Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Wei JT, Nygaard I, Richter HE, et al. A midurethral sling to reduce incontinence after vaginal prolapse repair. N Engl J Med 2012;366:2358-67.

Supplementary Appendix
Supplement to: Wei J, Nygaard I, Richter H, et al. Use of a Midurethral Sling to Prevent Urinary Incontinence Among Women Undergoing Vaginal Prolapse Repair

Contents

Supplementary Table 1. **Primary Study Endpoints.**

I. 3-month urinary incontinence or treatment endpoint was met if any of the following were present:

- A. Endorsement of any of the following questions from the PFDI with at least a moderate degree of bother:
  - 1. Do you usually experience urine leakage related to coughing, sneezing, or laughing?
  - 2. Do you usually experience urine leakage related to physical exercise such as walking, running, aerobics, or tennis?
  - 3. Do you usually experience urine leakage related to lifting or bending over?
  - 4. Do you usually experience urine leakage associated with a feeling of urgency, that is, a strong sensation of needing to go to the bathroom?
- B. Positive cough stress test on exam
- C. Need for treatment for any urinary incontinence after the index surgery (e.g., surgery, collagen injections, supervised pelvic muscle therapy, medication, pessary) for any urinary incontinence

II. 12-month urinary incontinence endpoint was met if criterion (IA) and/or (IB) above were satisfied.

Supplementary Table 2. **Demographics and Baseline Characteristics by Treatment Group (expanded)**

Variable	Sling Group (N=165)	Sham Group (N=172)
Age, yrs.- mean (SD)	63.4 (10.8)	62.2 (10.2)
Race [‡] *- no. (%)*		
White/Caucasian	143 (87%)	143 (83%)
Black/African American	10 (6%)	14 (8%)
Asian	3 (2%)	2 (1%)
Amer. Indian/Alaskan Native	0 (0%)	1 (1%)
Other	9 (5%)	12 (7%)
Ethnicity- no. (%)		
Hispanic	21 (13%)	27 (16%)
Non-Hispanic	144 (87%)	145 (84%)
BMI, kg/m^2- mean (SD)	27.8 (4.9)	28.1 (5.5)
POP, Q Stage [§] *- no. (%)*		
2	45 (27%)	48 (28%)
3	107 (65%)	106 (62%)
4	13 (8%)	18 (10%)
Income- no. (%)		
<$15,000	14 (22%)	10 (15%)
≥$15,000 to <$30,000	17 (27%)	17 (26%)
≥$30,000 to <$50,000	18 (28%)	18 (28%)

≥$50,000 to <$70,000	8 (12%)	11 (17%)
≥$70,000	7 (11%)	9 (14%)
Marital Status- no. (%)		
Married	121 (74%)	101 (63%)
Separated/Divorced	20 (12%)	26 (16%)
Widowed	20 (12%)	27 (17%)
Single/Never Married	2 (1%)	5 (3%)
Other	0 (0%)	2 (1%)
Education- no. (%)		
Less than High School	17 (10%)	26 (16%)
Completed High School or Equivalent	44 (27%)	45 (28%)
Some College/Associate Degree	56 (34.%)	44 (27%)
Completed 4 Year College	30 (18%)	29 (18%)
Graduate/Professional Degree	16 (10%)	17 (11%)
Baseline Stress Test- no. (%)		
Positive	54 (33%)	57 (33%)
Negative	107 (67%)	113 (67%)
Anterior Vaginal Prolapse Repair ¶- no. (%)		
Anterior Repair Only	20 (12%)	17 (10%)
Apical Suspension Only	32 (19%)	42 (24%)

Both Anterior and Apical	101 (62%)	100 (58%)
Colpocleisis	11 (7%)	13 (8%)
Posterior Vaginal Prolapse Repair- no. (%)		
Yes	74 (45%)	80 (46%)
No	90 (55%)	92 (54%)
Prior Hysterectomy – no. (%)	62 (38%)	66 (38%)
Concomitant Hysterectomy – no. (%)	82 (50%)	83 (48%)

All p-values are greater than 0.05.

‡ Race was self-reported and more than one category could have been selected.

