

The CDH Registry and Study Group

Past, Present and Future

At my age
I need glasses.



CDH Registry

- **Background of the Registry**
- **Current Status**
- **Major Publications**
- **Future Plans**





**EXTRACORPOREAL LIFE SUPPORT ORGANIZATION
Charter Meeting**

October 1-3, 1989

Ann Arbor, Michigan





**EXTRACORPOREAL LIFE SUPPORT ORGANIZATION
Charter Meeting**

October 1-3, 1989

Ann Arbor, Michigan



Members in attendance:

9/12/91

NAME

CENTER

Lucienne Sanchez	CNMC, Washington, D.C.
✓ Kevin Lally	Hermann Children's/Houston
- Jim Atkinson	CHLA/Los Angeles
- Charles Breaux, Jr.	Children's of Alabama
- Karen West	Riley Hospital/Indpls IN
Billie Lou Short	CNMC, Washington, D.C.
William Engle	Riley Hospital/Indpls IN
Bill Kernaghan for W.P. Kanto	Med College of Georgia
→ Michele Walsh-Sukys	Rainbow Babies, Cleveland
David P. Meagher, Jr.	Children's Hospital, Denver
Gerald M. Haase	Children's Hospital, Denver
✓ Jay Wilson	Boston Children's
✓ Desmond Bohn	Hospital For Sick Children
✓ Kyle Walker	Johns Hopkins Hospital
P. Pearl O'Rourke	Children's Hospital/Seattle

- 5 Neonatologists
- 7 Pediatric Surgeons
- 3 Intensivists

CDH STUDY GROUP

MINUTES OF CHARTER MEETING 9/12/91

The meeting was scheduled to begin at 15:30, and began shortly thereafter. It lasted for approximately one hour. Items of import discussed were as follows:

* There was universal agreement of a need for such a study group. The goals of the group were not completely defined, however 2 main goals were cited:

1) **Universal data collection of CDH patients.**

2) **Collective attempt to answer questions regarding CDH patients.** There was universal agreement that no single individual or institution had found "the answer" to the ubiquitous problem of CDH infants. There were numerous expressions of willingness to work together and attempt to put aside previous biases and large egos to collectively address CDH patient management and outcome.

CDH STUDY GROUP

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CDH Registry

- Existing data forms collated and modified
- Voluntary collection
- A priori plan to limit total amount of data
- Data collection begun 1995
- Data in secure, anonymized database
- Some PHI – DOB, DOS

The Congenital Diaphragmatic Study Group



MEETINGS

NONE OF US IS AS DUMB AS ALL OF US.

Versions of the CDH Registry

- Version 1 1995-2000
 - Defining the problem - medications, ventilator strategies, ECLS use

CONGENITAL DIAPHRAGMATIC HERNIA DATA FORM

Hospital: _____ DOB: ____/____/____ Time of Birth: _____
Initials: _____ Hosp. # _____ Admission Date: ____/____/____ Time: _____
Inborn Outborn **Group**(Circle one): No ECMO ECMO Pre-Repair ECMO Post-Repair
Sex: M F **Race:** Black White Hispanic Asian Other _____
Birthweight ____ Kgs **EGA(Exam)** ____ weeks
Prenatal Diagnosis: Yes No If Yes EGA@Dx(wks) ____ Polyhydramnios Yes No
Stomach in Chest Yes No Left Ventricular mass index(if known) _____
Liver in Chest Yes No Prenatal Repair Yes No Pregnancy terminated: Yes No
Delivery Data: Apgars (1/5/10) ____/____/____ Early death (<24 hrs) Yes No
Immediate Distress: Yes No CPR: Yes No Age at Dx:Date ____/____/____ Time ____
Age at Intubation:Date ____/____/____ Time _____

Associated Anomalies

Cardiac: Yes No If Yes: Hypoplastic Heart/TOF/TAPVR/VSD/ASD/Other _____
Chromosomal: Yes No If Yes: _____ Neural tube Anomaly: Yes No
Omphalocele: Yes No Other: _____

PHARMACOLOGIC DATA

Surfactant given: Yes No If Yes: Hours of Life: ____/____/____/____
If Yes: Survanta Exosurf Infracurf Other

<u>Drug Strategy(Circle)</u>			<u>Complications</u>
Vasopressors	Yes	No	_____
Intravenous Vasodilators	Yes	No	_____
Inhaled Vasodilators	Yes	No Don't Know	_____
Hyperoxia	Yes	No	_____
Sedation	Yes	No	_____
Alkalinization	Yes	No	_____
Neuromuscular Blockade	Yes	No	_____

Version 1

Repair Data:

