# Comparative Effectiveness of Stone Surgery for Pediatric Patients: The PKIDS Trial

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# Disclosures

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## Disclosures

All statements in this report, including its findings and conclusions, are solely those of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute (PCORI), its Board of Governors or Methodology Committee.

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PKIDS Pediatric KIDney Stone Care Improvement Network

# Evidence base

Uncomplicated ureteral stones <10 mm, clinicians should offer observation with or w/o MET using $\alpha$-blockers. **Level B**

URS or SWL for pediatric patients with ureteral stones unlikely to pass or who failed observation and/or MET, based on anatomy and body habitus. **Level B**

Clinicians should obtain a low-dose CT scan on pediatric patients prior to performing PCNL. **Level C**

In pediatric patients with ureteral stones, clinicians should not routinely place a stent prior to URS. **Expert Opinion**

In pediatric patients with a total renal stone burden ≤20 mm, clinicians may offer SWL or URS as first-line therapy. **Level C**

For total renal stone burden >20 mm, both PCNL and SWL are acceptable. If SWL is used, a ureteral stent or nephrostomy tube should be placed. **Expert Opinion**

Except in cases of coexisting anatomic abnormalities, open/laparoscopic/robotic surgery should not be routinely performed for upper tract stones. **Expert Opinion**

In pediatric patients with asymptomatic and non-obstructing renal stones, clinicians may utilize active surveillance with periodic ultrasonography. **Expert Opinion**

# American Urological Association Guidelines

In pediatric patients with a total renal stone burden ≤20 mm, clinicians may offer SWL or URS as first-line therapy. **Level C**

For total renal stone burden >20 mm, both PCNL and SWL are acceptable. If SWL is used, a ureteral stent or nephrostomy tube should be placed. **Expert Opinion**

# PKIDS

## Pediatric KIDney Stone Care Improvement Network


Cincinnati Children's
LEGES SINE MORIBUS VANAE
Children's Hospital of Richmond at VCU
Children's of Alabama
Monroe Carell Jr. Children's Hospital at Vanderbilt
Children's HOSPITAL • ST. LOUIS
children'shealth
Children's Wisconsin
Kids deserve the best.
Children's Healthcare of Atlanta
UNIVERSITY OF MICHIGAN
Nemours Children's Health System
Texas Children's Hospital
Northwell Health
NATIONWIDE CHILDREN'S
When your child needs a hospital,
Boston Children's Hospital
Intermountain Primary Children's Hospital
The Child First and Always
The UNIVERSITY of OKLAHOMA Health Sciences Center
UCLA
MATTEL Childrens Hospital
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AdventHealth for Children
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We Treat Kids Better
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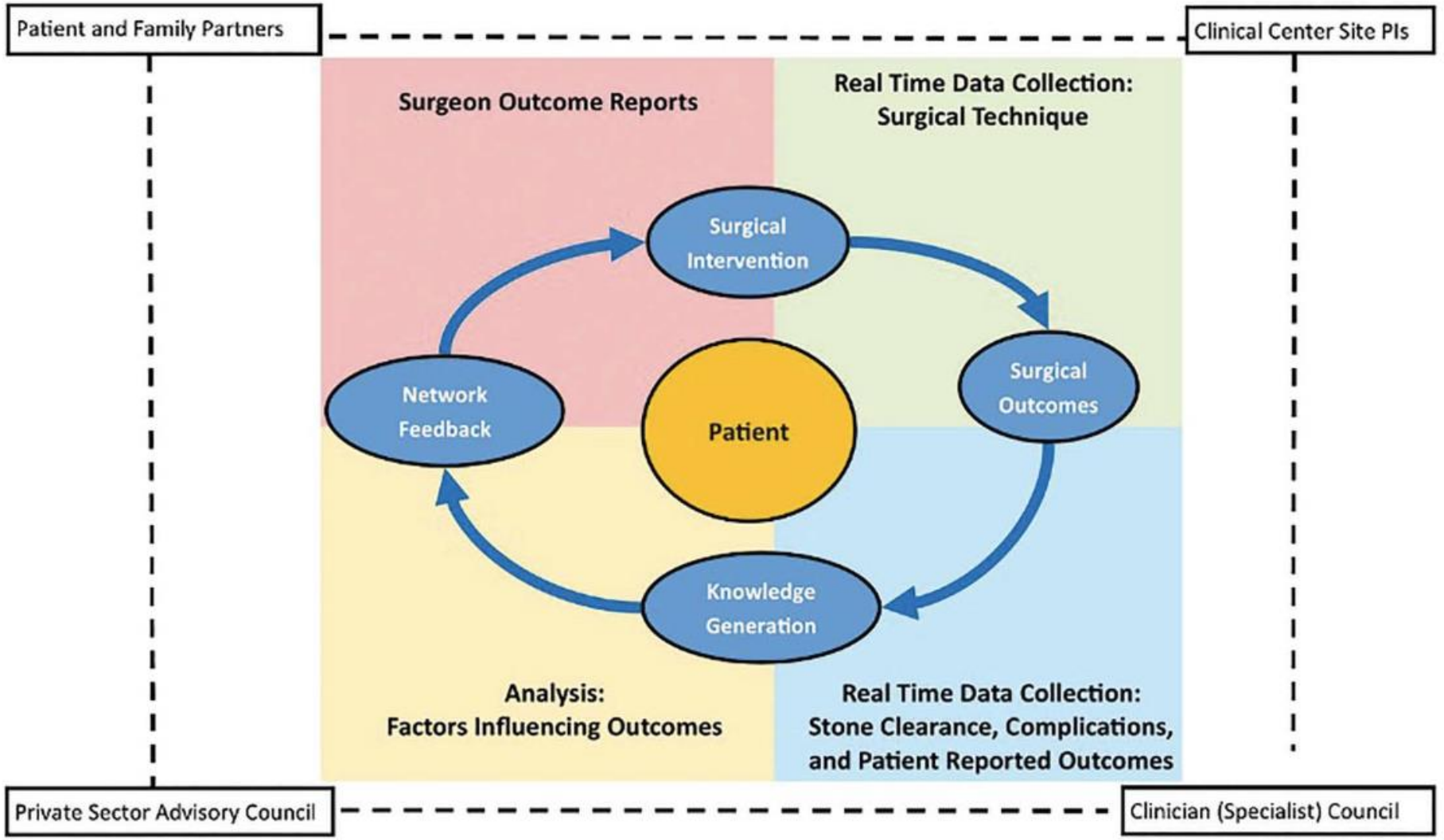
HOSPITAL · RESEARCH · FOUNDATION
SickKids
UFHealth
UNIVERSITY OF FLORIDA HEALTH

# Mission

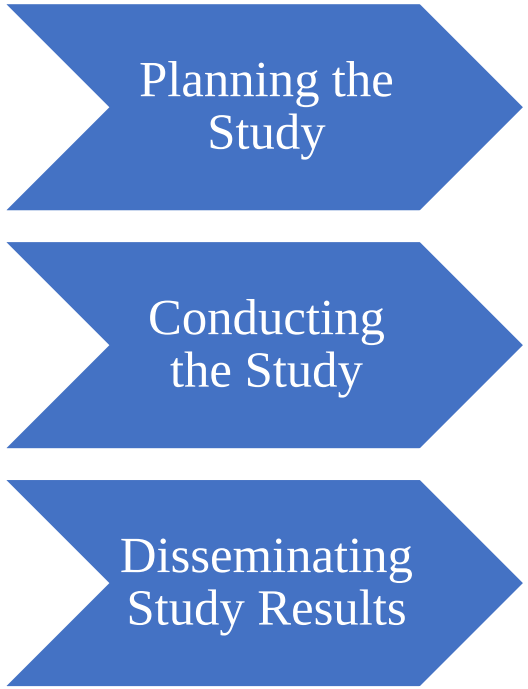
**To improve the health of children with kidney stone disease through collaborative patient-centered research**

# Surgical Learning Cycle



# Embracing Partnerships

- Patients
- Caregivers
- Clinicians
- Industry
- Payers
- Healthcare system leaders



