Can we predict and prevent pelvic floor dysfunction?

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Pelvic Floor Disorders (PFDs)

Pelvic Organ Prolapse (5-10%)
Urinary incontinence (30-60%)
Anal incontinence (11-15%)

Any form of pelvic floor disorder 46%

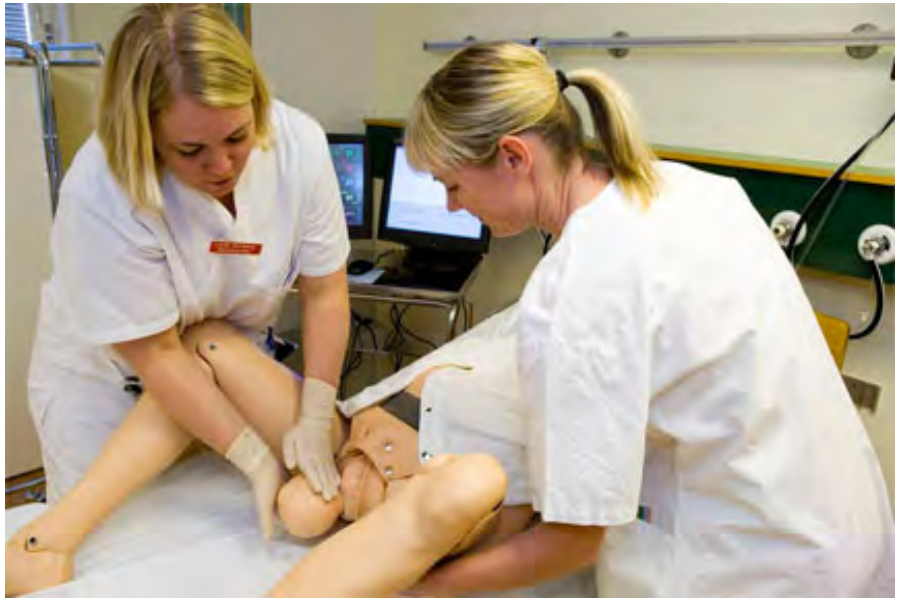
Common problems affecting millions of women throughout the world

Negative effect on:

Quality of life and Working ability

Sporting activities and Sexual activity

Global costs high



Milsom I, Altman D, Cartwright R, Lapitan MC, Nelson R, Sillén U, Tikkanen K. Epidemiology of Urinary Incontinence (UI) and other Lower Urinary Tract Symptoms (LUTS), Pelvic Organ Prolapse (POP) and Anal (AI) Incontinence. *In:* Incontinence, Editors Abrams, Cardozo, Kouhry and Wein. Health Publications Ltd, Paris 2013

Life-time risk of POP surgery

The lifetime risk of undergoing POP surgery alone has been reported to vary between 5 and 19%.[1] The highest life time risk for POP surgery,19%, has been reported from Western Australia[2]

De Boer[3] et al. estimated that 20.2% of Dutch women would undergo POP or continence surgery before 85 years of age

Wu et al.[4] estimated a similar rate of intervention in the United States

1. Haya et al. Am J Obstet Gynecol 2015;212:755.e1-755.e27.
2. Smith et al. Obstet Gynecol 2010;116:1096-1100
3. de Boer et al. Eur J Obstet Gynecol Reprod Biol 2011;158:343-349
4. Wu et al Obstet Gynecol 2014;123:1201-1216

What would be the demand for incontinence and prolapse surgery if vaginal birth was excluded?

Swedish National Quality Register of Gynecological Surgery, 2006-2016

- Of all prolapse procedures(n = 33 124)
  99% had at least one VD

- Of all incontinence procedures (n = 18 391)
  95% had at least one VD

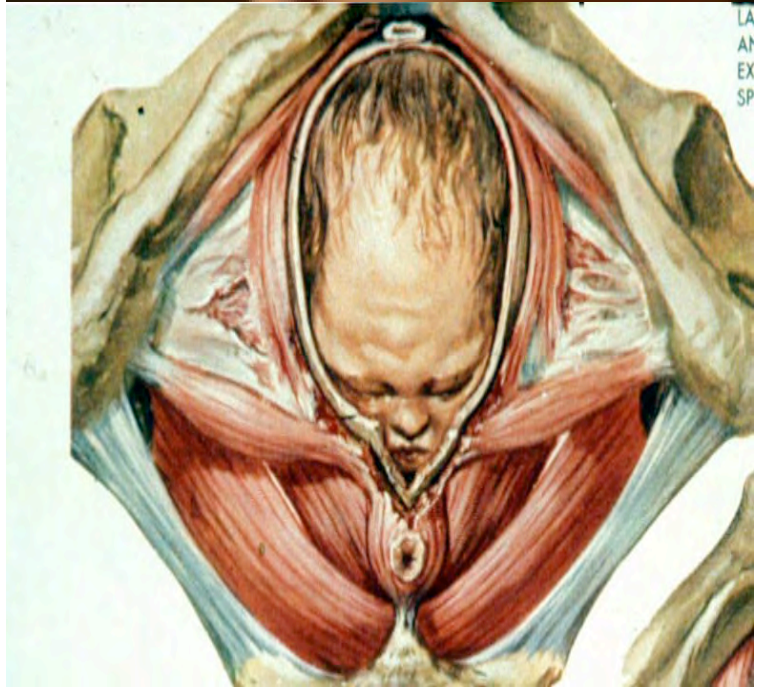
Larsudd-Kåverud J et al. Poster NFOG 2018, Odense, Denmark

Numerous risk factors for PFDs have been identified

Age
Hereditary factors
Hysterectomy
Obesity
Irritable Bowel syndrome
Ethnicity
Dementia
Physical activity
Neurological illnesses

Parity
Pregnancy
Delivery mode
Anal sphincter rupture
Postmenopausal
Multiple sclerosis
Parkinsons illness
Urinary tract infections
Diabetes mellitus

Milsom I, Altman D, Cartwright R, Lapitan MC, Nelson R, Sillén U, Tikkanen K. Epidemiology of Urinary Incontinence (UI) and other Lower Urinary Tract Symptoms (LUTS), Pelvic Organ Prolapse (POP) and Anal (AI) Incontinence. *In:* Incontinence, Editors Abrams, Cardozo, Kouhry and Wein. Health Publications Ltd, Paris 2013.



