Surgical Mesh for Transvaginal Repair of Pelvic Organ Prolapse in the Anterior Vaginal Compartment

Obstetrics and Gynecology Devices Panel

FDA Presentation

February 12, 2019

Presentation Overview

- Background
  - Kelly Colden, MD, MPH
- Medical Device Reports (MDRs) Published Literature
  - Jacqueline Cunkelman, MD, MPH
- Benefit/Risk Assessment
  - Angie Lee, MD

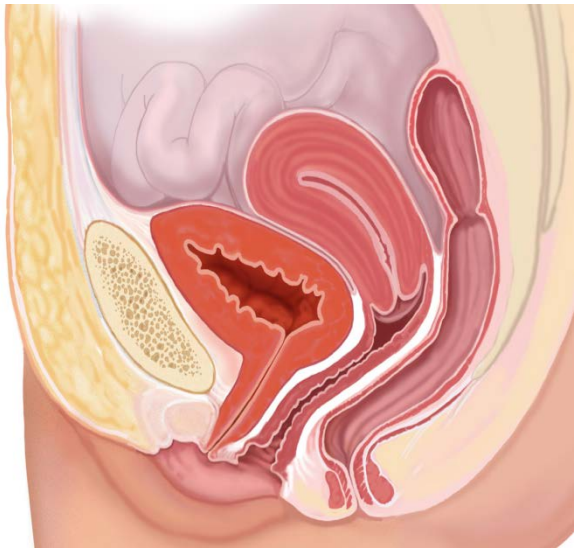
Background

Kelly Colden, MD, MPH, FACOG
Center for Devices and Radiological Health
Office of Device Evaluation

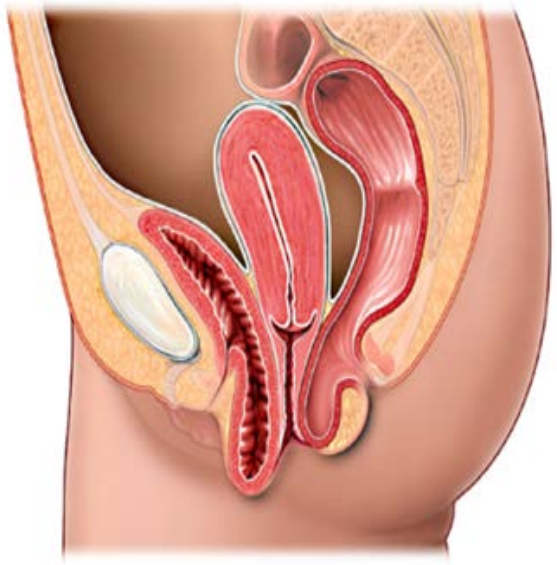
Outline

- Clinical Overview
- Device Description
- Regulatory History

Pelvic Organ Prolapse (POP)



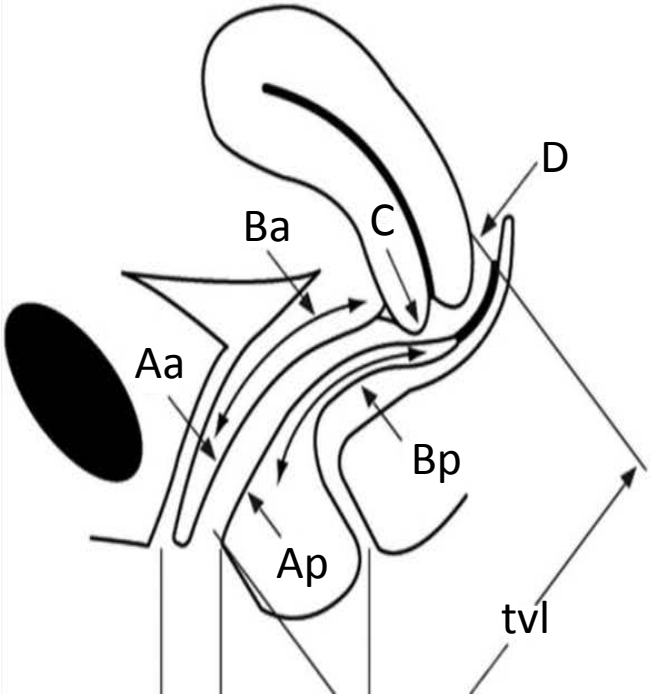
Normal



Cystocele

STAGING OF PROLAPSE

Pelvic Organ Prolapse Quantification (POP-Q) System



Point	Description	Range of Values
Aa	Anterior vaginal wall 3 cm proximal to the hymen	-3 cm to +3 cm
Ba	Most distal position of the remaining upper anterior vaginal wall	-3 cm to +tvl
C	Most distal edge of cervix or vaginal cuff scar	
D	Posterior fornix (N/A if post-hysterectomy)	
Ap	Posterior vaginal wall 3 cm proximal to the hymen	-3 cm to +3 cm
Bp	Most distal position of the remaining upper posterior vaginal wall	-3 cm to + tvl

Genital hiatus (gh) – Measured from middle of external urethral meatus to posterior midline hymen
Perineal body (pb) – Measured from posterior margin of gh to middle of anal opening
Total vaginal length (tvl) – Depth of vagina when point D or C is reduced to normal position

Rosati et al 2013

POP-Q System (cont.)

POP-Q Staging Criteria	
Stage 0	Aa, Ap, Ba, Bp = -3 cm and C or D ≤ – (tvl – 2) cm
Stage I	Stage 0 criteria not met and leading edge < -1 cm
Stage II	Leading edge ≥ -1 cm but ≤ +1 cm
Stage III	Leading edge > +1 cm but < + (tvl – 2) cm
Stage IV	Leading edge ≥ + (tvl – 2) cm

Rosati et al 2013

Risk Factors

- Advanced age
- Previous vaginal delivery
- High Body Mass Index (BMI)
- Race/ethnicity
- Previous hysterectomy or prolapse surgery

SYMPTOMS AND TREATMENT

Symptoms

- Most asymptomatic
- Varied symptoms: sensation of bulge, discomfort/pain, incontinence, and dyspareunia
- Treatment depends on type/severity of symptoms, compartment/stage, and age

Symptomatic POP-Treatment

Conservative/Non-surgical

- Pelvic floor exercises
- Pessaries

Surgical

- Transvaginal Repair
  - Mesh Augmentation
  - Native Tissue Repair
- Abdominal (sacrocolpopexy)

DEVICE DESCRIPTION

Surgical Mesh for POP

- Non-configured, Pre-configured
- Non-absorbable synthetic, absorbable synthetic, biologic, composite
  - Non-absorbable synthetic mesh described by type (1-4), classified by weave and density
  - Mesh from biologic material (human, bovine, porcine), cross-linked/non-cross-linked

Surgical Mesh for POP (cont.)

- Type I polypropylene
  - BSC Uphold LITE
  - Coloplast Restorelle DirectFix Anterior
- Fetal bovine, non-cross-linked
  - BSC Xenform

Boston Scientific Uphold LITE

Coloplast Restorelle DirectFix Anterior

Boston Scientific Xenform

REGULATORY HISTORY

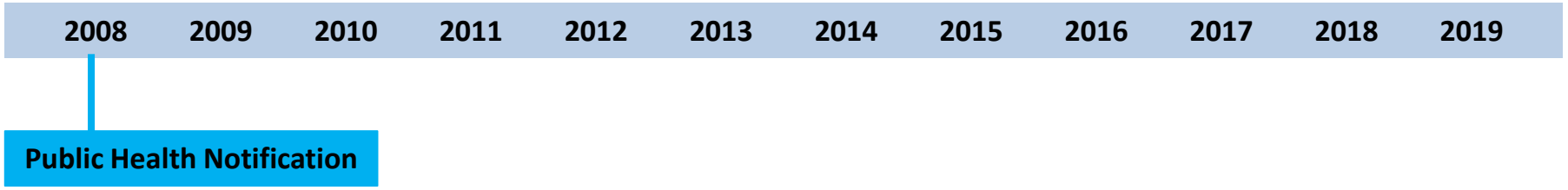
Regulatory History

- Surgical Mesh placed in Class II (21 CFR 878.3300) in 1988
  - Historically (1950s) General Surgery use for abdominal hernia repair
  - GYN use of hernia mesh for abdominal repair of POP 1970s and vaginal repair of POP 1990s

Regulatory History

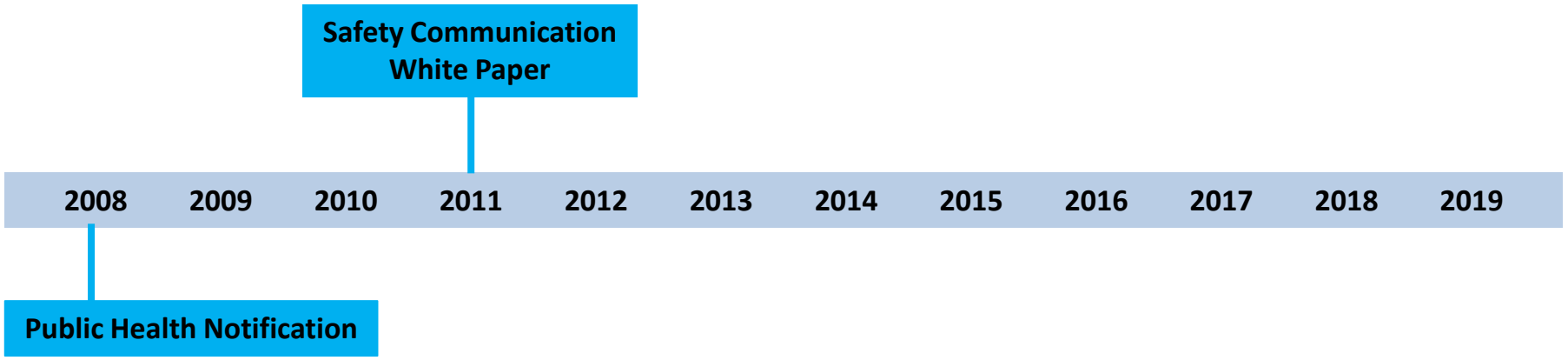
- 1996-510(k), Surgical Fabrics (ProteGen Sling)
- 2002-Pre-Configured, Gynemesh® PS
- 2004-Mesh Kits, AMS Apogee/Perigee Systems