# After surgery the experience can be drastically different:

*"The outcome was that this was a surgery that no one wanted to repeat."*

*"Wow! This experience was so different than my previous one."*

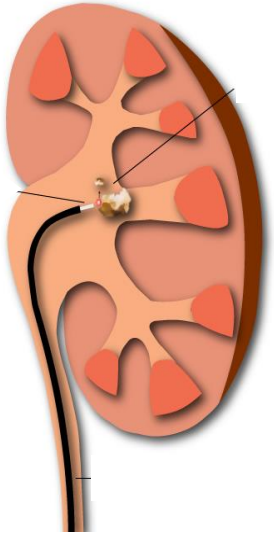

Children's Hospital of Philadelphia

PKIDS
Pediatric KIDney Stone
Care Improvement Network

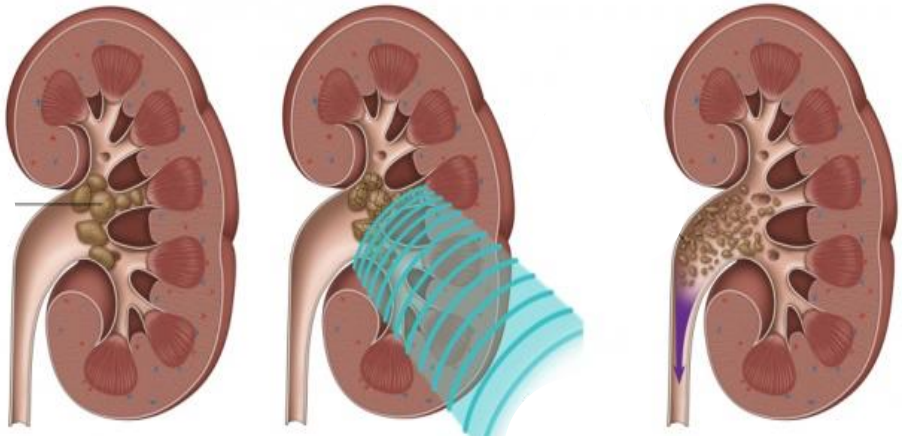
# Research question

**What is the best surgery for my child who has a kidney or ureteral stone?**

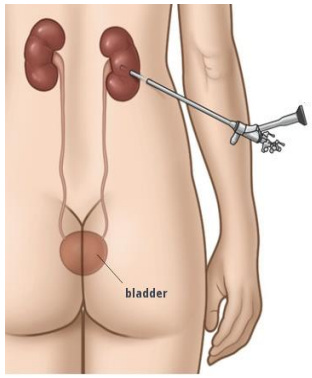
**Ureteroscopy (URS)**

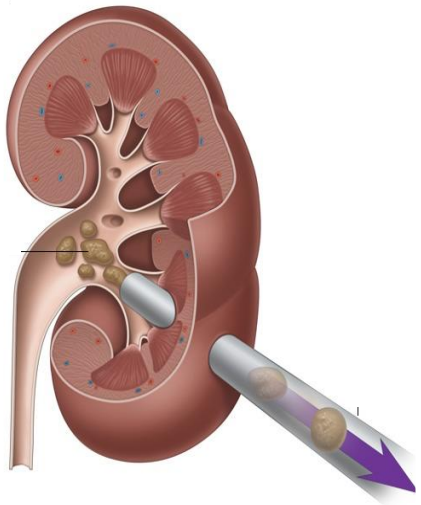


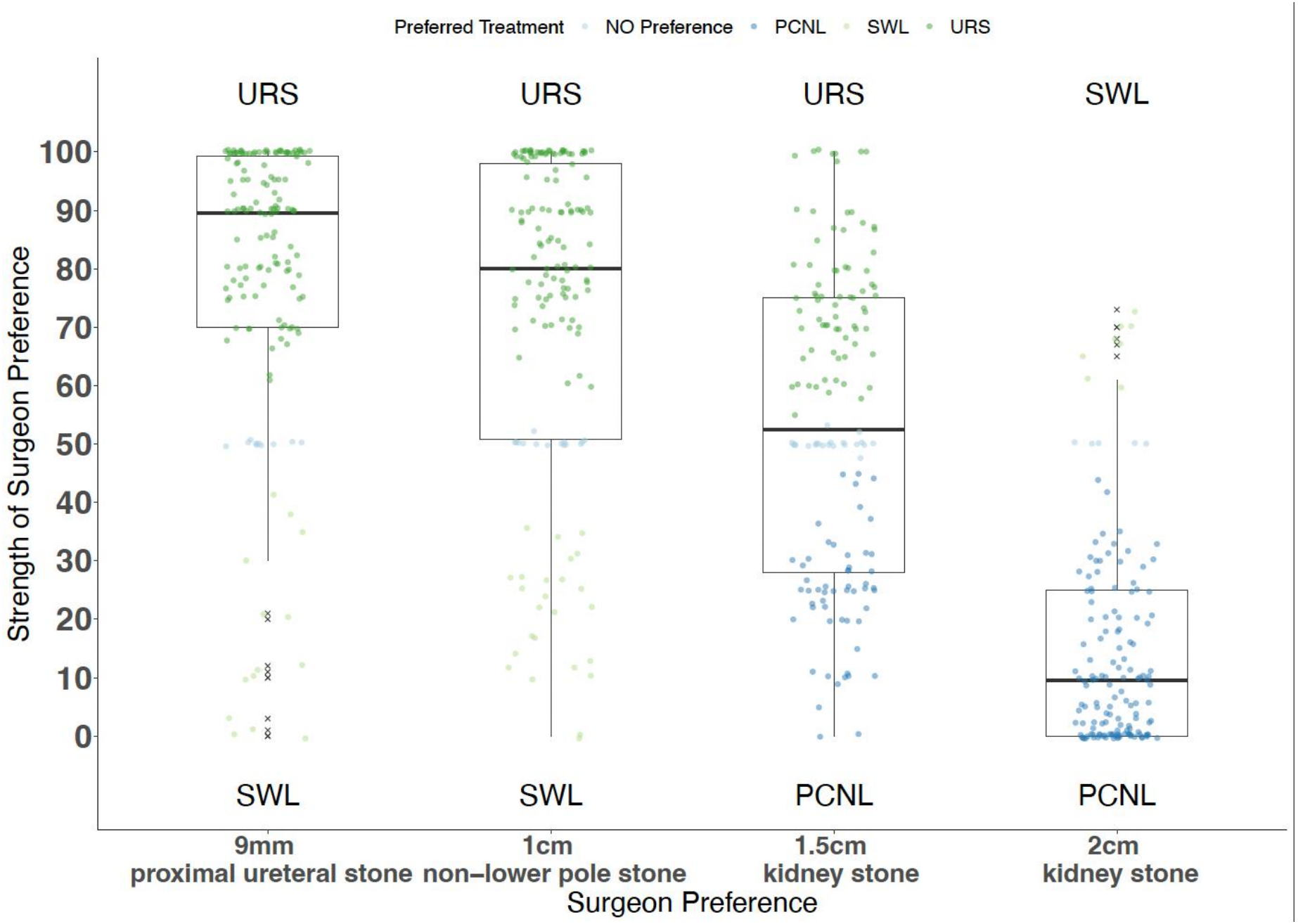
**Shockwave lithotripsy (SWL)**



**Percutaneous nephrolithotomy (PCNL)**




Preferred Treatment
NO Preference
PCNL
SWL
URS
URS
URS
URS
SWL
100
90
80
70
60
50
40
30
20
10
0
Strength of Surgeon Preference
SWL
SWL
PCNL
PCNL
9mm
proximal ureteral stone
1cm
non–lower pole stone
1.5cm
kidney stone
2cm
kidney stone
Surgeon Preference

# Study Design

## Prospective observational cohort study

# Population

## Broad Eligibility Criteria

### Inclusion

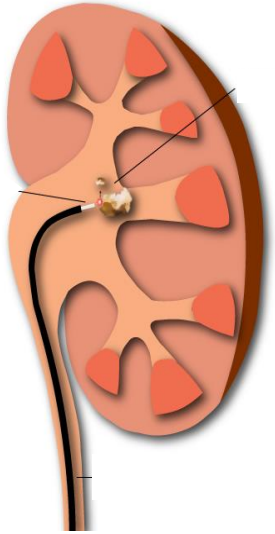
- Males or females, 8-21 years of age, undergoing URS, SWL, or PCNL for the removal of at least one kidney and/or ureteral stone

### Exclusion

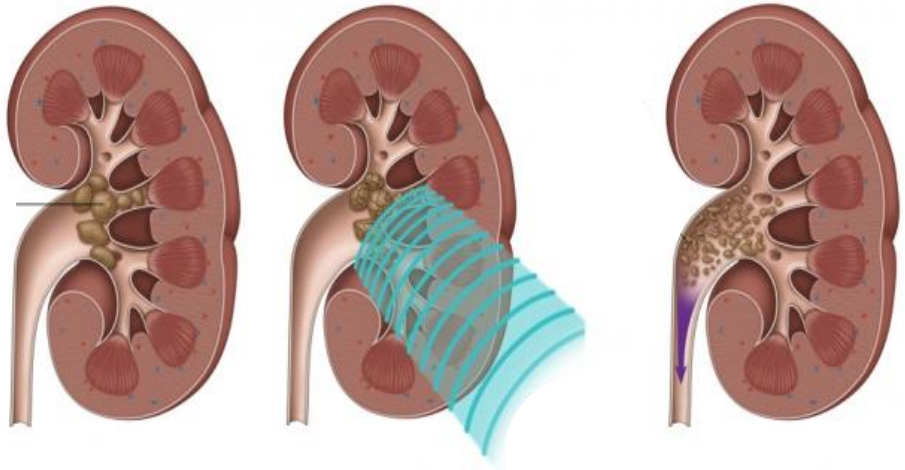
- Participants for whom informed consent would confer additional risk (e.g., obstructing ureteral stone with fever requiring emergency surgery)

