

# Effects of Anesthesia on Young Children

Khoa Phẫu thuật Gây mê Hồi sức  
BV nhi đồng 2

# MAYO ANESTHESIA SAFETY IN KIDS

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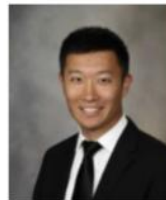
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*Andy Hanson*

# MASK Study

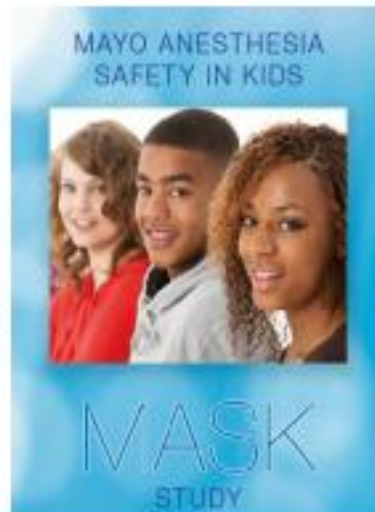
**Observational, population-based,  
propensity-matched designs**

*3 groups, defined by number of anesthetic  
exposures prior to 3rd birthday: 0, 1,  $\geq 2$*

↙

## Retrospective MASK study

*Replicate prior findings regarding  
behavior/learning in modern  
anesthesia practice*



↘

## Prospective MASK study

*Seek detailed phenotype of  
anesthesia-associated injury*

# MASK was Built on a Series of Retrospective Cohort Studies



## Early Exposure to Anesthesia and Learning Disabilities in a Population-based Birth Cohort

Robert T. Wilder, M.D., Ph.D.; Randall P. Flick, M.D., M.P.H.; Jura J. Sprung, M.D., Ph.D.; Slavica K. Katusic, M.D.; William J. Barbaresi, M.D.; et al



## Cognitive and Behavioral Outcomes After Early Exposure to Anesthesia and Surgery

**OBJECTIVE:** To determine whether exposure to anesthesia and surgery before the age of 2 years is associated with cognitive and behavioral outcomes in children. **DESIGN:** Retrospective cohort study. **SETTING:** Rochester, Minn. **PARTICIPANTS:** Children born in Rochester, Minn., between 1976 and 1982 who were exposed to anesthesia and surgery before the age of 2 years. **MEASUREMENTS AND MAIN RESULTS:** Children exposed to anesthesia and surgery before the age of 2 years had significantly lower scores on standardized tests of cognitive and behavioral outcomes compared with children who were not exposed. **CONCLUSIONS:** Exposure to anesthesia and surgery before the age of 2 years is associated with lower scores on standardized tests of cognitive and behavioral outcomes.

**WHAT IS KNOWN ON THIS SUBJECT:** Exposure to anesthesia and surgery before the age of 2 years has been shown to cause neurodevelopmental delay in young animals. Studies of learning and cognition in children exposed to anesthesia and surgery have been few, have relied on single outcome measures, and have not controlled for confounding.

**WHAT THIS STUDY ADDS:** In this study of children exposed to anesthesia and surgery before the age of 2 years, multiple gross and individual measures of learning and behavior are examined by using a matched design with adjustment for confounding using 2 separate methods.



Perioperative Medicine | August 2009

## Anesthesia for Cesarean Delivery and Learning Disabilities in a Population-based Birth Cohort

Jura J. Sprung, M.D., Ph.D.; Randall P. Flick, M.D., M.P.H.; Robert T. Wilder, M.D., Ph.D.; Slavica K. Katusic, M.D.; Tasha L. Pike, M.S.; et al