FDA Regulatory Actions



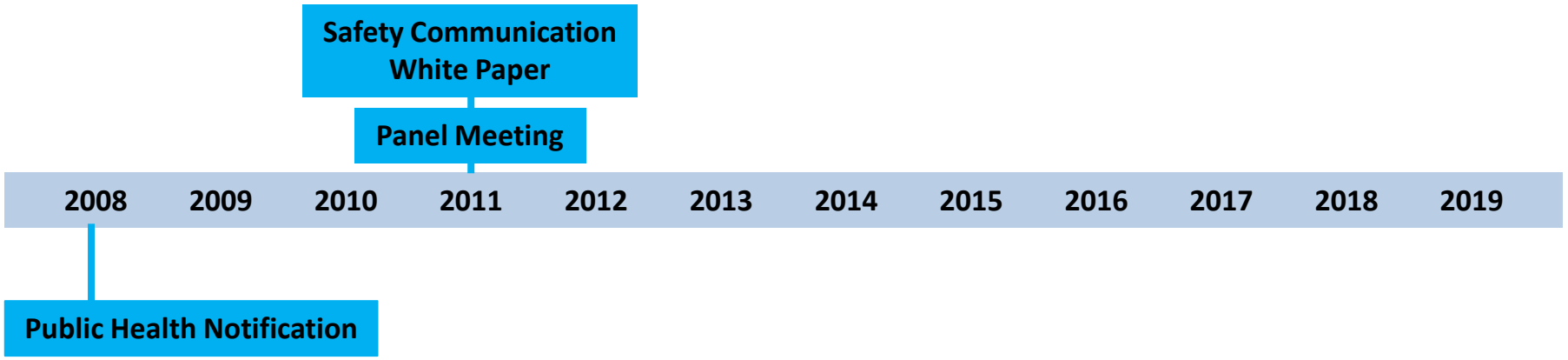
October 2008, Public Health Notification

FDA Regulatory Actions



July 13, 2011, Safety Communication "UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse" and White Paper, "Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse"

FDA Regulatory Actions



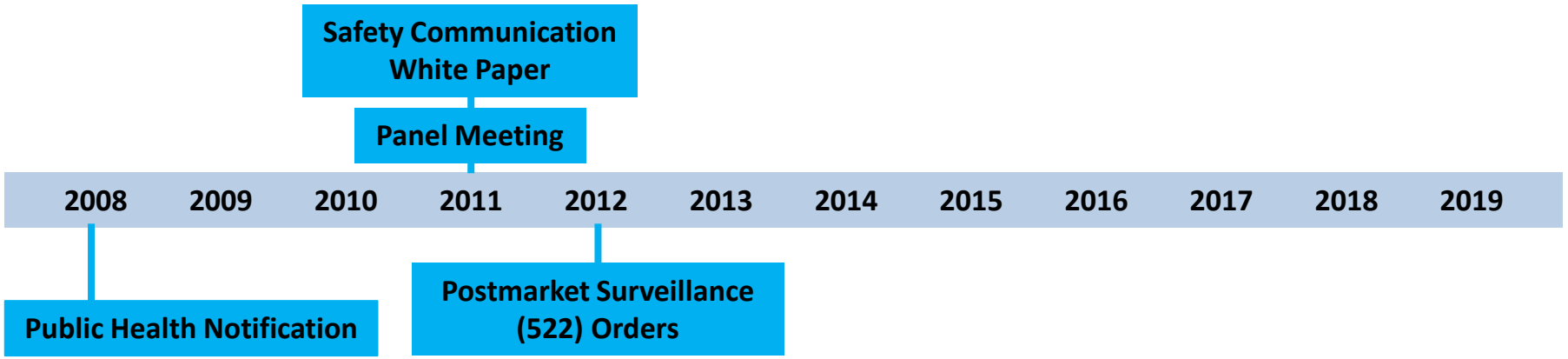
September 2011, Obstetrics and Gynecology Devices Panel of the Medical Device Advisory Committee

- Goal: Discuss safety and effectiveness of surgical mesh to treat POP and stress urinary incontinence (SUI)

2011 Panel Meeting

- Safety of surgical mesh for transvaginal POP repair not well established
- Depending on repair compartment, transvaginal placement of surgical mesh for POP repair may not be more effective than NTR
- Devices should be reclassified from class II to class III
- Issuance of postmarket surveillance study orders

FDA Regulatory Actions

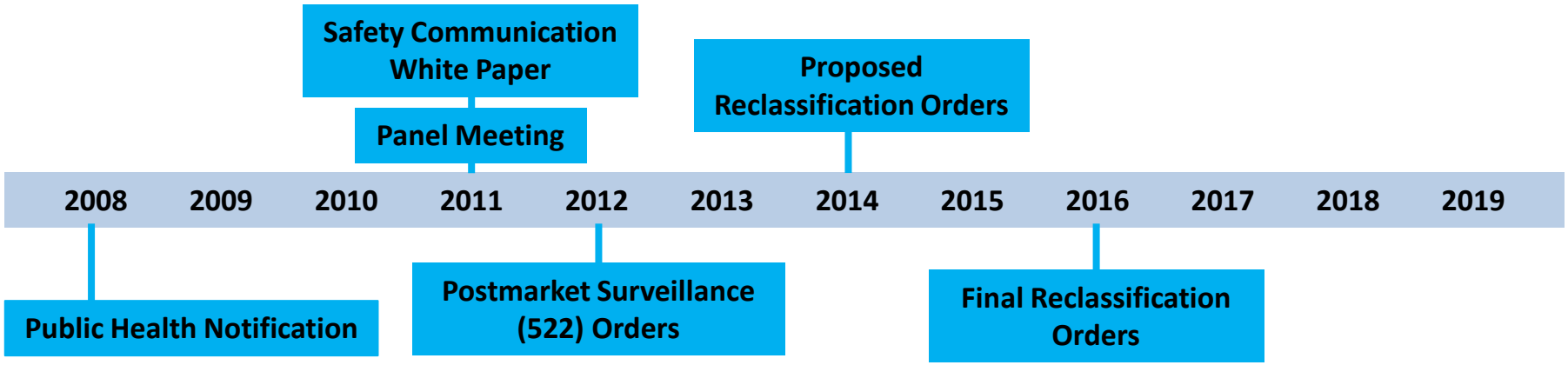


- January 2012, ordered manufacturers conduct postmarket surveillance studies (522 studies) to address specific safety and effectiveness concerns

522 Orders-Study Design

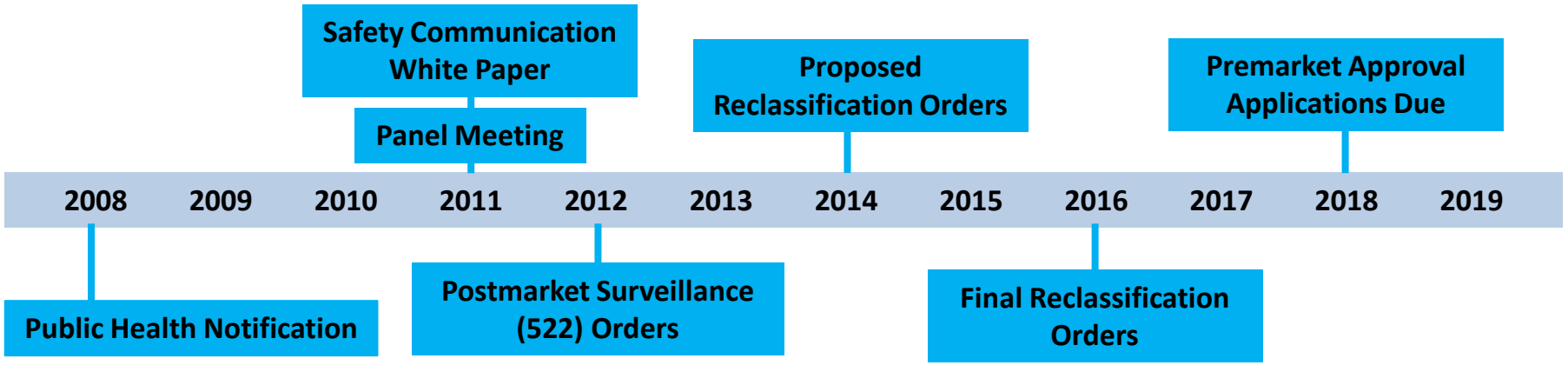
- Randomized controlled study or parallel cohort study comparing subject device to native tissue repair
- Effectiveness endpoints
  - anatomic/objective success
  - subjective success
  - retreatment for prolapse
- Safety endpoints
  - all device and procedure related adverse events
  - rate of individual adverse events of interest (mesh erosion, de novo urinary dysfunction, de novo dyspareunia, etc.)

FDA Regulatory Actions



- January 2016-Final Orders:
  - Reclassified surgical mesh for transvaginal POP repair-class II to class III (81 FR 353)
  - Required filing of PMA for surgical mesh (81 FR 363)

FDA Regulatory Actions



Premarket Approval Application

- Most stringent type of marketing application
- Approval based on valid scientific evidence to assure device is safe and effective each device reviewed based on individual data provided

Regulatory Actions Outside of the United States (OUS)

- May 2014, Health Canada-updated notice to hospitals regarding use of mesh placed transvaginally to treat POP/SUI
- December 2017, Australian Therapeutic Goods Administration (TGA)- “benefits of using transvaginal mesh products in the treatment of pelvic organ prolapse do not outweigh the risks these products pose to patients”
- 2018, United Kingdom and Ireland-pause on use of all surgical mesh placed transvaginally for POP/SUI
- 2018, Scotland-stopped all transvaginal mesh procedures until development/implementation of new ‘restricted use protocol’

PROFESSIONAL SOCIETY POSITIONS

Professional Society Positions

July/Aug 2012

- American Urogynecologic Society (AUGS) Guidelines for Providing Privileges and Credentials to Physicians for Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse

March 2013

- AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders

Professional Society Positions

<u>September/October 2017</u>

- (AUGS) Best Practice Statement: Evaluation and Counseling of Patients With Pelvic Organ Prolapse
  - "Surgeons offering various surgical treatments should be aware of the data on efficacy and complications of those procedures and offer these data to the patient during counseling."

