Full Cycle Safety and Quality Management Model Based on National Registry Database

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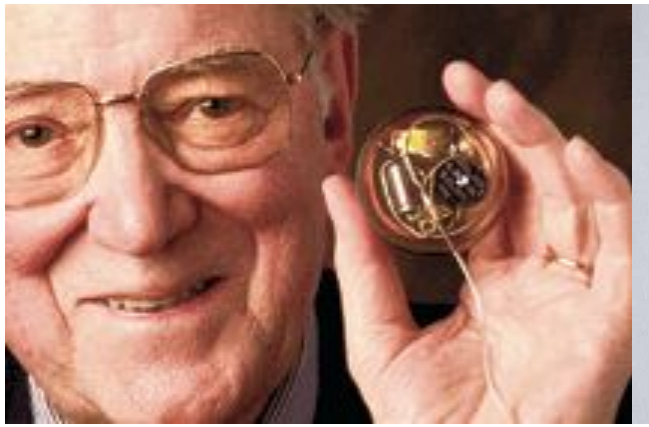
Human Implants

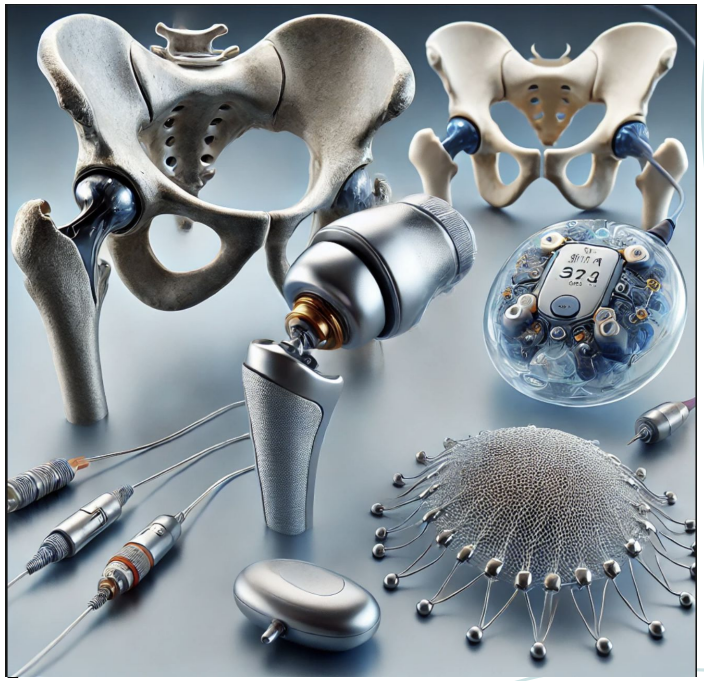


Åke Senning, together with the electrical engineer Rune Elmqvist, developed the first implantable pacemaker and implanted it in the 43-year-old patient Arne Larsson on 8 October 1958.

Medical implants

are devices or tissues that are placed inside or on the surface of the body.

- Many implants are prosthetics, intended to replace weakening body parts, such as *artificial joints*.
- Other implants deliver medication, monitor body functions, or provide support to organs and tissues, e.g. *breast implants, pacemakers and urogynecologic mesh*.



Urogynecologic Surgical Mesh Implants

Types of surgical mesh

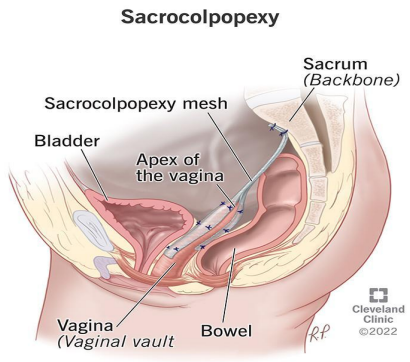
Synthetic mesh

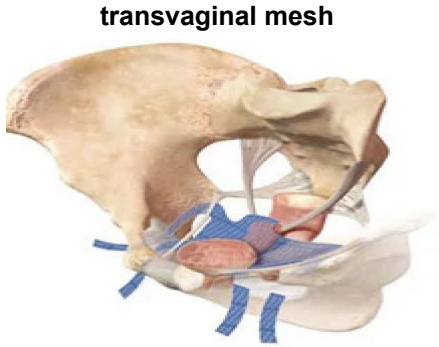
- Absorbable
- Non-absorbable
- A combination of absorbable and non-absorbable materials.

Animal-derived mesh (biological graft)

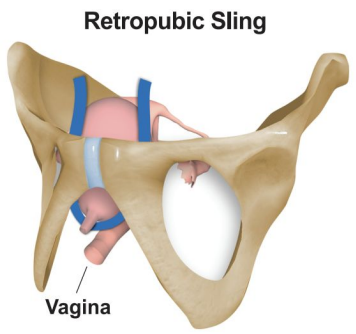
- Absorbable, tissues from a pig or cow

Uses for Surgical Mesh

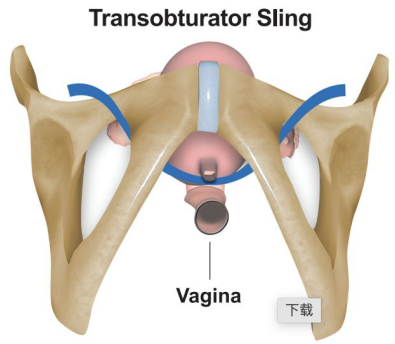




Transabdominal/tranvaginal mesh to treat pelvic organ prolapse (POP)



The placement of the retropubic sling is like a U



The placement of the transobturator is a "smile"

