FDA Perspective on Surgical Mesh for Stress Urinary Incontinence (SUI)

September 9, 2010

Gaithersburg, MD

FDA Overview - SUI

- MDR Analysis
- Systematic Literature Review
- Clinical Overview
- Concluding Remarks and Panel Questions

Analysis of MDR Reports Associated with the Use of Surgical Mesh for SUI Repair

Presented by:
Nancy Pressly
Associate Director
Division of Postmarket Surveillance
Office of Surveillance and Biometrics

Analysis performed by:
Nasrin Mirsaidi, RN, MSN
Division of Postmarket Surveillance
Office of Surveillance and Biometrics

September 9, 2011

Gaithersburg, Maryland

Outline

- Overview of Medical Device Reporting (MDR)
- Search Methodology
- Limitations
- Results

What is MDR?

- MDR refers to Medical Device Reporting
  - Required under 21 CFR Part 803
  - Manufacturers are required to report deaths, injuries and malfunctions related to their devices to FDA.
  - User Facilities are required to report medical device related deaths to FDA and the manufacturer and Injuries to the manufacturer.
  - The MDR regulation is a mechanism for FDA and manufacturers to identify and monitor significant adverse events involving marketed medical devices.

Voluntary Reporting

- Anyone can file a voluntary report through FDA's MedWatch program

  http://www.fda.gov/Safety/MedWatch/default.htm

- Mandatory and Voluntary reports are entered into the Manufacturer and User Facility Device Experience (MAUDE) Database
- In 2010, FDA received more than 300,000 reports covering all medical devices

MDR Reports

- Provide a qualitative snapshot of adverse events for a specific device or device type
- Vary in quality and usefulness due to the information provided
- Include both problem codes as well as narrative text
- May be coded with multiple problem codes

Limitations of MDRs

- Under reporting of events
- Insufficient or inadequate information
- Inability to establish causality
- Inability to establish rate of adverse events
- “Trends” in numbers should be interpreted cautiously

Methodology

- Search Criteria
  - Product Codes FTL & FTM
  - Date Entered Between Jan 1, 2008 and Dec 31, 2010

- The following MDRs were removed:
  - Non-urogyn meshes,
  - Duplicate reports,
  - Reports with unknown device specifications,
  - Miscoded reports

Methodology (cont.)

- Remaining meshes sorted into POP or SUI
  - Based on the indicated use of the product reported
- Analysis completed using semantic text mining techniques as well as traditional analytical methods

Limitations Specific to this Search

- Multiple procedures in one operation
- Multiple meshes used
- Voluntary reporters used layman terminologies

MDR Reports for SUI

Year	# of Reports
2008	368
2009	513
2010	490
Total	**1371**

* Previous time period – 2005-2007 approx. 835 reports

Death Reports n=3

Age	Summary of Report's Narrative	Type of Procedure
73	Bowel perforation & adhesion – died next day	Mid-Urethral Sling
UNK	Bowel Perforation – died of toxic shock and cardiac arrest	Sling Procedure
61	Erosion & bleeding; on life support after mesh removal; died after life support discontinued	Sacrocolpopexy & Sling Procedure

Top 10 Adverse Events for SUI Reports

Rank	Adverse Events	# of MDRs	Percentile Rate
1	Pain	479	34.9%
2	Erosion	436	31.8%
3	Infection	260	18.9%
4	Urinary Problems	220	16.0%
5	Organ Perforation	110	8.3%
6	Recurrence, Incontinence	103	7.5%
6	Bleeding	103	7.5%
8	Dyspareunia	73	5.3%
9	Neuro-muscular problems	50	3.6%
10	Vaginal scarring	22	1.6%

Total number of adverse events is larger than total number of MDRs because the majority of MDRs reported more than one adverse event

Most Frequently Reported Required Interventions

Intervention	Number
Additional Surgical Procedure	394
Partial or complete mesh explant	162
Hospitalization	58

Summary

- Persistent signal related to the use of surgical mesh for SUI
- Serious, life-altering adverse events associated with the use of surgical mesh for SUI continue to be reported

Epidemiological Overview of Published Literature on Stress Urinary Incontinence and Need For Post-Approval Studies

Cara Krulewitch, CNM PhD FACNM
Branch Chief
Division of Epidemiology
Office of Surveillance and Biometrics

September 9, 2011

Outline

- Background
- Methods
- Findings
- Postmarket Regulatory Options

Background

- FDA purpose of reviewing the literature
  - Increase in adverse event reports
- Objectives of the FDA literature review
  - POP presented yesterday
  - Focus today SUI