Pelvic floor dysfunction

Which are the most important risk factors

Pregnancy per se?

(non modifiable!!!!)

or is it related to:

Delivery parameters

(potentially modifiable)

Mode of delivery

(potentially modifiable)

For ethical and practical reasons, randomised controlled trials to evaluate the causal effects of vaginal and caesarean delivery on the pelvic floor will never be performed

We therefore have to rely on:

Objective Pathophysiological data

Epidemiological data

Objective Pathophysiological data

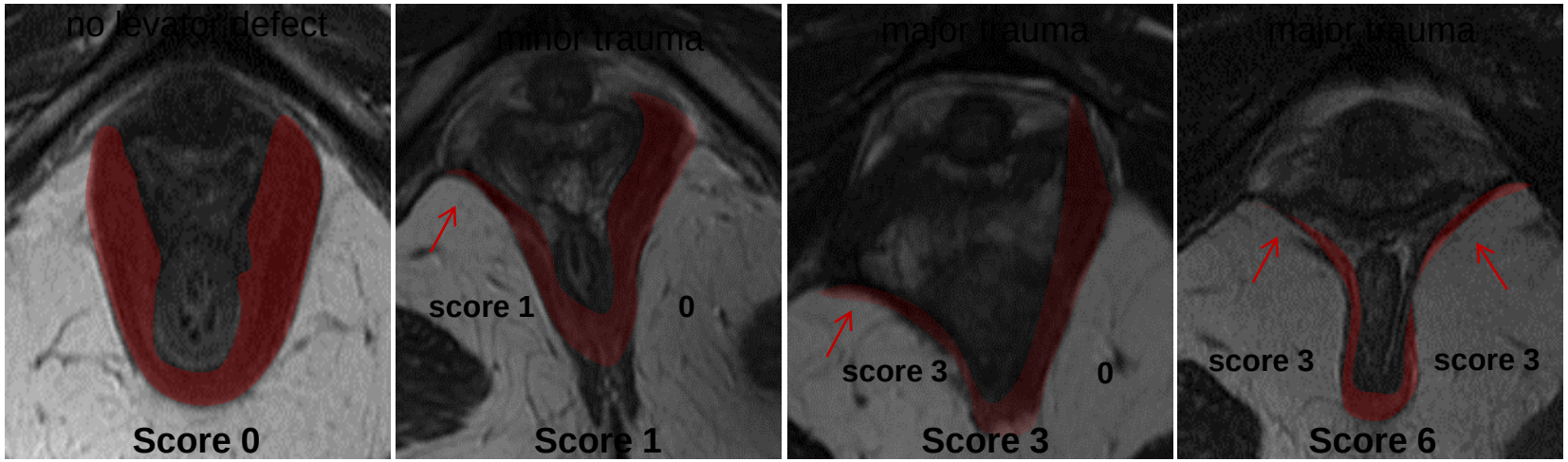
Magnetic resonance imaging
Ultrasound
Electrophysiological data

MRI Levator ani injury postpartum

6-10% after spontaneous vaginal delivery
17-33% after vacuum extraction
67-71% after forceps delivery

but was not identified in nulliparous women or after caesarean section

Kearney R, Fitzpatrick M, Brennan S, Behan M, Miller J, Keane D, O'Herlihy C, DeLancey JO. Int J Gynaecol Obstet. 2010