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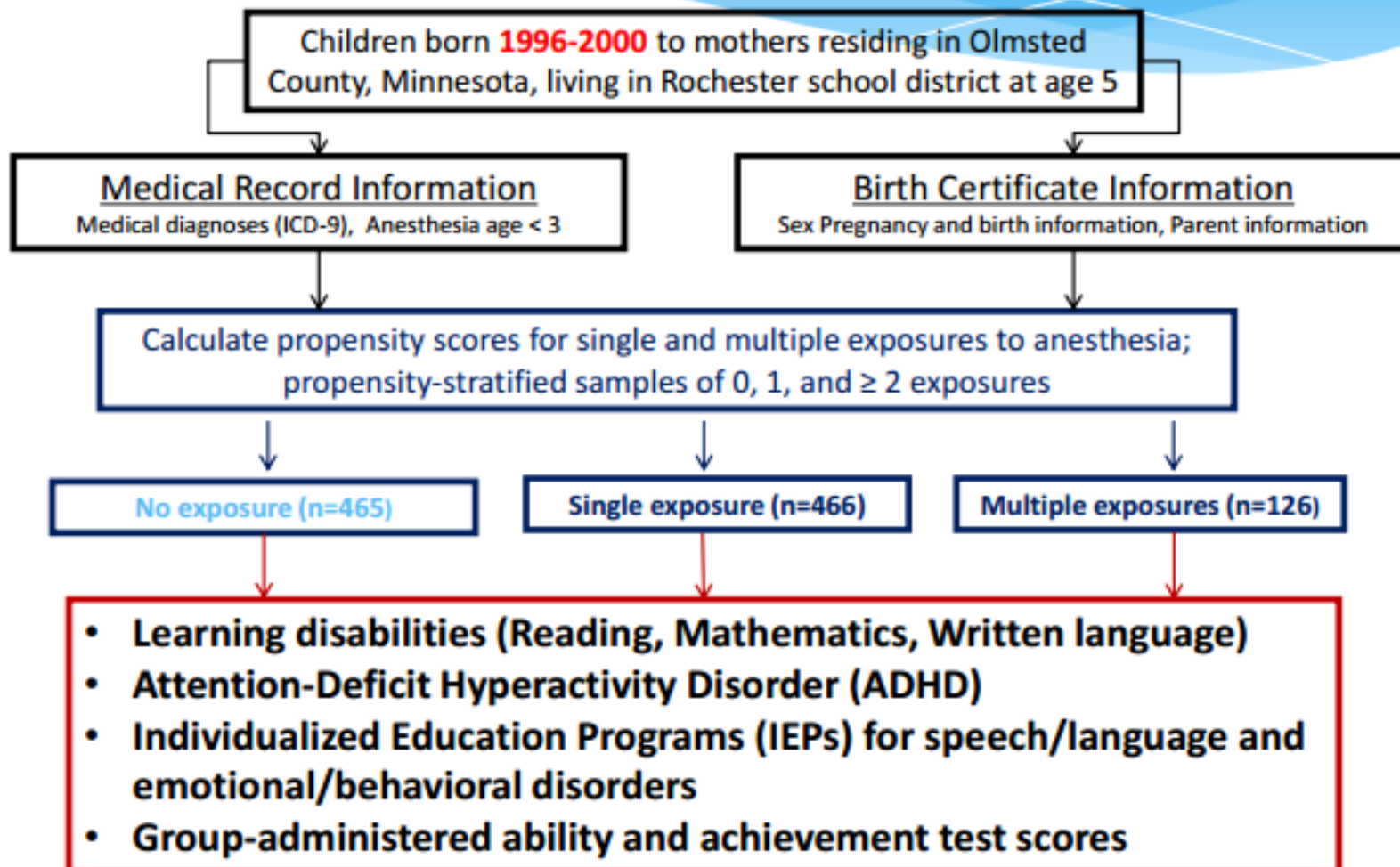
## Attention-Deficit/Hyperactivity Disorder After Early Exposure to Procedures Requiring General Anesthesia