# Comparators

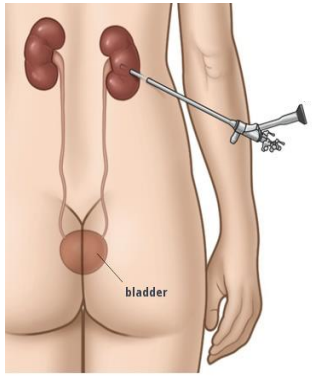
**Ureteroscopy (URS)**

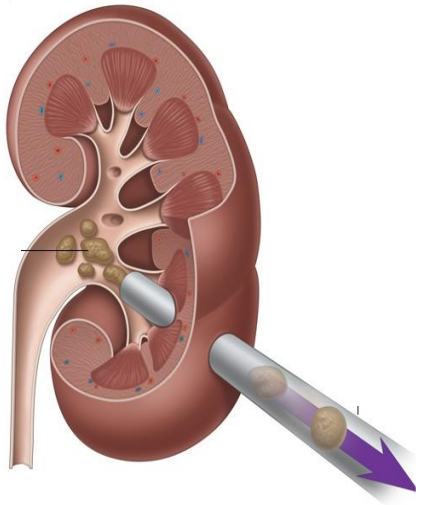


**Shockwave lithotripsy (SWL)**



**Percutaneous nephrolithotomy (PCNL)**



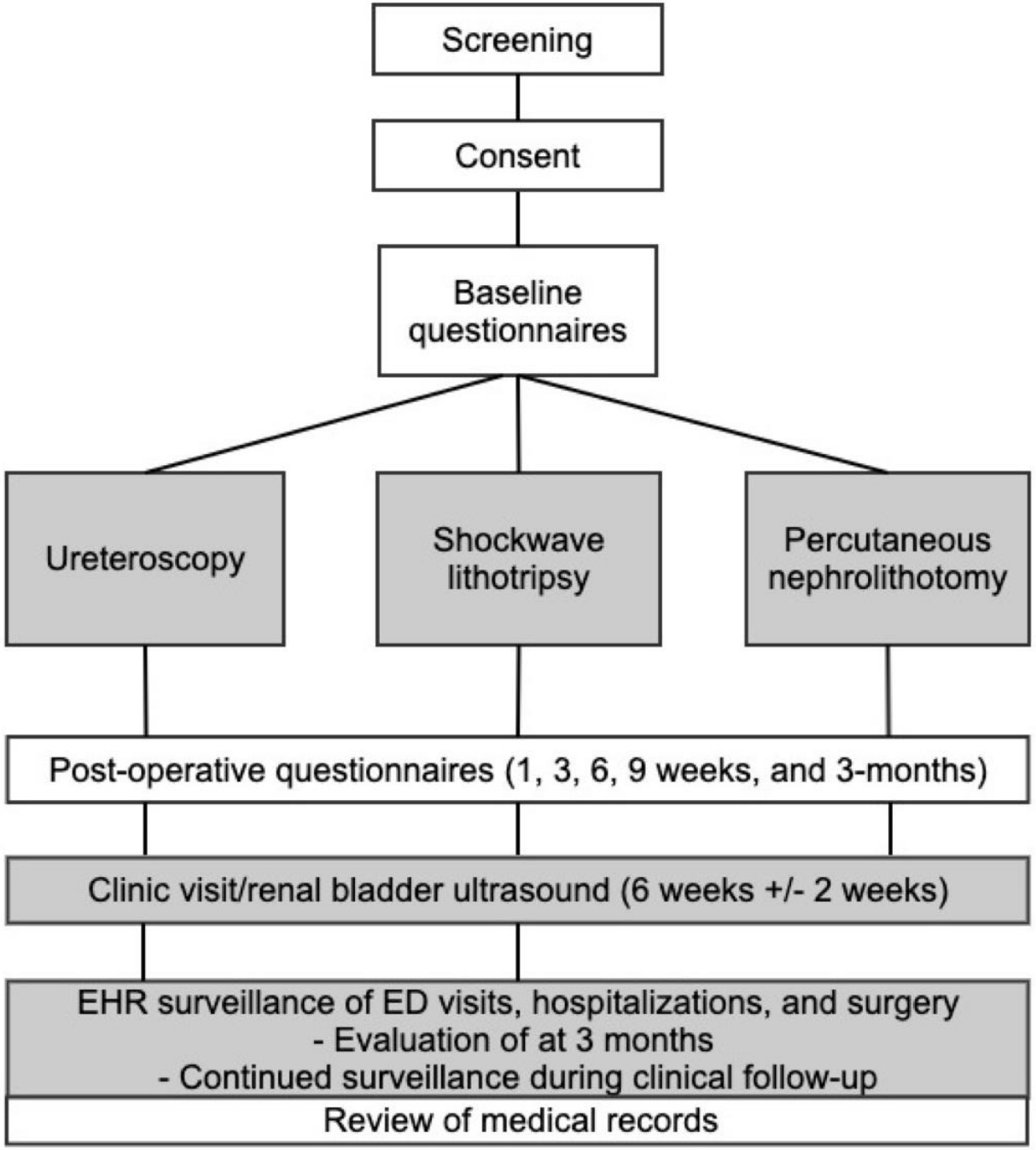
# Outcomes: Patient selected and prioritized

**Primary Outcome: Stone clearance**
HTE by stone size and stone location

- Absence of any stone >4mm
- Standardized ultrasound at 6 +/- 2 weeks

**Secondary: Physical, social, and emotional health**
HTE by age and sex

- PROMIS measures
  - Pain intensity
  - Pain interference
  - Anxiety
  - Sleep disturbance
  - Psychological stress
  - Peer relationships
- Urinary symptoms
  - DVSS
  - QUIKSS
- Missed school/work
- ED visits, repeat surgery, admissions




* All boxes in grey shade reflect clinical care (not study) procedures.

# Analysis

Propensity score development

- Identify patient, surgeon, and institutional characteristics that could impact selection of treatment and outcomes
  - Clinician importance
  - Principal components analysis
  - Correlation

Inverse propensity score weighting to balance patient, surgeon, and institutional characteristics across groups

- Weighted generalized linear models for stone clearance
- Weighted ANCOVA for PROs

# Analysis

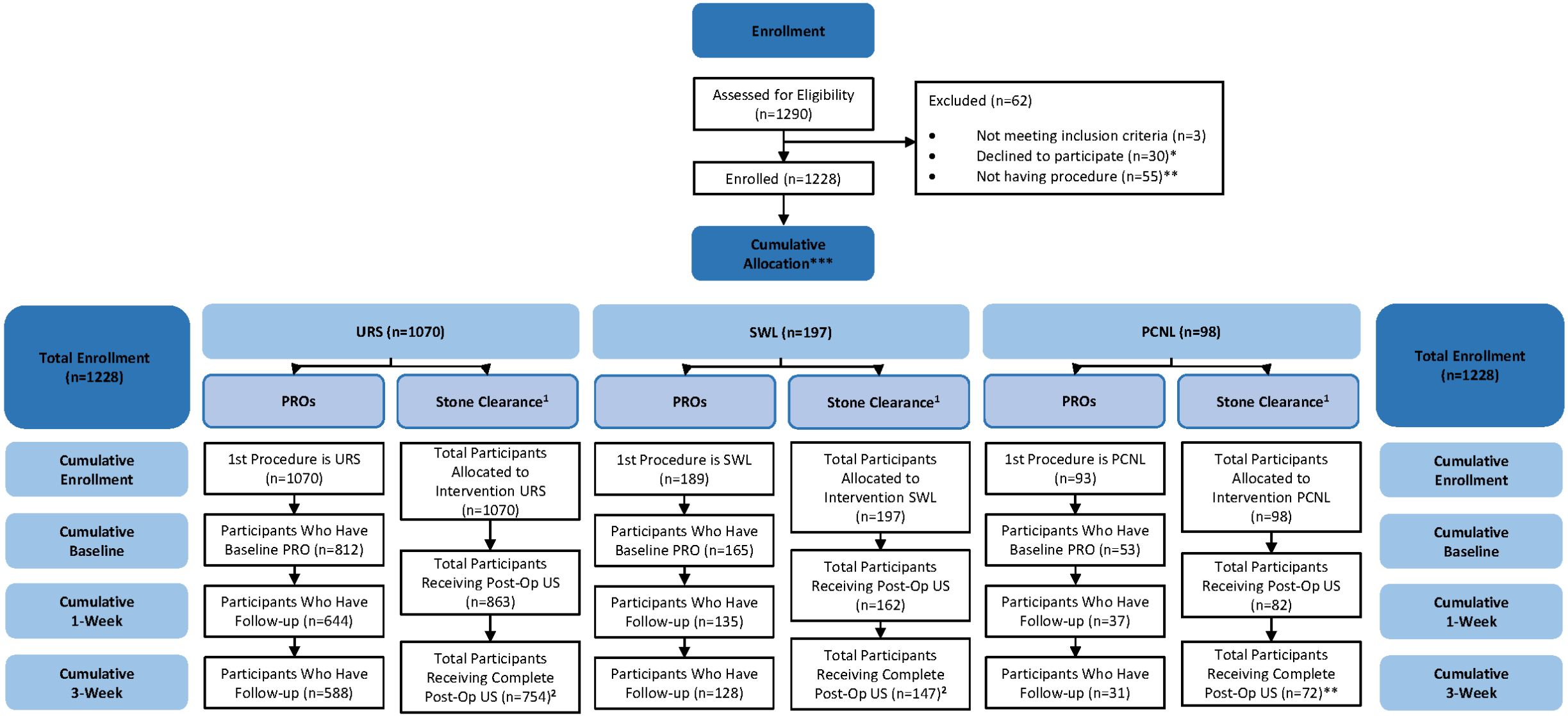
Multiple imputation for missing data

Centralized review of random sample of 10% of pre- and post-operative ultrasounds

- Blinded single reviewer
- Determine change and direction of change of primary outcome

Comparison of trial participants to PCORnet

- Patients at PCORnet sites that participate in PKIDS
- Patients at PCORnet sites that do not participate in PKIDS




* Participants who withdraw but permit data collection will remain in the analysis cohort
** Participants did not receive URS, SWL, or PCNL
*** Cumulative allocation is by patient side
[1] Cumulative allocation is by patient side
[2] Complete means US studies either reported 'No stone present" OR "had measured stone size"

# Participant characteristics

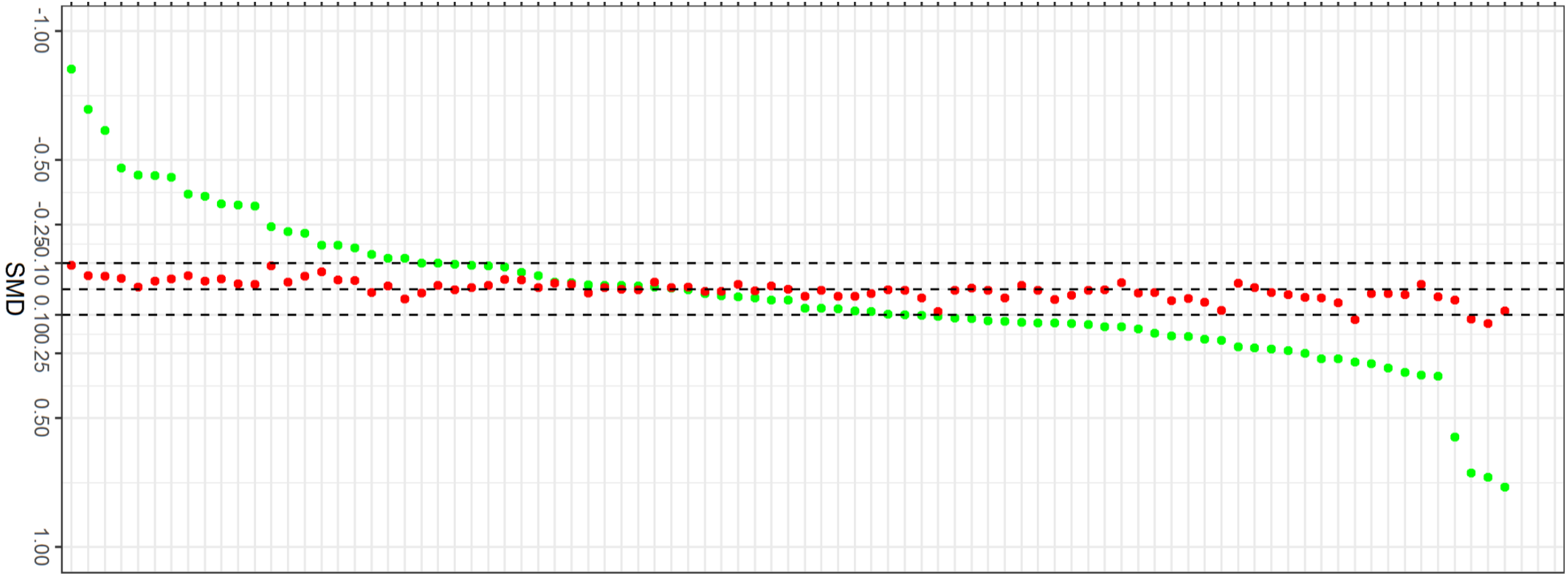
| Characteristics | URS (n = 1070) | SWL (n = 197) | PCNL (n = 93) |
|---|---|---|---|
| **Median age in years, (IQR)** | 15.6 (12.6, 17.3) | 15.6 (12.5, 17.6) | 15.0 (11.8, 17.5) |
| **Female sex, n (%)** | 659 (61.6%) | 103 (52.3%) | 39 (45.3%) |
| **Race, n (%)** | | | |
| White | 834 (77.9%) | 153 (77.7%) | 54 (62.8%) |
| Black | 42 (3.9%) | 3 (1.5%) | 2 (2.3%) |
| Asian | 15 (1.4%) | 1 (0.5%) | 1 (1.2%) |
| **Hispanic ethnicity**, n (%) | 124 (11.6%) | 20 (10.2%) | 18 (20.9%) |
| **Number of stones in treated kidney**, median (IQR) | 1 (1, 2) | 1.00 (1, 2) | 2.0(1.0, 3.0) |
| **Largest stone size in treated kidney**, mm, median (IQR) | 6 (4, 9) | 7.00 (6, 9) | 14.0(8.5, 20.0) |
| **Stone Location** | | | |
| No stone | 63 (5.9%) | 2 (1.0%) | 1 (1.2%) |
| Lower pole kidney | 198 (18.5%) | 68 (34.5%) | 25 (29.1%) |
| Non-lower pole kidney | 311 (29.1%) | 98 (49.7%) | 46 (53.5%) |
| Ureter (includes UPJ) | 480 (44.9%) | 28 (14.2%) | 13 (15.1%) |
| **Primary indication for surgery** | | | |
| Elective | 111 (10.4%) | 69 (35.0%) | 4 (4.7%) |
| Pain | 702 (65.6%) | 75 (38.1%) | 26 (30.2%) |
| UTI | 207 (19.3%) | 50 (25.4%) | 48 (55.8%) |