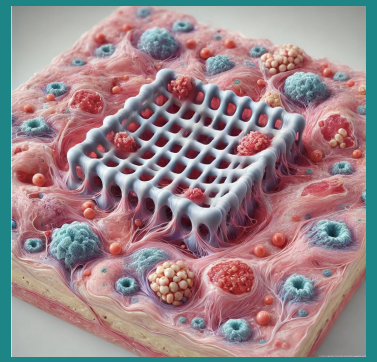
Retropubic/transobturator slings to treat stress urinary incontinence(SUI)

Safety issues of Medical Implants

1

Rejection by the Body

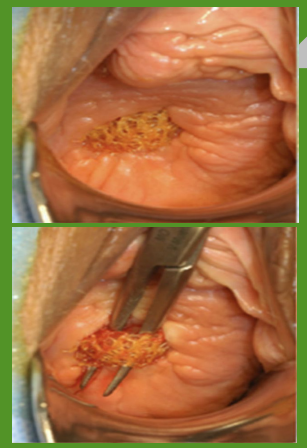
- *Immune response*
- *Material biocompatibility*
- *Allergic reactions*
- *Toxicity*



2

Health Effects

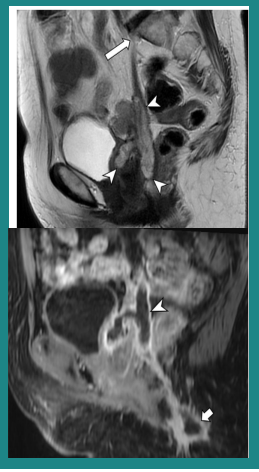
- *Surgical risks during placement or removal*
- *Mesh exposure*
- *Chronic pelvic pain*



3

Infection risks

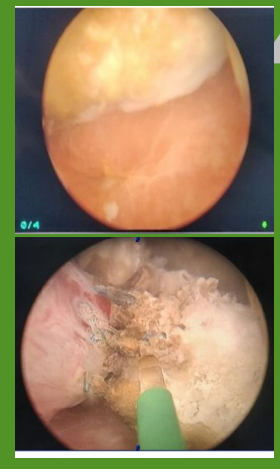
- *During and after the surgical procedure to insert the implants*



4

Mechanical Failures

- *Material wear*
- *Breakdown*
- *Migration*
- *Malfunction*

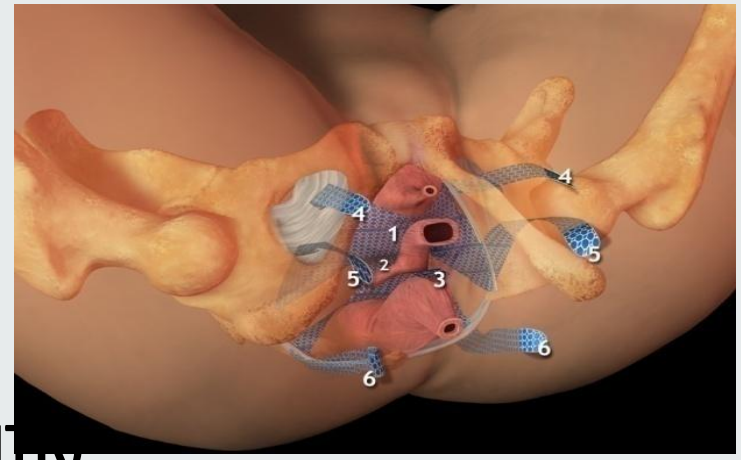


Transvaginal Mesh (TVM) Repair

- **Cochrane Database 2012[1]: TVM kits（Level I evidence）**

  - High anatomical success rate (87%～96%) ;

  - Mesh exposure/erosion rate 11.4～18%, reopeartion rate 11%



- **Cocharane Database 2024[2] : TVM repair vs native tissue repair(NTR)**

  - Lower rates of awareness of prolapse, repeat surgery for prolapse.

  - Higher rates of total repeat surgery (for prolapse, SUI, or mesh exposure), bladder injury, and de novo SUI.

1. Maher C, Feiner B, Baessler K, et al. Cochrane Database Syst Rev. 2013 Apr 30;(4):CD004014.
2.Yeung E, Baessler K, Christmann-Schmid C,et al. Cochrane Database Syst Rev. 2024 Mar 13;3(3):CD012079.

Timeline of Transvaginal Mesh

1996

- The FDA approve Boston Scientific to manufacture and market first TVM patch, Protegen.

2002

- The first mesh device for transvaginal repair of POP was cleared for use as a class II moderate-risk device.

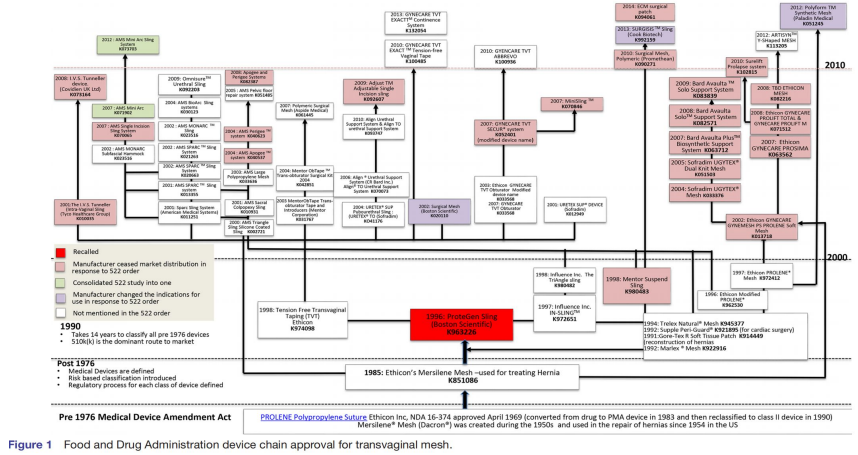


Figure 1 Food and Drug Administration device chain approval for transvaginal mesh.