Professional Society Positions

American College of Obstetricians and Gynecologists (ACOG) and AUGS joint publications

April 2017

- Committee Opinion, Management of Mesh and Graft Complications in Gynecologic Surgery

November 2017

- Practice Bulletin, Pelvic Organ Prolapse

Overview of Clinical Evidence

Jacqueline Cunkelman, MD, MPH
Center for Devices and Radiological Health
Office of Device Evaluation

Overview of Clinical Evidence

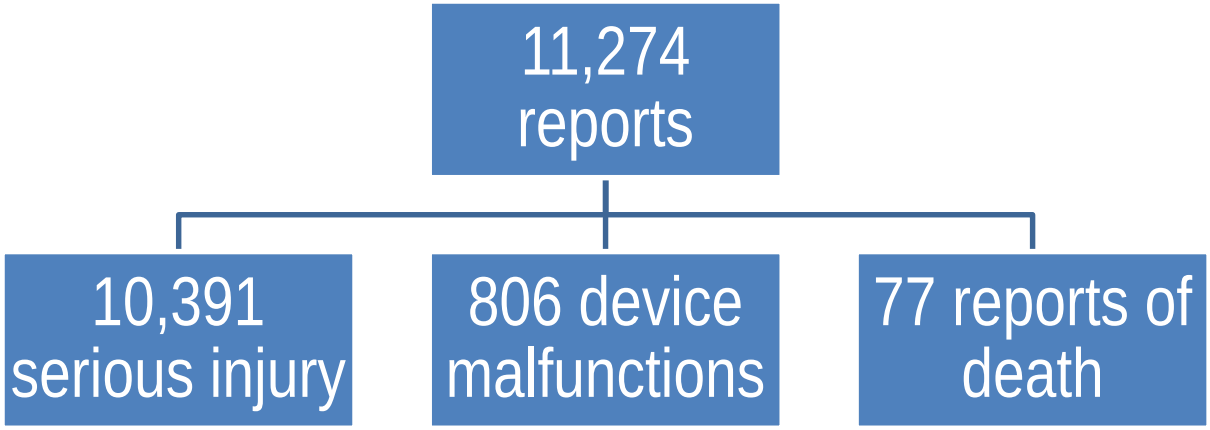
- Medical Device Reports
- Literature Review

FDA U.S. FOOD & DRUG ADMINISTRATION

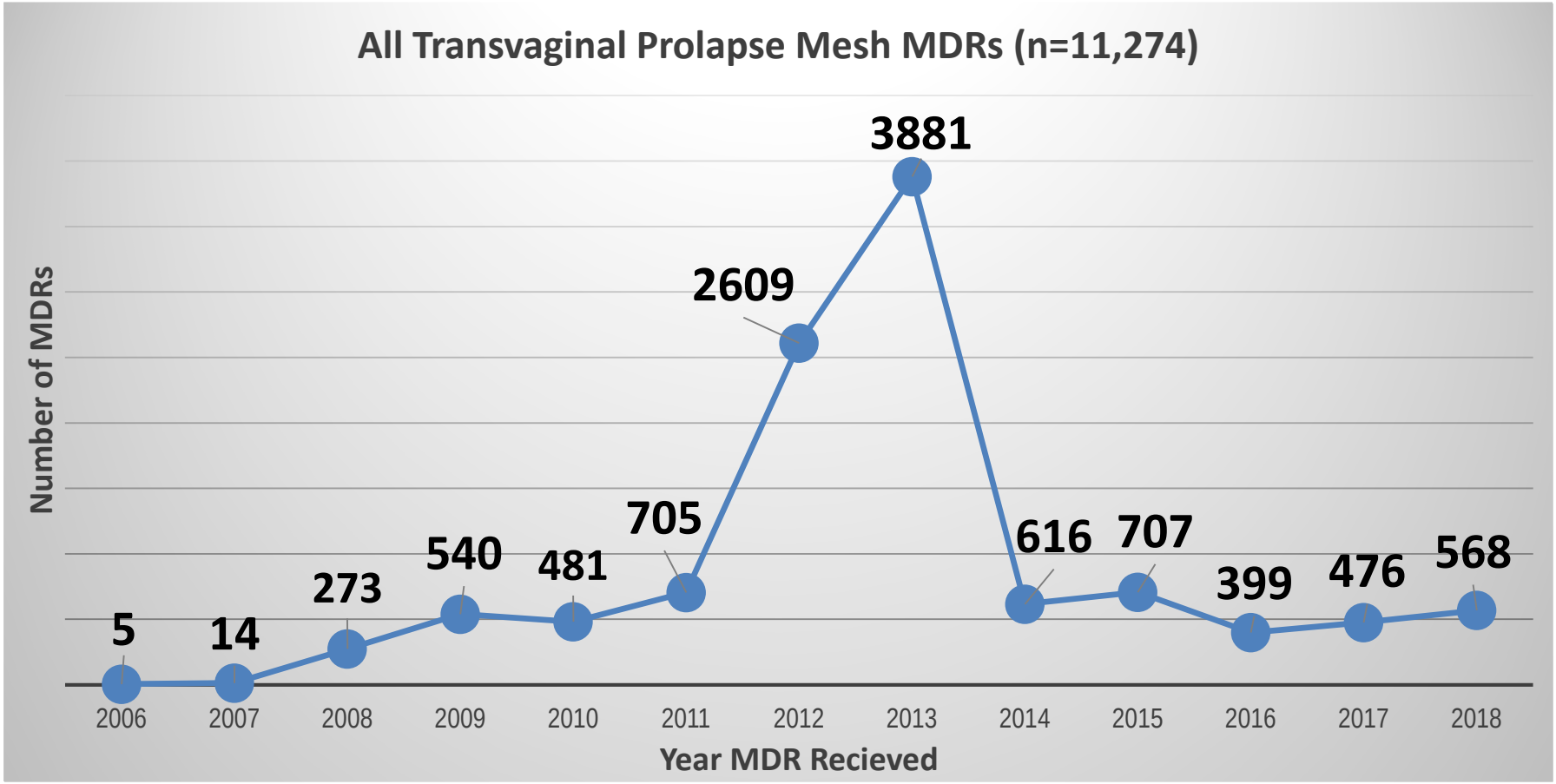
Medical Device Reports

Search Methods

- Date range January 1, 2008-September 30, 2018
- Specific to anterior/apical repair



MDR Trend by Year—All Anterior Mesh



Top MDRs –All Anterior Mesh

	Patient Problem	Count
1	Pain	3717
2	Erosion/Exposure	3509
3	Infection	1794
4	Injury	1701
5	Incontinence	814
6	Scar Tissue	761
7	Bleeding	475
8	Infection, Urinary Tract	371
9	Disability	339
10	Neurological Deficit/Dysfunction	272

Panel Question #3

The following adverse events have been associated with mesh and/or native tissue repair and are being collected in the 522 studies:

- Pelvic pain
- Erosion/exposure
- Dyspareunia
- De novo voiding dysfunction (e.g., incontinence)
- Infection
- Vaginal shortening
- Atypical vaginal discharge
- Neuromuscular problems
- Vaginal scarring
- De novo vaginal bleeding
- Fistula formation

Please discuss these adverse events and consider their importance, potential to be debilitating, how they should be assessed, when they should be assessed, and key considerations related to the mesh material or other mesh characteristics. Please also comment on any important adverse events that may be missing.

Limitations

- Cannot establish or compare rates
- Report ≠ Causation
- Data is highly susceptible to reporting bias
- MDR data is not comprehensive

U.S. FOOD & DRUG ADMINISTRATION

Literature Review

Literature Review

- Methods and Limitations
- Effectiveness
- Safety
- Concomitant Procedures
- Patient Characteristics
- Surgeon Characteristics

U.S. FOOD & DRUG ADMINISTRATION

Literature Review
Methods and Limitations

Search Methods

January 1, 2008-November 1, 2018

The PubMed database was searched using the following search strategy:

("pelvic organ prolapse"[MeSH terms]) AND ("surgical mesh" OR "transvaginal mesh" OR "vaginal mesh")

Methods

Eligibility Criteria:

1. English
2. Relevant to transvaginal mesh (any brand/type) used for anterior and/or apical pelvic organ prolapse repair; mesh repair for posterior prolapse must include anterior/apical as well
3. Clinical research study with live human participants OR meta-analysis of randomized controlled trials
4. Clinical outcome data (safety and/or effectiveness) for at least 12 months of follow-up, and N ≥ 25 patients
5. For cohort studies: prospectively collected data relevant to at least one device of interest

Result:

Methods

Study designs of the 73 papers included for analysis:

- Randomized controlled trials (RCT): N=39
- Prospective cohort with a device of interest (Uphold/Uphold LITE, Restorelle, or Xenform): N=8
- Large database or registry study: N=14
- Meta-analysis of RCTs: N=9
- Markov analysis: N=3

Limitations

- Length of follow-up
- Heterogeneity of study design
  - Inclusion/exclusion criteria, age, concomitant procedures, definitions of success, classifications of adverse events, devices evaluated (not all available in the US), etc.

FDA U.S. FOOD & DRUG ADMINISTRATION

Literature Review

Effectiveness

FDA Position & Panel Question #1

In light of its increased risks compared to native tissue repair, to demonstrate reasonable assurance of effectiveness, FDA believes that surgical mesh used in the anterior or anterior/apical vaginal compartment for transvaginal prolapse repair should be superior to native tissue repair. Does the Panel agree?

- If yes, at what timepoint should superiority be demonstrated, e.g., 12, 24, 36 months, or longer?
- If no, how should the effectiveness of mesh compare to native tissue repair and at what timepoint should the effectiveness be assessed?
- Does the Panel have additional comments related to the mesh material (e.g., polypropylene or non-crosslinked biologic) or other mesh characteristics ?

FDA Position & Panel Question #2

The FDA literature review identified that while anatomic/objective outcomes generally favor mesh, subjective outcomes demonstrate similar effectiveness for mesh and native tissue repair. FDA believes that both anatomic/objective and subjective outcomes should be used to assess the effectiveness of transvaginal anterior or anterior/apical mesh repair compared to native tissue repair.