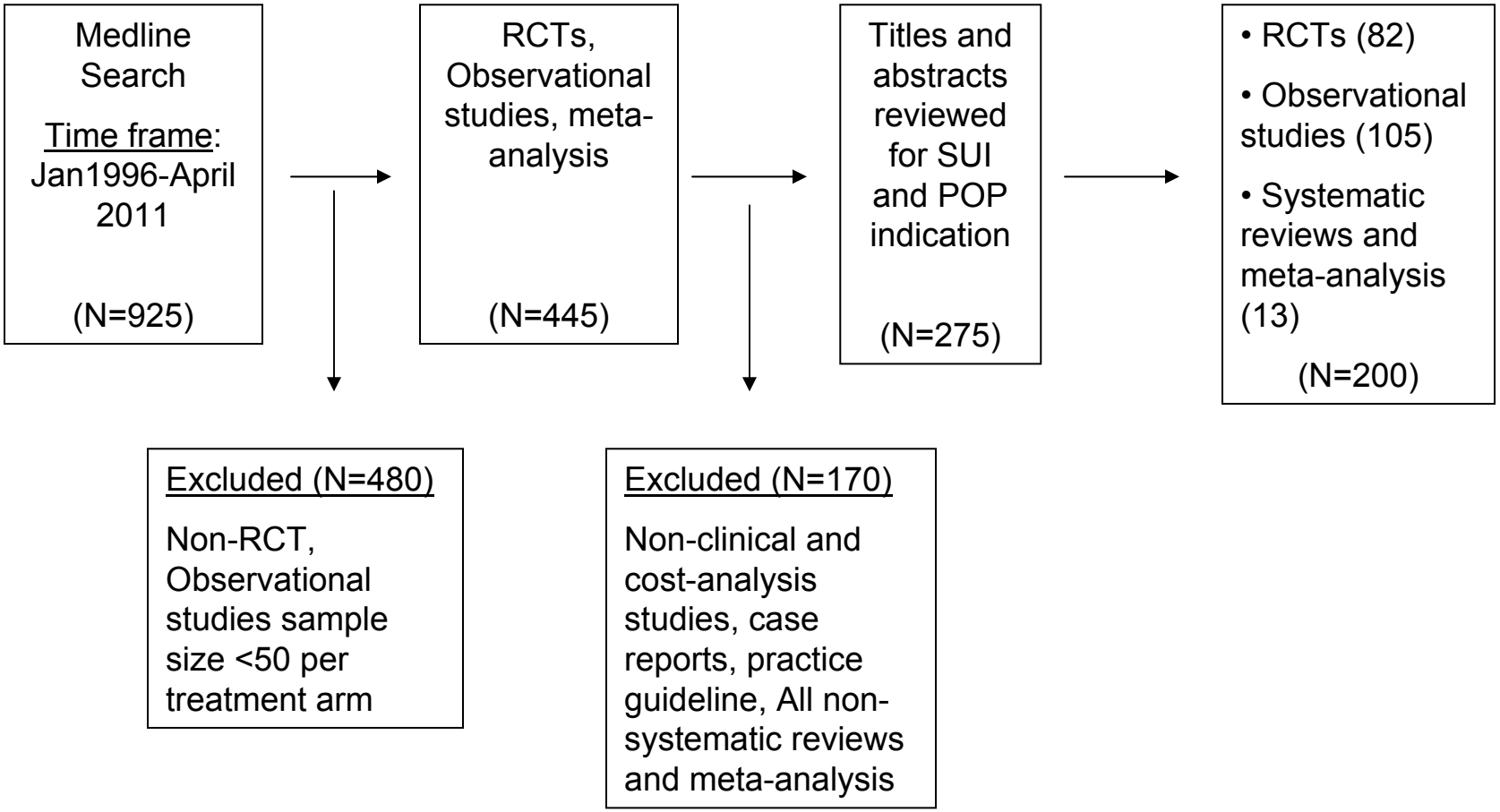
Methods

- Medline database search on the treatment of SUI using surgical mesh
  - RCTs
  - Observational studies

- Time frame January 1996 to April 2011

Inclusion Criteria

- RCT any sample size
- Observational Studies
  - Multiple (at least one mesh) cohorts
    - Total ≥ 100
  - Single mesh cohorts
    - Total ≥ 50


Medline Search
Time frame: Jan1996-April 2011
(N=925)
RCTs, Observational studies, meta-analysis
(N=445)
Titles and abstracts reviewed for SUI and POP indication
(N=275)
• RCTs (82)
• Observational studies (105)
• Systematic reviews and meta-analysis (13)
(N=200)
Excluded (N=480)
Non-RCT, Observational studies sample size <50 per treatment arm
Excluded (N=170)
Non-clinical and cost-analysis studies, case reports, practice guideline, All non-systematic reviews and meta-analysis

Methods

- Title and abstract review of RCTs indicated many methodological limitations
  - Unmasked studies
  - Confounding
  - Non-hypothesis driven trials
  - Differential loss to follow-up
- Variations in measures of effectiveness
- Patients from observational studies and RCTs were grouped together safety only

Methods-Weighted Mean Averages

Percentage occurrence of each adverse event (AE) within a study treatment group or "cohort" was calculated for each time period as follows:

$$\frac{\text{\# patients with AE}}{\text{\# patients within treatment group}}$$

The percentages for each timeframe were then averaged across cohorts, weighting the percentage in each cohort according to the number of patients in the cohort