Side : Left Right Bilateral Repair Done Yes No
 Type Repair: 1°: Yes No Patch: Yes No Material: PTFE Dura Other ____
 Size of Defect: 1/4 1/2 Agensis
 Approach: Subcostal Thoracic Other _____ Abdomen Closure: 1° Hernia Silo Expander
 Chest Tube: Yes No Suction Yes No Malrotation Procedure: Yes No
 Appendectomy: Yes No Other procedure: _____
 Repair on ECMO: Yes No If Yes: Hours of ECMO when Repair _____ Fibrin glue: Yes No
 Date of Operation: ____/____/____ Time: _____
 Length of Operation (mins.) _____ EBL: _____ Introp Probs: _____
 Operation Indication: ABG's Age ECHO PFT's Can Wean from ECMO Inability to Wean
 Complications: Yes No If Yes: Bleeding Infection
 Describe _____

ECMO DATA

ECMO Criteria: OI > ____ x ____ Hrs AaDO₂ > ____ x ____ Hrs
 Acute Deterioration ____ It's Time ____
 Date on ECMO: ____/____/____ Time on ECMO: _____
 Date off ECMO: ____/____/____ Time off ECMO: _____
 ECMO Mode: - VA VA(+V) VV(DL) VV to VA
 Amicar: Yes No Second Run: Yes No If Y (Duration of 2nd run hrs) _____
 Complications: ICH Renal Failure Other _____
 Bleeding: Neck Amount(Total) _____
 Wound Amount(Total) _____
 GI Tract Amount(Total) _____
 Other Amount(Total) _____ (Site) _____

Version 1

Versions of the CDH Registry

- **Version 1** 1995-2000
 - Defining the problem - medications, ventilator strategies, ECLS use
- **Version 2** 2001-2006
 - Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies

CDH Registry – Why it has worked Management (2000 – 2019)



CONGENITAL DIAPHRAGMATIC HERNIA FORM
(To be used for patients born 10/1/2000 – 12/31/2006)

Year of Birth: _____ Center #: _____ Patient #: _____

Patient Date of Birth: ___/___/___ Time of Birth: _____

- Inborn
- Outborn: Admission Date : ___/___/___ Time: _____

Sex: M / F
Race: Black / White / Hispanic / Asian / Native American / Other: _____

Birthweight: _____ kg Head Circ: _____ cm Length: _____ cm
EGA (at birth): _____ wks APGAR (1/5/10): ___/___/___

Method of delivery: Vaginal (Spontaneous) Vaginal (Induced)
C-Section (Elective) C-Section (Urgent or Non-Elective)
If C-S, indication: _____

Immediate Distress: Yes / No CPR Given: Yes / No
Prenatal diagnosis of CDH: Yes / No If Yes, diagnosis made at ___ weeks gestation
Prenatal steroids given: Yes / No / Unknown
If Yes, steroids given at gestational ages (in wks): ___/___/___/___

Associated Non-Cardiac Anomalies (Check all that apply and please provide DX if known):

- Chromosomal – If Yes, please describe: _____
- Neural Tube Defect – If Yes, please describe: _____
- Omphalocele
- Other Anomalies – If Yes, please describe: _____

Associated Structural Cardiac Anomalies (Check all that apply):

- ASD
- VSD
- AVSD (AV Canal)
- Pulmonic Stenosis
- Pulmonary Atresia
- TOF (Tetralogy of Fallot)
- Coarctation of Aorta
- TOGV (Transposition of Great Vessels or Transposition of Great Arteries)
- Truncus Arteriosus
- Complex Biventricular anatomy (i.e. heterotaxy syndrome)
- Anomalous Pulmonary Venous Return: please describe: _____
- Single Ventricle Variant (hypoplastic left heart syndrome):
please describe: _____
- Other: please describe: _____

Treatment of Cardiac Anomaly (Check all that apply):

- Prostaglandins required
- Cardiac Surgery performed
If Yes, type of procedure(s) and date(s) performed: _____

ECMO needed post Cardiac Surgery

Versions of the CDH Registry

- **Version 1** 1995-2000
 - Defining the problem - medications, ventilator strategies, ECLS use
- **Version 2** 2001-2006
 - Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies
- **Version 3** 2007-2014
 - Staging - classifying defect size, pulmonary hypertension

Pulmonary Hypertension (PHTN):

First Echo on date: ___/___/___

PHTN: None < 2/3 systemic between 2/3 and systemic > systemic

Ductus: Open Closed

Ductal Shunt: L to R Bidirectional R to L

Atrial Shunt: Yes No

Tricuspid regurgitation: Yes No

Last Echo on date: ___/___/___

PHTN: None < 2/3 systemic between 2/3 and systemic > systemic

Ductus: Open Closed

Ductal Shunt: L to R Bidirectional R to L

Atrial Shunt: Yes No

Tricuspid regurgitation: Yes No

Treatment of Pulmonary Hypertension:

Check if used		Date Started	Date Ended
<input type="checkbox"/>	Inhaled Nitric Oxide – Maximum dose: ___ ppm	___/___/___	___/___/___
<input type="checkbox"/>	Sildenafil <input type="checkbox"/> Oral <input type="checkbox"/> iv	___/___/___	___/___/___
<input type="checkbox"/>	Endothelial Receptor Blockade	___/___/___	___/___/___
<input type="checkbox"/>	Prostacyclin	___/___/___	___/___/___
<input type="checkbox"/>	Alprostadil (PGE1)	___/___/___	___/___/___
<input type="checkbox"/>	Milrinone	___/___/___	___/___/___
<input type="checkbox"/>	Other (specify): _____	___/___/___	___/___/___

Ventilation:

Intubated at: date: ___/___/___, time: _____

Extubated at date: ___/___/___ (Never extubated)

Actual Values in the first 24 hours of life (pre-ECMO):

Highest pre -ductal PaO ₂ : ___ mm Hg O ₂ sat: ___ % <input type="checkbox"/> Not available	Highest post -ductal PaO ₂ : ___ mm Hg O ₂ sat: ___ % <input type="checkbox"/> Not available
Highest PaCO ₂ : ___ mm Hg <input type="checkbox"/> Not available	Lowest PaCO ₂ : ___ mm Hg <input type="checkbox"/> Not available
Highest Lactate in first 24 hours: ___ mmol/L)	Highest Lactate in first 72 hours: ___ mmol/L)

Version 3

Page 2 of 6

Side of Diaphragmatic Hernia: Left Right Bilateral/Central

No Repair:

Reasons repair not done (select best):

- Unable to stabilize patient
- Patient felt to be non-survivable / not candidate for ECMO:
 - PaO₂ never greater than _____
 - PaCO₂ never lower than _____
 - Anomaly: Cardiac / Chromosomal / Other
 - Parents requested no further therapy
 - Other: _____
- Patient felt to be survivable / not candidate for ECMO:
 - Prematurity / low birth weight
 - IVH or cerebral hemorrhage pre-ECMO
 - Parents requested no further therapy
 - Other: _____
- Patient felt to be survivable / placed on ECMO but no repair done:
 - IVH or cerebral hemorrhage on ECMO
 - Other ECMO complication: _____
 - Parents requested no further therapy
 - Unable to wean off ECMO
 - Late diagnosis of anomaly: Cardiac / Chromosomal / Other
 - Other: _____
- Patient came off ECMO but was not repaired:
 - Refractory hypoxia
 - Refractory hypercarbia
 - Anomaly: Cardiac / Chromosomal / Other
 - Parents requested no further therapy
 - Multisystem organ failure
 - Sepsis
 - Other: _____

Repair Done:

Repair done on date: ___/___/___ time: _____

Diaphragm Defect: A B C D



(Have surgeon identify which diagram (A, B, C, D) most closely approximates defect noted intra-operatively. Orientation: diagram drawn with the diaphragm (defect) on the patient's left and you are looking up from the abdomen towards the chest.)

- Type Repair: Primary Patch
 If Patch, type patch: PTFE Surgisis Mesh plug Alloderm Other
- Hernia Sac: Yes No
- Liver: Chest Abdomen
- Approach: Subcostal Thoracic Both Thoracoscopic Laparoscopic
 Other: _____
- Abdominal Closure: Primary Ventral hernia Silo Patch Other: _____
- Chest Tube: Yes No