- Does the Panel agree that both objective and subject outcomes should be used to assess the effectiveness of mesh compared to native tissue repair?
- If the Panel agrees that both anatomic/objective and subjective outcomes should be used to assess effectiveness, should improvement in both outcomes be required to consider a patient to be a success? Why or why not?
- Should the assessment of anatomic/objective outcomes be completed by a blinded evaluator?
- FDA believes improvement or resolution of patient symptoms are an important component in demonstrating effectiveness of a mesh versus native tissue repair. Please address the following:
  - How should symptoms be measured (e.g., validated questionnaire)?
  - How should we assess if a patient has a meaningful/significant improvement (e.g., what if a patient has symptoms but is not bothered by the symptoms)?
  - How is a patient's assessment of her symptoms affected by sexual activity (or other patient factors) (e.g., would a patient who is not sexually active find her prolapse less bothersome compared to a sexually active patient)?
  - When patients are not blinded to their treatment (mesh or native tissue repair), how might that affect their assessment of symptoms?
- Does the Panel have additional comments related to the mesh material or other mesh characteristics?

Literature Review - Effectiveness

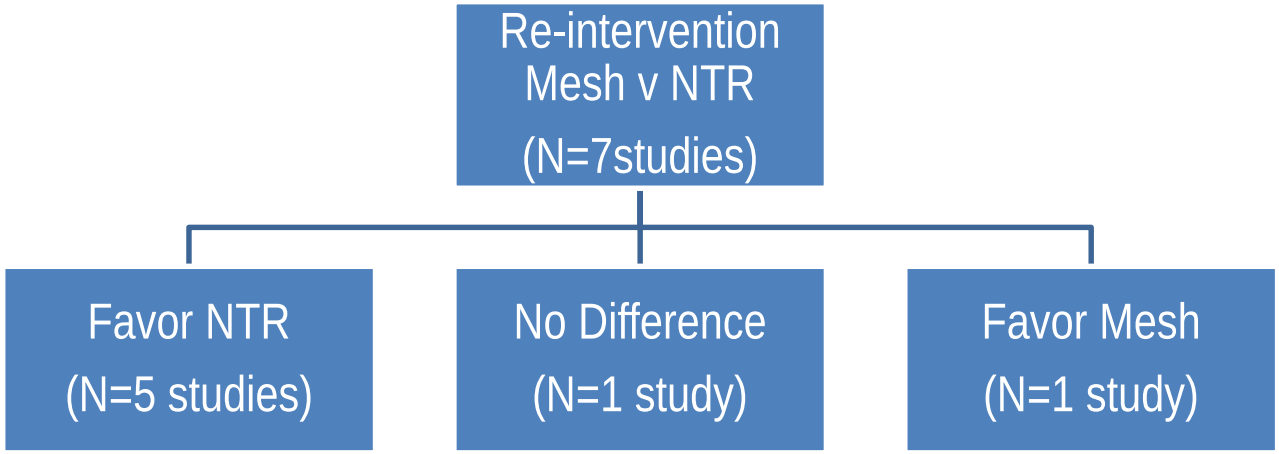
- Meta-analyses
- Database Studies
- Randomized Controlled Trials
- Prospective Cohort Studies
- Markov Analyses
- Effectiveness by Timepoint
- Effectiveness by Material
- Conclusions

Effectiveness—Meta-analyses RCTs

Favor Mesh	• Objective cure • Surgery for recurrent POP
No Difference	• Subjective outcomes—satisfaction, QoL, sexual function
Favor NTR	• Re-operation, including mesh complications

Effectiveness—Databases

Overall rate of re-operation 5-6% for mesh patients for 1-5 years of follow-up.



One registry reported subjective outcomes (cure, satisfaction, improvement, feeling of protrusion) → favored mesh (Jonsson Funk, 2013).

Effectiveness—RCTs

Generally favor mesh for objective outcomes; similar for subjective outcomes for 1-3 years follow-up.

Largest trial—NIHR-funded PROSPECT—found no significant differences in POP-Q/re-operation for synthetic mesh or biologic graft compared to NTR.

(Glazener, 2016) (Glazener, 2017)

Effectiveness—Prospective Cohorts

Uphold/Uphold LITE (4 studies)	Xenform (1 study)	Restorelle (2 studies)
• Objective cure 94-97% • Composite cure 74-97% • Reoperation 1-7% • No difference compared to NTR (1 study)	• Improvement in objective/subjective outcomes at 12 months.	• Objective cure 92-95% • Reoperation 8.5%

Effectiveness—Markov Analyses

30-70% probability of re-operation for recurrent apical prolapse over 2 years of follow-up compared to NTR

(Dieter, 2015)

Effectiveness by Material

Mixed results
Polypropylene may have advantage over biologic graft when compared to NTR

(Maher, 2017)

Effectiveness by Timepoint

Longest follow-up (5 years) for apical repair (Truven MarketScan and Medicare databases)

No significant differences in re-operation for recurrent prolapse between mesh and native tissue repair

(Dandolu, 2017) (Jonsson Funk, 2013)

Re-intervention is not limited to the 1st year post-implantation.

(Forde, 2017)

Effectiveness Conclusions

- Between 1-3 years follow up, mesh may have some advantage over NTR for objective, but not subjective, outcomes.
- Mesh outcomes are similar to NTR over 5 years, but mesh complications may lead to higher rates of re-operation.

FDA U.S. FOOD & DRUG ADMINISTRATION

Literature Review Safety

FDA Position & Panel Question #4

To demonstrate reasonable assurance of safety, FDA believes the adverse event profile for mesh placed in the anterior or anterior/apical vaginal compartment should be comparable to native tissue repair, or any increase in risk should be offset by a corresponding improvement in effectiveness. FDA also believes that all adverse events (not just those adjudicated as device or procedure related adverse events or serious adverse events) should be considered, along with their severity/seriousness, timing, resolution, and relatedness to the device and/or procedure should be used to evaluate the safety of mesh compared to native tissue repair.

- Does the Panel agree with this approach?
- What are the effectiveness scenarios where an increased safety risk may be acceptable (e.g., patient with recurrent prolapse)?
- At what timepoint should comparable safety (or increase in risk offset by a corresponding improvement in effectiveness) be demonstrated, e.g., 12, 24, 36 months, or longer ?
- Does the Panel have additional comments related to the mesh material or other mesh characteristics?

Literature Review - Safety

- Erosion/Exposure
- De Novo SUI
- De Novo Dyspareunia
- Other Adverse Events
- Safety by Timepoint
- Safety by Material
- Conclusions

Safety—Erosion/Exposure

FDA Review Meta-Analysis

- 3-15%

Cochrane Review

- 11.3% Anterior
- 18% Apical

(Maher, 2016) (Maher, 2017)

Safety—SUI

Cochrane Review (Maher, 2017)

- De novo SUI—mesh v NTR similar
- Overall SUI—biologic v NTR no difference
- Not enough evidence—absorbable mesh v NTR

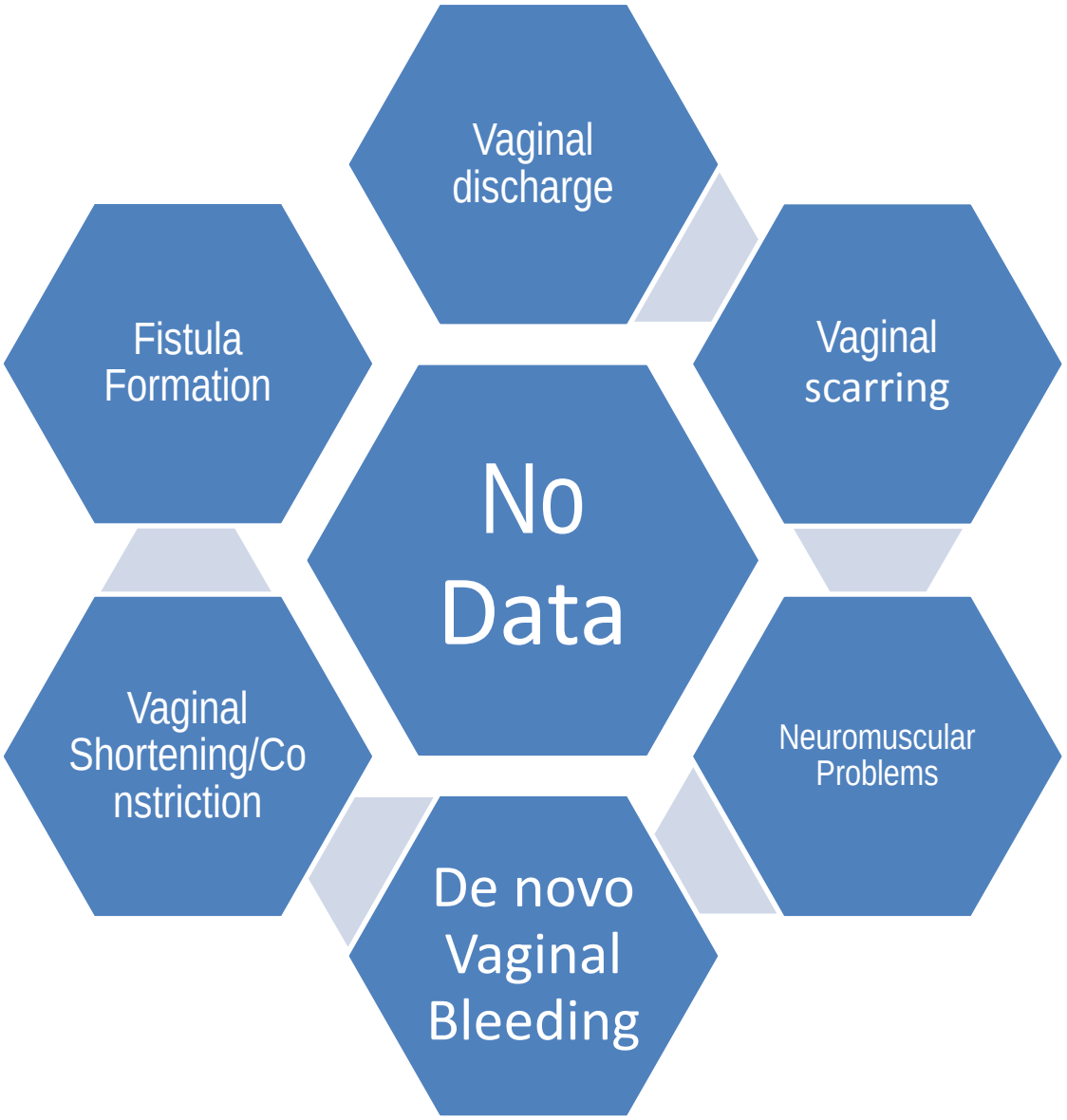
RCTs/Database Studies

- Mixed results

Safety—Dyspareunia

- Meta analyses ➡ No significant between group differences in dyspareunia/de novo dyspareunia.
- One RCT reported a small but significant difference in dyspareunia at 1 yr (2.7% mesh, 0% NTR). (Rudnicki, 2014)
- Other papers were mixed—either not significant or not tested.