Treatment Cohorts

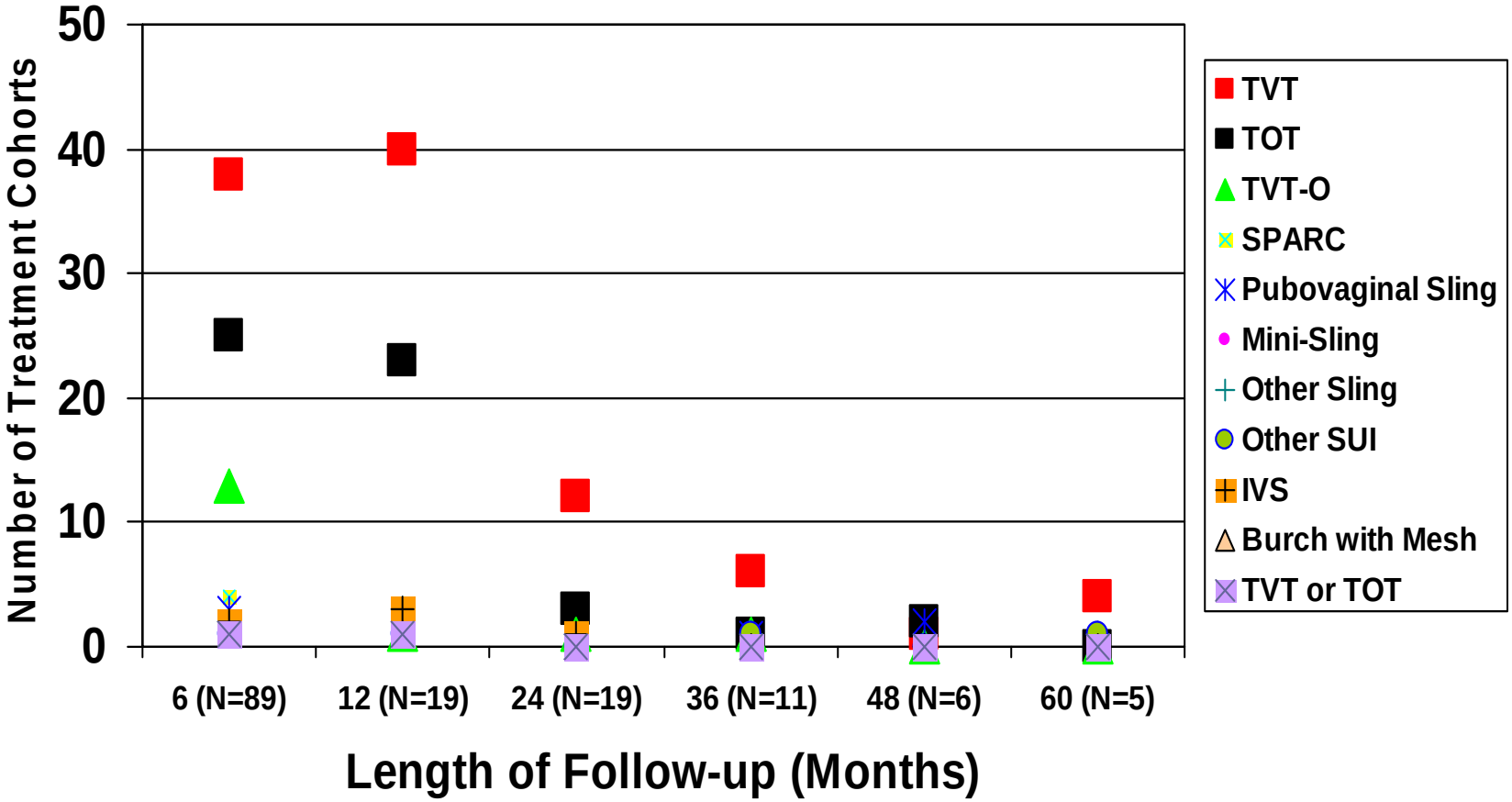
- There were 391 treatment cohorts that met inclusion criteria for SUI
  - Range of treatment cohorts 1 to 3
  - Range of sample sizes in each treatment cohort 10 to 2795

Number of Surgical Mesh Treatment Groups/Cohorts by Surgical Procedures for the Perioperative Period N=391

Type of Surgery	Number of Arms
TVT	148
TOT	63
TVT-O	30
Other Sling	16
Pubovaginal Sling	10
Other where number of studies < 10*	36

*Includes SPARC (8), IVS (6), **Mini-Sling (5),** TVT or TOT (5), Burch with mesh (4), Other (8)

Number Of Surgical Mesh Treatment Groups/Cohorts By Surgical Procedures and Follow-up Period In Months



Most Commonly Reported Adverse Events

- Erosion
- *de novo* dyspareunia
- Infection (including UTI)
- Pain
- Urinary problems
  - *de novo* SUI
  - Urgency, frequency and overactive bladder
  - Re-surgery

Most Common Peri-operative Complications

- Hemorrhage/Bleeding* (31.7%)
- Pain (6%)
- Infection (5%)
- Organ perforation (3.9%)
- Hematoma (1.0%)

*The definitions for hemorrhage or bleeding were disparate across the literature, and any conclusions to its clinical significance cannot be made.