2011

- FDA issued FDA Safety Communication and ordered to conduct postmarket surveillance studies (“522 orders”) to 34 manufacturers of surgical mesh for transvaginal repair of POP.

2016

- The FDA reclassified TVM products of POP into the highest risk class of devices (class III)

Timeline of Transvaginal Mesh

2019 April

- Mesh kit product was withdrawn from U.S due to the lack of the 36 month safety and efficacy data comparing TVM to native tissue repairs（NTR）.

2021 August

- Final results of the Boston Scientific Transvaginal Mesh (522 study).

2022 October

- Final results of the Coloplast Transvaginal Mesh (522 study).

Although the study results showed both transvaginal POP mesh had similar effectiveness and safety outcomes to native tissue repair at 36 months， the FDA maintains that these devices do not have a favorable benefit-risk profile.

Pelvic Floor Surgery Registry

Received: 31 January 2019 | Revised: 21 May 2019 | Accepted: 26 July 2019 | First published online: 20 August 2019
DOI: 10.1002/ijgo.12932

REVIEW ARTICLE
Gynecology

WILEY
INTERNATIONAL GYNECOLOGY OBSTETRICS FIGO

FIGO review of statements on use of synthetic mesh for pelvic organ prolapse and stress urinary incontinence

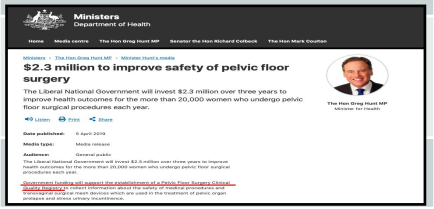
Aiste Ugianskiene[1] | G. Willy Davila[2,*] | Tsung-Hsien Su[3] | for the FIGO Urogynecology and Pelvic Floor Committee

FIGO review: agree with AUGS [3]

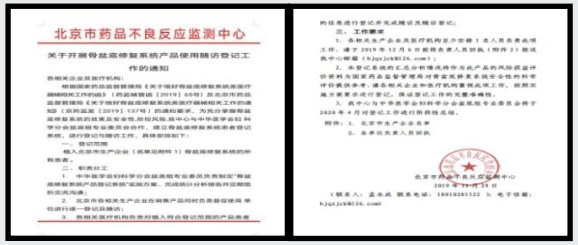
“ instead of a ban on mesh implementation, evidence-based guidelines should be established so that mesh procedures are performed only by qualified surgeons and there is a formal mechanism for patient follow-up ！”

3. Ugianskiene A, Davila GW, Tsung-Hsien S,Int J Gynaecol Obstet. 2019 Nov;147(2):147-155.

National Pelvic Floor Surgery Databases

Insitutions	The Pelvic Floor Registry Database	
AUGS & FDA， USA	2016，the Pelvic Floor Disorders Registry https://www.augs.org/clinical-practice/pfd-research-registry/	
NICE，BSUG，UK	British Society of Urogynaecology (BSUG) database (National Health Service England interim report). Ruben DT，et alInt Urogynecol J (2018) 29:899–904；2019 NICE Guideline；	
National Health Service National Services Scotland, Edinburgh, UK	2017，A first, single incontinence procedure or prolapse procedure during 1997–98 to 2015–16 identified from a national hospital admission database Joanne RM，et al. Lancet 2017; 389: 629–40	
International Urogynecology Association（IUGA）	2018，IUGA Surgical Database，（2023 closed） https://www.iuga.org/tools/surgical-database	
Health Minister，Australia	2019，Australasian Pelvic Floor Procedure Registry (APFPR)	
Sweden	2019，the Swedish National Quality Register of Gynecological Surgery(GynOP) Nüssler EK,et al. Int Urogynecol J. 2019 Sep;30(9):1533-1539.	
France	2019，VIGI-MESH registry BJOG 2020;127:88–97；BJOG 2022;129:656–663.	
CUPRSA，China	2017，27 members from CUPRSA reported complications（preliminary work） 2019，Chinese Pelvic Floor Reconstruction Surgery with Implants (Mesh) Registry，PRIMES Registry	

Chinese National Medical Products Administration（NMPA）pushed forward the PRIMES Registry(TVM repair)


北京市药品不良反应监测中心

关于开展骨盆底修复系统产品使用随访登记工作的通知

2019. 5. 28

01 Hearing on "complications of TVM repair"

2019. 10. 29

02 NMPA and CURPSA reached an agreement:
to establish a Chinese TVM surgical complication registry study

2019. 11. 8

03 Issue post-market surveillance study:
Register each case and follow-up long-term

2019. 11. 29

04 NMPA Official Order：
Designated as the only cooperation platform

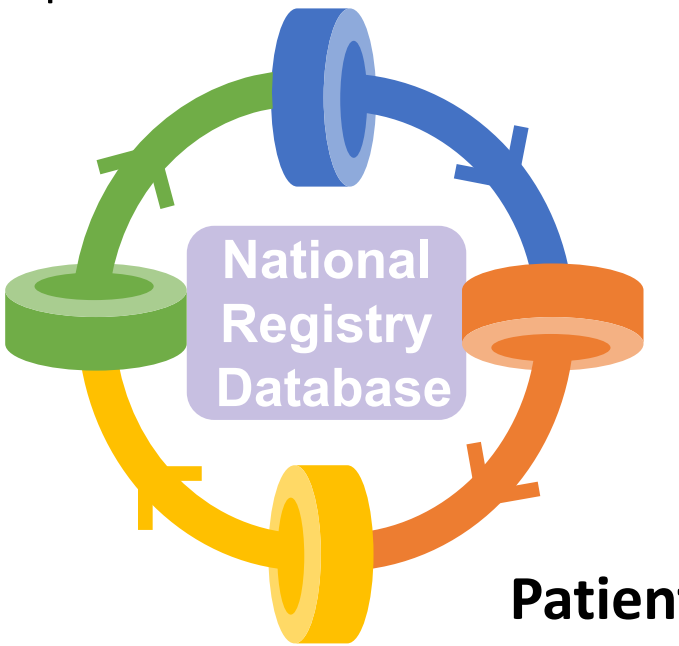
-Submitted safety reports by June 2020；
-1051 cases for Interim Analysis：
perioperative and postoperative early-stage complications were very low.