DeLancey JO et al. Obstet Gynecol 2003;209:295-302

Epidemiological data

Urinary Incontinence after Vaginal Delivery or Caesarean Section

Rortveit G et al. N Engl J Med 2003;348: 900-907

EPINCONT study - community based cohort (n = 15 307), younger than 65 years

Prevalence of UI

Nulliparous 10.1%

Vaginal delivery group 21.0%

Cesarean section group 15.9%

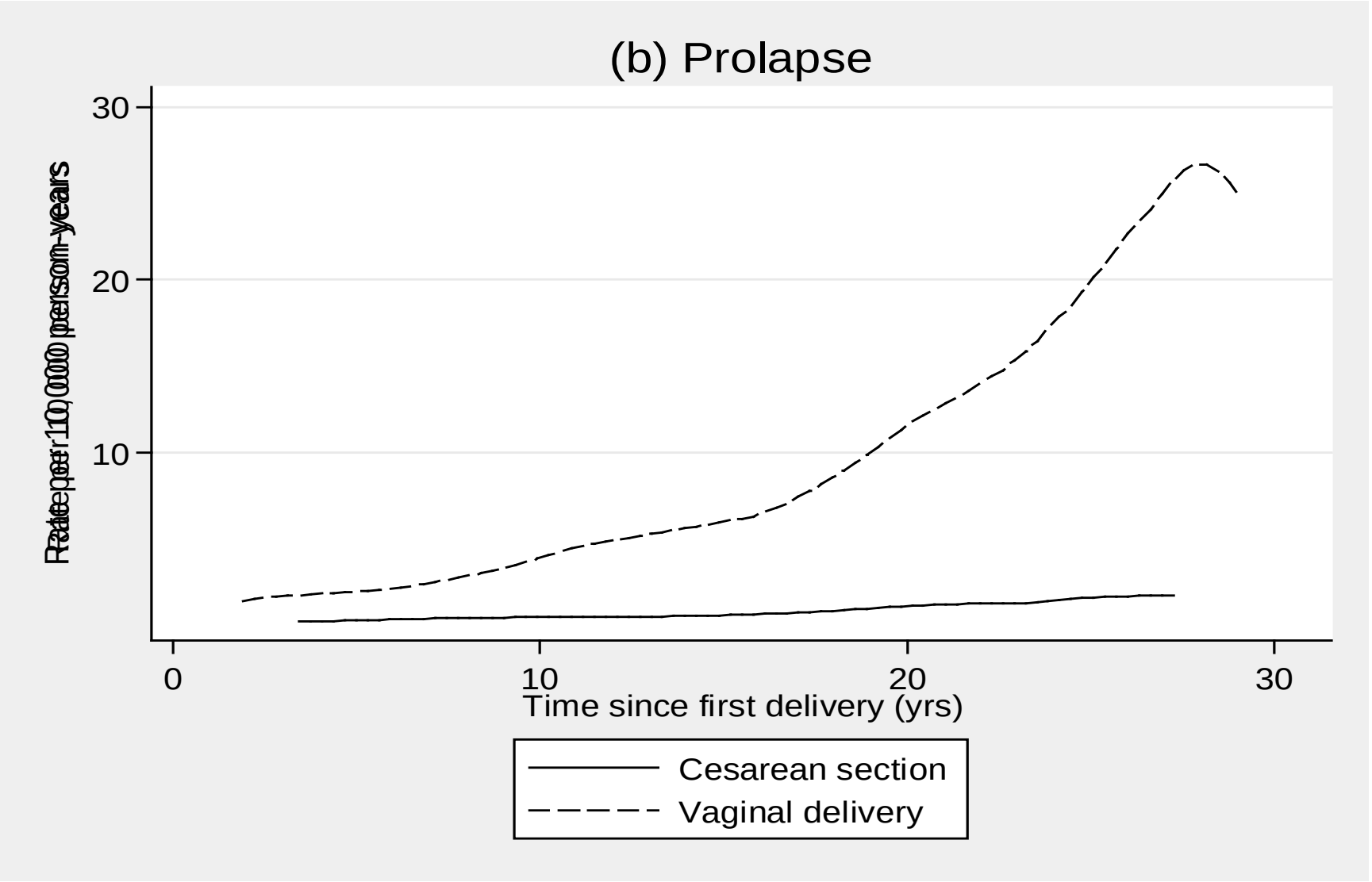
Odds ratio UI

Nulliparous - CS 1.5 (95% CI 1.2-1.9)

VD - CS 1.7 (95% CI 1.3-2.1)

Rate of pelvic organ prolapse surgery in relation to mode of delivery and time from first childbirth

(Leijonhufvud Å et al. Am J Obstet Gynecol 2011;204(1):70.e1-7)



***SWE**dish **P**regnancy, **O**besity and **P**elvic floor study*
SWEPOP-study

Earlier Studies

- mixed parity
- mixed mode of delivery
- poor control of confounding factors
- control group (CS) too small leading to underpowered analysis
- to short follow up
- recall data

SWEPOP-study

- homogenous (1-parae)
- vaginal or caesarean birth
- BMI, maternal age, infant birth weight
- large cohorts
- long term assessment
- registry data and validated questionnaires

SWEPOP-study

SWEdish Pregnancy, Obesity and Pelvic floor study

- **The risk increase after VD compared to CS was 67% for UI and 275% for UI>10 years**
- **The prevalence of sPOP was 14.6% after vaginal delivery and 6.3% after caesarean section and the risk increase associated with VD was 255% compared to CS**
- **Vaginally delivered women had a more than tripled prevalence and risk of having the combination sPOP and UI compared to CS**
- **The prevalence of UI, UI>10 years and sPOP did not differ between elective CS and acute CS**

Gyhagen et al. BJOG. 2013 Jan;120(2):144-51.
Gyhagen et al. BJOG. 2013 Jan;120(2):152-60.

SWEPOP-study

SWEdish Pregnancy, Obesity and Pelvic floor study

Vaginal delivery, maternal age at delivery, family history of UI and a high current BMI were independent risk factors for the development of UI[1]

Vaginal delivery, infant birth weight, family history of POP and a high current BMI were independent risk factors for the development of sPOP[2]