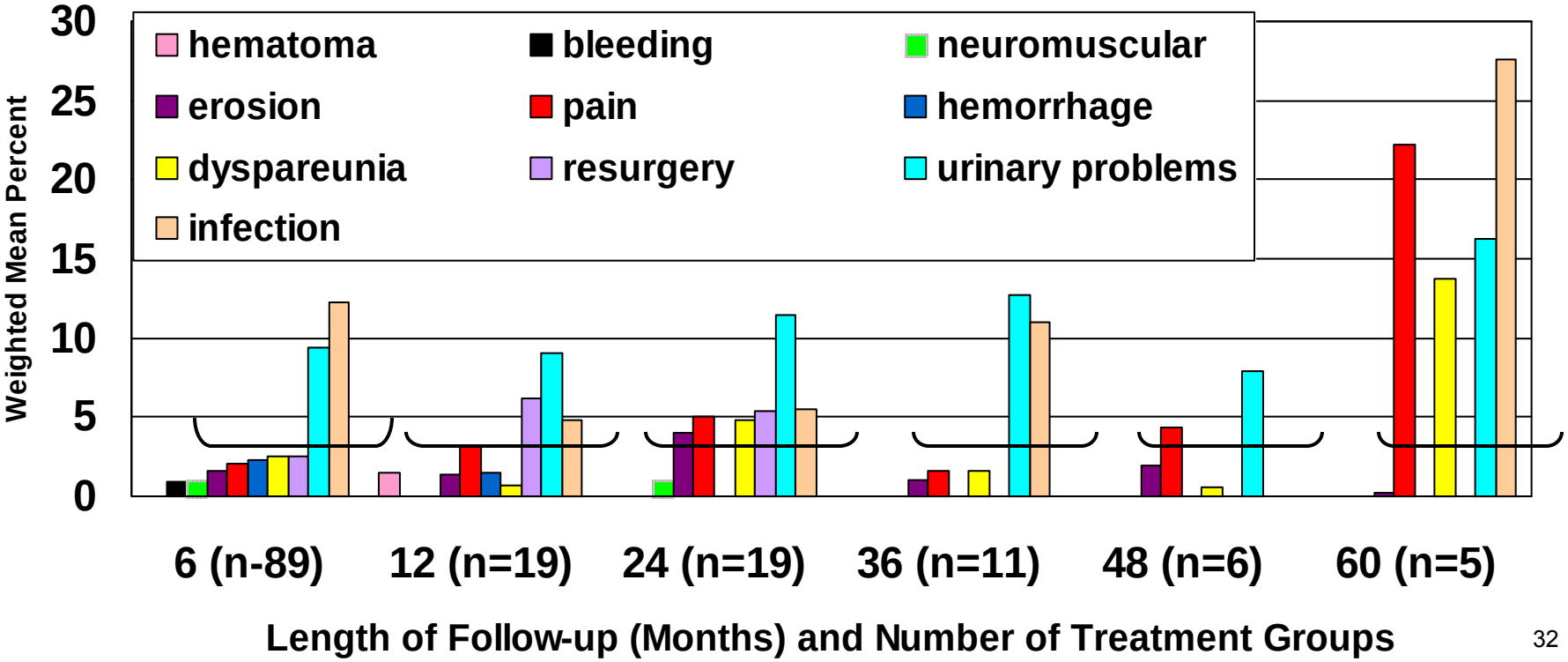
Reported Adverse Events at Follow-Up

	Range of Weighted Mean Percentages (%)	Range of Follow-Up (months)
Erosion	0.25 - 4.1	6 - 48
Resurgery	2.6 - 6.2	6 - 24
Dyspareunia	0.6 - 13.7	6 - 60
Pain	1.6 - 22.2	6 - 60
Urinary Problems	7.9 - 16.2	6 - 60
Infection*	4.8 - 27.4	6 - 60

* includes urinary tract infection

NOTE: Insufficient information exists in literature to provide quantitative measures of these adverse events among women with "non-mesh" surgeries

Weighted Mean Percentages Of AE Across Literature For The Treatment Of SUI Using Mesh Procedures By Follow-up Period



Conclusions

- There were a number of long-term adverse outcomes
- Some higher at later time points up to 60 months
- Fewer treatment cohorts to evaluate after 36 months

Mini-Sling Findings

- Adverse events reported for second generation synthetic slings or “single incision mini-slings”
  - Greater intraoperative blood loss
  - Lead to higher rates of vaginal mesh erosion compared to first generation slings

Limitations of Literature

- Literature on SUI includes a variety of approaches
- Lack of statistical power for many studies
- Comparators vary for effectiveness measures
- Evaluator masking not present
- Many studies involve concomitant surgical procedures
- Adverse event reporting is inconsistent across the studies and not the focus for many studies
- Inclusion/exclusion criteria are incompletely documented
- Length of follow-up varies
- Causality cannot be determined

Postmarket Studies

We believe postmarket studies are warranted and can help more immediately answer questions regarding the long term safety and effectiveness of vaginal mesh used for SUI repair already on the market

Need of Postmarket Studies

- Available scientific literature raises concerns of long-term safety profile for all SUI procedures
- Little scientific evidence for mini-slings (5 treatment cohorts)

The panel will be asked to consider whether postmarket studies are needed for cleared mini-slings, or all cleared surgical mesh indicated for SUI, and if so, should it be for all or a subset of these devices.

Design Options Available For 522 Studies Of Mesh For SUI

- May recommend RCT or prospective cohort study design that compares the device(s) to a control
- Sponsors responsible for study plans
  - RCT
  - Prospective cohort
  - Single sponsor registry
  - Multi-sponsor or society registry
  - RCT nested in registry

522 Recommendations

- Women 18 or older
- Documented SUI
- Surgery is scheduled
- Adjustment for pertinent risk factors

Safety and Effectiveness of Suburethral Mesh Slings for Surgical Repair of Stress Urinary Incontinence (SUI): ODE Clinical Review

Julia Carey-Corrado, MD

Obstetrics and Gynecology Devices Branch
Division of Reproductive, Gastro-Renal, and Urological Devices
Office of Device Evaluation (ODE)

General Issue Device Panel

- Generic view of device category (suburethral mesh slings for SUI)
  - Custom features (e.g. needle passers, sleeves, tissue anchors, etc.) will not be discussed

Outline

- SUI: Public Health Perspective
- Non-pharmacologic therapies for female SUI
- Comparative safety and effectiveness outcomes on 1st generation minimally invasive mesh slings
  - Cochrane Collaboration Reviews
  - Richter *et al*. 2010 NEJM
- Preliminary findings and comparative data on 2nd generation mesh “mini-slings”
- Clinical summary
  - Premarket, postmarket (ODE viewpoint)

Prevalence of Female Urinary Incontinence

- 15.7%[1]
  - All types of incontinence
  - Moderate to severe leakage
- Types of urinary incontinence[2]
  - Stress urinary incontinence (SUI) 48%
  - Urge incontinence 17%
  - Mixed incontinence 34%
- 11% lifetime risk of surgery for prolapse or incontinence[3]

[1] 2005-2006 National Health and Nutrition Examination Survey (NHANES)
[2] Nitti VW Rev Urology (2001)
[3] Olsen et al. Obstet Gynecol (1997)