Full Cycle Safety and Quality Management Model based on National Registry Database

Developers & Manufacturers
Design & optimize

Doctors

Drive continuous improving cycle of safety & quality control



NMPA
Approve & monitor

Patients

Use & feed back

1.Establishing a Collaboration Working Group

Professional society:
Chinese Urogynecology & Reconstructive Pelvic Surgery Association
（CURPSA）

Dorctors & Hospital representatives

Collaboration working group

Regulatory agency:
Chinese National Medical Products Administrtion (NMPA)

Developers & Manufacturers

Regular Meetings per 3 months

- to discuss mesh safety and quality management issues
- to report and analysis mesh complication cases
- to develop related policies and standards
- to control post-market surveillance data quality（Registry）

Regular meetings held by the Collaboration Working Group

9月5日 周二 2023年

614 622 623

华北地区盆底植入物并发症登...

时间：08:00 发起人：北京协和医院...

9月2日 周六 2023年

730 853 456

盆底植入物并发症登记东北区...

时间：16:05 发起人：北京协和医院...

9月22日 周五 2023年

793 841 363

华中地区盆底植入物并发症登记及质控培训会 >

时间：20:13 发起人：北京协和医院梁硕

9月17日 周日 2023年

780 219 882

西北地区盆底植入物并发症登记及质控培训... >

时间：05:04 发起人：北京协和医院梁硕

9月28日 周四 2023年

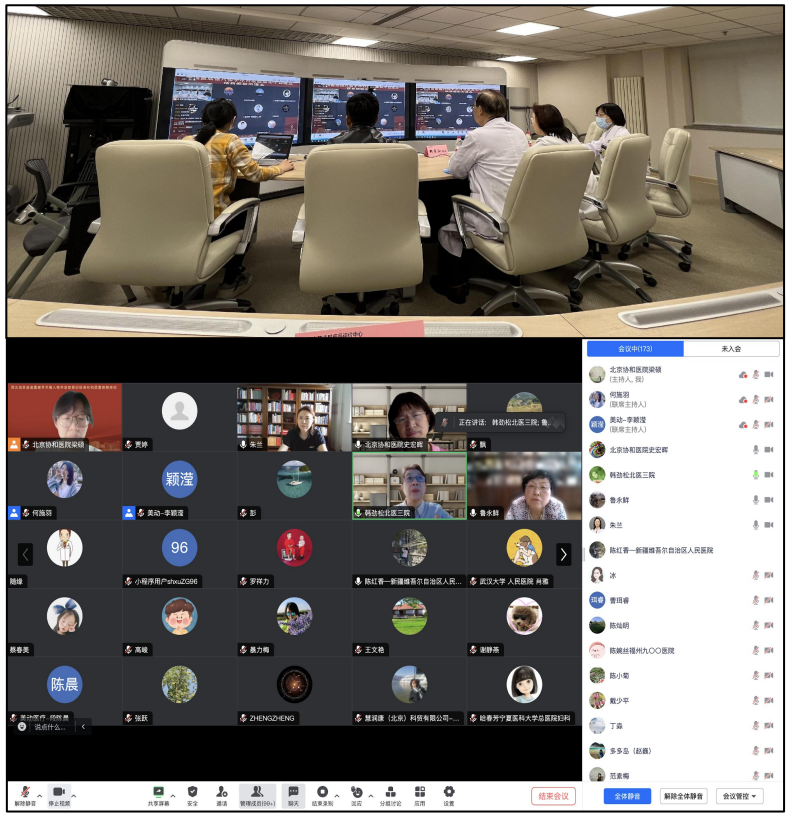
778 930 293

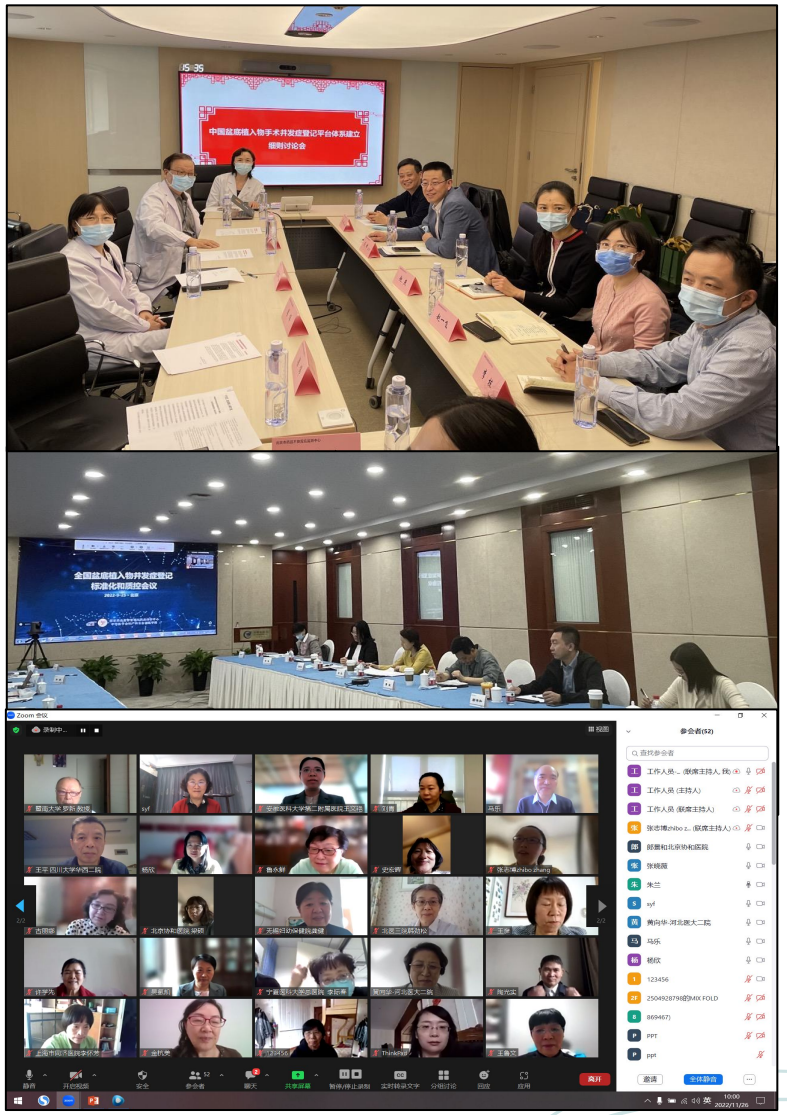
华东地区盆底植入物并发症登记质控培训会议 >

时间：14:50 发起人：北京协和医院梁硕

Strengthening the NMPA and CURPSA's regulatory oversight to protect patients.

One mesh, one record!





2. Establishing the National Pelvic Floor Surgery Database

- The database project was initiaed in August 2018 and officially launched for registration on July 1, 2019.