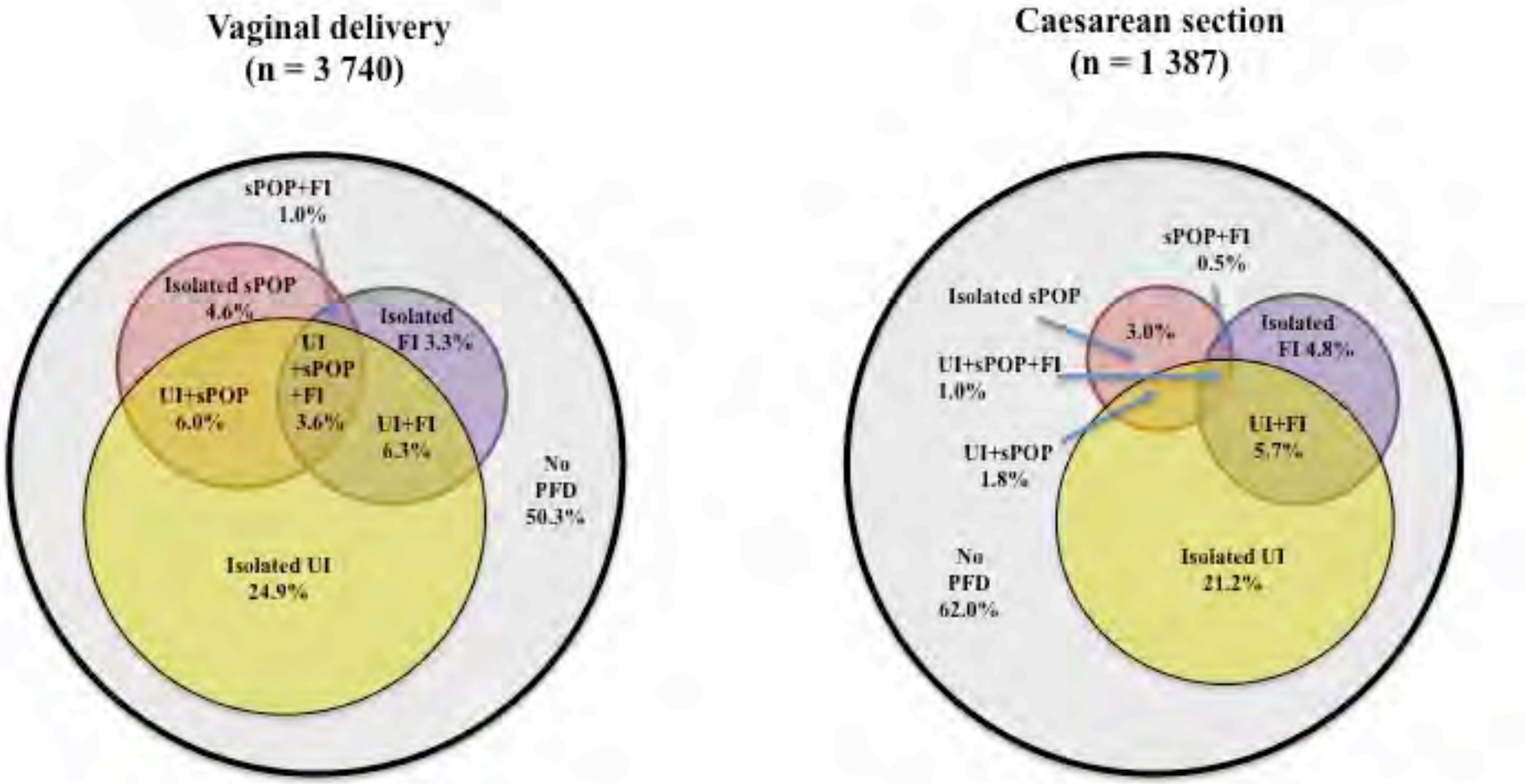
The prevalence of co-occurring PFDs 20 years after birth was high. Approximately one third of the women with a PFD had two or more PFDs[3]

The prevalence of co-occurring PFDs was doubled in women after VD compared to CS[3]

Risk factors for clustering of PFDs were: VD, family history, ≥2 degree tears maternal age and current BMI[3]

1. Gyhagen et al. BJOG. 2013;120:144-51; 2. Gyhagen et al. BJOG. 2013;120:152-60;
3. Gyhagen et al Int Urogynecol J. 2015;26:1115-1121.

Clustering of pelvic floor disorders 20 years after one vaginal or one caesarean birth



Gyhagen et al. Int Urogynecol J 2015 26:1115-1121

UR-CHOICE – Can we provide mothers-to-be with information about the risk of future pelvic floor dysfunction?

Don Wilson, James Dornan, Ian Milsom, Robert Freeman

Int Urogynecol J 2014; 25: 1449 – 1452

The hypothesis suggested that the following physical features of the Mother and the Baby can be scored and used to determine the most suitable route of delivery

U - Presence or absence of antenatal UI

R - Race/Ethnicity

C - Childbearing started at what age

H - Height of mother

O - Overweight? (mothers BMI)

I - Inheritance (family history)

C - Children (number of children desired

E - Estimated fetal weight

Predictive Modelling Cooperation

SWEPOP Study Group

Sahlgrenska Academy, Gothenburg

Maria Gyhagen, Jwan Othman, Ida Nilsson, Björn Areskoug, Ian Milsom

PROLONG Study Group

Aberdeen, Glasgow and Otago

Don Wilson, Charis Glazener, Suzanne Hagen, Andrew Elders

CLEVELAND CLINIC Group

Cleveland

Matt Barber, Eric Jelovsek, Michael Kattan, Kevin Chagin

Study Population

Data from 2 longitudinal, prospective cohorts

1. **Swedish Pregnancy, Obesity and Pelvic Floor Study (SwePOP)**
   - **Only Primiparous women delivered 1985-1988 (n = 9423)**
   - **Swedish Medical Birth Register data**
   - **Linked to Postal Questionnaire 20 years after delivery**
2. **ProLong study from UK/New Zealand**
   - **All deliveries w/n 12 months (1993-94)**
   - **7883 participated 3 months after index birth**
   - **Aberdeen (UK), Birmingham (UK), Dunedin (New Zealand)**
   - **Followed up to 12 years after delivery**