Safety—Other



Adverse Events—Timepoint

At 12-36 months follow-up, most studies favored the NTR.

Primarily due to mesh erosion/exposure rates for the mesh arm; higher rates of de novo dyspareunia and de novo SUI were also observed in the mesh arm.

Adverse Events—Mesh Material

- The PROSPECT RCT reported that mesh-related complications were higher in patients who received synthetic mesh (6% versus <1% in native tissue repair); complications were similar between biologic and native tissue repair (both <1%). (Glazener, 2016) (Glazener, 2017)
- Compared to biologic graft, polypropylene mesh is associated with a higher rate of erosion (6.3% v 0%) (Natale 2009)
- Goldstein (2010) reported no graft related erosions or pain lasting more than 30 days when using Xenform
- Polypropylene mesh is associated with a higher rate of erosion (1 year) than partially absorbable (polypropylene with polyglycolic acid/caprolactone) (Farthmann 2013)

Safety—Conclusions

- All timepoints favor NTR
- Complications continue beyond the first year of follow up and through 5 years
- Mesh complications are more common for synthetic mesh than for biologic graft
- The risks of using mesh in the anterior vaginal compartment are greater than native tissue repair, particularly with respect to re-operation for all indications

Clinical Factors and Benefit/Risk

Angie Lee, MD, FACOG
Center for Devices and Radiological Health
Office of Device Evaluation

Outline

- Patient Population
- Patient Characteristics
- Surgeon Characteristics
- Benefit/Risk Assessment

Patient Population

Panel Question 5: Patient Population

The FDA literature review identified concomitant procedures (hysterectomy and sling placement) and surgical/medical history (age, obesity, current level of sexual activity, parity, premenopausal estrogen therapy, diabetes, and smoking) that may affect the safety or effectiveness outcomes of an anterior or anterior/apical mesh or native tissue repair.

a. Does the Panel agree that the identified concomitant procedures and surgical/medical history may affect the safety or effectiveness of a mesh or native tissue repair?

b. Which additional concomitant procedures or surgical/medical history could affect the safety or effectiveness outcomes of mesh or native tissue repair in the target compartment?

c. How should FDA factor concomitant procedures and surgical/medical history in its interpretation/evaluation of study results (e.g., balance of these characteristics between study arms, assessment of adverse events associated with concomitant procedure vs primary procedure)?

Concomitant Procedures

- Another surgery may be required at the time of the transvaginal prolapse repair of the anterior vaginal compartment
- Concomitant procedures may affect safety and effectiveness outcomes
- Challenging to distinguish between outcomes

Concomitant Procedures

- Effect on patient assignment
  - Some women prefer uterine-sparing surgery
- Most common concomitant procedures
  - Midurethral sling
  - Hysterectomy

Most Common Concomitant Procedures

- Midurethral sling for SUI
- Hysterectomy

Concomitant Midurethral Sling

Author	Patient dataset	Concomitant sling in mesh prolapse repair group	Concomitant sling in non-mesh/NTR prolapse repair group	Concomitant sling in prolapse repair surgery (mesh and non-mesh)
Chughtai 2015	NY SPARCS	20.0%	14.4%	
Jonsson Funk 2013	MarketScan database	70.6%	62.4%	
Anger 2014	Medicare beneficiaries	48.2%		15%

- Concomitant sling at time of POP surgery is fairly common

Concomitant Midurethral Sling & Erosions/Reoperations

Chughtai 2017	With concomitant sling	Without concomitant sling (POP repair only)
Erosions	2.7%	1.9%
Reoperations	5.6%	4.3%

- Higher rates of mesh erosion and reoperation with concomitant sling

Most Common Concomitant Procedures

- Midurethral sling
- Hysterectomy

Concomitant Hysterectomy

Author	Patient dataset	Concomitant hysterectomy in mesh prolapse repair group	Concomitant hysterectomy in NTR prolapse repair group
Jonsson Funk 2013	MarketScan database	18.4%	38.3%
Dandolu 2017	Truven CCAE, Medicare Supplemental databases	9.2%	23.5%
Chughtai 2015	New York Statewide Planning and Research Cooperative System (SPARCS)	38.5%	51.3%

- Concomitant hysterectomy at time of POP surgery is fairly common

Concomitant Hysterectomy & Mesh Erosion/Exposure

FDA

More Erosion

- 1.46x more mesh erosion (95% CI: 1.03-2.07), Deng 2016

More Exposure

- 3.8x more mesh exposure (95% CI: 1.46-9.89), Farthmann 2013

No Difference

- No significant difference in 3-yr reintervention rates, Forde 2017

Patient Characteristics

Panel Question 6: Patient Population

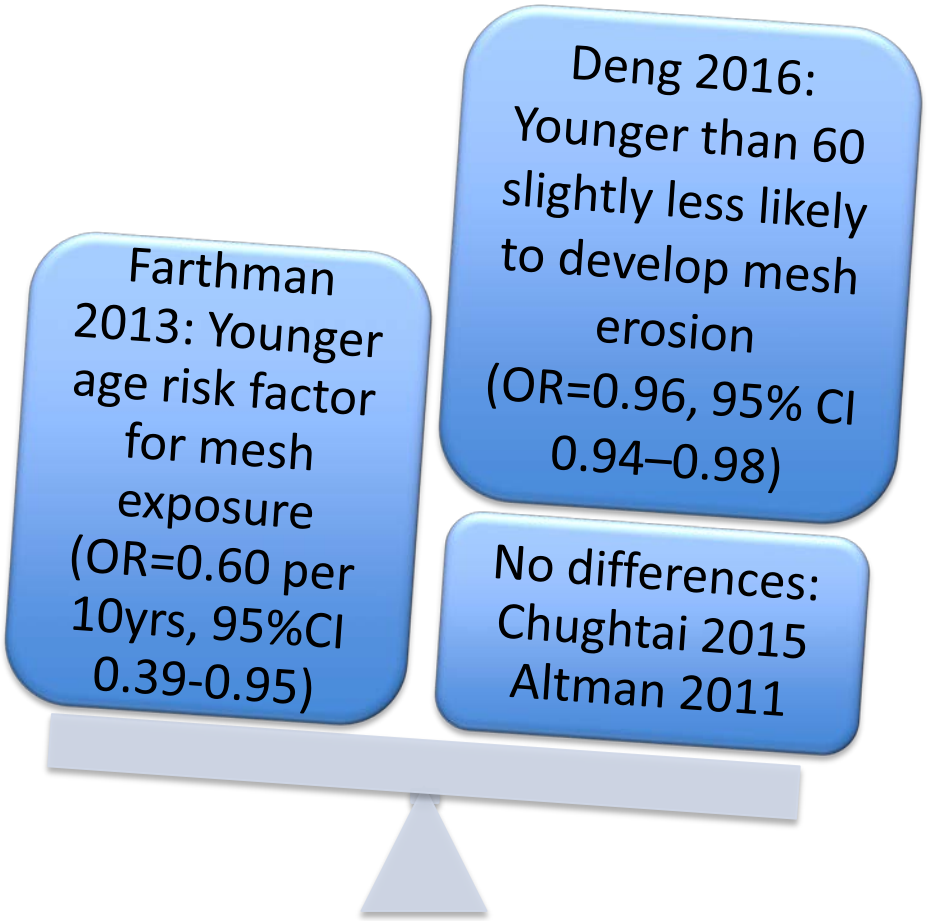
In non-randomized studies, selection bias can influence safety and effectiveness outcomes. FDA believes the following factors may determine whether a patient undergoes a mesh versus native tissue repair.

- Patient (e.g., recurrent prolapse, severity of prolapse, age, obesity, sexual activity, parity, other surgical/medical history)
- Procedure (e.g., need for a concomitant procedure)
- Clinical Site (e.g., whether site offers only mesh versus native tissue repair, whether the site is a specialty center for one type of repair)
- Surgeon (e.g., experience with mesh versus native tissue repair, surgeon preference based on individual patient characteristics)

Please discuss how these factors or any additional factors may bias the safety and effectiveness outcomes of a native tissue or mesh repair.

