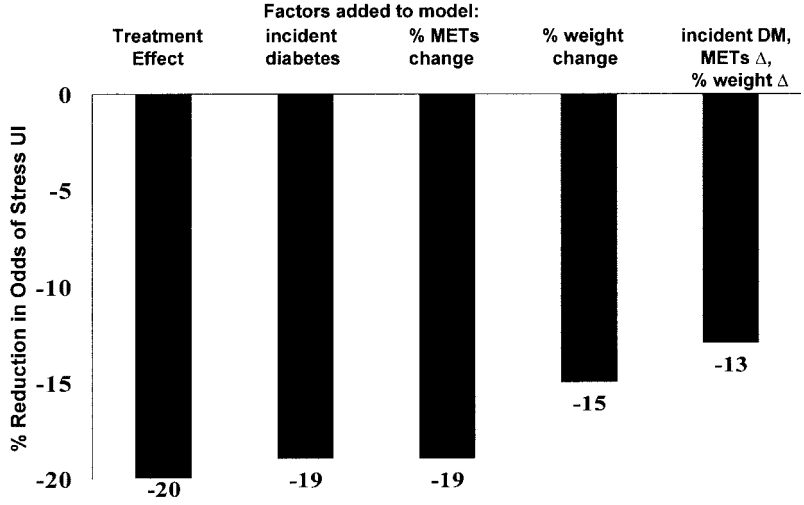

Figure 1—*Percent reduction in odds for weekly or more stress urinary incontinence in the intensive lifestyle intervention group versus the placebo/standard lifestyle group. Each model is adjusted for baseline hormone therapy use, general health status, and 2-h postchallenge glucose test results. Sequential models are adjusted for the indicated change variables. DM, diabetes.*

5–10% weight loss in women with urinary incontinence resulted in marked improvement of incontinence, and it has been suggested that improved incontinence may motivate overweight and obese women to lose weight (11,13).

Increased physical activity did not significantly affect the beneficial treatment effect of the intensive lifestyle intervention on urinary incontinence. In other studies, over 40% of middle-aged women reported leaking urine during exercise, and a similar proportion reported avoiding exercise because of urinary incontinence (14). Running and high-impact aerobics have been reported as the most common forms of exercise associated with incontinence (15). It has been suggested that walking is less likely to provoke incontinence and therefore is a more common form of exercise chosen by women with incontinence. A majority of the subjects in the intensive lifestyle intervention arm of the DPP chose walking as their physical activity.

Although type 2 diabetes increases risk for incontinence, it is not surprising that incident diabetes among the DPP treatment groups did not mediate the benefit observed in urinary incontinence with lifestyle intervention. The early detection of diabetes in the DPP was associated with blood glucose levels that are not usually high enough to cause an osmotic diuresis. Moreover, microvascular complications associated with type 2 diabetes that may damage the innervation of the bladder or alter detrusor muscle function (23–25) have not occurred in early disease. For similar reasons, pre-diabetes most likely does not promote incontinence.

The DPP had a diverse population of women in a wide age range and excellent measures of body weight, physical activity, and incident diabetes through the trial, but we did not have baseline measures of urinary incontinence and could not examine net improvement in incontinence symptoms. However, since the groups were balanced with respect to most variables, there is no reason to suspect that these groups would have differed in relation to urinary incontinence prevalence at baseline. Adjustment for the three variables that were imbalanced by group at baseline did not materially alter the results. Another potential limitation includes limited power to evaluate modification of treatment effect by various baseline covariates.

In conclusion, women at high risk for diabetes who were randomly assigned to an intensive lifestyle intervention involving weight loss and exercise had a substantially lower prevalence of stress urinary incontinence. Increased low-impact exercise did not appear to have an adverse effect on incontinence. Health care providers may use the message that weight loss and lifestyle intervention may lower the risk of urinary incontinence. Lower prevalence of urinary incontinence may be a powerful motivating factor for women with pre-diabetes to choose a lifestyle modification in order to prevent diabetes.