Gyhagen M, Bullarbo M, Nielsen T, Milsom I. BJOG 2013
MacArthur C, Glazener C, Lancashire R, Herbison P, Wilson D, BJOG 2011

Complete dataset and candidate predictors

SwePOP
(N=4991)
+
ProLong
(N=3638)
=
Dataset
(N=8629)

Variables	Median (IQR) or N(%)
Parity	1 (1, 1)
Missing	742 (8%)
Age	29 (25, 33)
Missing	10 (0%)
Pre-Pregnancy Weight	61 (55, 68)
Missing	1433 (16%)
Mother's Height	165 (161, 170)
Missing	61 (1%)
Infant's Weight	3480 (3130, 3860)
Missing	67 (1%)
Laceration	
Yes	1606 (18%)
No	7047 (80%)
Missing	130 (1%)
Circumference	35 (34, 36)
Missing	255 (3%)
Delivery Mode	
Vaginal Unassisted	5762 (66%)
Vaginal - Forceps	331 (4%)
Vaginal - Vacuum	877 (10%)
Acute C-Section	715 (8%)
Elective C-Section	1098 (13%)
Epidural	
Yes	2726 (31%)
No	6033 (69%)
Missing	24 (0%)
Family History of POP	
Yes	1269 (14%)
No	6044 (69%)
Missing	1470 (17%)
Episiotomy	
Yes	1244 (14%)
No	7409 (84%)
Missing	130 (1%)

Jelovsek et al. Am J Obstet Gynecol 2018

Hypotheses

- Models can be developed to predict the likelihood of developing PFDs (outcomes) 12-20 years after delivery that:
  - Discriminate better than chance (i.e. concordance index=0.5)
  - Reasonable to calibrate and are internally and externally validated
  - Can be used in an ***on-line calculator*** to permit prediction on an individual basis

Jelovsek et al. Am J Obstet Gynecol 2018

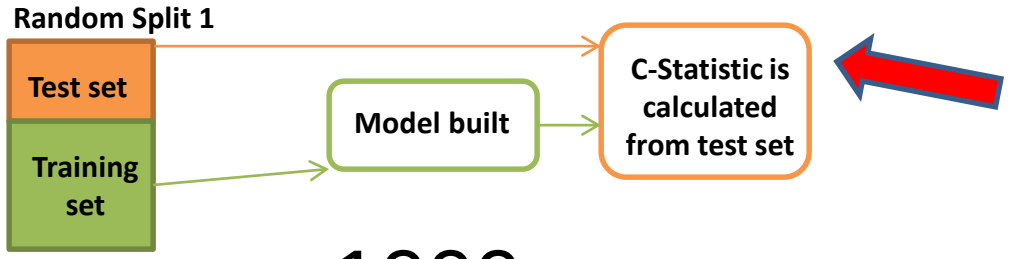
Prediction modelling- methodology

We examined predictors from 8629 primiparous and multiparous women from two longitudinal, prospective cohorts from Sweden (the SwePOP cohort, N=4991) and UK/New Zealand (ProLong cohort, N=3638).

Two thirds of data were randomly placed into a training set for model building.
Multiple logistic models were fit to the data and reduced using backwards elimination.
Model internal validation was assessed using 1000 bootstrap samples generating a bias-corrected concordance index.
Each model was then externally validated on the remaining 1/3 of the data.

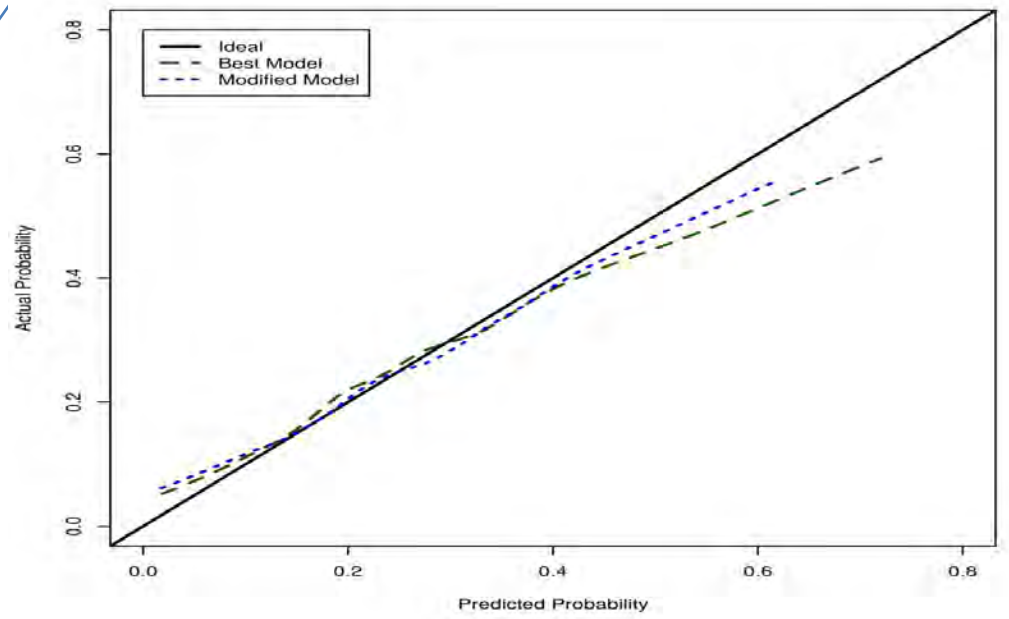
Jelovsek et al. Am J Obstet Gynecol 2018