- Over the past five years, the database expanded from the initial 42 institutions to 232 hospitals covering 29 provinces municipalities, and autonomous regions across China.
- A total of 306 doctors registered.

National center → Regional center →Centers/hospitals→Doctors

Registration	Follow-up management	Early alerts	EDC platform	Specialized disease database
1 View cohort data	1 Process patient-filled follow-up visits	1 Handle alerts	1 Process the follow-up data	1 Advanced search/ simple search
2 Create a new patient reigistry record	2 Give follow-up opinions	2 Doctor-patient communication	2 Transcription data	2 Set up target variables
3 Create follow-up/fill in follow-up	3 Raise doubts	3 Doctor gudiance for alerts	3 Raise doubts	3 Data quality inspection
4 Create dropout			4 Lock the databse	4 Statistical analysis
5 Complete follow-up				

Patients

Follow-up	Handle doubts	Handle alerts
1 Review registration information	1 View follow-up questions	1 View alert data
2 Review follow-up data	2 Reply to questions	2 Doctor-patient interaction for alert issues
3 Fill in follow-up forms	3 Doctor-Patient communication	
4 View follow-up opinions		

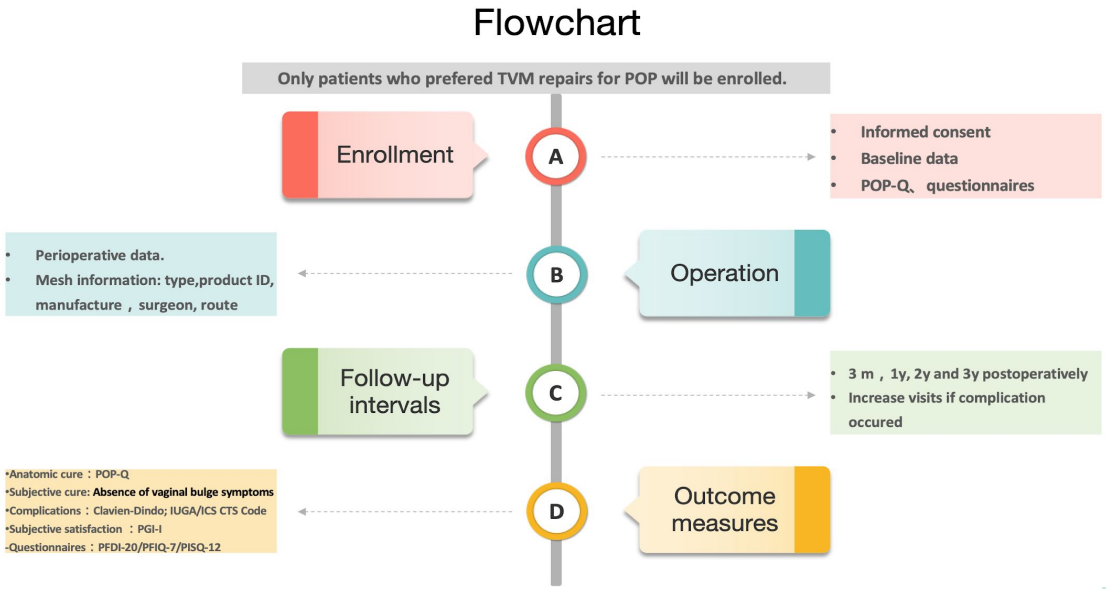
PRIMES registry

ClinicalTrials.Gov Registration Information: NCT04025047

- **Design**: A prospective, observational registry study
- **Setting :** Multicenter
- **Leaders:**

  - Chinese Urogynecology and Reconstructive Pelvic Surgery Association (CURPSA)

  - Chinese National Medical Products Administration (NMPA)