Three patients had SWL for stones >15mm

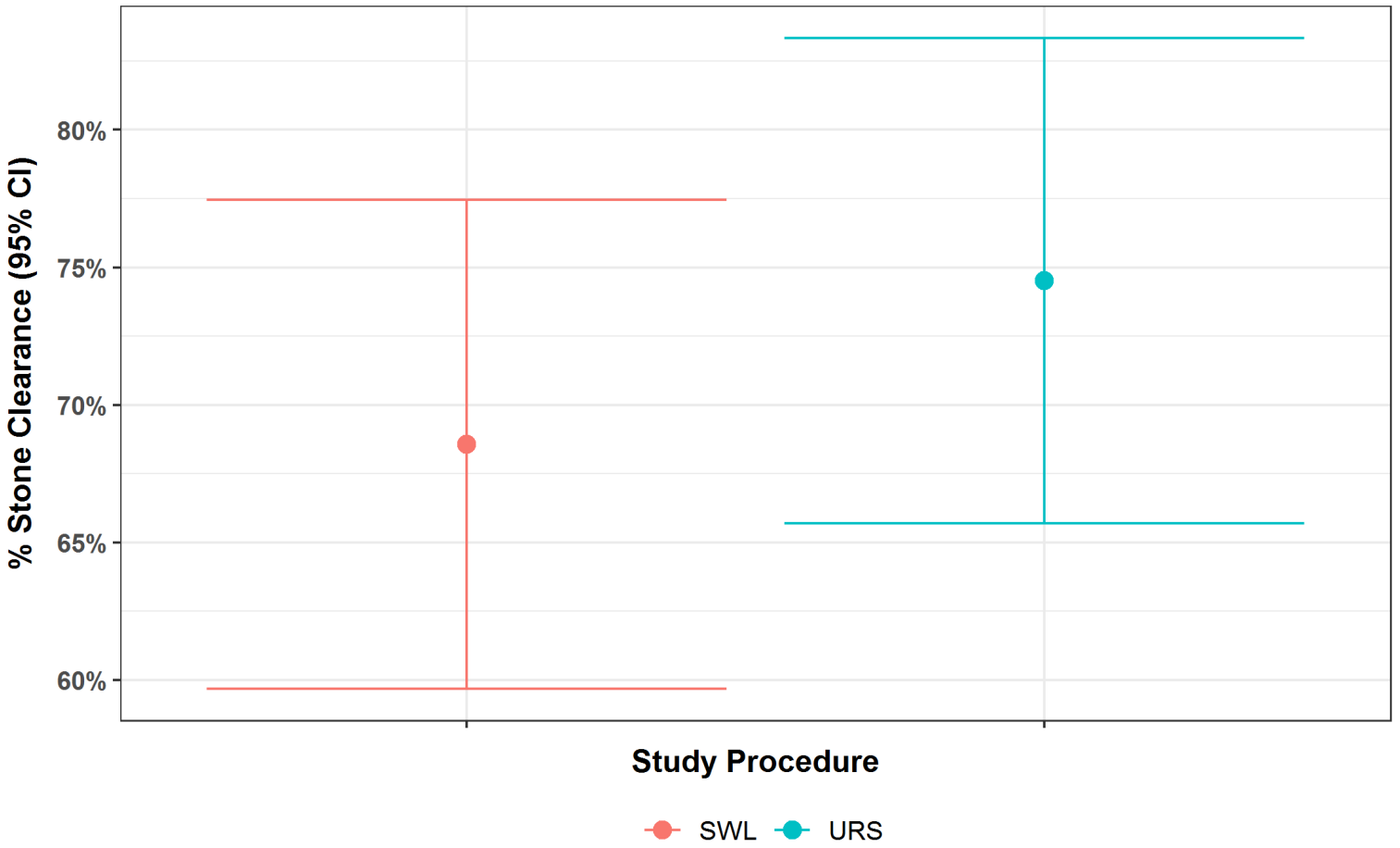
# URS vs SWL

In pediatric patients with a total renal stone burden ≤20 mm, clinicians may offer SWL or URS as first-line therapy. **Level C**

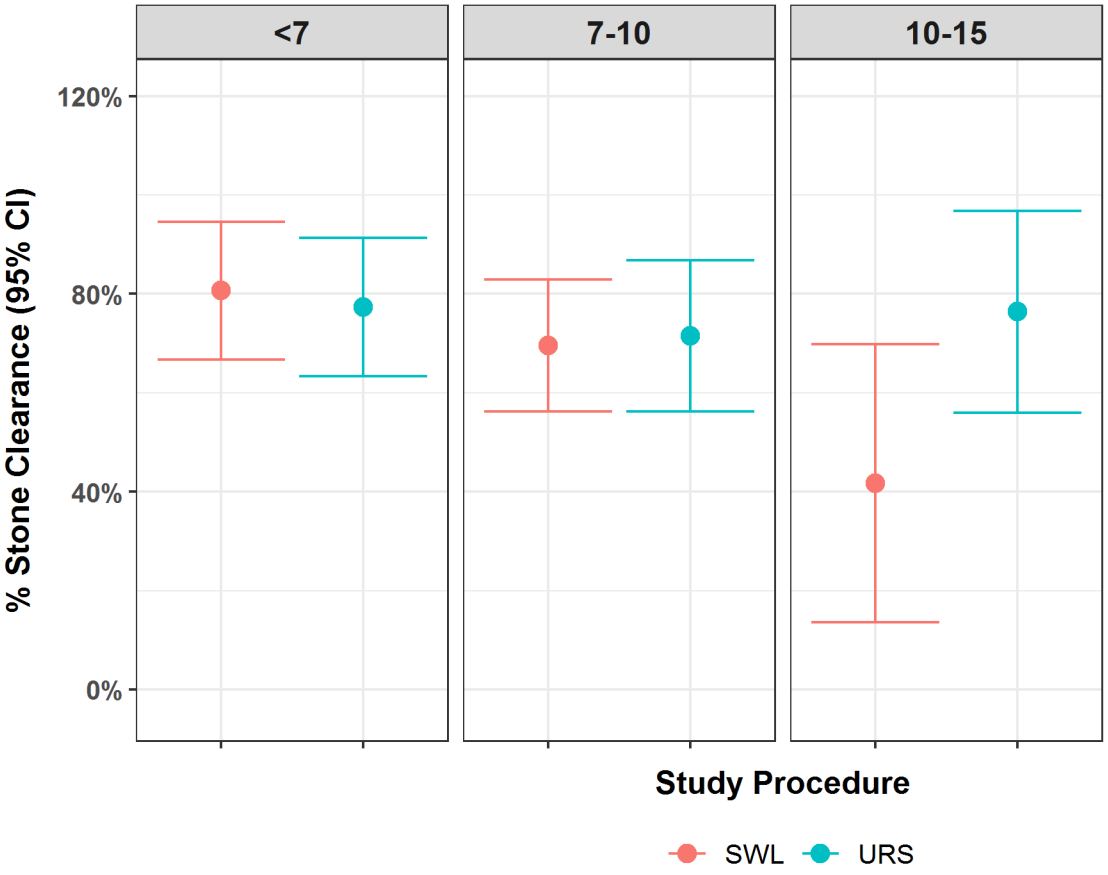
# URS vs SWL
# Covariate balance before and after propensity score weighting