Jura J. Sprung,<sup>1,2</sup> Randall P. Flick,<sup>3</sup> Slavica K. Katusic,<sup>4</sup> Robert C. Colligan,<sup>5</sup> William J. Barbaresi,<sup>1</sup> Katarina Rojanic,<sup>6</sup> Tasha L. Welch,<sup>7</sup> Michael D. Olson,<sup>8</sup> Andrew C. Hanson,<sup>9</sup> Darrell R. Schroeder,<sup>9</sup> Robert T. Wilder,<sup>9</sup> and David O. Warner<sup>8</sup>

**All used a birth cohort (1976-82) assembled in Rochester, MN designed to define the incidence of learning disabilities in a population**

# Retrospective MASK Study – Design

Slide courtesy of D.O. Warner



# MASK Retrospective

Repeated our earlier study using a cohort born 1996-2000 :

- 116/457/463 multiple/single/unexposed prior to age 3 yrs
- Modern anesthetic (sevoflurane)
- Pulse oximetry and capnography
- Pediatric anesthesiologists

Results essentially unchanged among multiply exposed

- 1. Doubling in the incidence of LD and ADHD
- 2. Modest reductions in performance on group tests of achievement/ability.

Single exposure - reductions in reading performance only

# Summary of Retrospective MASK

- \* Multiple, but not single, exposures to “modern” anesthesia prior to age 3 still associated with LD (all three types) and ADHD
  - 57% of multiply-exposed had both ADHD and LD, compared with ~25% of singly- and un-exposed
- \* Multiple exposures associated with modest decreases in standardized tests of ability and achievement
- \* Single exposures associated with modest decreases in subdomain of reading, not mathematics and spelling
- \* No evidence of factors moderating associations
  - Including sex, socioeconomic status, birthweight, gestational age

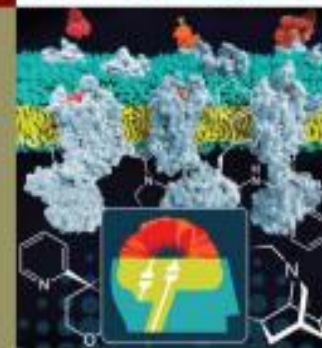
# Mask Prospective (Ambidirectional)

## Neuropsychological and Behavioral Outcomes after Exposure of Young Children to Procedures Requiring General Anesthesia

### *The Mayo Anesthesia Safety in Kids (MASK) Study*

David O. Warner, M.D., Michael J. Zaccariello, Ph.D., L.P., Slavica K. Katusic, M.D., Darrell R. Schroeder, M.S., Andrew C. Hanson, B.S., Phillip J. Schulte, Ph.D., Shonie L. Buenvenida, R.N., Stephen J. Gleich, M.D., Robert T. Wilder, M.D., Juraj Sprung, M.D., Danqing Hu, M.D., Robert G. Voigt, M.D., Merle G. Paule, Ph.D., John J. Chelonis, Ph.D., Randall P. Flick, M.D., M.P.H.