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References

1. Davidson MB, Landsman PB, Alexander CM: Lowering the criterion for impaired fasting glucose will not provide clinical benefit. *Diabetes Care* 26:3329–3330, 2003
2. Benjamin SM, Valdez R, Geiss LS, Rolka DB, Narayan KMV: Estimated number of adults with prediabetes in the U.S. in 2000: opportunities for prevention. *Diabetes Care* 26:645–649, 2003
3. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
4. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, Keinänen-Kiukaanniemi S, Laakso M, Louheranta A, Rastas M, Salminen V, Uusitupa M: Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 344:1343–1350, 2001
5. Wetle T, Scherr P, Branch LG, Resnick NM, Harris T, Evans D, Taylor JO: Difficulty with holding urine among older persons in a geographically defined community: prevalence and correlates. *J Am Geriatr Soc* 43:349–355, 1995
6. Sampselle CM, Harlow SD, Skurnick J, Brubaker L, Bondarenko I: Urinary incontinence predictors and life impact in ethnically diverse perimenopausal women. *Obstet Gynecol* 100:1230–1238, 2002
7. Varmus H: *Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support*. Washington, DC, U.S. Govt. Printing Office, Department of Health and Human Services, National Institutes of Health, Office of the Director, 1997, p. Appendix
8. Wilson L, Brown JS, Shin GP, Luc KO, Subak LL: Annual direct cost of urinary incontinence. *Obstet Gynecol* 98:398–406, 2001
9. Jackson RA, Vittinghoff E, Kanaya AM, Miles TP, Resnick HE, Kritchevsky SB, Simonsick EM, Brown JS: Urinary incontinence in elderly women: findings from the Health, Aging, and Body Composition Study. *Obstet Gynecol* 104:301–307, 2004
10. Brown J, Grady D, Ouslander J, Herzog A, Varner R, Posner S: Prevalence of urinary incontinence and associated risk factors in postmenopausal women: Heart & Estrogen/Progestin Replacement Study (HERS) Research Group. *Obstet Gynecol* 94:66–70, 1999
11. Subak LL, Johnson C, Whitcomb E, Boban D, Saxton J, Brown JS: Does weight loss improve incontinence in moderately obese women? *Int Urogynecol J Pelvic Floor Dysfunct* 13:40–43, 2002
12. Bump R, Sugerman H, Fantl J, McClish D: Obesity and lower urinary tract function in women: effect of surgically induced weight loss. *Am J Obstet Gynecol* 166:392–399, 1992
13. Subak LL, Whitcomb E, Shen H, Saxton J, Vittinghoff E, Brown JS: Weight loss: a novel and effective treatment for urinary incontinence. *J Urol* 174:190–195, 2005
14. Brown WJ, Miller YD: Too wet to exercise? Leaking urine as a barrier to physical activity in women. *J Sci Med Sport* 4:373–378, 2001
15. Nygaard I, DeLancey J, Arnsdorf L, Murphy E: Exercise and incontinence. *Obstet Gynecol* 75:848–851, 1990
16. The Diabetes Prevention Program Research Group: Design and methods for a clinical trial in the prevention of type 2 diabetes. *Diabetes Care* 22:623–634, 1999
17. The Diabetes Prevention Program (DPP) Research Group: Description of lifestyle intervention. *Diabetes Care* 25:2165–2171, 2002

18. Kriska AM, Caspersen CJ: Introduction to a collection of physical activity questionnaires. *Med Sci Sports Exerc* 29:S5–S9, 1997
19. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 20:1183–1197, 1997
20. Grady D, Brown JS, Vittinghoff E, Applegate W, Varner E, Snyder T: Postmenopausal hormones and incontinence: the Heart and Estrogen/Progestin Replacement Study. *Obstet Gynecol* 97:116–120, 2001
21. Hannestad YS, Rortveit G, Sandvik H, Hunskaar S: A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT study: epidemiology of incontinence in the county of Nord-Trondelag. *J Clin Epidemiol* 53:1150–1157, 2000
22. Sandvik H, Hunskaar S, Vanvik A, Bratt H, Seim A, Hermstad R: Diagnostic classification of female urinary incontinence: an epidemiological survey corrected for validity. *J Clin Epidemiol* 48:339–343, 1995
23. Ellenberg M: Development of urinary bladder dysfunction in diabetes mellitus. *Ann Intern Med* 92:321–323, 1980
24. Ueda T, Yoshimura N, Yoshida O: Diabetic cystopathy: relationship to autonomic neuropathy detected by sympathetic skin response. *J Urol* 157:580–584, 1997
25. Brown JS, Nyberg LM, Kusek JW, Burgio KL, Diokno AC, Foldspang A, Fultz NH, Herzog AR, Hunskaar S, Milsom I, Nygaard I, Subak LL, Thom DH: Proceedings of the National Institute of Diabetes and Digestive and Kidney Diseases International Symposium on Epidemiologic Issues in Urinary Incontinence in Women. *Am J Obstet Gynecol* 188:S77–S88, 2003