Internal Validation Bootstrapping Schematic



1000x

2/3 of Dataset



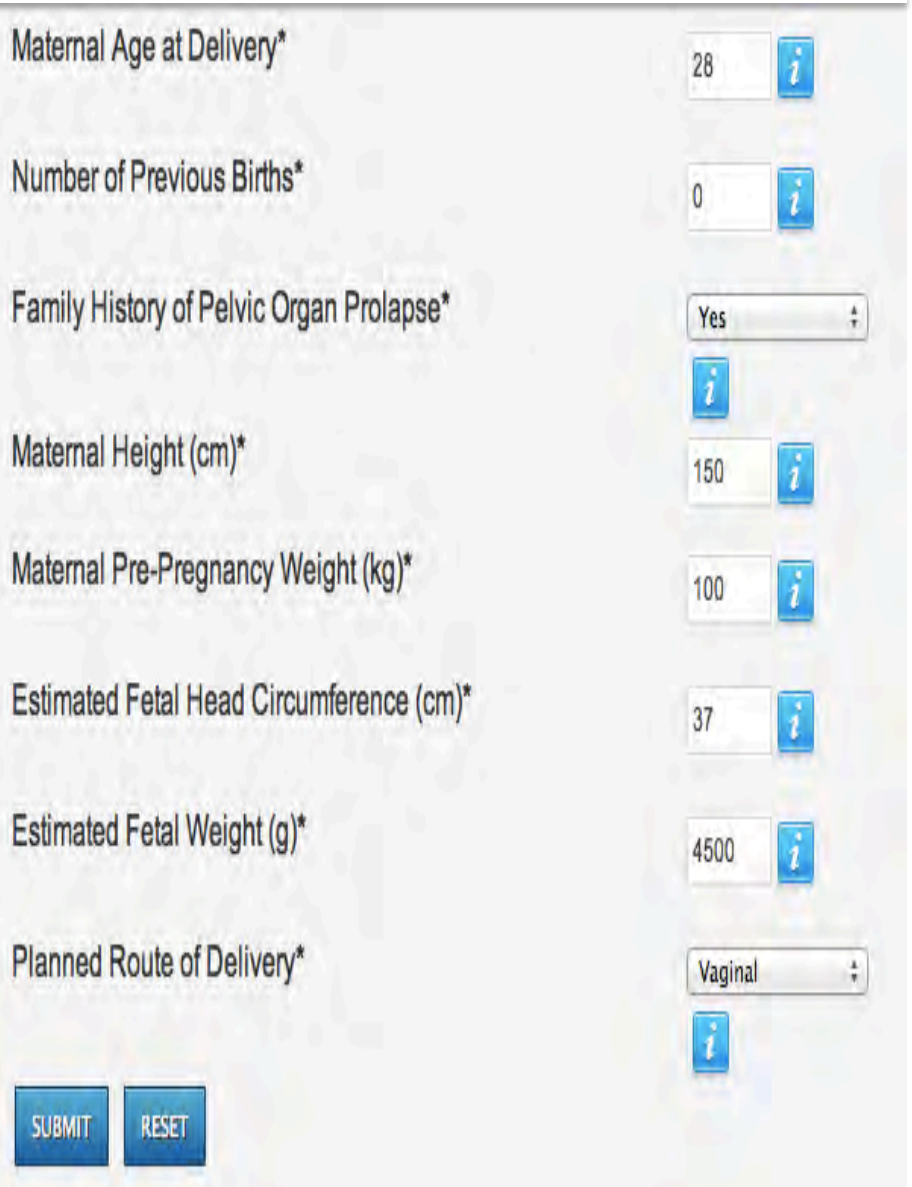
1/3 of Dataset

Discriminatory ability expressed as concordance indices or C-statistic (95% CI) varied between 0.607-0.773

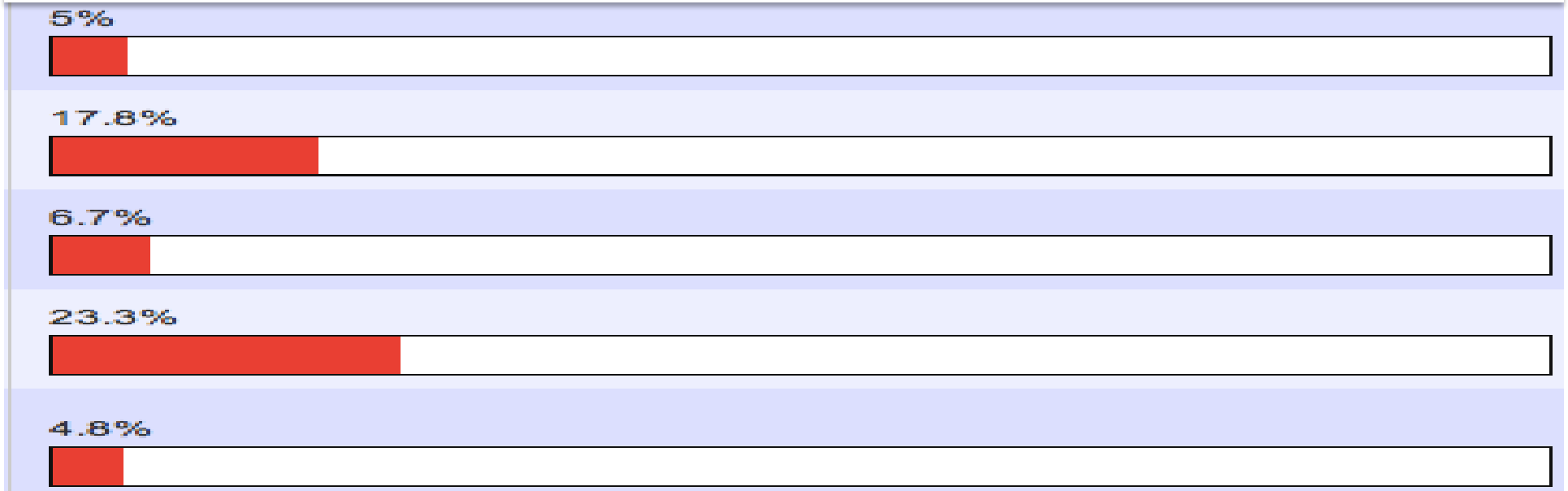
Jelovsek et al. Am J Obstet Gynecol 2018