Treatment Options for SUI

- Pelvic Floor Muscle Training
- Mechanical Support Devices
- Transurethral Bulking Agents
- Transurethral RF Tissue Remodeling
- Surgery (bladder neck and mid-urethral support)

Bladder Neck and Suburethral Support Surgery

More Invasive

- Open retropubic colposuspension
- Pubovaginal sling*
- Bladder neck needle suspension

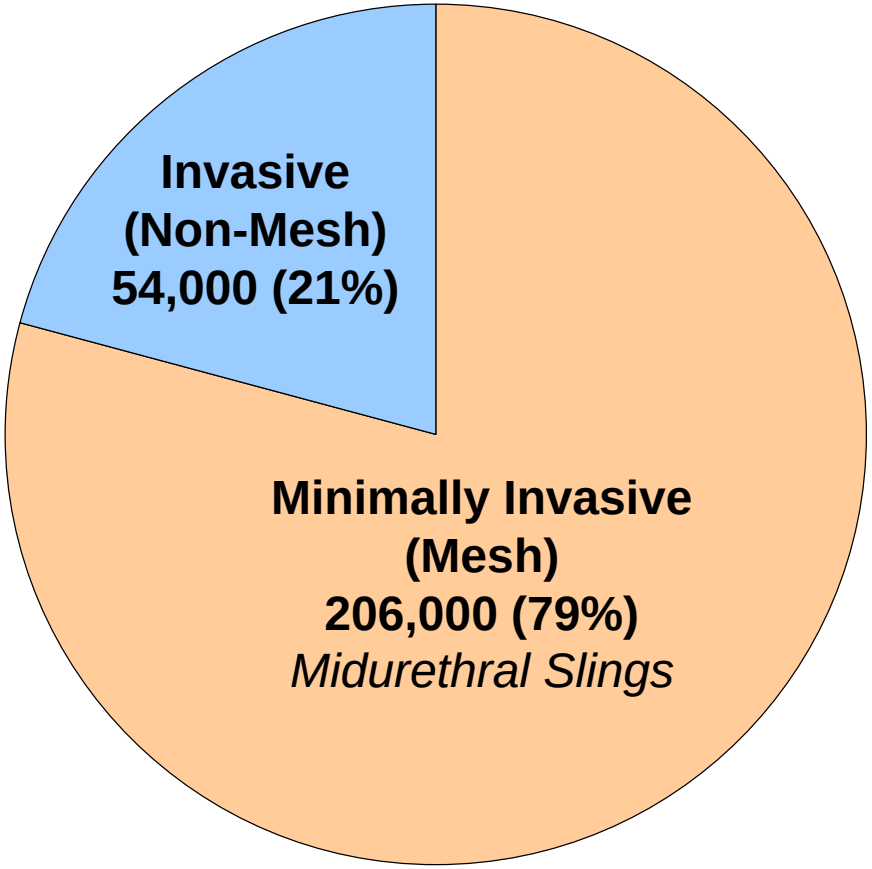
Minimally Invasive – Use Mesh

- (1st generation) suburethral mesh sling
- (2nd generation) single-incision mini-sling

* May use mesh

Surgical Procedures for SUI (2010)

Invasive and Minimally Invasive



Industry Source

1st Generation Minimally-Invasive Suburethral Slings

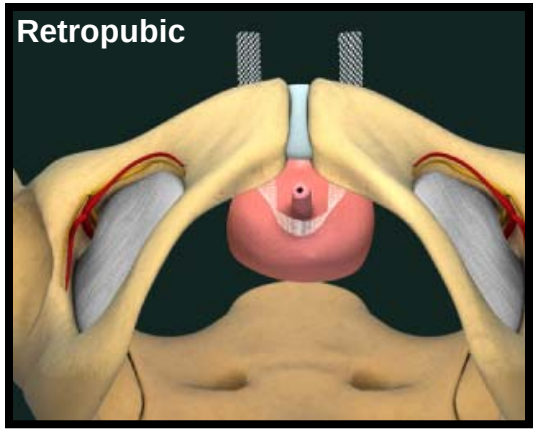
- Provide mechanical support for urethra

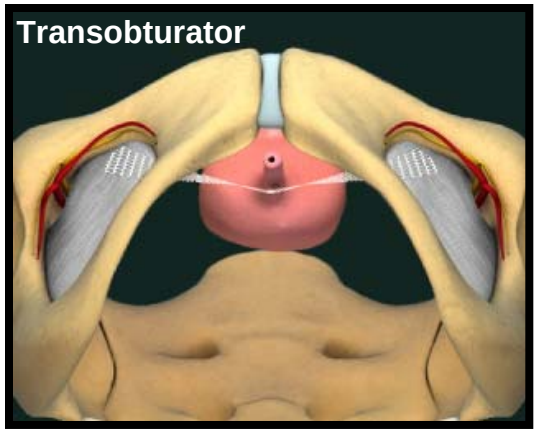
<u>Retropubic</u>

– bottom-to-top
– top-to-bottom

<u>Transobturator</u>

– medial-to-lateral
– lateral-to-medial





Images courtesy of C.R. Bard

FDA Clinical Review: Cochrane Collaboration Systematic Reviews

- Cochrane Collaboration
  - Prospective RCTs (Quality Level I evidence)*
  - (At least) one study arm randomized to mesh
  - Comparative data for all outcomes evaluated
  - Meta-analytic technique for pooling multiple data sets

* US Preventive Services Task Force

FDA Clinical Review: Cochrane Collaboration Meta-Analysis

- Definition of “cure/failure” not uniform across studies
- Uneven weighting of studies
- Possible bias (e.g. unmasked treatment arm)
- No subgroup analyses for
  - Symptoms
  - Diagnosis
  - Prior failed surgery
  - Single or multiple procedure (e.g. prolapse)
  - Surgeon experience