Patient Characteristics - Age

Mixed evidence that age affects treatment outcomes



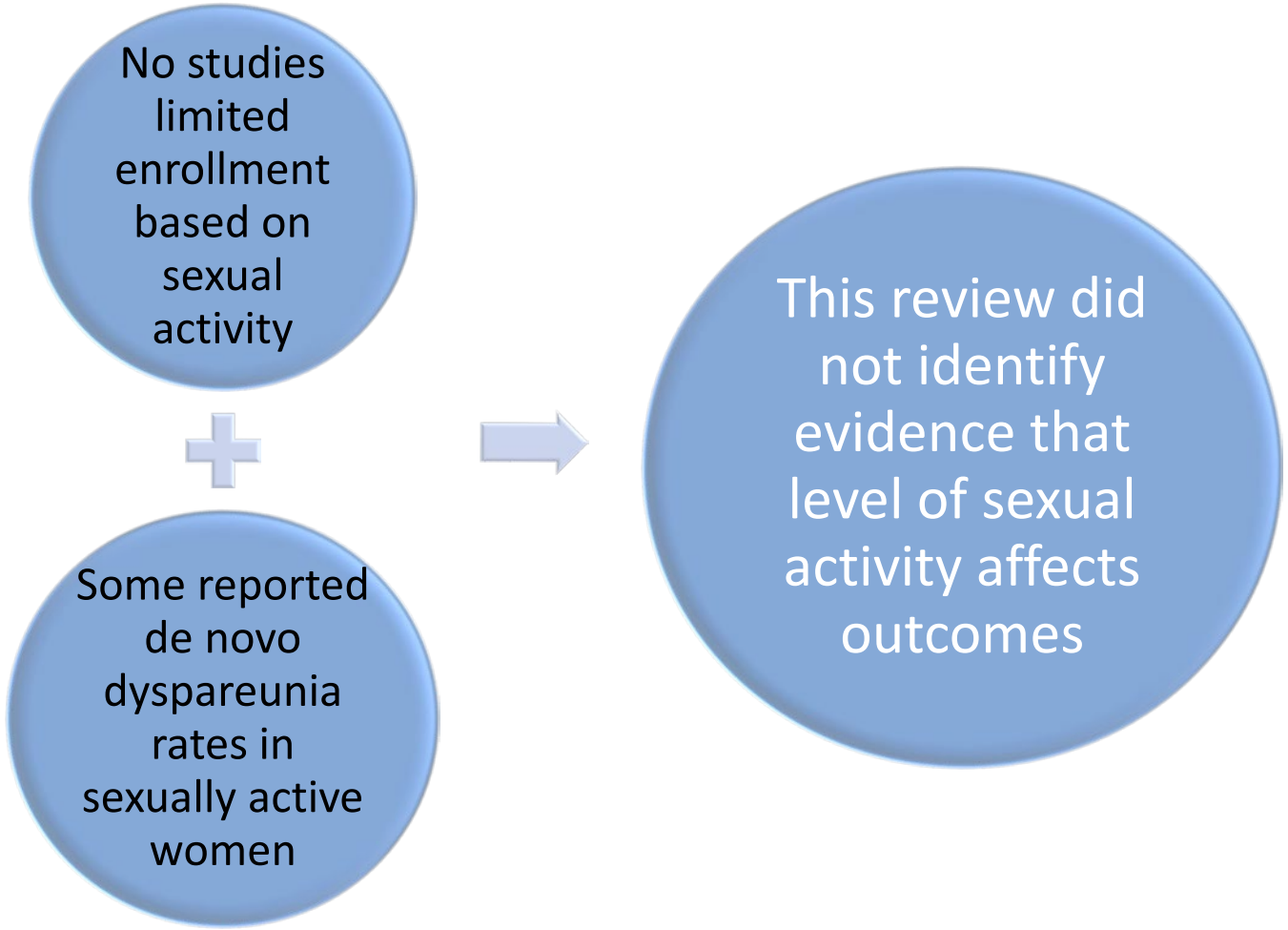
Patient Characteristics - Obesity

Mesh erosion and exposure – no significant differences with BMI

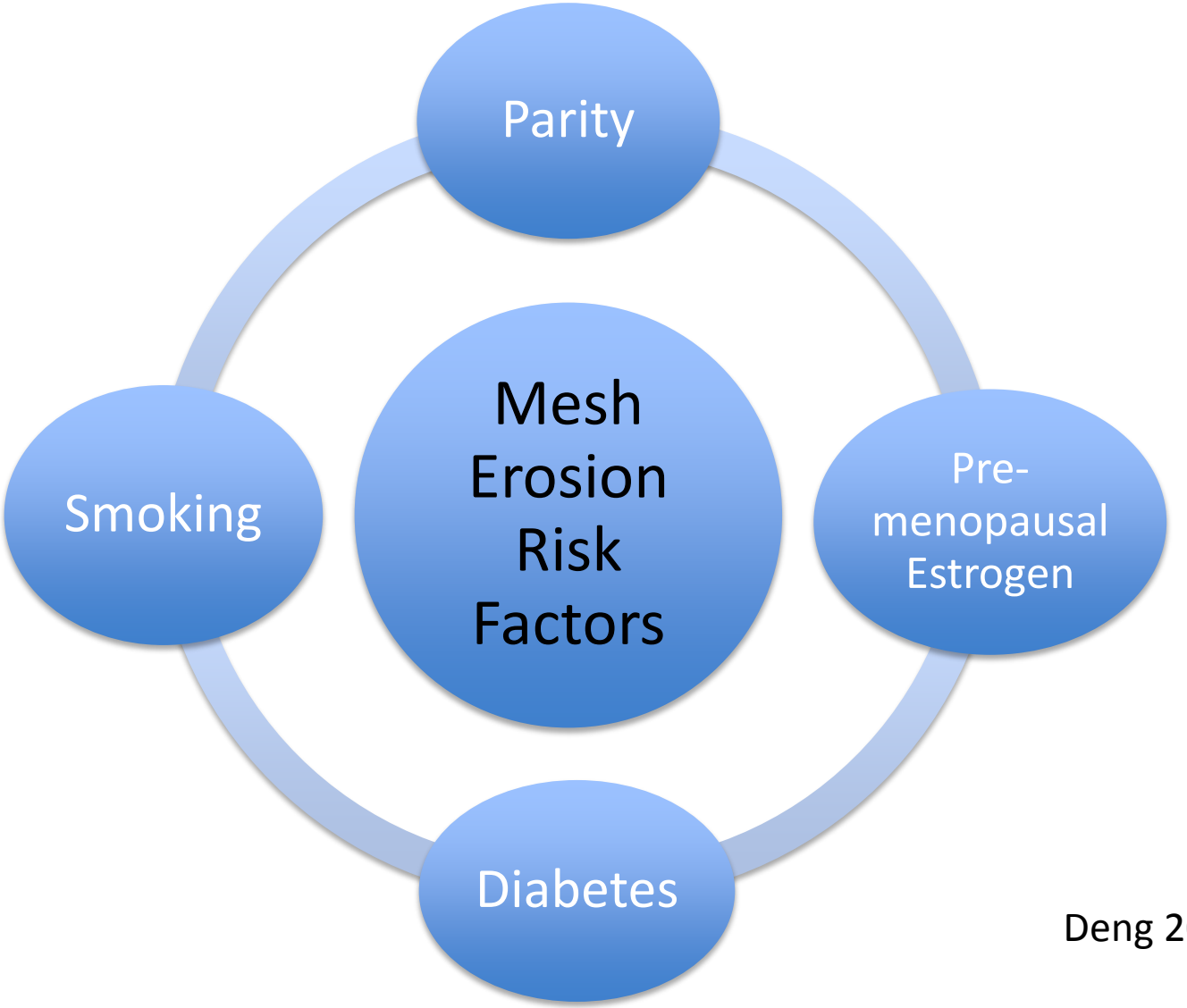
Mesh erosions
Deng 2016

Mesh exposures
Farthmann 2013

Patient Characteristics – Sexual Activity Level

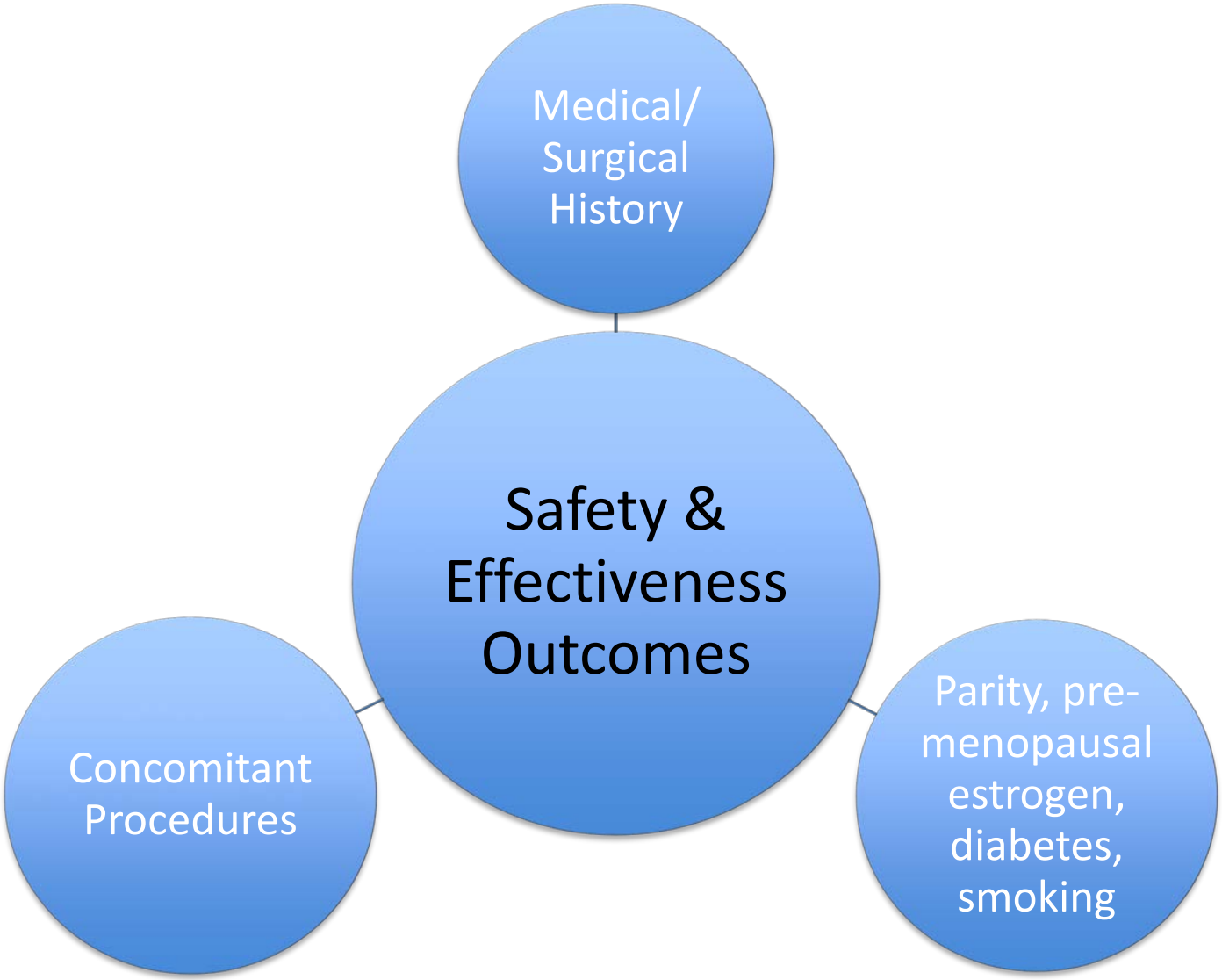


Patient Characteristics – Other



Deng 2016

Recap of Patient Characteristics



Surgeon Characteristics

Panel Question 7: Training

The FDA literature review indicated that surgeon experience may affect safety and effectiveness outcomes of a mesh or native tissue repair.

a. Please comment on how a physician's level of training and experience affects safety and effectiveness outcomes for mesh versus native tissue repair.

b. How should FDA incorporate the level of training and experience of investigators in a clinical study in its interpretation/evaluation of study results (e.g., need for comparable experience between study arms, clinical study results may not reflect real world results)?