28 year old primip, family history of POP
Otherwise low risk

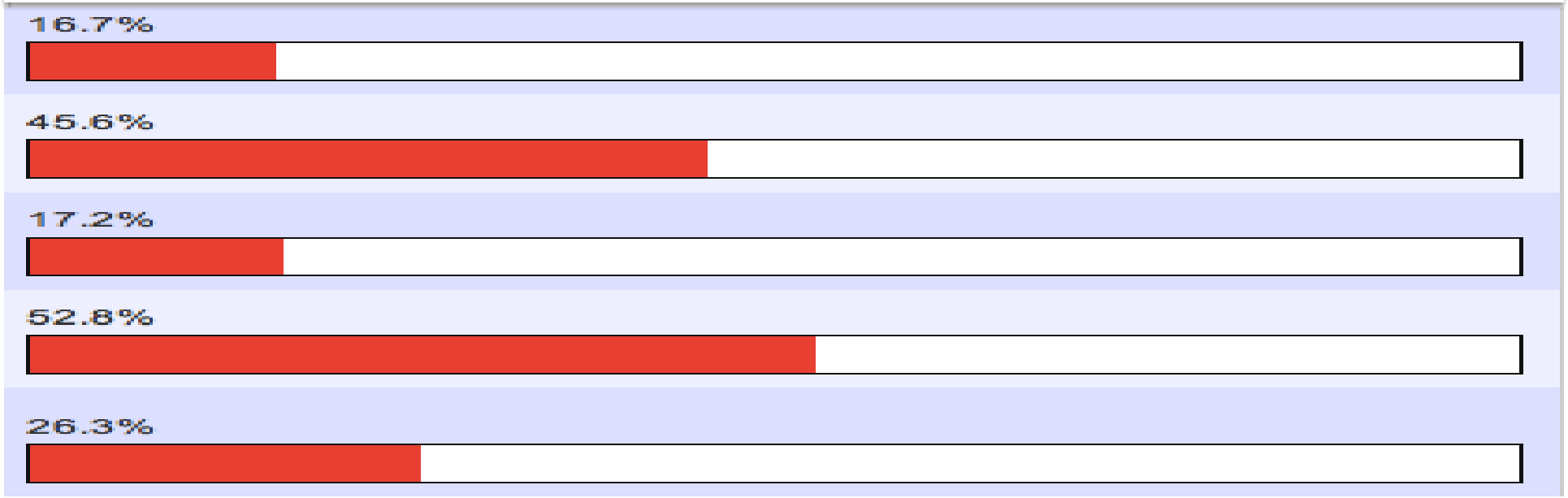
28 year old primip, family history of POP
High risk



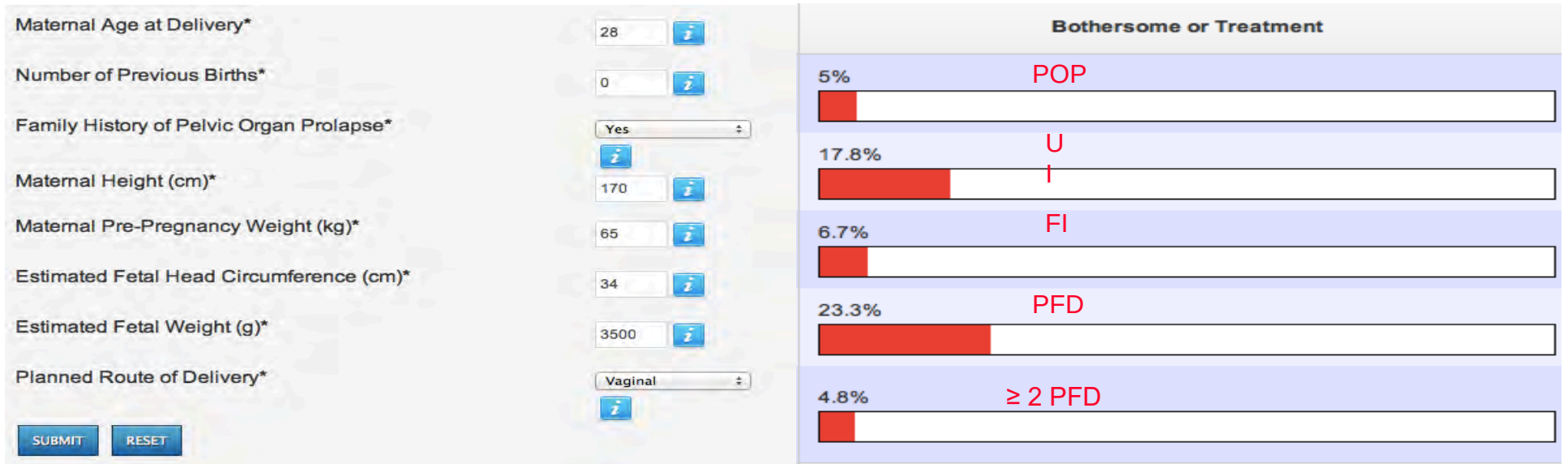
28 year old primip, family history of POP, low risk