ANESTHESIOLOGY

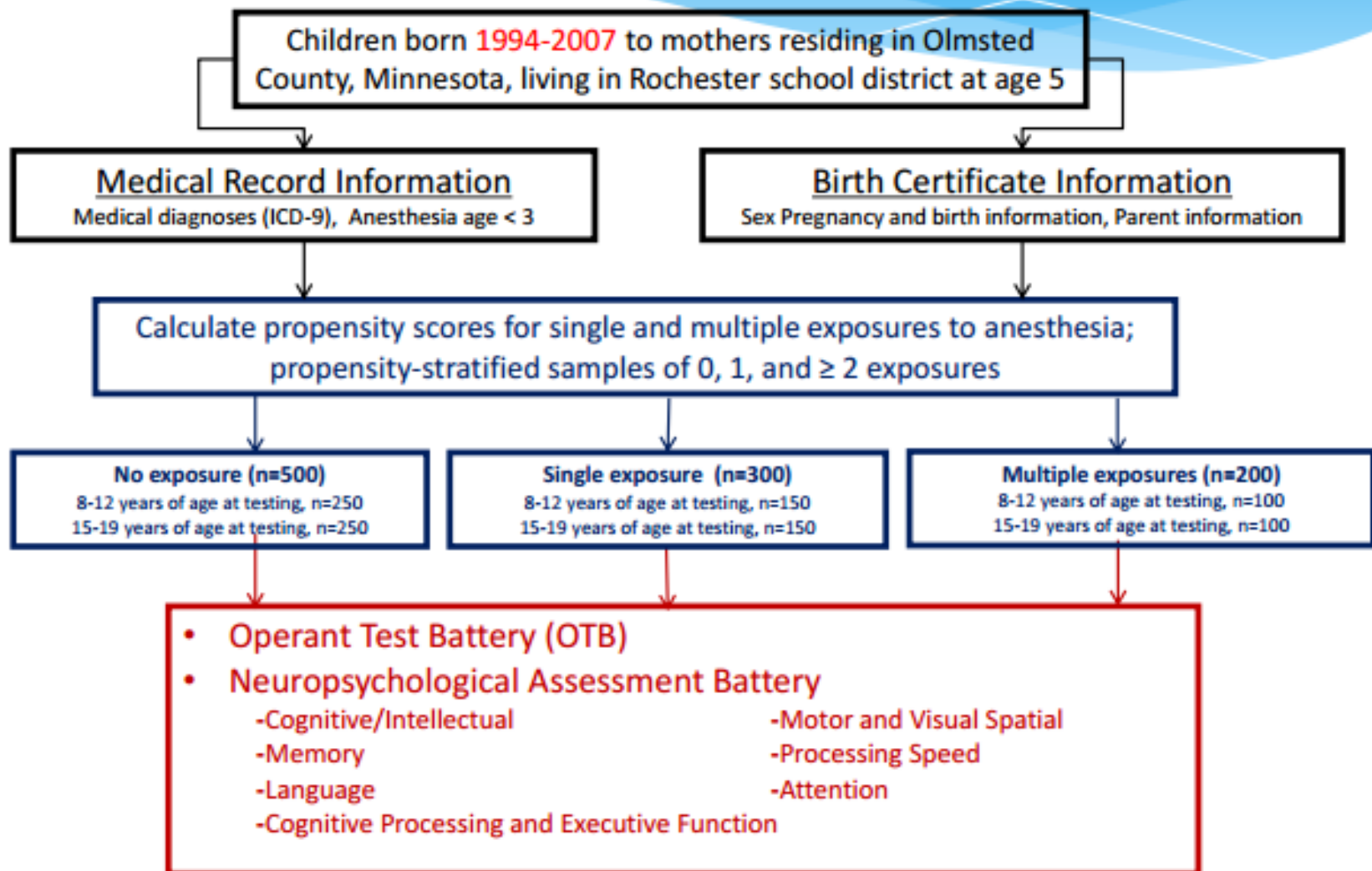


## MASK Prospective Hypothesis ...

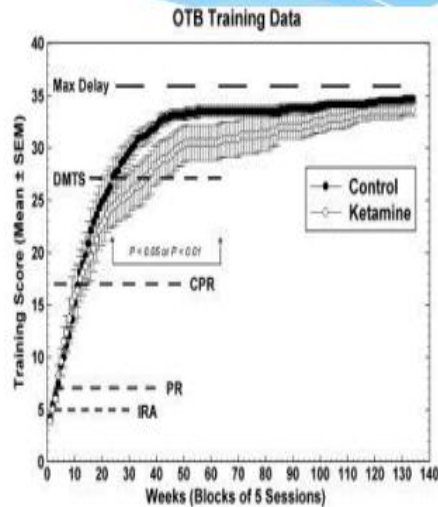
**Exposure to multiple but not single procedures requiring anesthesia prior to the third birthday is associated with adverse neurodevelopmental outcomes.**



# Prospective MASK Study - Design



# Operant Test Battery



Paule et al, Neurotoxicology and Teratology, 2011



# Psychometrist Assessments\*

## Global Cognitive Function

Full Scale IQ, WASI

### Visual/Motor Integration

Berry VMI

### Visual and Verbal\* Memory

WRAML-2 (7 subtests)