Version 3

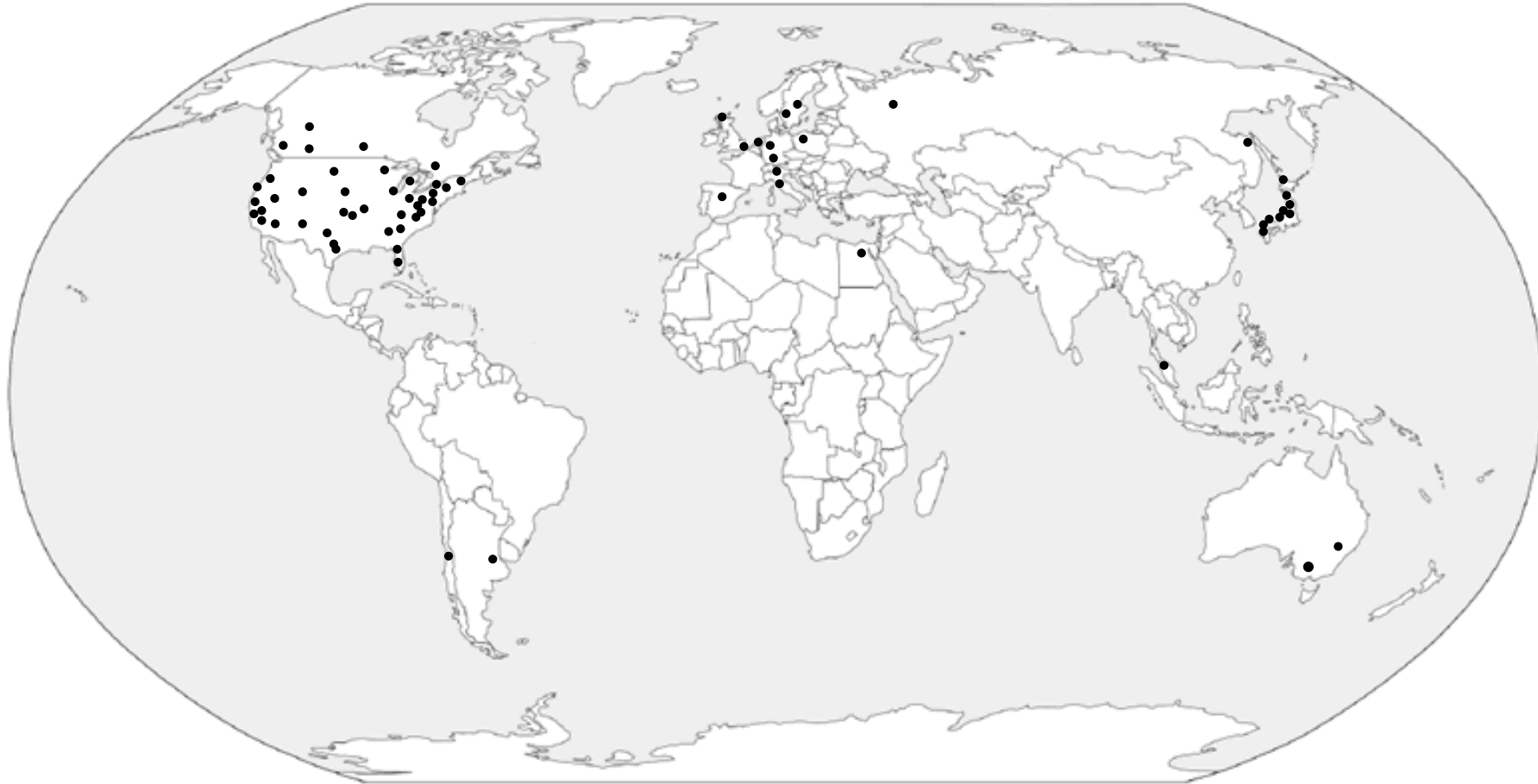
Versions of the CDH Registry

- **Version 1** 1995-2000
 - Defining the problem - medications, ventilator strategies, ECLS use
- **Version 2** 2001-2006
 - Understanding the details - delivery, oxygen/carbon dioxide, discharge status, cardiac anomalies
- **Version 3** 2007-2014
 - Staging - classifying defect size
- **Version 4** 2015-present
 - The role of the heart and PH, prenatal dx