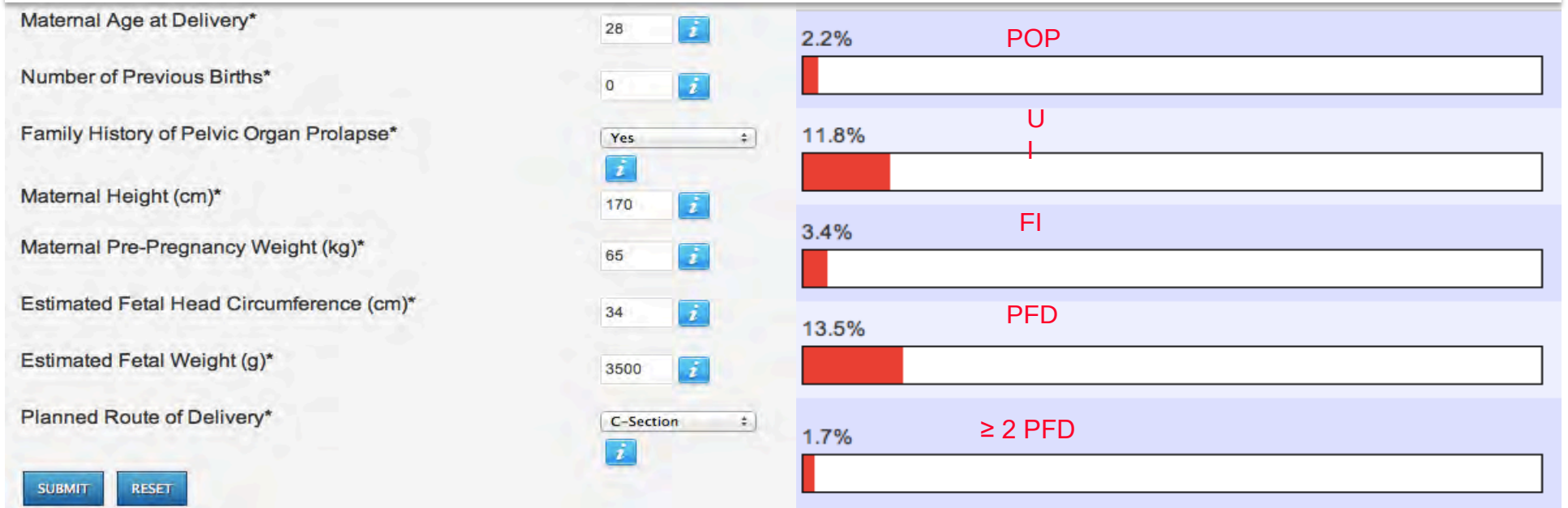


28 year old primip, family history of POP, high risk



28 year old primip, family history of POP, low risk





Limitations & Strengths

- **Models are not perfect (c-stat = 1)**
- **Several over predict when patients are very high risk.**
- **Significantly advance our ability to counsel women before and after delivery**
- **Identify women for future prevention studies**

Conclusions

- **Models provide valid individualized risk estimates for the development of PFDs 12-20 years after delivery.**
- **The models in this analysis provide similar discrimination to other predictive models currently used in clinical practice whose concordance index generally range from 0.6 to 0.8 including widely-used models such as the National Cancer Institute Gail model for prediction of Breast Cancer risk (concordance index 0.59) and the Framingham Cardiovascular Risk Model (concordance index 0.72).**

Conclusions

- **Significantly advance our ability to identify women for prevention Future studies should investigate:**
  - **How do women and providers interpret and use prediction tools?**
  - **High risk, what can be done about it?**
- **Predicting risk is a major step in prevention.**
- **The risk calculator is freely available on line:**

http://riskcalc.org:3838/UR CHOICE/

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3 - 6 September 2019

Leading Continence Research and Education

Call for Abstracts: 1 March - 1 April 2019

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ICS 2019 GOTHENBURG

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The Scientific program

We are planning an action-packed, innovative, scientific program covering all aspects of continence care

State of the Art Lectures

Kari Bo

" Is physical activity good or bad for the pelvic floor"

Professor, Norwegian School of Sport Sciences, Dept of Sports Medicine

J Eric Jelovsek, MD, MMEd

"Risk prognostication in prolapse and incontinence following childbirth"

2nd degree connection2nd/Vice Chair, Education for OBGYN, Associate Professor at Duke University School of Medicine/Durham, North Carolina

State of the Art Lectures

Linda Brubaker

"The urinary microbiome"

Linda Brubaker, MD, MS is a Professor in the Department of Reproductive Medicine at the University of California San Diego and a board-certified specialist in Female Pelvic Medicine and Reconstructive Surgery. Dr. Brubaker is a prolific researcher with multiple NIH awards including a recently awarded R01 and is a PI within the NIDDK PLUS network to study bladder health.

Andrea Tubaro

"Prostatic controversies"

Professor Tubaro graduated in Medicine and Surgery at Sapienza University of Rome where he completed his postgraduate training in urology. Andrea Tubaro is Professor and Chairman of the Department of Urology in Sant'Andrea Hospital – Sapienza University of Rome, Italy

VIDEO….

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