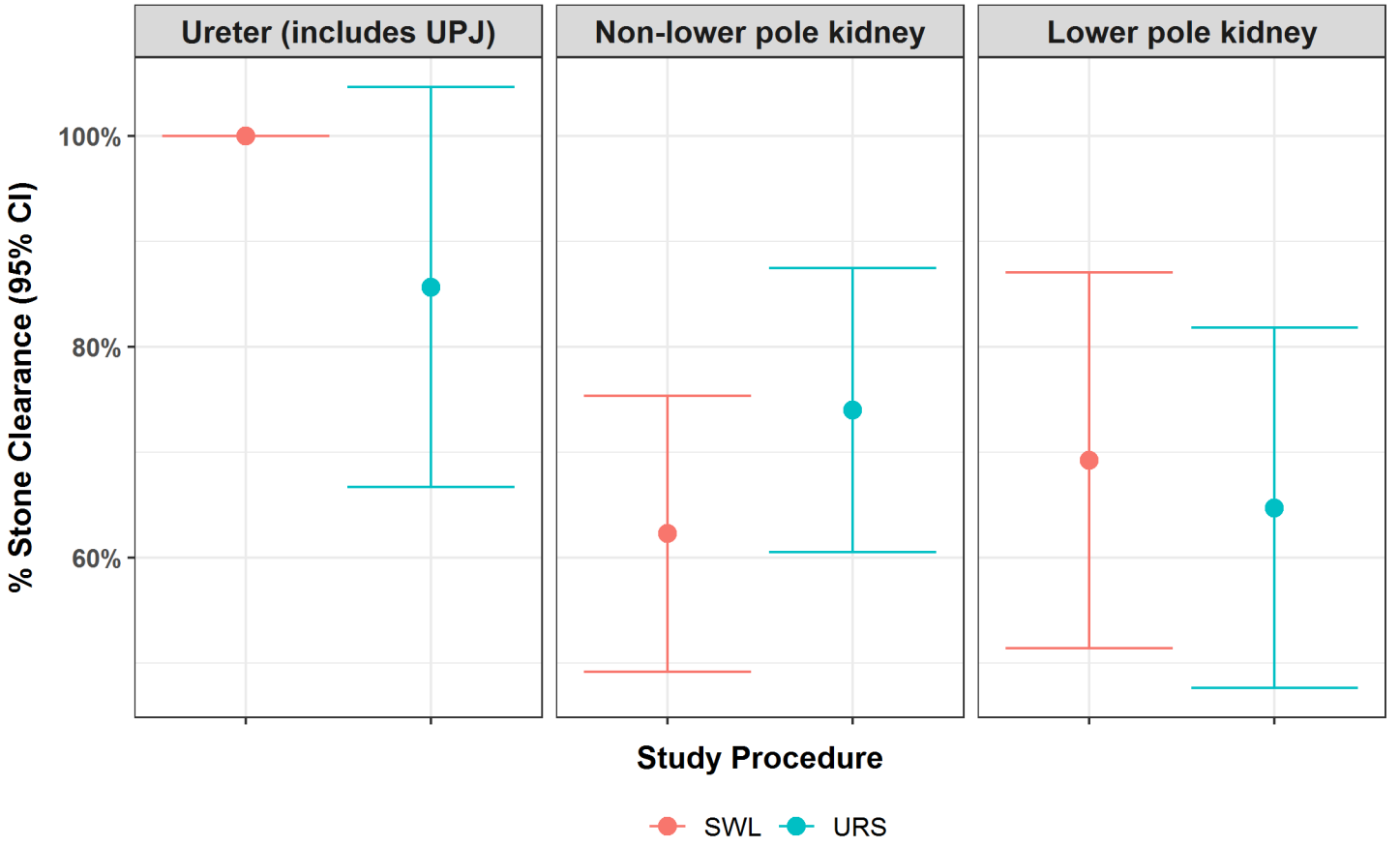


# URS vs SWL: overall treatment effect
# No difference in stone clearance



# URS vs SWL: HTE by size and location
# No difference in stone clearance (remaining uncertainty 10-15mm)



# Impact of URS Compared to SWL on PROs of Physical, Emotional, and Social Health at One week after Surgery

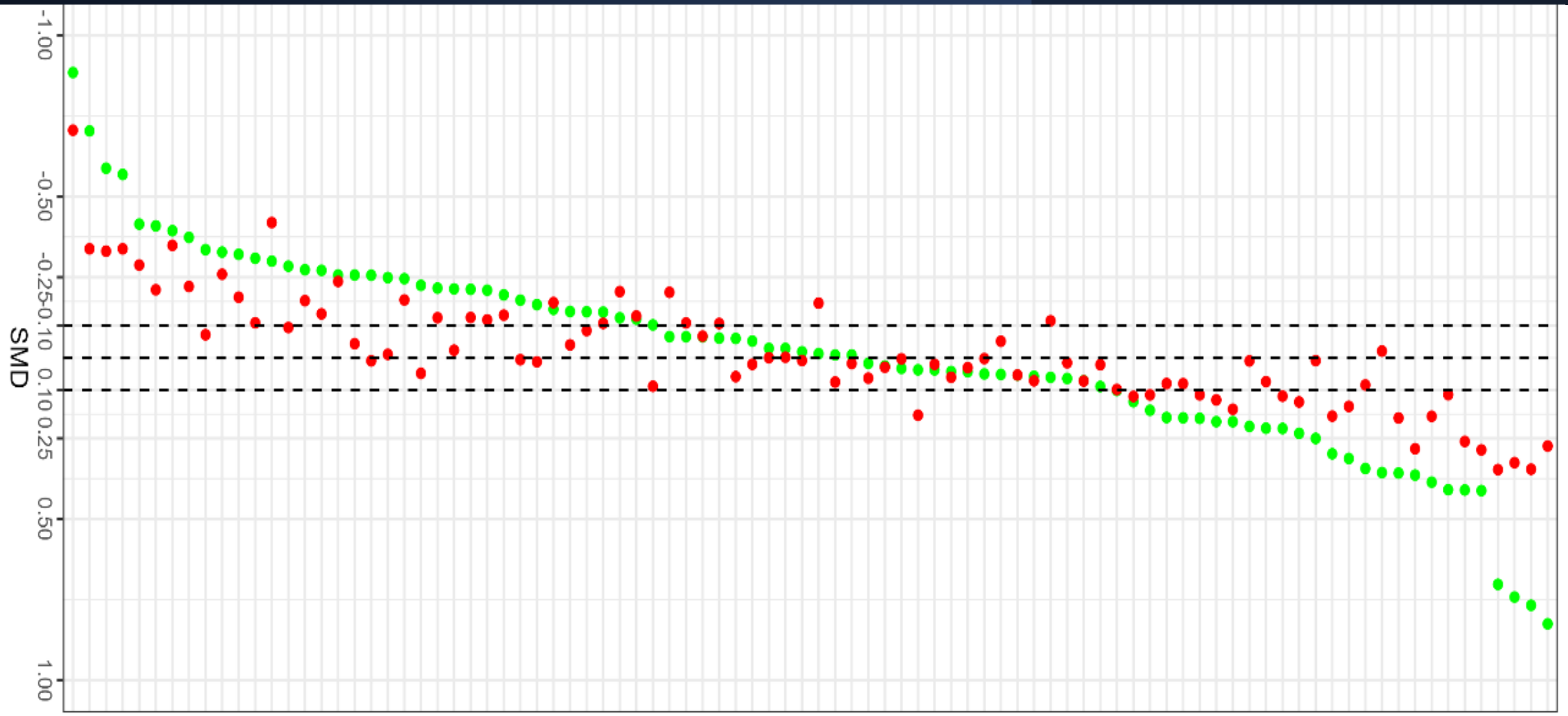
| PRO | Procedure | Baseline effect (β, 95% CI) | Procedure effect (β, 95% CI) |
|---|---|---|---|
| **Urinary symptoms** | URS | **0.5 (0.36, 0.65)** | **5.86 (3.32, 8.39)** |
| **Anxiety** | URS | **0.73 (0.58, 0.88)** | 2.7 (-0.12, 5.52) |
| **Pain Intensity** | URS | **0.34 (0.12, 0.56)** | **4.76 (1.6, 7.91)** |
| **Pain Interference** | URS | **0.33 (0.2, 0.47)** | **8.09 (4.73, 11.45)** |
| **Peer Relationships** | URS | **0.67 (0.5, 0.85)** | -1.22 (-3.64, 1.19) |
| **Sleep Disturbance** | URS | **0.68 (0.51, 0.84)** | 1.37 (-1, 3.73) |
| **Stress Experiences** | URS | **0.68 (0.6, 0.77)** | 1.42 (-0.57, 3.42) |

# PCNL vs URS (not SWL)

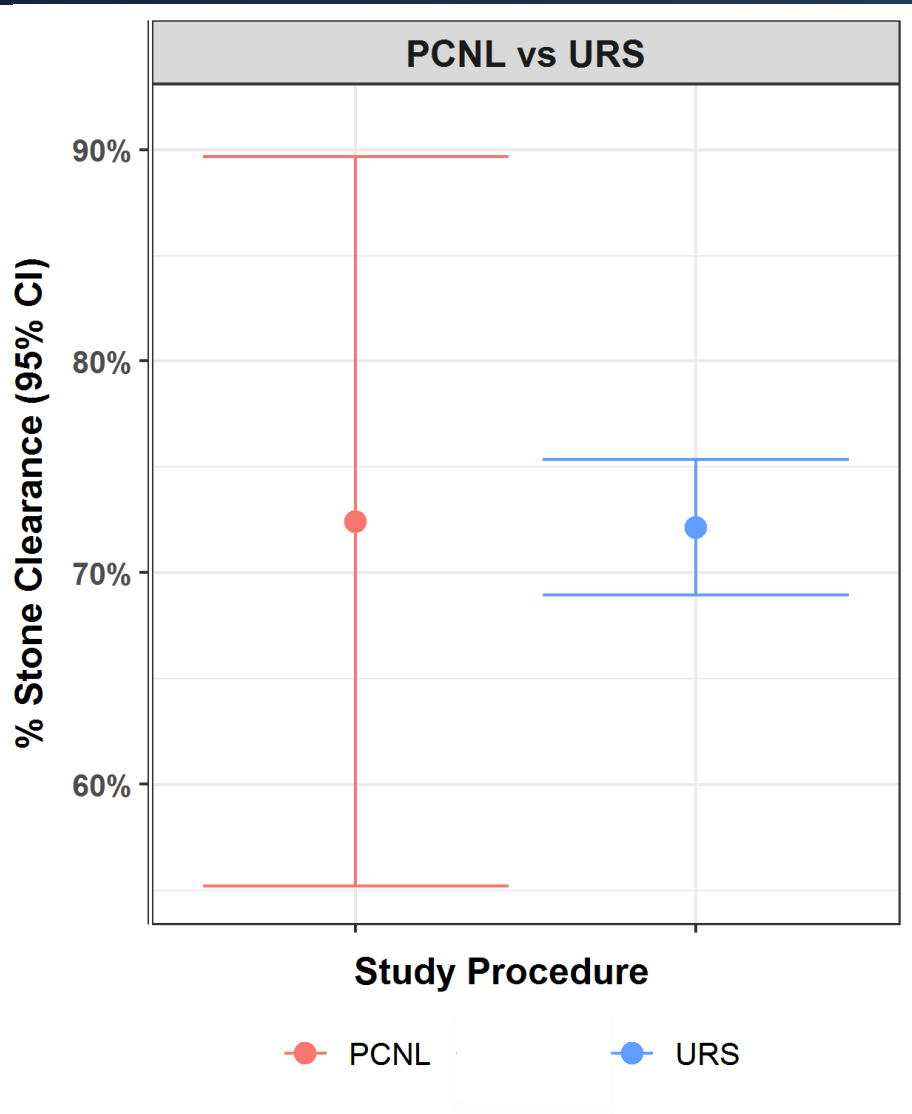
For total renal stone burden >20 mm, both PCNL and SWL are acceptable. If SWL is used, a ureteral stent or nephrostomy tube should be placed.