1st Generation Mesh Slings: Cochrane Comparative Effectiveness Outcomes

- Colposuspension vs. 1st Generation Mesh Sling[4]
  - Cochrane Meta-Analysis
  - Ward KL *et al*. 6-month, 2- and 5-year outcomes

- Mesh Sling vs. Mesh Sling[5]
  - Retropubic vs. Transobturator
  - (Retropubic bottom-to-top vs. top-to-bottom)
  - (Transobturator medial-to-lateral vs. lateral-to-medial)

[4] Lapitan MCM *et al*. Cochrane Database Sys Rev (2009)
[5] Ogah J *et al*. Cochrane Database Sys Rev (2010)

Comparative Effectiveness of Colposuspension vs. 1st Generation Mesh Slings[4]

		Open Colposuspension	1st Generation Mesh Sling	Risk Ratio (95% CI)
***1 Year* Failure**	Subjective (3 studies; N=400)	26%	31%	0.85 (0.63, 1.17)
	Objective (2 studies; N=368)	19%	19%	1.02 (0.67, 1.56)

[4] Lapitan MCM, *et al.* Cochrane Database Sys Rev (2009)

Comparative Effectiveness of Colposuspension vs. 1st Generation (Retropubic) Mesh Slings[4]

		Open Colposuspension	1st Generation Mesh Sling	Risk Ratio (95% CI)
***1-5 Year* Failure**	Subjective (2 studies; N=320)	29%	32%	0.92 (0.67, 1.26)
	Objective (2 studies; N=304)	17%	14%	1.22 (0.72, 2.06)

[4] Lapitan MCM, *et al.* Cochrane Database Sys Rev (2009)

Comparative Effectiveness of Colposuspension vs. 1st Generation (Retropubic) Mesh Slings[4a]

		Open Colposuspension (N=169)	1st Generation Mesh Sling (N=175)	P-value
6-Month Cure	Subjective*	71%	66%	0.95
	Objective∓ (ITT; withdrawals failures)	57%	66%	0.099

* Bristol Female Lower Urinary Tract Symptoms Questionnaire (e.g. any symptom of ***stress* incontinence**)

∓ Negative stress test on urodynamic testing + negative 1-hour pad test (< 1g change weight)

[4a] Ward KL *et al*. BMJ (2002)

Comparative Effectiveness of Colposuspension vs. 1st Generation (Retropubic) Mesh Slings[4b]

		Open Colposuspension (N=169)	1st Generation Mesh Sling (N=175)	P-value
***2 Year* Cure**	Subjective*	78%	79%	0.26
	Objective∓ (ITT; withdrawals failures)	51%	63%	0.02

* Bristol Female Lower Urinary Tract Symptoms Questionnaire (e.g. any symptom of ***stress incontinence***)

∓ Negative stress test on urodynamic testing + negative 1-hour pad test (< 1g change weight)

[4b] Ward KL et al. Am J Obstet Gynecol (2004)

Comparative Effectiveness of Colposuspension vs. 1st Generation (Retropubic) Mesh Slings[4c]

		Open Colposuspension (N=49)	1st Generation Mesh Sling (N=72)	P-value
***5 Year* Cure**	Subjective*	76%	71%	0.54
	Objective∓ (Evaluable Patients)	90%	81%	0.21

* Bristol Female Lower Urinary Tract Symptoms Questionnaire (e.g. any symptom of ***stress* incontinence**)

∓ Negative 1-hour pad test (< 1g change weight)

[4c] Ward KL *et al*. BJOG (2007)

Comparative Effectiveness of 1st Generation Mesh Slings (Mesh vs. Mesh)[5]

		Transobturator	Retropubic	Risk Ratio (95% CI)
1 Year Cure	Subjective (10 studies; N=1281)	85%	84%	1.00 (0.96, 1.05)
	Objective (17 studies; N=2434)	84%	88%	0.96 (0.93, 0.99)

[5] Ogah J *et al*. Cochrane Database Sys Rev (2010)

Comparative Effectiveness of 1st Generation Mesh Slings (Mesh vs. Mesh)[6]

		Transobturator (N=292)	Retropubic (N=291)	% Point Difference (95% CI)
1 Year Cure	Subjective*	56%	62%	6% (-1.6, 14.3)
	Objective∓ (Per Protocol)	78%	81%	3% (-3.6, 9.6)

* No self reported symptoms (Medical, Epidemiological and Social Aspects of Aging (MESA) Questionnaire; no leak 3-day diary)

∓ Negative provocative stress test + negative 24-hour pad test + no retreatment

[6] Richter HE *et al*. NEJM (2010)

1st Generation Mesh Slings: Comparative Safety Outcomes

- Colposuspension vs. 1st Generation Mesh Slings
- Mesh Sling v. Mesh Sling
  - Transobturator vs. Retropubic
  - (Retropubic bottom-to-top vs. top-to-bottom)
  - (Transobturator medial-to-lateral vs. lateral-to-medial)

Comparative Safety of Colposuspension vs. 1st Generation Slings (at 6-12 months)[4]

Comparative Safety of Colposuspension vs. 1st Generation Slings (at 6 months)[4a]

	Open Colposuspension (N=146)	1st Generation Mesh Sling (N=170)	RR (95% CI) P-value
Peri-operative Surgical Complications (2 studies; N=121)	8.3%	9.8%	0.85 (0.28, 2.61)
Bladder Injury Bladder Perforation (5 studies; N=653)	2% 1%	9% 7.1%	0.19 (0.07, 0.52)
Vascular Injury	0%	1%	
Voiding Difficulty (4 studies; N=501)	5.4%	5.7%	0.92 (0.46, 1.85)
Mesh Erosion	NA	1%	
Repeat Incontinence Surgery (1 study; N=316)	3.4%	1.8%	1.94 (0.47, 7.98)