Surgeon Experience

- Low volume mesh surgeons- higher reoperation rates

	Low volume (1 case per yr)	Intermediate (2 cases per yr)	High volume (3+ cases per yr)
Reoperation Rate per Eilber 2015	6%	2%	3%

- More than half of procedures performed by low volume surgeons
- 4% reoperation rate for both gynecologists and urologists

High-volume surgeons

- *"We observed lower reoperation rates among high-volume surgeons and propose that increased surgeon experience has an influential role in outcomes of vaginal surgery with mesh."*

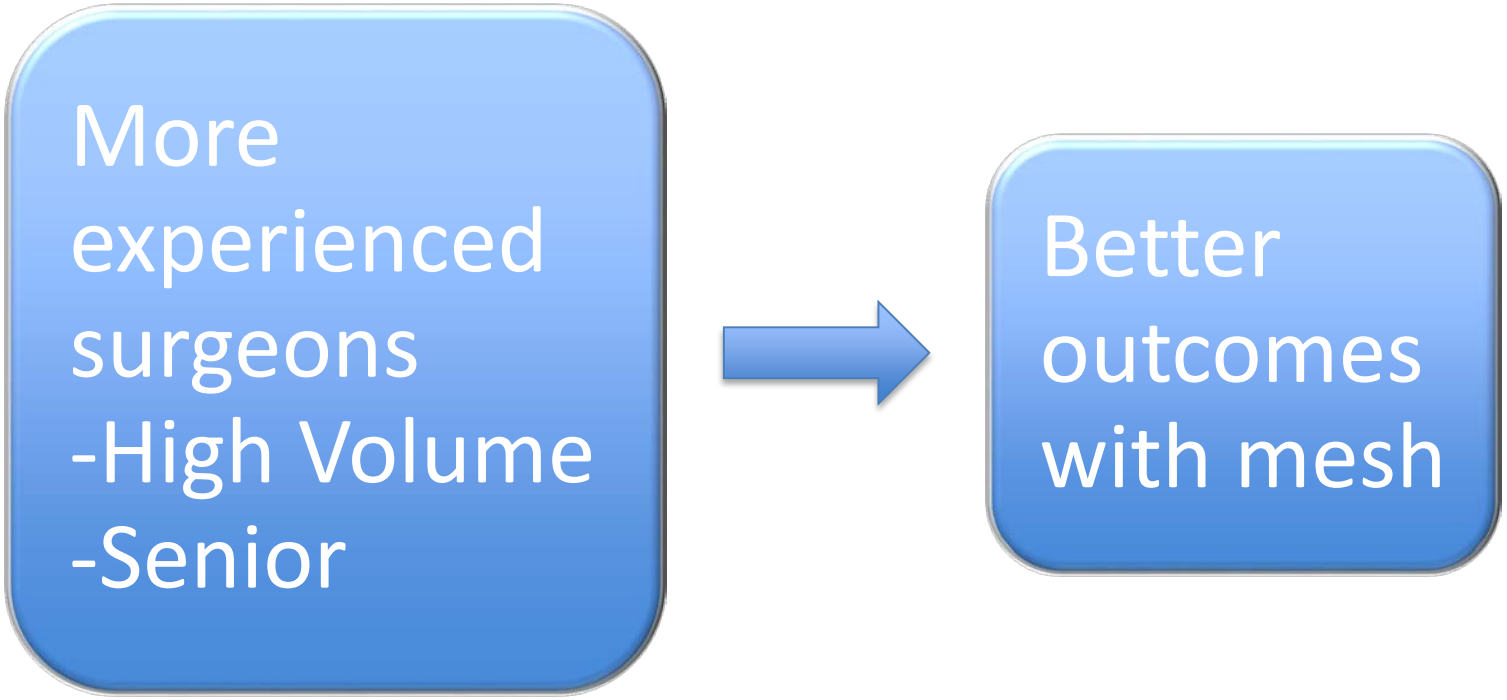
  - Eilber 2015

Senior surgeons – lower mesh erosions

Mesh erosion risk was significantly lower in patients who had surgery performed by a senior surgeon compared to a junior surgeon (OR 0.42, 95% CI 0.30–0.58, $p < 0.001$)

Deng 2016

Recap of Surgeon Characteristics



Benefit/Risk Assessment

Panel Question 8: Benefit/Risk

Surgical mesh for transvaginal repair of POP in the anterior or anterior/apical compartment is an implant, and its benefit/risk profile may change over time.

a. What is the appropriate expectation for the durability of a mesh repair and native tissue repair (e.g., remainder of the patient's lifetime)?

b. How quickly should the data demonstrate the benefit of a mesh repair versus a native tissue repair?

c. In broad terms, a device subject to PMA is approved for marketing when the benefit/risk profile is favorable for its proposed indications for use, with a reasonable assurance of safety and effectiveness. In light of this, what is the most appropriate time point to assess benefit/risk to support a marketing application, e.g., 12, 24, 36 months, or longer?

d. What is the appropriate duration of follow up needed to support marketing approval versus the follow up needed postmarket? What data should be collected postmarket? Please consider rare adverse events, long term durability, and use of real world evidence to collect safety and effectiveness outcomes.

e. Does the Panel have additional comments related to the mesh material or other mesh characteristics?

Benefit/Risk Assessment

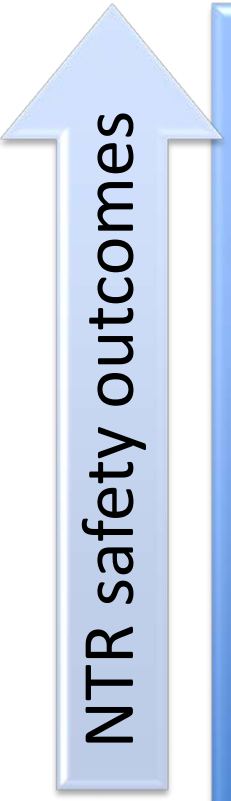
Comparison should be made to native tissue repair

-Randomized control trial or parallel cohort study

Use of surgical mesh should offer an advantage over the same repair without use of mesh

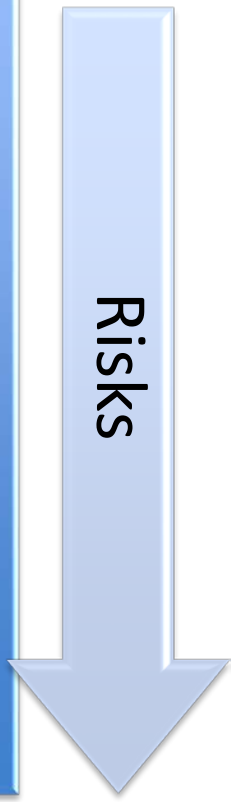
- Advantage over the lifetime of the repair
- Or may be specific to a certain patient population

Benefit/Risk Assessment



Evidence from RCTs favor safety outcomes of native tissue repair at 12, 24, and 36 months

- Mesh risk profile less favorable than native tissue repair
- Mesh exposure/erosion rate ~ 11-18%
- Mesh exposure/erosion may require further surgery
  - Some mesh adverse events will increase over time
  - Mesh-specific adverse events can occur as late as 3 yrs postop



Benefit/Risk Assessment

Comparison should be made to native tissue repair

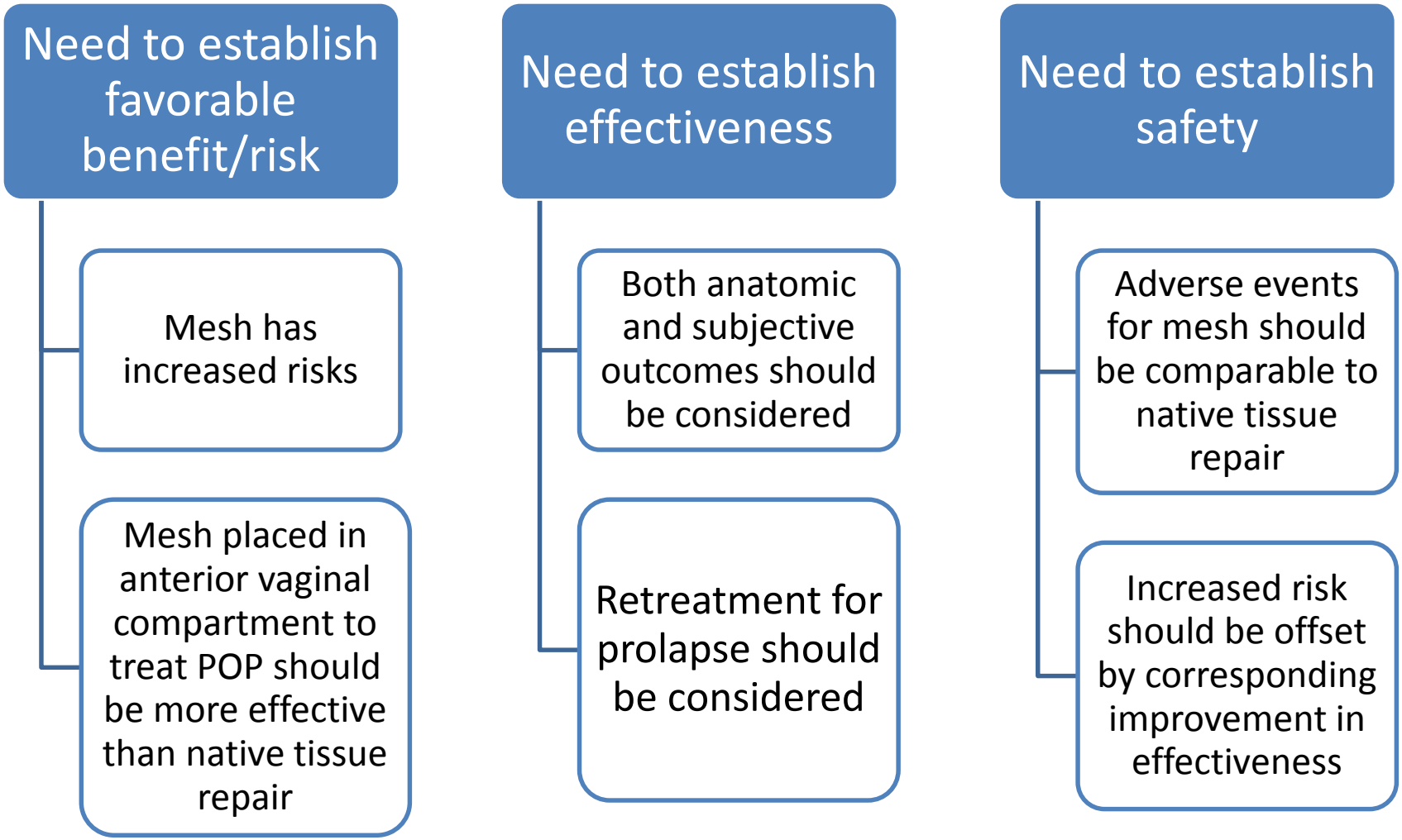
-Randomized control trial or parallel cohort study