**Expert Opinion**

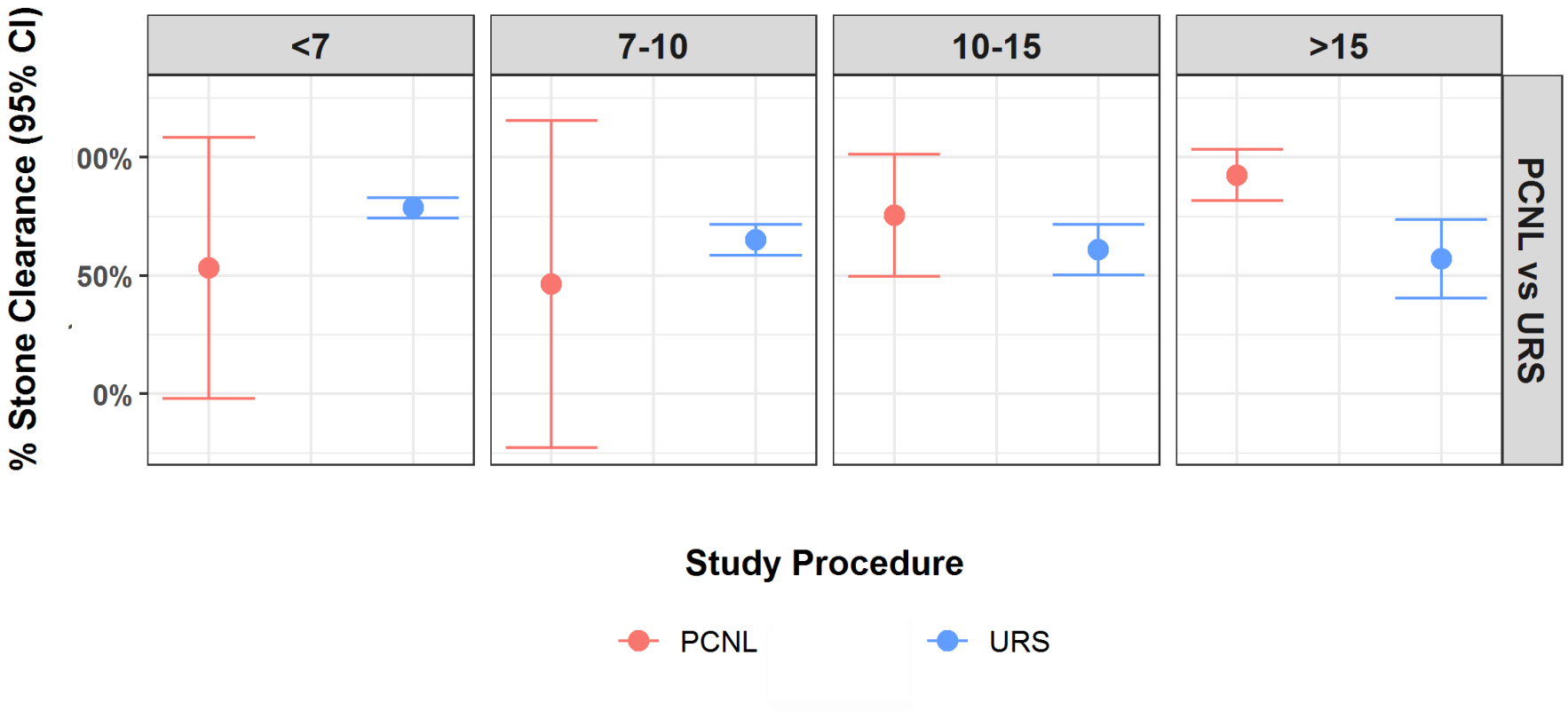
# PCNL vs URS:
# Covariate balance before and after propensity score weighting



# PCNL vs URS: Overall treatment effect
# No difference in stone clearance



# PCNL vs URS: THE by size and location
# Greater stone clearance for stones >15mm



# Impact of PCNL Compared to URS on Patient-Reported Outcomes of Physical, Emotional, and Social Health at One week after Surgery

| PRO | Procedure | Baseline effect (β, 95% CI) | Procedure effect (β, 95% CI) |
|---|---|---|---|
| **Urinary symptoms** | PCNL | **0.31 (0.21, 0.4)** | **-6.37 (-11.71, -1.03)** |
| **Anxiety** | PCNL | **0.61 (0.54, 0.68)** | **-5.74 (-9.26, -2.22)** |
| **Pain Intensity** | PCNL | **0.26 (0.19, 0.33)** | **-5.42 (-10.38, -0.46)** |
| **Pain Interference** | PCNL | **0.24 (0.17, 0.31)** | **-5.88 (-11.02, -0.75)** |
| **Peer Relationships** | PCNL | **0.67 (0.6, 0.74)** | 1.63 (-1.94, 5.2) |
| **Sleep Disturbances** | PCNL | **0.53 (0.45, 0.6)** | **-5.57 (-8.56, -2.58)** |
| **Stress Experiences** | PCNL | **0.66 (0.6, 0.73)** | **-7.9 (-13.13, -2.67)** |

# The PKIDS trial supports revision of AUA guidelines

1) A new size threshold of 15mm for kidney stones

2) Recommend SWL over URS for stones <10mm

3) Consider possible greater stone clearance and worse patient experiences with URS for kidney stones 10-15mm

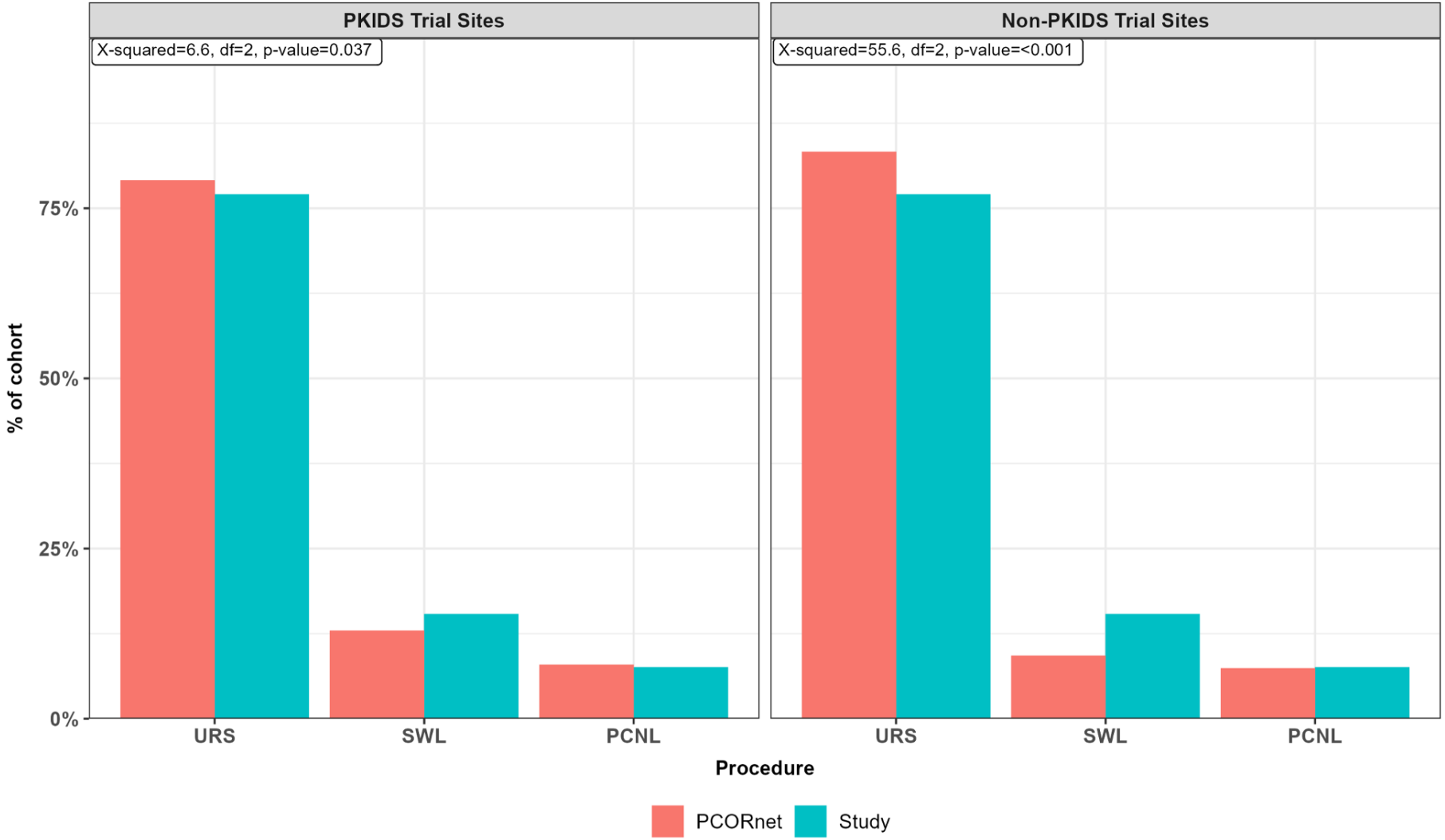
4) Remove SWL from guidelines for stones >15mm