[4a] Ward KL *et al.* BMJ (2002)
[4] Lapitan MCM *et al.* Cochrane Database Sys Rev (2009)

Comparative Safety of Colposuspension vs. 1st Generation Slings (at 6 months)[4a]

	Open Colposuspension (N=146)	1st Generation Mesh Sling (N=170)	P-value
Bladder Injury	2%	9%	0.013
Vascular Injury	0%	1%	1.0
Mesh Erosion	NA	1%	

[4a] Ward KL *et al.* BMJ (2002)

Comparative Safety of Colposuspension vs. 1st Generation Slings (at 5 years)[4c]

	Open Colposuspension	1st Generation Mesh Sling	P-value
Mesh Erosion	NA	3.5%	
Prolapse Surgery	7.5%	1.8%	0.025
Repeat Incontinence Surgery	3.4%	2.3%	0.74

[4c] Ward KL et al. BJOG (2007)

Comparative Safety of 1st Generation Mesh Slings[5]

	Transobturator	Retropubic	RR (95% CI)
Bladder/Urethral Perforation (18 studies; N=2674)	0.3%	5.5%	0.14 (0.07, 0.26)
Post-Op Voiding Difficulty (14 studies; N=2085)	4.3%	7.1%	0.63 (0.44, 0.89)
Vaginal Mesh Erosion (14 studies; N=2017)	2.1%	1.3%	1.58 (0.83, 3.00)
Groin pain/retropubic pain (8 studies; N=1050	12.0%	1.5%	5.95 (3.22, 11.02)
Repeat Incontinence Surgery (5 studies; N=746)	7.6%	5.1%	1.52 (0.90, 2.59)

[5] Ogah J et al. Cochrane Database Sys Rev (2010)

Comparative Safety 1st Generation Mesh Slings[6]

	Transobturator (N=299)	Retropubic (N=298)	P Value
Patients with Any Serious Adverse Event (SAE)	6.4%	13.8%	0.003
Wound-Related SAE (includes mesh erosion)	1.7%	3%	0.30
Genitourinary SAE	4.3%	7.7%	0.09
Voiding Dysfunction	0%	2.7%	0.004

[6] Richter HE *et al*. NEJM (2010)

Clinical Conclusions: 1st Generation Mesh Slings

Effectiveness

- 1st generation minimally-invasive mesh slings as effective as open colposuspension
- large body of comparative outcomes data for mesh vs. mesh demonstrates effectiveness
  - cure/failure rates ~consistent across studies
  - limited data beyond 1 year

Safety

- Vaginal mesh erosion up to 3.5%
  - vaginal erosion from SUI mesh (3.5%) lower compared to POP mesh (10%)
- Retropubic v. Transobturator trade-off
  - ↑ risk of bladder injury
  - ↑ risk of voiding dysfunction
  - ↓risk of groin pain

*Average overall incidence reported as 6% in Stanford EJ *et al* J Min Invas Gynecol (2008)

2nd Generation Slings: Single-Incision Mini-Slings

- Goal to decrease risk of:
  - groin pain
  - bladder perforation

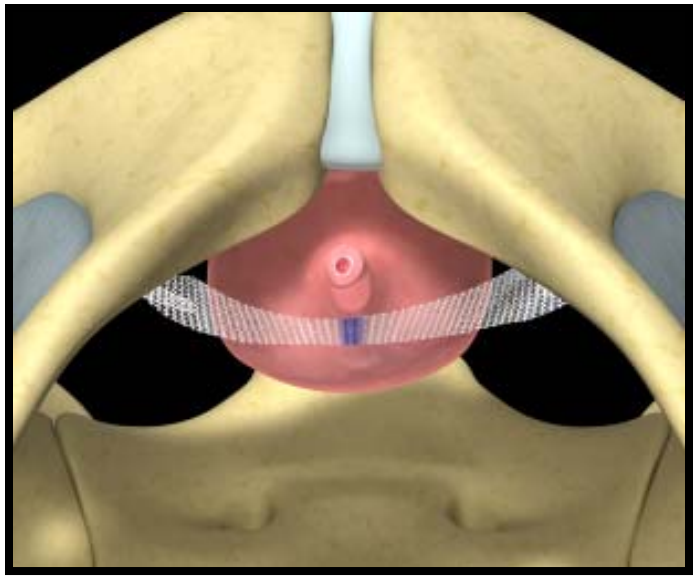


Image courtesy of C.R. Bard

Effectiveness of 2nd Generation Mesh Sling: Meta-Analysis of 12-month Outcomes[7]

- Subjective Cure 76% (8 studies; N=1024)
- Objective Cure 76% (6 studies; N=683)

[7] Walsh CA BJU Internat (2011)

Safety of 2nd Generation Mesh Sling: Meta-Analysis of 12-month Outcomes[7]

- Complications
  - Vaginal Mesh Exposure 2.4% (10 studies; N=1178)
  - Recurrent SUI 5% (5 studies; N=799)
  - De Novo Overactive Bladder 10% (8 studies; N=832)

[7] Walsh CA BJU Internat (2011)

Comparative Effectiveness of 1st Generation Mesh Sling vs. 2nd Generation Mesh Mini-Sling[8]

	1st Generation Mesh Sling (N=38)	2nd Generation Mesh Sling (Mini-Sling) (N=37)
1 Year Cure* (Objective)	81.6%	83.8%