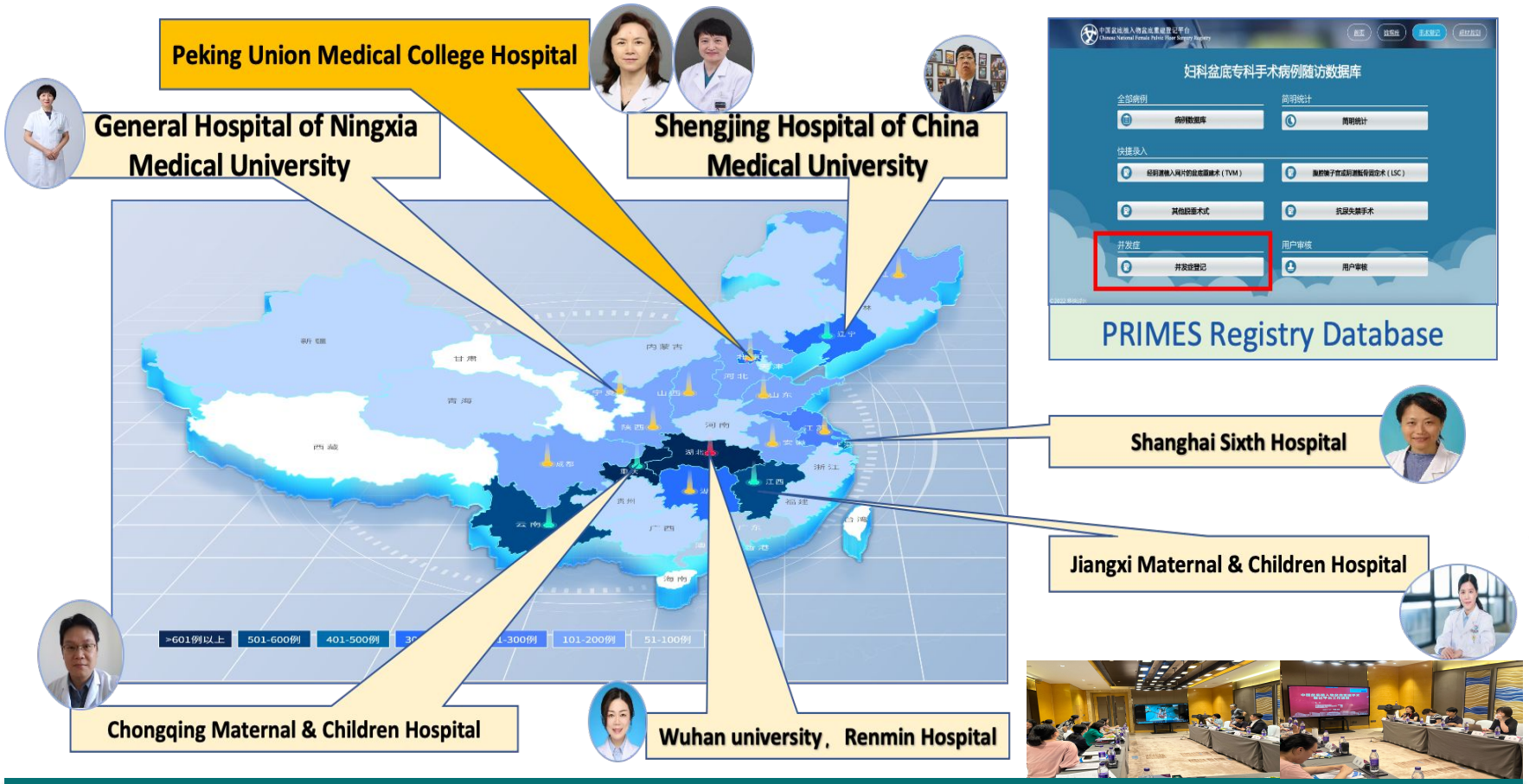
- **Objective:**

To study the effectiveness, safety and functional improvement of pelvic floor repair surgery with mesh(TVM, sacrocolpopexy, lateral suspension) and tapes for pelvic organ prolapse and stress urinary incontinence.

2019.07.01~2024.08.15 registered procedures using mesh

- **13206 TVM repairs**
- **3408 Sacrocolpopexies**
- **655 Lateral suspensions**
- **3817 TVT slings**

3. Establishing Adverse Event Reporting Network based on the PRIMES Registry Database



PRIMES Registry Database

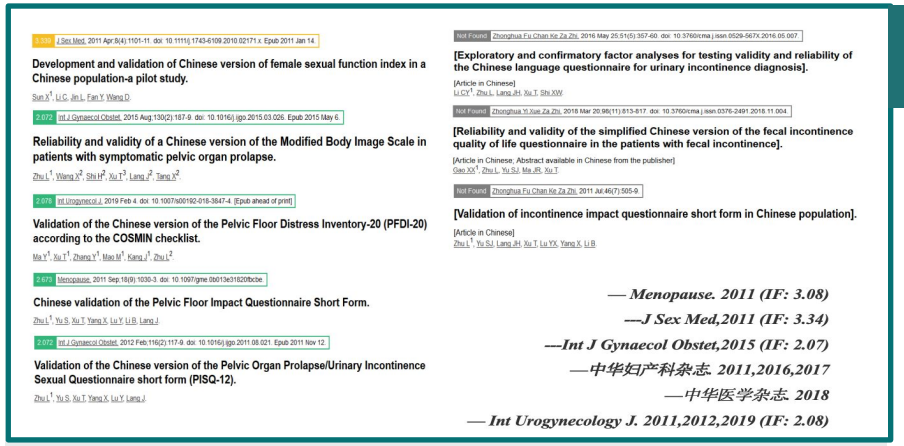
National center ← 7 Regional centers ←Local centers/doctors

- **Under supervision of NMPA, regular seminars held for AE reports, analysis and feed-back.**
- **Quick response and resolution of AEs.**
- **So far,**

✔ 617 complications reported from TVM prospective cohort;

✔ 371 cases referred from local centers.

4. Establishing Procedures Standards and Terminology



Development and validation of Chinese version of female sexual function index in a Chinese population-a pilot study.

Validation of the Chinese version of the Pelvic Floor Distress Inventory-20 (PFDI-20) according to the COSMIN checklist.

Chinese validation of the Pelvic Floor Impact Questionnaire Short Form.