§ POP Q stages are ordinal categories based on the lowest point of prolapse with stage 1 (lowest point of prolapse is > 1 cm above hymen), stage 2, (lowest point of prolapse is within 1 cm above or below to the hymen), stage 3 (lowest point of prolapse >1 cm below hymen but protrudes no more than 2 cm less than the total vaginal length) and stage 4 (complete vaginal eversion)

¶ Anterior repairs included paravaginal repairs, colporrhaphy, mesh augmentation and apical suspensions included uterosacral ligament suspension, sacrospinous ligament suspension, McCall culdoplasty, Iliococcygeal repair, Pursestring repair of enterocele, Apical suspension kit.

Supplementary Table 3. **Demographic and Baseline Characteristics by Cohort**

Variable	Group	
	Randomized Cohort	**Patient Preference Cohort**
	N=337	**N=129**
Age- yrs.		
Mean (SD)	62.8 (10.2)	64.4 (10.0)
Age- no. (%)		
>30 and <=40	9 (2.7%)	1 (0.8%)
>40 and <=50	23 (6.8%)	7 (5.4%)
>50 and <=60	90 (26.7%)	34 (26.4%)
>60 and <=70	144 (42.7%)	50 (38.8%)
>70 and <=80	60 (17.8%)	27 (20.9%)
>80	11 (3.3%)	10 (7.8%)
*Race ‡- no. (%)**		
White/Caucasian	286 (84.9%)	123 (95.4%)
Black/African American	24 (7.1%)	4 (3.1%)
Asian	5 (1.5%)	1 (0.8%)
American Indian/Alaskan Native	1 (0.3%)	0 (0.0%)
Other	21 (6.2%)	1 (0.8%)
Ethnicity- no. (%)		
Hispanic	48 (14%)	14 (10.9%)
Non-Hispanic	289 (86%)	115 (89.2%)
BMI- kg/m^2		
Mean (SD)	28.0 (5.2)	27.9 (5.3)
POP, Q Stage §- no. (%)		
2	93 (28%)	44 (34.4%)
3	213 (63%)	77 (60.2%)
4	31 (9%)	7 (5.5%)
Income- no. (%)		
<$15,000	24 (18.6%)	3 (5.7%)
≥$15,000 to <$30,000	34 (26.4%)	17 (32.1%)
≥$30,000 to <$50,000	36 (27.9%)	12 (22.6%)
≥$50,000 to <$70,000	19 (14.7%)	10 (18.9%)
≥$70,000	16 (12.4%)	11 (20.8%)

Marital Status- no. (%)		
Married	222 (68.5%)	78 (63.4%)
Separated/Divorced	46 (14.2%)	21 (17.1%)
Widowed	47 (14.5%)	21 (17.1%)
Single, never married	7 (2.2%)	2 (1.6%)
Other	2 (0.6%)	1 (0.8%)
Education- no. (%)		
Less than high school	43 (13.3%)	12 (9.8%)
Completed high school or equivalent	89 (27.5%)	28 (22.8%)
Some college/Associate degree	100 (30.9%)	34 (27.6%)
Completed 4 years of college	59 (18.2%)	26 (21.1%)
Graduate/Professional degree	33 (10.2%)	23 (18.7%)
Baseline Stress Test- no. (%)		
Positive	111 (33.5%)	51 (40.2%)
Negative	220 (66.5%)	76 (59.8%)
*Anterior Vaginal Prolapse Repair ¶ - no. (%)**		
Anterior repair only	37 (11.0%)	11 (8.5%)
Apical suspension only	74 (22.0%)	45 (34.9%)
Both anterior and apical	201 (59.8%)	60 (46.5%)
Colpocleisis	24 (7.1%)	13 (10.1%)
Posterior Vaginal Prolapse Repair- no. (%)	154 (45.8%)	54 (41.9%)
Prior Hysterectomy – no. (%)	128 (38.0)	48 (37.5)
Concomitant Hysterectomy – no. (%)	165 (49.1)	70 (54.3)
Pre-Surgery UI Medication Use- no. (%)	15 (4.5%)	9 (7.0%)
Estimated Blood Loss- cc		
Mean (SD)	156.0 (113.6)	144.0 (97.7)
Operative Time- min.		
Mean (SD)	135.3 (52.4)	130.4 (47.8)

* P<0.05

‡ Race was self-reported and more than one category could have been selected.