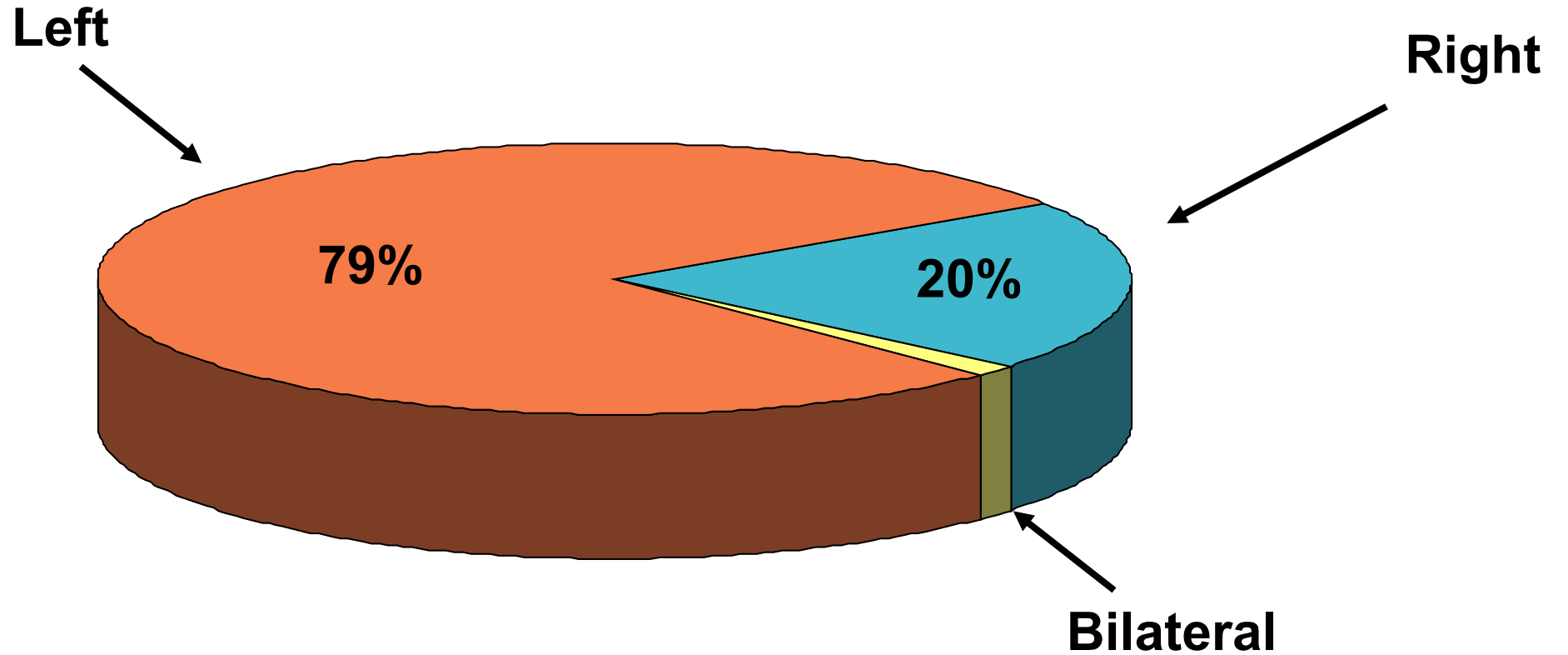
Issues addressed by version 4

- Timing of surgical repair when receiving ECLS
- Cardiac dysfunction in CDH
- CDH-associated pulmonary hypertension
- Prenatal diagnosis / prediction in CDH