5) Recommend PCNL over URS for stone >15mm

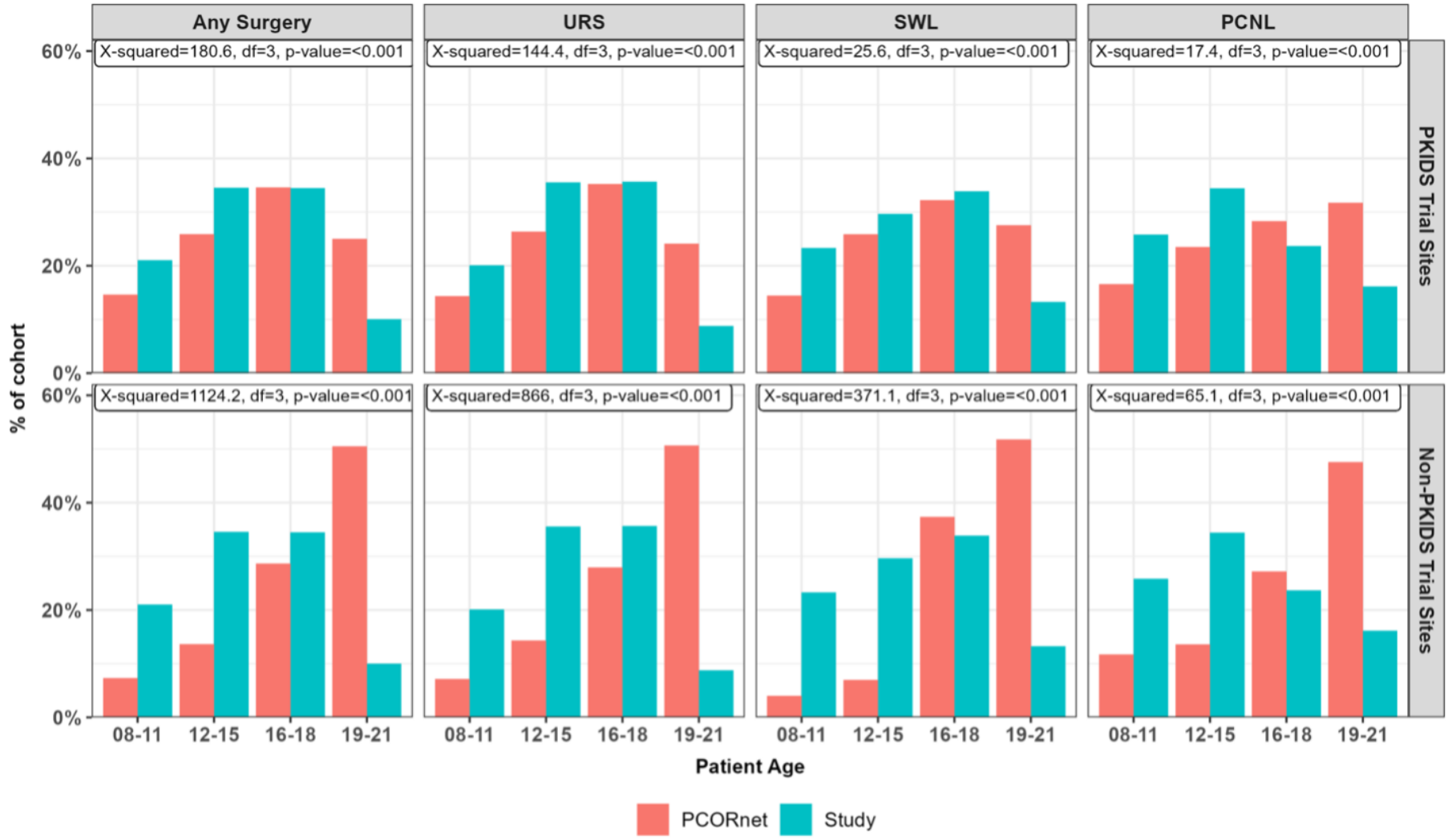
# Internal & External Validity and Generalizability

- 5.4% of stone clearance outcomes changed on central review
  - Bias towards decreasing stone clearance
  - Non-differential across modalities
- No change in direction or statistical significance of point estimates on imputed data analysis

# Internal & External Validity and Generalizability



# Internal & External Validity and Generalizability



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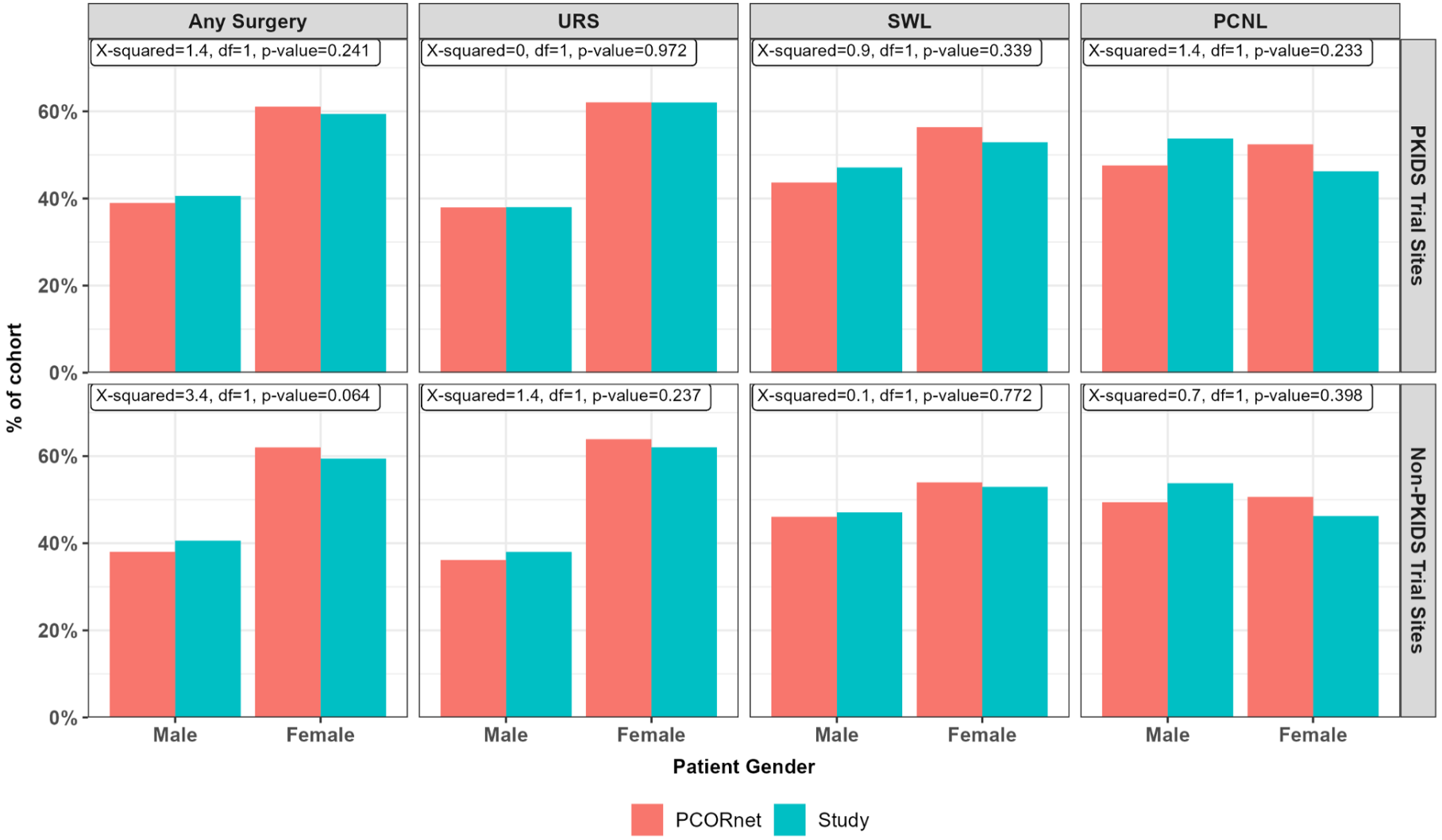

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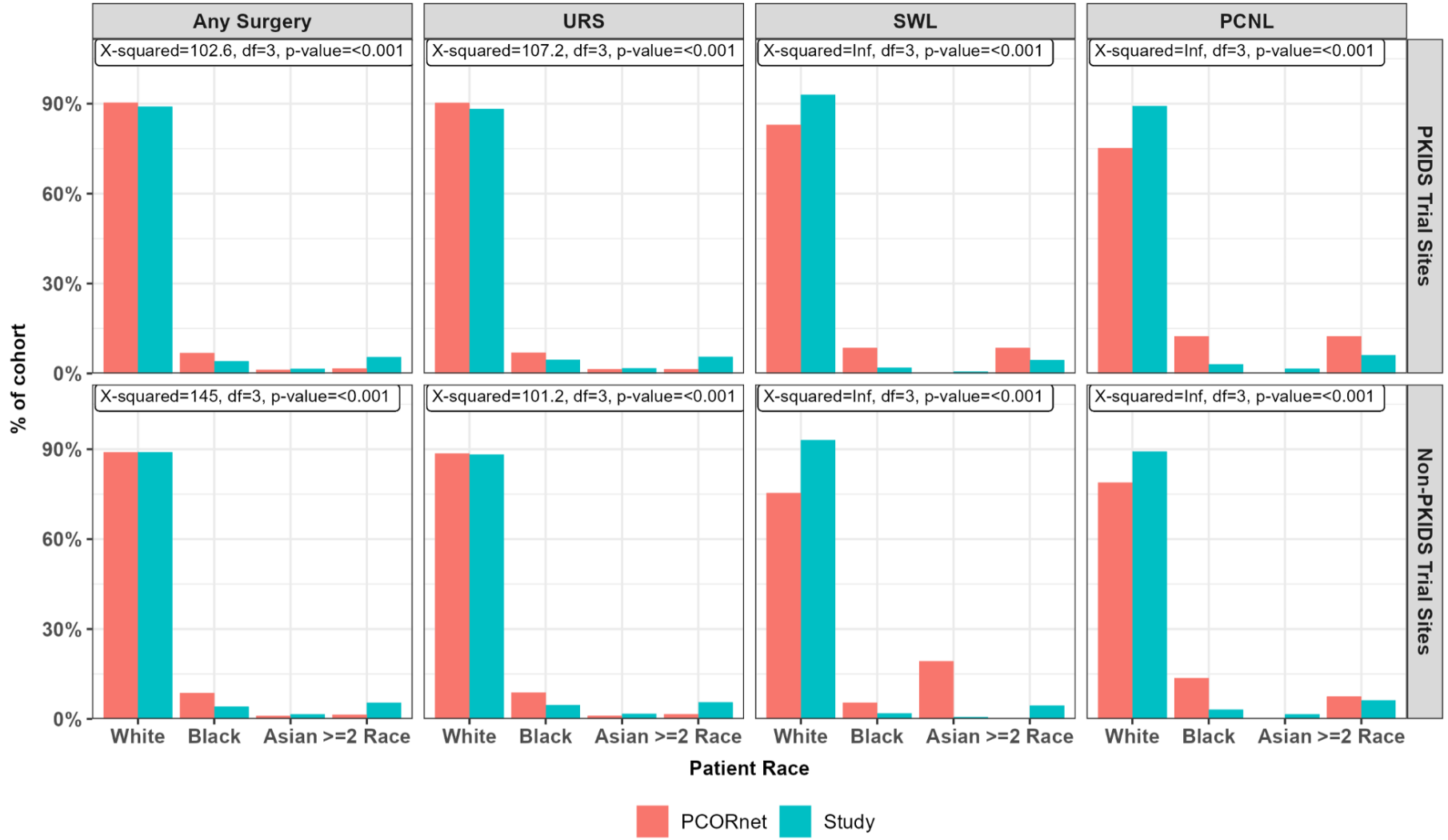