§ POP Q stages are ordinal categories based on the lowest point of prolapse with stage 1 (lowest point of prolapse is > 1 cm above hymen), stage 2, (lowest point of prolapse is within 1 cm above or below to the hymen), stage 3 (lowest point of prolapse >1 cm below hymen but protrudes no more than 2 cm less than the total vaginal length) and stage 4 (complete vaginal eversion)

¶ Anterior repairs included paravaginal repairs, colporrhaphy, mesh augmentation and apical suspensions included uterosacral ligament suspension, sacrospinous ligament suspension, McCall culdoplasty, Iliococcygeal repair, Pursestring repair of enterocele, Apical suspension kit.

Supplementary Table 4. **Additional Patient Reported Outcomes by Treatment Group in the Randomized Cohort.**

Variable[‡]	**Treatment Group**		**Treatment Difference**[†]
	Sling Group	**Sham Group**	**(95%CI)**
	N=165	**N=172**	
PFDI Pelvic Organ Prolapse Distress Index (POPDI)			
Change from Baseline to 3 Months			
No.	160	158	
Mean (SD)	-74.1 (68.59)	-74.7 (61.18)	0.6 (-13.7, 15.0)
Change from Baseline to 12 Months			
No.	157	154	
Mean (SD)	-73.8 (65.07)	-74.6 (60.4)	0.7 (-13.3, 14.7)
PFDI Colo-Rectal Anal Distress Index (CRADI)			
Change from Baseline to 3 Months			
No.	157	154	
Mean (SD)	-35.6 (66.45)	-33.0 (65.19)	-2.5 (-17.2, 12.1)
Change from Baseline to 12 Months			
No.	157	153	
Mean (SD)	-38.2 (63.12)	-37.9 (63.56)	-0.3 (-14.5, 13.8)
PFIQ Urinary Impact Questionnaire (UIQ)			
Change from Baseline to 3 Months			
No.	153	152	
Mean (SD)	-48.4 (75.07)	-38.3 (71.63)	-10.1 (-26.7, 6.4)
Change from Baseline to 12 Months			
No.	151	150	
Mean (SD)	-50.3 (71.29)	-48.0 (65.89)	-2.4 (-18.0, 13.2)
PFIQ Pelvic Organ Prolapse Impact Questionnaire (POPIQ)			
Change from Baseline to 3 Months			
No.	154	152	
Mean (SD)	-57.1 (79.38)	-47.0 (73.91)	-10.0 (-27.3, 7.2)
Change from Baseline to 12 Months			
No.	152	150	
Mean (SD)	-57.6 (79.23)	-51.6 (70.88)	-6.1 (-23.1, 11.0)

PFIQ Colo-Rectal Anal Impact Questionnaire (CRAIQ)			
Change from Baseline to 3 Months			
No.	153	152	
Mean (SD)	-22.8 (59.16)	-19.2 (59.82)	-3.6 (-17.0, 9.8)
Change from Baseline to 12 Months			
No.	151	150	
Mean (SD)	-24.9 (65.71)	-24.3 (64.21)	-0.6 (-15.3, 14.2)
PISQ-12 Total Score			
Change from Baseline to 3 Months			
No.	57	48	
Mean (SD)	2.8 (4.56)	3.2 (5.32)	-0.4 (-2.3, 1.5)
Change from Baseline to 12 Months			
No.	66	52	
Mean (SD)	4.0 (4.93)	3.5 (4.30)	0.5 (-1.2, 2.2)
Average Weekly Pain			
Change from Baseline to 3 Months			
No.	159	158	
Mean (SD)	-1.4 (2.53)	-1.2 (2.45)	-0.2 (-0.8, 0.3)
Change from Baseline to 12 Months			
No.	156	154	
Mean (SD)	-1.7 (2.61)	-1.4 (2.47)	-0.3 (-0.9, 0.3)