* Cough stress test, urodynamic evaluation

[8] Tommaselli GA *et al*. Int Urogyn J (2010)

Comparative Effectiveness of 1st Generation Mesh Sling vs. 2nd Generation Mesh Mini-Sling[9]

		1st Generation Mesh Sling (N=92)	2nd Generation Mesh Sling (Mini-Sling) (N=96)	P-value
1 Year Failure	Objective*	2.4%	16.4%	0.002
	Subjective∮	8.3%	24.0%	0.008

* Standing cough stress test w/bladder volume 300cc or >70% max capacity

∮ Any incontinence episode during previous month

[9] Hinoul P *et al*. J Urol (2011)

Comparative Safety of 1st Generation Mesh Sling vs. 2nd Generation Mesh Mini-Sling[8]

	1st Generation Mesh Sling (N=38)	2nd Generation Mesh Sling (Mini-Sling) (N=37)	P-Value
Urinary Retention	5.2% (2/38)	0% (0/37)	0.49
Vaginal Erosion	0% (0/38)	2.7% (1/37)	0.49
Leg Pain	7.9% (3/38)	0% (0/37)	0.24
De Novo Urgency	2.6% (1/38)	5.4% (2/37)	0.61

[8] Tommaselli GA *et al*. Int Urogyn J (2010)

Comparative Safety of 1st Generation Mesh Sling vs. 2nd Generation Mesh Mini-Sling[9]

	1st Generation Mesh Sling (N=92)	2nd Generation Mesh Sling (Mini-Sling) (N=96)	Odds Ratio (95% CI)
Vaginal Mesh Erosion	1%	7%	7.6 (0.8, 74.0)
Reoperation for SUI within 12 months	0%	15%	2.3 (1.9, 2.7)

[9] Hinoul P *et al*. J Urol (2011)

Clinical Conclusions: 2nd Generation Mesh Slings

Effectiveness

- Possibly less effective at 12 months compared to 1st generation mesh slings
  - Meta-analysis dominated by non-randomized studies
  - limited prospective comparative outcomes data
  - Possible “learning curve” bias

Safety

- Similar types of risks as 1st generation mesh
  - Too early to quantitate level of risk

ODE Clinical Conclusions

- Premarket Review: New SUI Mesh Slings
  - No premarket data for 1st Generation Slings
  - Premarket data for 2nd Generation Mini-Slings
    - Class II comparison to 1st Generation Sling

- Post-Market Review: FDA cleared, legally marketed
  - No postmarket data for 1st Generation Slings
  - Postmarket data for 2nd Generation Mini-Slings

Surgical Mesh for SUI

Recap and Panel Questions

Jill Brown, MD/MPH, FACOG
CDR USPHS
Office of Device Evaluation

Key Messages

- Safety
  - persistent MDR signal
  - serious adverse events reported in literature
  - erosion < 5%
- Effectiveness
  - 1st generation slings as effective as non-mesh surgery; clinically accepted standard of care
- Limited data on mini-slings

Concerns with SUI Data

- Question whether existing data affords sufficient understanding of risks for all serious AEs
- Heterogeneous outcome measures may limit comparability across studies
- Majority of data 1-year follow-up
- Indication of lower success rates and higher complication rates for mini-slings

Regulatory Conclusions

- Pre-market: clinical data needed for new mini-slings (not 1st generation slings)
  - can compare to 1st generation slings
  - 510(k) still appropriate for SUI indication
  - up-classification to Class III not necessary
- Post-market: different viewpoints
  - Post-market studies needed for entire class

    vs.
  - Post-market studies only needed for mini-slings

Viewpoints on SUI Data

- One view
  - existing data does not afford sufficient understanding of risks for all serious AEs
  - postmarket data needed for entire class
- Other view
  - risks for 1st generation devices adequately characterized in existing literature
  - postmarket data only needed for mini-slings

- Asking Panel to weigh in on these questions

Thank you!

Questions?

Panel Questions

Question 1 Part a:

Effectiveness of surgical mesh for SUI repair

Considering the available evidence, is there reasonable assurance that first-generation minimally invasive suburethral slings for SUI repair are effective?

Question 1 Part b:
Safety of surgical mesh for SUI repair

- Is the list of risks prepared by FDA complete and accurate?
- Given the available evidence on incidence and severity of these adverse events, is there reasonable assurance of safety?

Question 1 Part c

Surgical mesh for SUI repair

Considering the available evidence, do the benefits outweigh the risks?

Question 1 Part d

Surgical mesh for SUI repair

- Are clinical studies needed before FDA clears/approves new surgical mesh products for SUI repair?
- If yes, what type(s) of clinical studies?
  - Consider patient selection/exclusion (e.g., concomitant surgeries), outcome measures, follow-up duration, and controls.

Question 1 Part e

Surgical Mesh for SUI Repair: Postmarket Studies

- Are postmarket studies needed for currently marketed surgical mesh products for SUI repair?
- If so, what type(s) of studies are needed?

Question 2 Part a

Single incision mini-slings

Based on the available scientific evidence, is there adequate safety and effectiveness data to support the use of single-incision mini-slings?

Question 2 Part b

Single incision mini-slings

- Are clinical studies needed before FDA clears/approves new single incision mini-slings?
- If yes, what type(s) of clinical studies?
  - Consider patient selection/exclusion (e.g., concomitant surgeries), outcome measures, follow-up duration, and controls.

Question 2 Part c

Single incision mini-slings: Postmarket Studies

- Are postmarket studies needed for currently marketed single incision mini-slings?
- If so, what type(s) of studies are needed?
  - Consider patient selection/exclusion (e.g., concomitant surgeries), outcome measures, follow-up duration, and controls.

Thank You