Use of surgical mesh should offer an advantage over the same repair without use of mesh

- Advantage over the lifetime of the repair
- Or may be specific to a certain patient population

All adverse events should be considered (not just those adjudicated as device- or procedure-related), along with their severity, timing, resolution, and relatedness to the device and/or procedure

Benefit/Risk Assessment



Benefit/Risk Assessment

Permanent implant should establish a long term favorable benefit/risk assessment

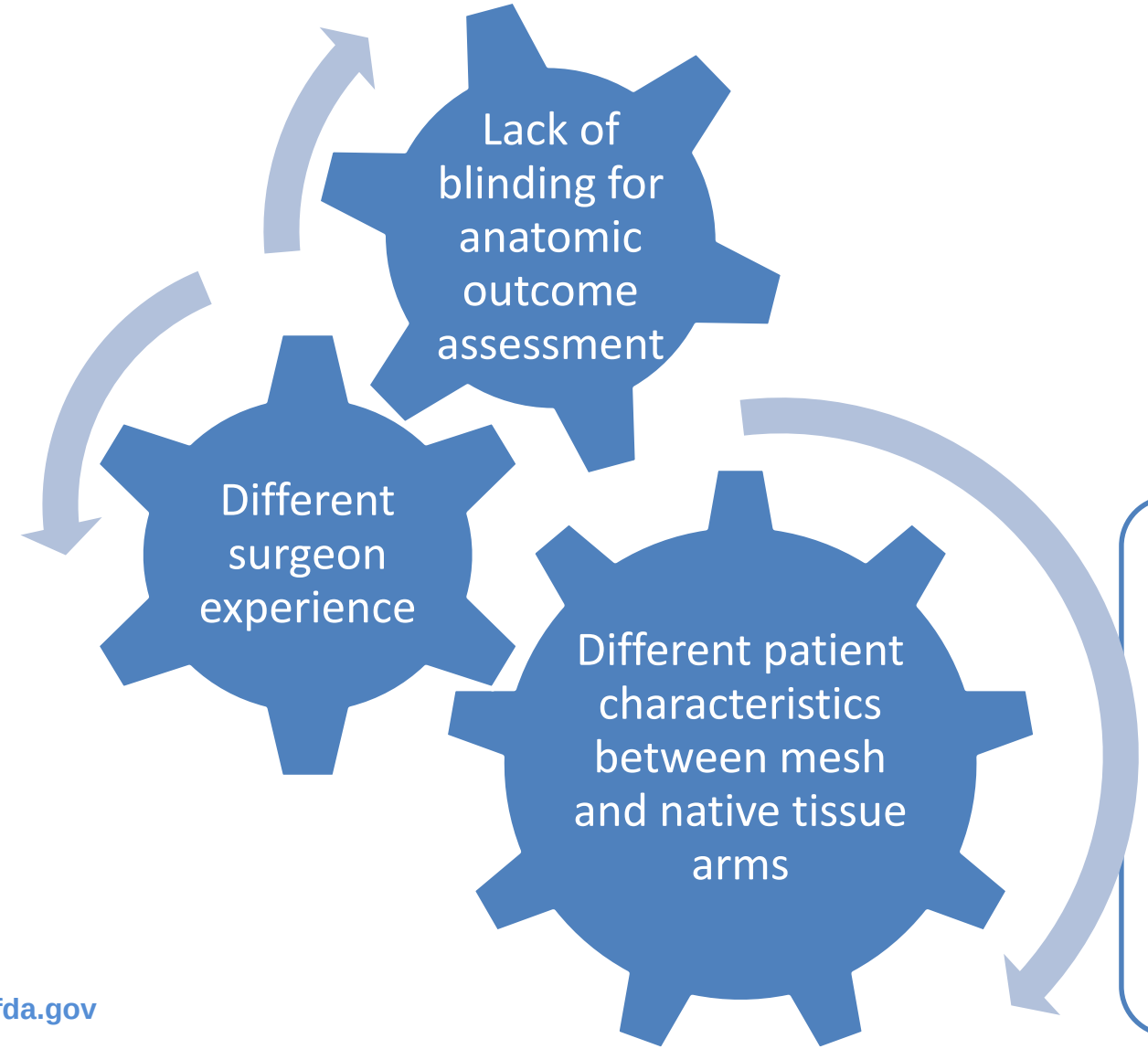
Safety and effectiveness outcomes beyond 12-months are necessary

Continued postmarket follow up

- Long term adverse events
- Durability of the repair

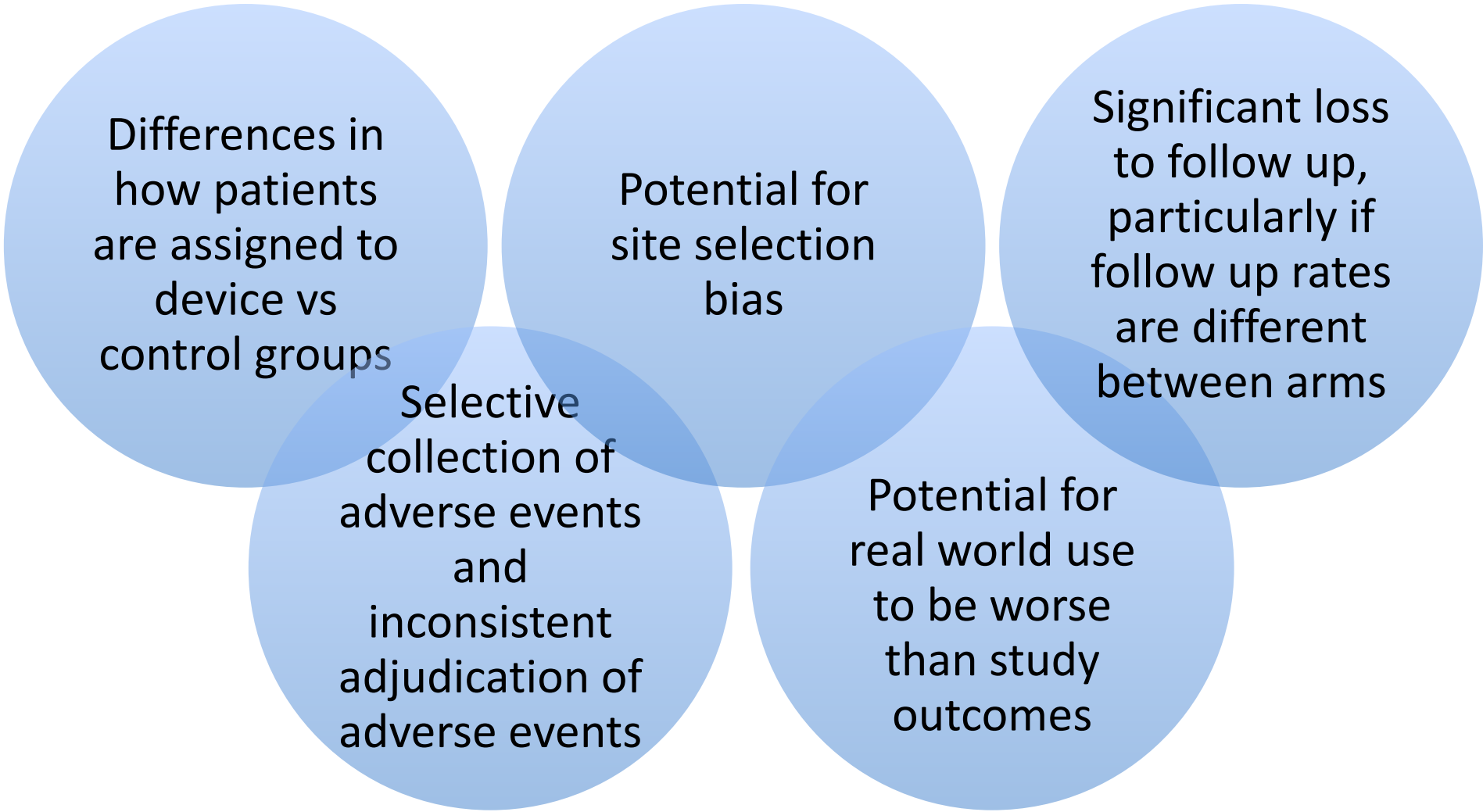
Currently, there are limited long term data, particularly beyond 3 years

Challenging Benefit/Risk Assessment



- Severity of prolapse
- Age
- Sexual activity
- BMI
- Menopausal status
- Medical and past surgical history
- Concomitant procedures

Challenging Benefit/Risk Assessment



Conclusion

Challenging Benefit/Risk assessment

Request expertise and input of the Panel

U.S. FOOD & DRUG ADMINISTRATION

Panel Questions to FDA


FDA
U.S. FOOD & DRUG
ADMINISTRATION