† All p-values greater than 0.05

‡ Pelvic Floor Distress Inventory POPDI domain (range 0-300 with higher score indicating more symptoms); Pelvic Floor Distress Inventory CRADI domain (range 0-400 with higher score indicating more symptoms); Pelvic Floor Impact Questionnaire domains (range 0-400 with higher score indicating greater impact); Pelvic Organ Prolapse/Urinary Incontinence Sexual Functioning Questionnaire Short Form (range 0-48 with higher score better sexual function); analogue pain scale adapted for suprapubic pain (range 0-10 with higher score indicating more pain)

Supplementary Table 5. **Likelihood of Incontinence at 3 months Stratified by Preoperative Prolapse Reduction Stress Test in the Randomized Cohort.**

	Treatment Group		
Baseline Stress Test†	**Prolapse Repair plus Sling**	**Prolapse Repair plus Sham**	**All**
	N=165	**N=172**	
	3 month endpoint		
Positive	16/54 (29.6%)	41/57 (71.9%)	57/111 (51.4%)
Negative	22/107 (20.6%)	43/113 (38.1%)	65/220 (29.5%)
	12 month endpoint		
Positive	19/54 (35.2%)	34/57 (59.7%)	53/111 (44.7%)
Negative	30/107 (28.0%)	46/113 (40.7%)	76/220 (34.5%)

† Positive Stress Tests: the bladder is filled retrograde to 300 ml, (at baseline, the prolapse was replaced inside the vagina using one or two large swabs). If the woman demonstrates leakage with coughing or straining in either the supine or standing position, the test is considered positive. P-value is 0.06 at 3 months and 0.16 at 12 months based on test of interaction between stress test and treatment group from model, stratifying by surgeon, and controlling for type of prolapse repair procedure (colpocleisis, apical suspension and/or anterior repair.

Supplementary Table 6. **Proportion with Urinary Incontinence (UI) Endpoints at 3 and 12 Months in the Patient Preference Cohort†**

Study Endpoint	Sling Group (N=64)	Prolapse Repair Only (N=65)	Treatment Difference (95% CI)	Adjusted Odds Ratio (95% CI)
UI/Treatment at 3 Months†- no. (%)	14/64 (21.9%)	30/65 (46.2%)	-24.3%^ (-40.6%, -7.9%)	0.31* (0.11, 0.86)
Positive Cough Stress Test‡- no. (%)	2/58 (3.5%)	14/55 (25.5%)	-22% *** (-34.9, -9.1)	
Symptoms§- no. (%)	4/62 (6.5%)	5/61 (8.2%)	-1.7% (-10.9, 7.5)	
UI Treatments¶- no. (%)	4/64 (6.3%)	7/65 (10.8%)	-4.5% (-14.2, 5.1)	
				Adjusted Odds Ratio (95% CI)
UI at 12 Months† - no. (%)	17/64 (26.6%)	30/65 (46.2%)	-19.6%^ (-36.2%, -3.0%)	0.54 (0.21, 1.39)
Positive Cough Stress Test‡- no. (%)	2/54 (3.7%)	13/50 (26%)	-22.3% ** (-35.8, -8.8)	
Symptoms§- no. (%)	3/56 (5.4%)	5/60 (8.3%)	-3.0% (-12.2, 6.3)	

* P<0.05;** P<0.01; *** P<0.001; ^not done

†3 Month endpoint includes any positive cough stress tests, symptoms, or additional urinary incontinence treatment whereas 12 month endpoint includes positive cough stress tests or symptoms only. P-value from model, stratifying by surgeon, and controlling for type of prolapse repair procedure (colpocleisis, apical suspension and/or anterior repair).

‡ Positive Stress Tests: Leakage of urine with coughing or straining in either the supine or standing position with the bladder filled retrograde to 300 ml.

§ Symptoms: of UI that are also characterized as being at least moderately bothersome to the subject (as measured by a "moderately" or "quite a bit" response to any of the four items from the Pelvic Floor Distress Inventory regarding leakage).

¶ UI Treatment: need for treatment for any urinary incontinence including surgery, UI medication, pessary for incontinence, supervised pelvic muscle exercises, timed voiding & fluid management, periurethal injection, botulinum injection, neuromodulation, or other treatment for incontinence.