### Visual/Spatial Abilities†

Berry Visual Perception  
Judgement of Line Orientation

### Expressive Language†

Boston Naming  
D-KEFs Category Fluency

### Attention

WRAML-2, Attention  
CPTII, Hit Reaction

### Executive Function

D-KEFs Tower, Trail making 4  
Wisconsin Card Sort

### Processing speed

CTOPP, Rapid naming

### Fine Motor Skills†

Berry Motor Coordination  
Grooved Pegboard

\*36 individual measures; 16 a priori summary measures mapped to 9 domains

†Study-specific composite

# Summary of Prospective MASK

- \* Exposure not associated with primary outcome of IQ
  - \* Effect sizes consistent with prior studies (~1 IQ point)
- \* Multiple exposures associated with
  - \* Modest decreases in processing speed and fine motor skills
  - \* No other changes in neuropsychological testing domains
  - \* Parental reports of more problems with reading (not math), behavior, and executive function
- \* Single exposures associated with
  - \* No changes in neuropsychological testing domains
  - \* Parental reports of more problems with reading and executive function
- \* No evidence of factors moderating associations
  - \* Including sex, socioeconomic status, birthweight, GA, age at testing

# Limitations

- \* All observational studies are subject to confounding both known and unknown despite propensity guided approach.
  - \* Confounding by indication – children who need procedures are different than those who do not (Neuro and CV; Specific pattern).
  - \* Anesthesia and surgery cannot be separated.
  - \* Selection (volunteer) bias although population is very similar to retrospective studies where selection is not a concern.
- \* Statistical artifact
  - \* imbalances in factors known to impact outcomes (IPTW)
    - \* Pattern remained unchanged regardless of adjustment methods
  - \* Multiple comparisons (type I error)
    - \* Composites/*a priori analysis plan*
- \* Sample size/power (Glatz findings)
- \* And others....

# Conclusions

No significant effect on IQ

- 0,5p reduction sigle exposure
- 1,3p reduction multiple exposure

Multiple exposure asociated with

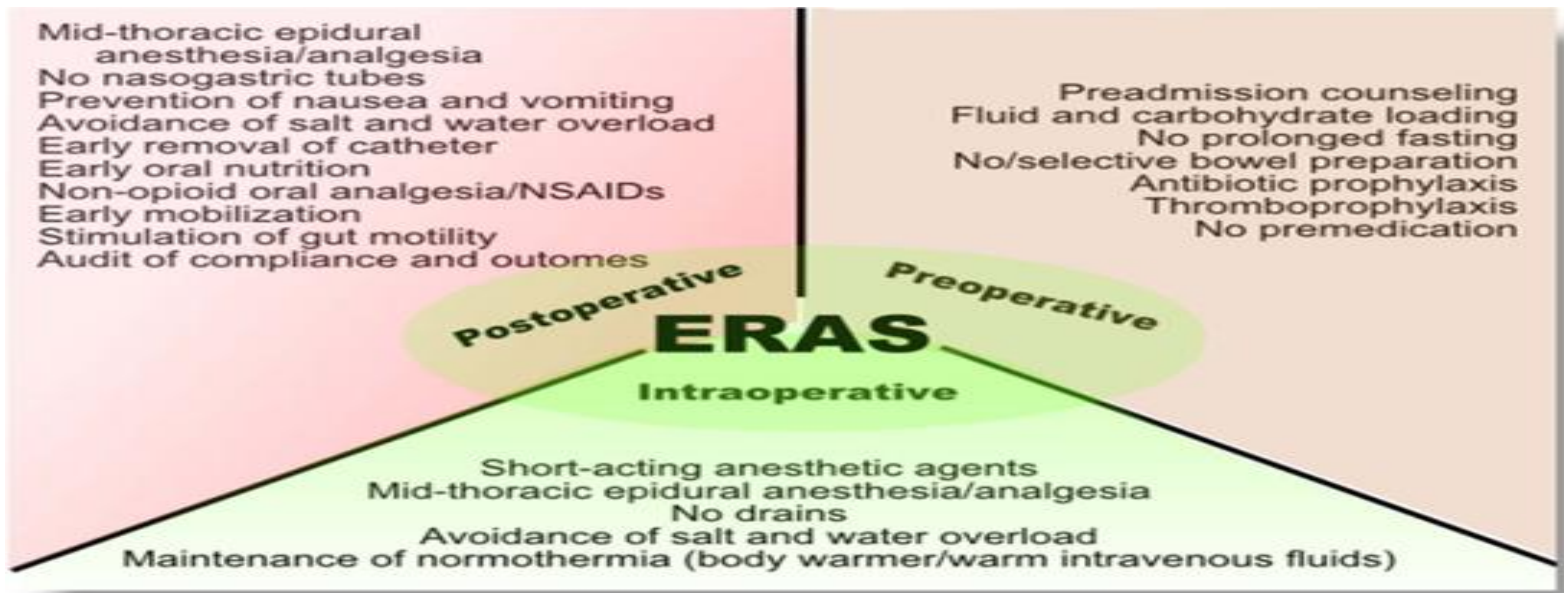
- fine motor
- processing speed
- Parental reports of difficulties in reading, behavior and executive function ( but not math)