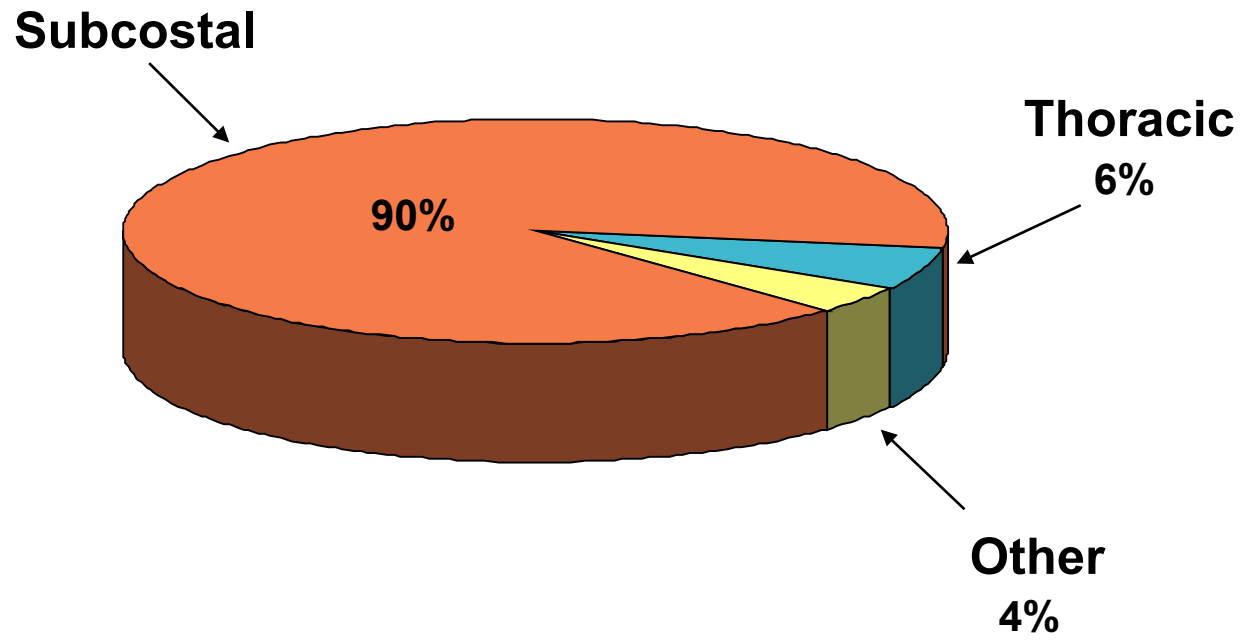
85 Centers/17 countries/12,000 Patients



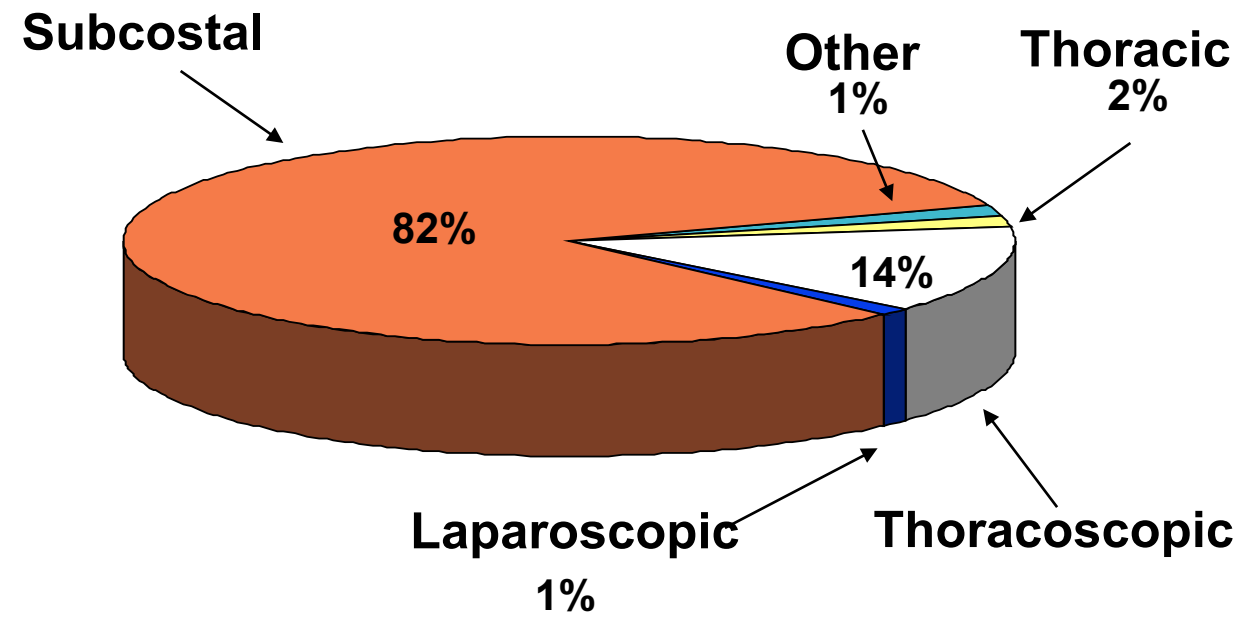
Hernia Side



Operative Approach

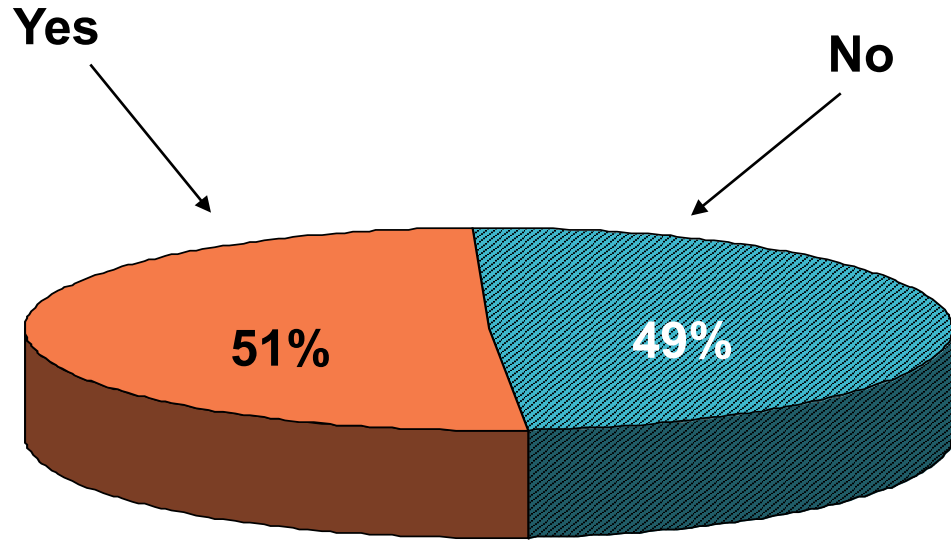


1995-1996