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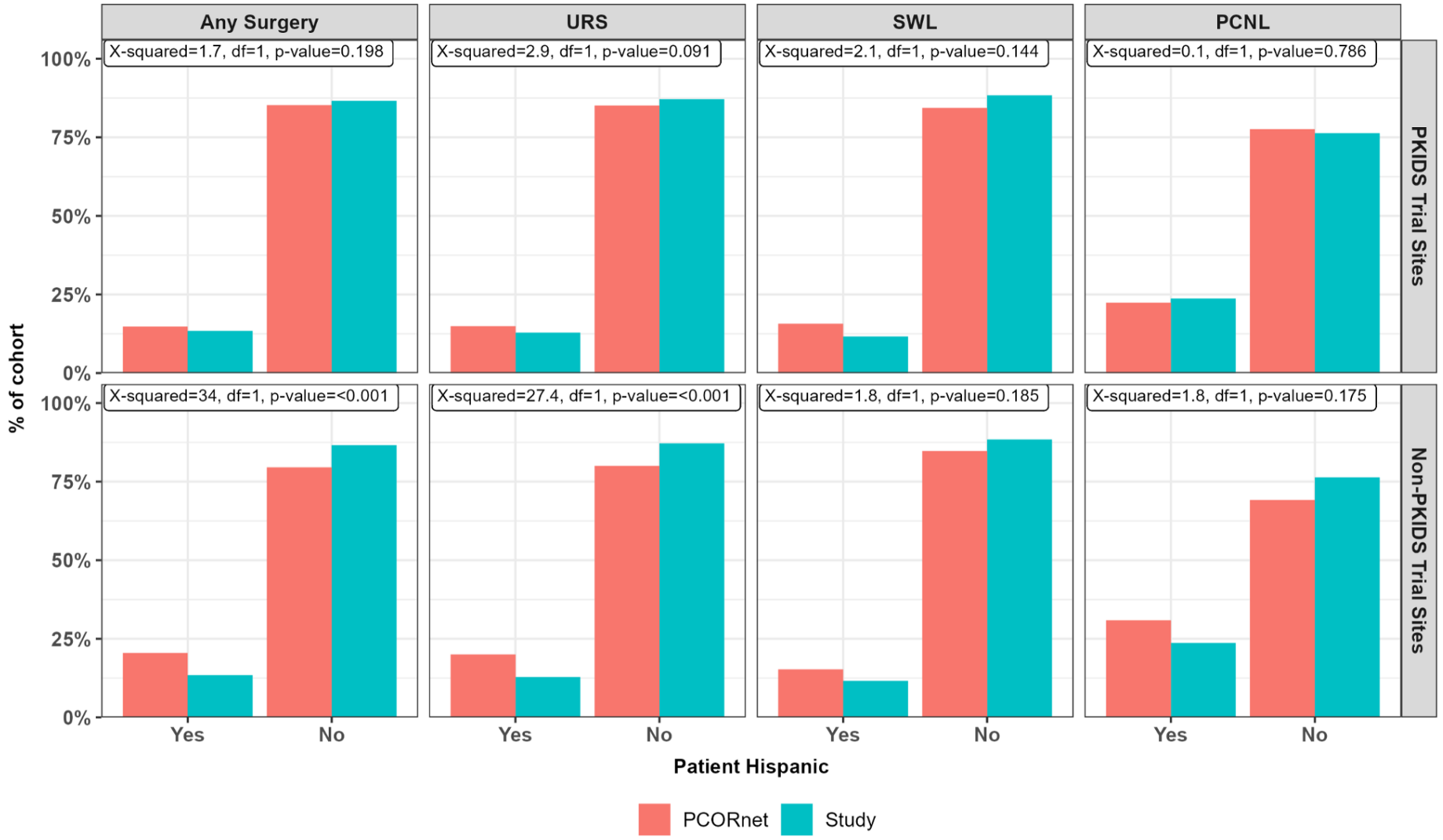


# Study Design

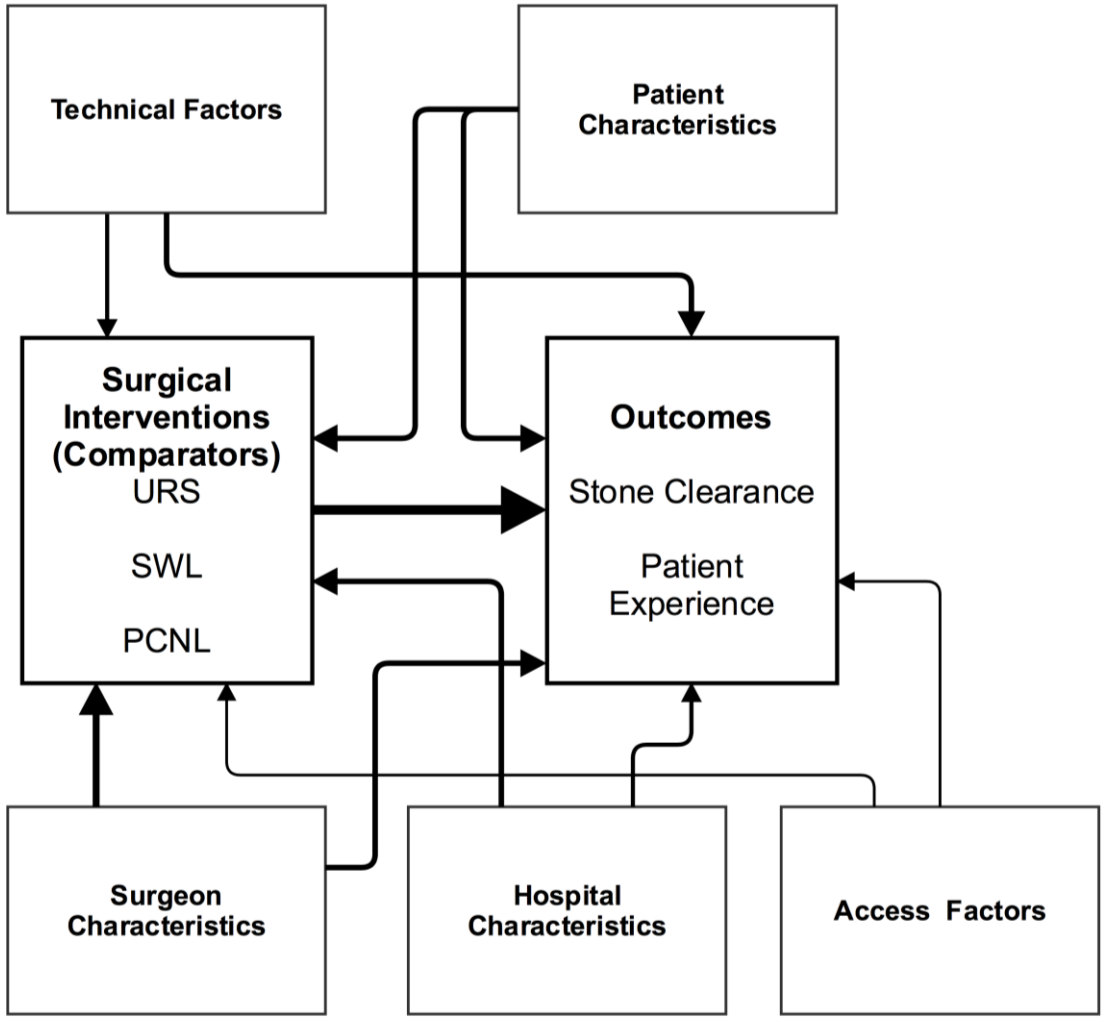
## Prospective observational cohort study

- Embedded in real-world clinical care
- Greater generalizability
- Threats of bias and unmeasured confounding

## Why not a RCT?

- Lack of clinical equipoise
  - treatment is heavily influenced by surgeons' experience, training, and local practices.
  - Surgeons and patients may be unwilling to have surgical decisions determined by chance alone → failure to enroll

# Study Design



# Enhancing Participation

Introduce the PKIDS trial to *every* patient undergoing surgery

- Trust
  - Operating surgeon introduces study
- Altruism
  - Participation will help families make decisions about surgery by generating knowledge about outcomes that matter most to them
- Financial motivation
  - $100 compensation
- Burden
  - No study visits
  - Questionnaires can be completed remotely

# Retention/Data Missingness

Ultrasound completion reflects real-world care in non-Covid times

- Need to link to real-world clinical outcomes

Very good but not excellent capture of technical aspects of surgery

- Need better ways to recognize missing data at the point of care within time window of ascertainment and intervene

# Implementation

**Changing care needs more than improved shared decision making**

Surgeon and patients

- Informing of evidence and understanding priorities but…

Use of SWL and PCNL determined by

- Surgeon training and skill
- Surgeon bias
- Equipment availability
- Equipment type


PKIDS
Pediatric KIDney Stone
Care Improvement Network
PKIDS is a network of over 26 pediatric healthcare systems in North America with mission of generating and applying knowledge to improve patient-centered outcomes in pediatric kidney stone disease.
Scan the QR code or contact pkids@chop.edu to learn more!
Hunter Beck
Media, PA


If you were
a Kidney
I'd Be your
Stone
Chocolate by Mueller
Chocolate by Mueller