Validation of the Chinese version of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form (PISQ-12).

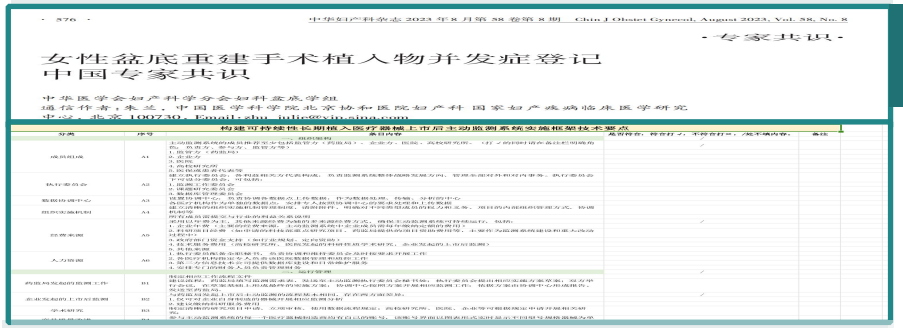
[Exploratory and confirmatory factor analyses for testing validity and reliability of the Chinese language questionnaire for urinary incontinence diagnosis].

[Reliability and validity of the simplified Chinese version of the fecal incontinence quality of life questionnaire in the patients with fecal incontinence].

[Validation of incontinence impact questionnaire short form in Chinese population].

— Menopause. 2011 (IF: 3.08)
—J Sex Med,2011 (IF: 3.34)
—Int J Gynaecol Obstet,2015 (IF: 2.07)
—中华妇产科杂志. 2011,2016,2017
—中华医学杂志. 2018
— Int Urogynecology J. 2011,2012,2019 (IF: 2.08)

✔ **Validation of patient reported outcomes(PROMs) questionnaires in Chinese women.**



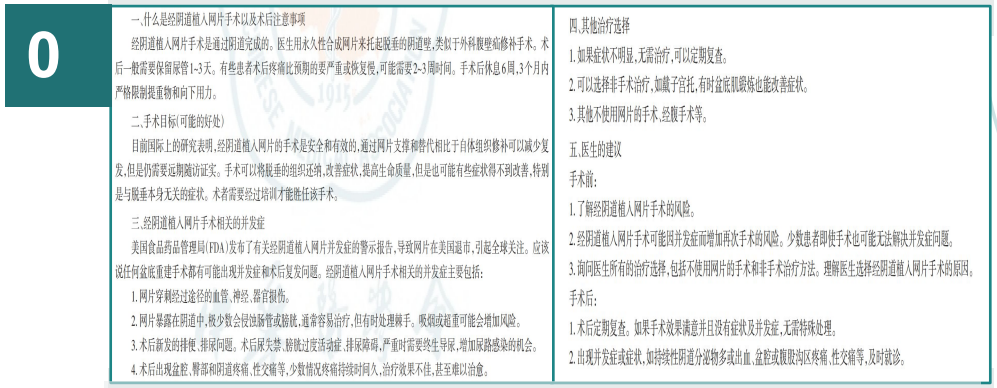
女性盆底重建手术植入物并发症登记
中国专家共识

构建可持续性长期植入医疗器械上市后主动监测系统实施框架技术要点

✔ **Establisment of consensus on implant registration and industry standards for active monitoring of implantable device with NMPA.**

骨盆底修复系统类产品故障类不良事件术语

✔ **Formulation a glossary of Chinese pelvic floor implant complications terminology with NMPA.**



一、什么是经阴道植入网片手术以及术后注意事项

二、手术目标(可能的好处)

三、经阴道植入网片手术相关的并发症

四、其他治疗选择

五、医生的建议

手术前:

手术后:

✔ **Development of a unified template for "Informed Consent Form for Transvaginal Synthetic Mesh Surgery".**

Education and Policy Support

5. Training and Education

- Provide regular professional training to R&D personnel, clinicians and hospital administrators to ensure they are up-to-date on the latest technologies, regulations and operating practices.

6. Policy Support

- The NMPA issued the documents requiring relevant medical device manufacturers or agents to cooperate with doctors' work.
- Professional groups encourage hospitals and doctors to actively participate in the comprehensive management of mesh.

Mid-Term Follow-Up Results of the PRIMES Registry

- **2019.7.1~2022.12.31，5621 TVM procedures prospectively included.**
- **4940 (87.9%) at least once follow-up，3759 (76.1 %) clinic visits，1174(23.8%) via telephone or WeChat，7(0.1%) death.**
- **Median follow up interval 11.0（1~45.9）months.**
- ***Primary outcomes :***
- ***Perioperative complications* were reported in 3.9% (217/5621) of the patients in the total cohort, with 17 cases (0.30%) categorized as Clavien-Dindo grade-III and -IV complications.**

Table1. Specific and serious perioperative complications related to TVM (N=5621)

Period of follow-up	Specific and serious complications	Sum, n(%)
Perioperative complications	Urinary retention	85(1.60)
	Hematoma or bleeding >500 cc	33(0.62)
	Blood transfusion	13(0.23)
	Urinary system injury（Urethra, bladder, ureter）	14(0.25)
	Infection	30(0.57)
	VTE（DVT & PE）	33(0.62)

Mid-Term Follow-Up Results of the PRIMES Registry

- ***Mesh exposures risks :***

1.0% at 3 mo, 2.4% at 1 year, 4.4% at 2 year postoperative f/u.