Single exposure associated with

- Parental report of difficulties in reading and executive function ( but not math)

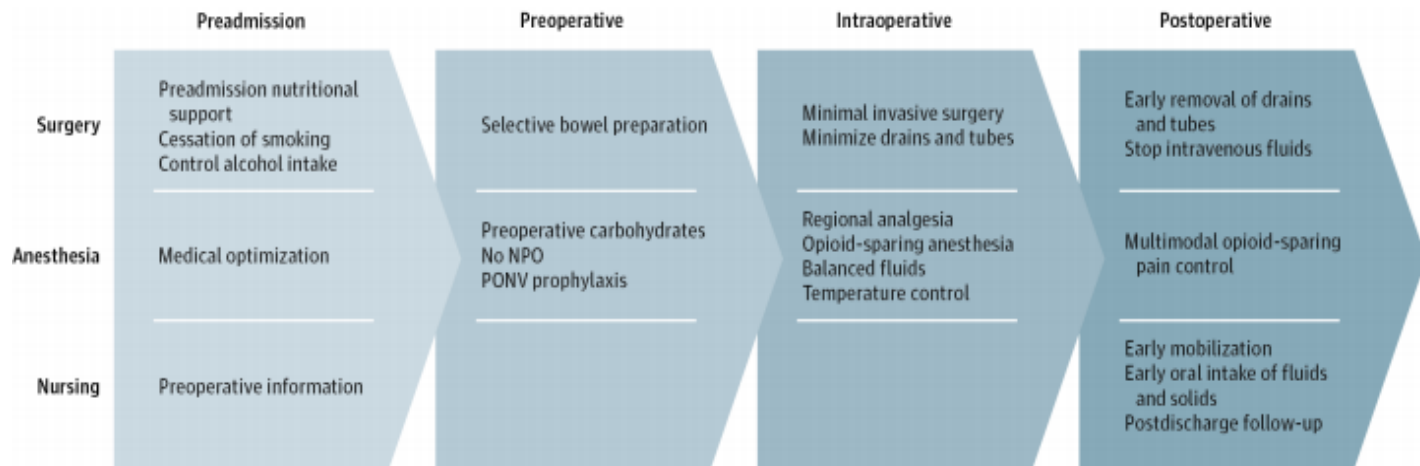
# Conclusions

- Deferral of elective procedures beyond the first few years of life should be contemplated.
- Parents should be counselled to not avoid necessary invasive procedures for fear of a currently ill-defined risk.
- Enhanced Recovery After Surgery



Integrated ERAS protocol

Figure. Enhanced Recovery After Surgery (ERAS) Flowchart



Thank you!