Supplementary Table 7. **Serious Adverse Events by Body System**[†]

Body System	Treatment Group	SAE Description
Cardiovascular	Sling	Arrhythmia
	Sling	Congestive heart failure
	Sling	Decreased pulse, abnormal EKG
	Sham	Post-operative hypoxia and hypotension
	Sham	Dizziness
	Sham	Chest pain
Cardiovascular and Urological	Sling	Fluid overload, shortness of breath, urinary tract infection
GI	Sling	Dehydration and diarrhea
	Sling	Surgery for recurrent rectal prolapse
	Sling	Acute appendicitis
	Sling	Acute ischemic colitis
	Sling	Nausea and vomiting secondary to Percocet, requiring hospitalization
	Sling	Diverticulitis
	Sling	Small bowel obstruction
	Sling	Appendicitis
	Sham	Post-operative nausea and vomiting
	Sham	Rectal prolapse
	Sham	Small bowel obstruction
Gynecologic	Sling	Surgery for recurrent vaginal vault prolapse
	Sling	Rectocele repair
	Sling	Surgery for recurrent vaginal vault prolapse[‡]
	Sling	Surgery for recurrent pelvic organ prolapse
	Sling	Surgery for recurrent pelvic organ prolapse
	Sling	Surgery for recurrent apical prolapse
	Sham	Surgery for recurrent pelvic organ prolapse
Hematologic/Bleeding	Sling	Intraoperative retropubic hematoma[‡]
	Sling	Post-operative hemorrhage
	Sling	Post-operative anemia
Miscellaneous	Sham	Goiter
Musculoskeletal	Sling	Hip Replacement
	Sling	Knee fracture

	Sling	Total knee replacement
	Sham	Knee replacement
	Sham	Hip degenerative joint disease
	Sham	Lumbar stenosis
	Sham	Arthritis both knees with valgus deformity
Neoplastic	Sham	Colon cancer
	Sham	Colon cancer
	Sham	Abnormal mammogram malignant right breast
Neurological	Sling	Post-operative pain
	Sling	Herniated disc
	Sling	Leg pain
	Sham	Transient ischemic attack
Pulmonary	Sling	Spontaneous pneumothorax
Urological	Sling	Kidney stone, urinary tract infection
	Sham	Pyelonephritis‡
	Sham	Stitch abscess, pelvic pain, urinary frequency
Wound	Sling	Post-operative vaginal edge bleeding
	Sham	Post-operative vaginal edge bleeding
	Sham	Post-operative vaginal bleeding
	Sham	Vaginal cuff abscess
	Sham	Abscess

† Serious adverse events: Any untoward medical occurrence (whether or not related to index surgery) that resulted in death, is life threatening, requires inpatient hospitalization, results in persistent or significant disability or incapacity, in a congenital anomaly/birth defect, or is another medically important condition

‡ SAE that is plausibly related to mid-urethral sling as determined by independent adjudication committee. Using Fisher's exact test, there was no differences in the occurrence of plausibly related SAEs between Sling and Sham groups (p=0.62)

Supplementary Table 8. **Unexpected Adverse Events by Body system**[†]

Body System	Treatment Group	SAE Description
GI	Sling	Planned laparoscopic assisted vaginal hysterectomy unable to be performed due to adhesive disease.
	Sling	Rectal proctotomy
	Sling	Constipation
	Sham	Constipation
Gynecologic	Sham	Vaginal adhesions
	Sham	Mesh complication
Infection	Sham	Methicillin resistant staphylococcus infection
Miscellaneous	Sham	Fatigue
	Sham	Lost needle
	Sham	Scabies
Musculoskeletal	Sham	Hip fracture
Neurological	Sling	Pain
	Sling	Pain
	Sham	Inguinal nerve injury
	Sham	Vestibulitis
	Sham	Pain
	Sham	Nerve pain
Urological	Sling	Ureteral injury[‡]
	Sling	Ureteral injury[‡]
	Sling	Ureteral injury[‡]
	Sling	Ureteral injury[‡]
	Sling	Ureteral injury[‡]
	Sling	Ureteral injury[‡]
	Sham	Ureteral injury[‡]
	Sham	Ureteral injury[‡]
	Sham	Ureteral injury[‡]
Wound	Sling	Granulation
	Sling	Granulation
	Sling	Granulation
	Sling	Granulation
	Sham	Intraoperative vaginal bleeding