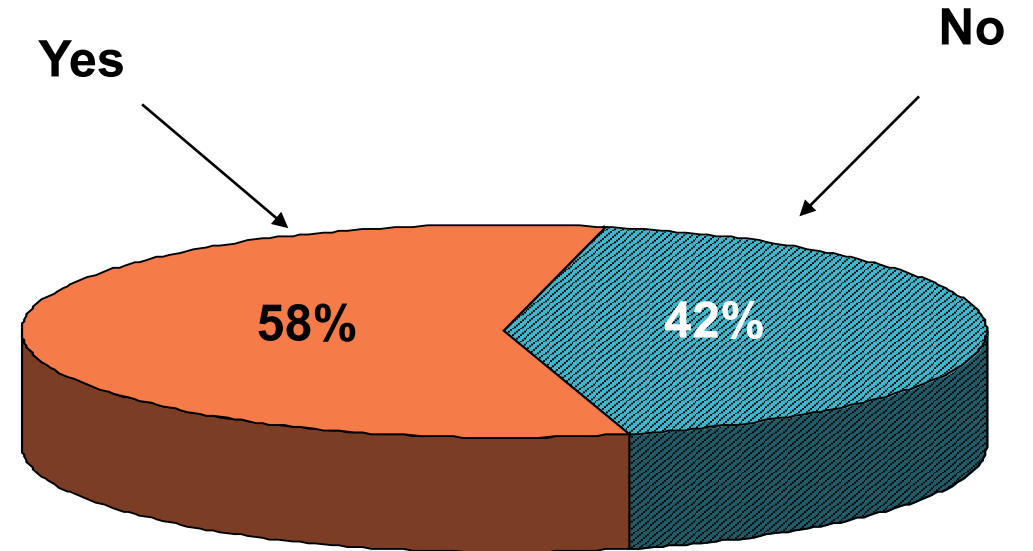


2017-2018

Patch Used In Repair

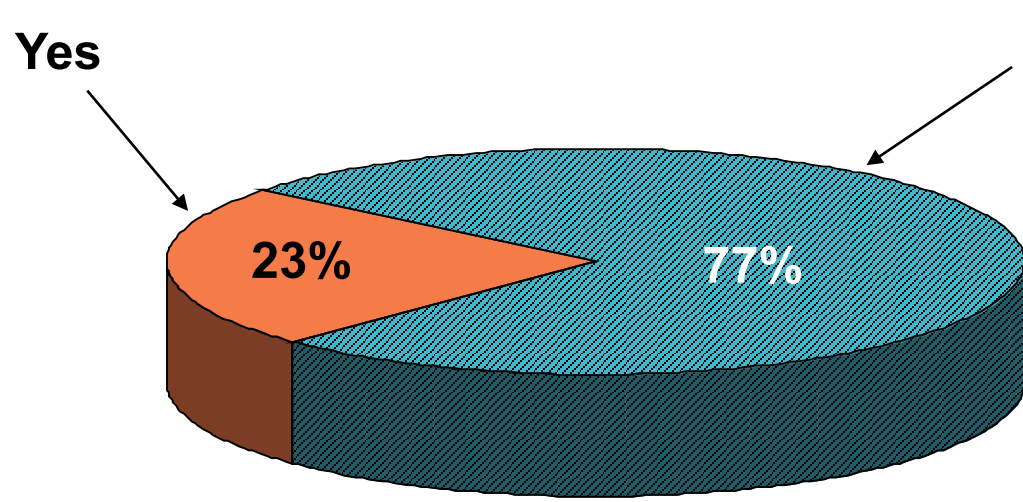


1995-1996

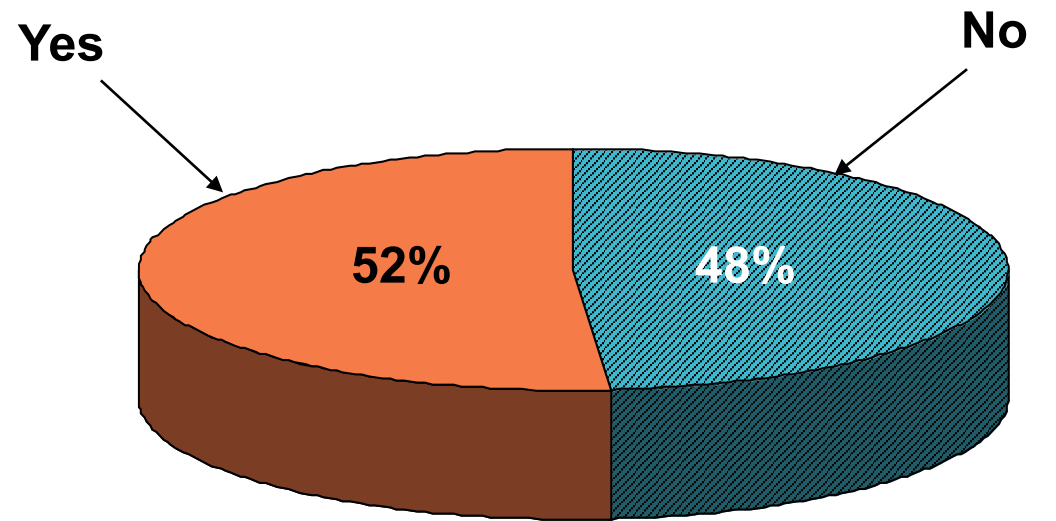


2017-2018

Repair On ECMO (Of all ECMO)