- **Overall, 83 mesh exposure cases reported, 91.5%（76/83）less than 1cm^2, 55.4%(46/83) of cases were asymptomatic and successfully cured at clinic.**
- **Reoperation rate for partial mesh removal at OR is 0.14%(7/4940).**
- **Possible protective factors: uterus preservation; surgical volume>130cases/surgeon (Figure 2A, 2B).**

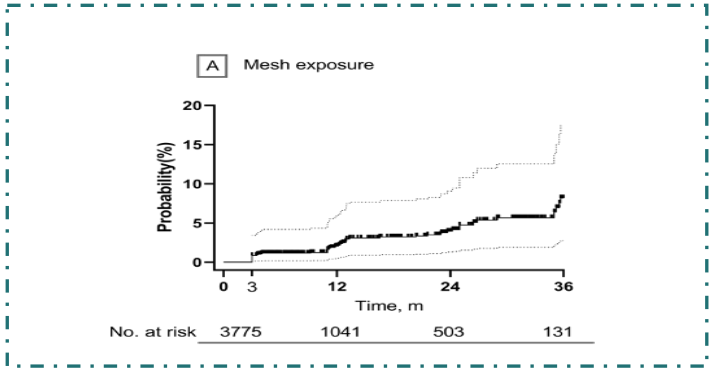


Figure1A. Kaplan-Meier Survival Curves for Mesh exposure of TVM Repair in Treating POP Through 11months（median）follow-up.

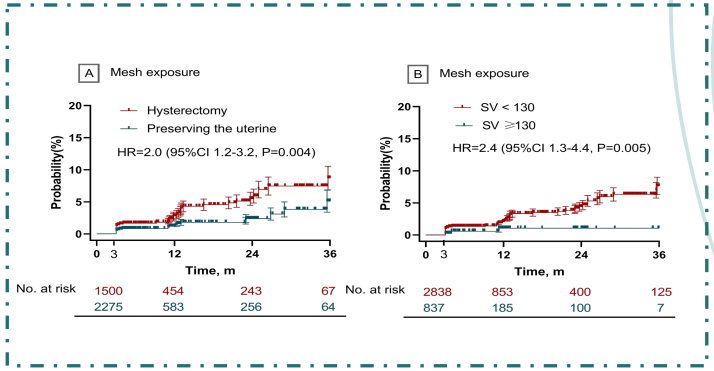


Figure 2. Kaplan-Meier Survival Curves for Mesh exposure in treating POP patients by different variables.
A Red, patients underwent hysterectomy; green, patients with uterus preservation.
B SV exceed 130 in red, less than and 130 in green.

Table2 Estimated Probability of Mesh Exposure After TVM Repair

Outcomes	(%) No. With Outcome/Total No.	Estimated probability based on K-M（95%CI）
Primary : Mesh exposure		
3 mo	1.0 (37/3775)	**1.0（0.1-4.0）**
1 year	1.3 (20/1486)	**2.4（0.6-6.3）**
2 year	1.1 (8/731)	**4.4（1.6-9.6）**

Mid-Term Follow-Up Results of the PRIMES Registry

Table3 Estimated Probability of Surgical Effectiveness After TVM Repair

Outcomes	(%) No. With Outcome/Total No.	Estimated probability based on K-M (95%CI)
Secondary:		
Anatomic cure		
3 mo	96.9 (3659/3775)	97.3(96.8-97.8)
1 year	98.9 (1470/1486)	94.4(93.3-95.3)
2 year	97.0 (709/731)	91.9(90.2-93.3)
Absence of vaginal bulge symptom		
3 mo	96.4 (4656/4832)	96.4(95.8-96.9)
1 year	98.9 (2270/2295)	94.5(93.7-95.2)
2 year	99.1 (1262/1274)	93.3(92.3-94.2)
Composite success		
3 mo	93.4 (3525/3775)	95.3(94.6-95.9)
1 year	98.2 (1459/1486)	92.2(91.3-93.0)
2 year	96.4 (705/731)	90.5 (89.3-91.6)

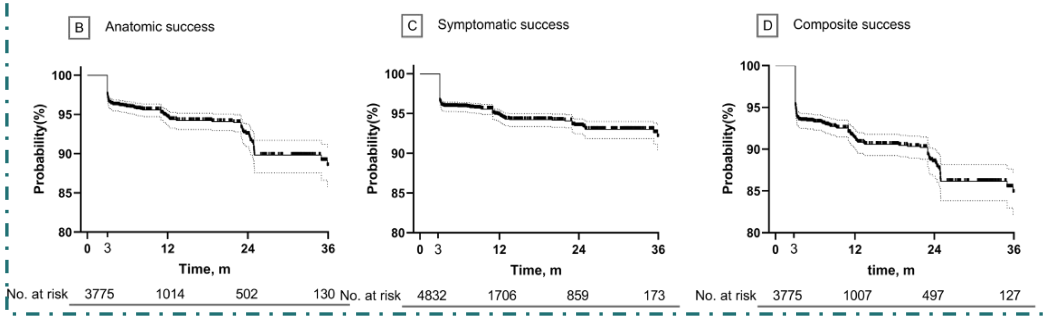


Figure1B-D. Kaplan-Meier Survival Curves for Surgical Effectiveness for POP Through 11months (median) Follow-up.

- ***Secondary Outcomes***
- **2-year postoperative effectiveness of TVM repairs:**
- ***anatomic cure (91.9%)***
- ***bulge symptom improvement (93.3%)***
- ***composite success (90.5%)***
- **TVM repairs showed satisfactory anatomical and subjective outcomes with relatively low mesh exposure rates.**

Acknowledgements

- **Chinese National Medical Products Administration（NMPA）Adverse Effect Monitoring Center**
- **Chinese Pelvic Floor Reconstruction Surgery with Implants (Mesh，Tape) Registry（PRIMES Regitry）**

- Keep ongoing efforts on monitoring urogynecologic surgical mesh for PFD women's health!
- Report the prospective long-term（36months）safety and effectiveness outcomes of TVM repairs cohort this year!
- ***One mesh, one record!***

Thank you!