† Unexpected adverse events: Any other untoward event that is not qualified as an expected adverse event (as listed in manuscript Table 4)

‡ Transient ureteral obstruction diagnosed during cystoscopy in the operating room, which was resolved with removal of uterosacral suspension sutures

OPUS Primary Analysis Manuscript Acknowledgments

Pelvic Floor Disorders Network:

Cleveland Clinic

Mathew D. Barber, MD, MHS, Principal Investigator

Marie Fidela R. Paraiso, MD, Co-Investigator

Mark D. Walters, MD, Co-Investigator

J. Eric Jelovsek, MD, Co-Investigator

Linda McElrath, RN, Research Nurse Coordinator

Donel Murphy, RN, MSN, Research Nurse

Cheryl Williams, Research Assistant

Duke University

Anthony G. Visco, MD, Principal Investigator

Jennifer Wu, MD, Co-Investigator

Alison Weidner, MD, Co-Investigator

Cindy Amundsen, MD, Co-Investigator

Mary J. Loomis, RN, BSN, Research Coordinator

Loyola University

Linda Brubaker, MD, MS, Principal Investigator

Kimberly Kenton, MD, MS, Investigator

MaryPat FitzGerald, MD, MS, Investigator

Elizabeth Mueller, MD, MSME, Investigator

Mary Tulke, RN, Research Nurse Coordinator

Kathy Jesse, RN, Research Nurse Coordinator

Kathy Marchese, RN, Research Nurse Coordinator

University of Alabama at Birmingham

Holly E. Richter, PhD, MD, Principal Investigator

Kathryn L. Burgio, PhD, Co-Principal Investigator

R. Edward Varner, MD, Co-Investigator

Robert L. Holley, MD, Co-Investigator

W. Jerod Greer, MD, Co-Investigator

Patricia S. Goode, MD, Co-Investigator

L. Keith Lloyd, MD, Co-Investigator

Alayne D. Markland, DO, Co-Investigator

Tracey Wilson, MD, Co-Investigator

Velria Willis, RN, BSN, Research Nurse Coordinator

Nancy Saxon, BSN, Research Nurse Clinician

LaChele Ward, LPN, Research Specialist

Lisa S. Pair, CRNP

University of California, San Diego and Kaiser Permanente, San Diego

Charles W. Nager, MD Principal Investigator

Shawn A. Menefee, MD, Co- Investigator

Emily Lukacz, MD, Co-Investigator

Margie Kahn, MD, Co-Investigator

Karl M. Luber, MD, Co-Investigator

Leah Merrin, Research Coordinator

Giselle Zazueta-Damian, Research Coordinator

Patsy Riley, R.N.

Lynn Hall, R.N.

Judy M. Condino, RN

University of Michigan

Cathie Spino, DSc, Principal Investigator

John T. Wei, MD, MS, Co-Principal Investigator

Morton B. Brown, PhD, Co-Investigator

Donna DiFranco, BS, Clinical Monitor

John O.L. DeLancey, MD, Co-Investigator

Dee Fenner, MD, Co-Investigator

Nancy K. Janz, PhD, Co-Investigator

Zhen Chen, MS, Statistician

Fang Xiang, Statistician

Yang Wang Casher, MS, Database Programmer

University of Texas, Southwestern

Joseph Schaffer MD, Principal Investigator

David Rahn, MD, Co-Investigator

Clifford Wai, MD, Co-Investigator

Marlene Corton, MD, Co-Investigator

Gary Lemack, MD, Co-Investigator

Philippe Zimmern, MD Co-Investigator

Kelly Moore - Research Coordinator

Shanna Atnip, NP

Margaret Hull, NP

Pam Martinez, NP

Deborah Lawson, NP

University of Utah

Ingrid Nygaard, MD, Principal Investigator

Peggy Norton, MD, Co-Investigator

Yvonne Hsu, MD, Co-Investigator

Linda Freeman, RN, Research Coordinator

Steering Committee Chair

Katherine E. Hartmann, MD, PhD

NIH Project Scientist

Susan Meikle, MD, MSPH