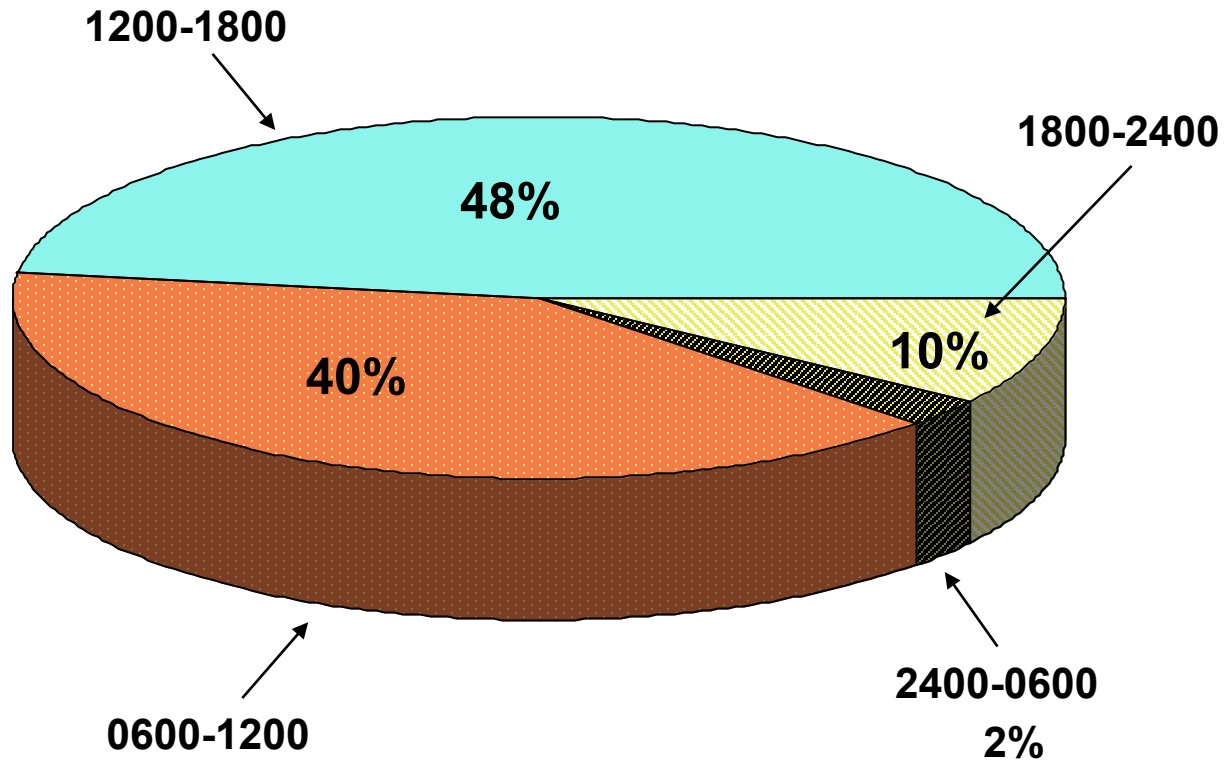


1995-1996

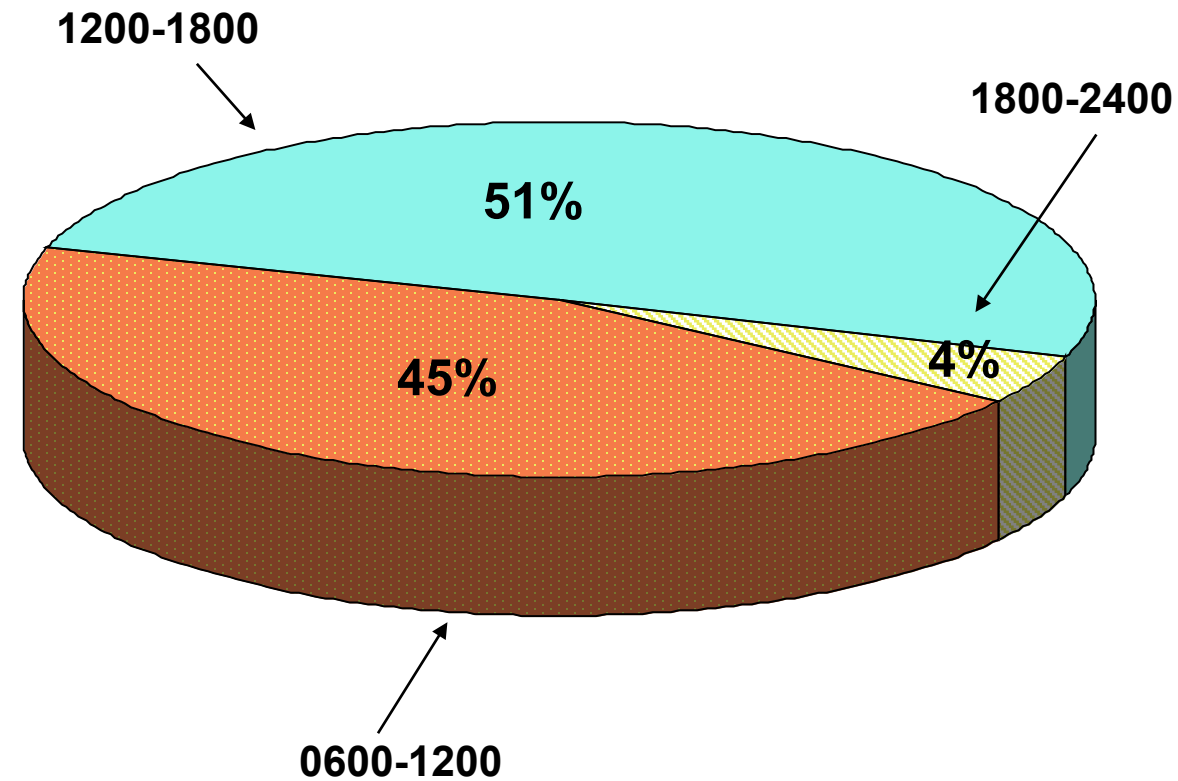


2017-2018

Time of Day For Repair

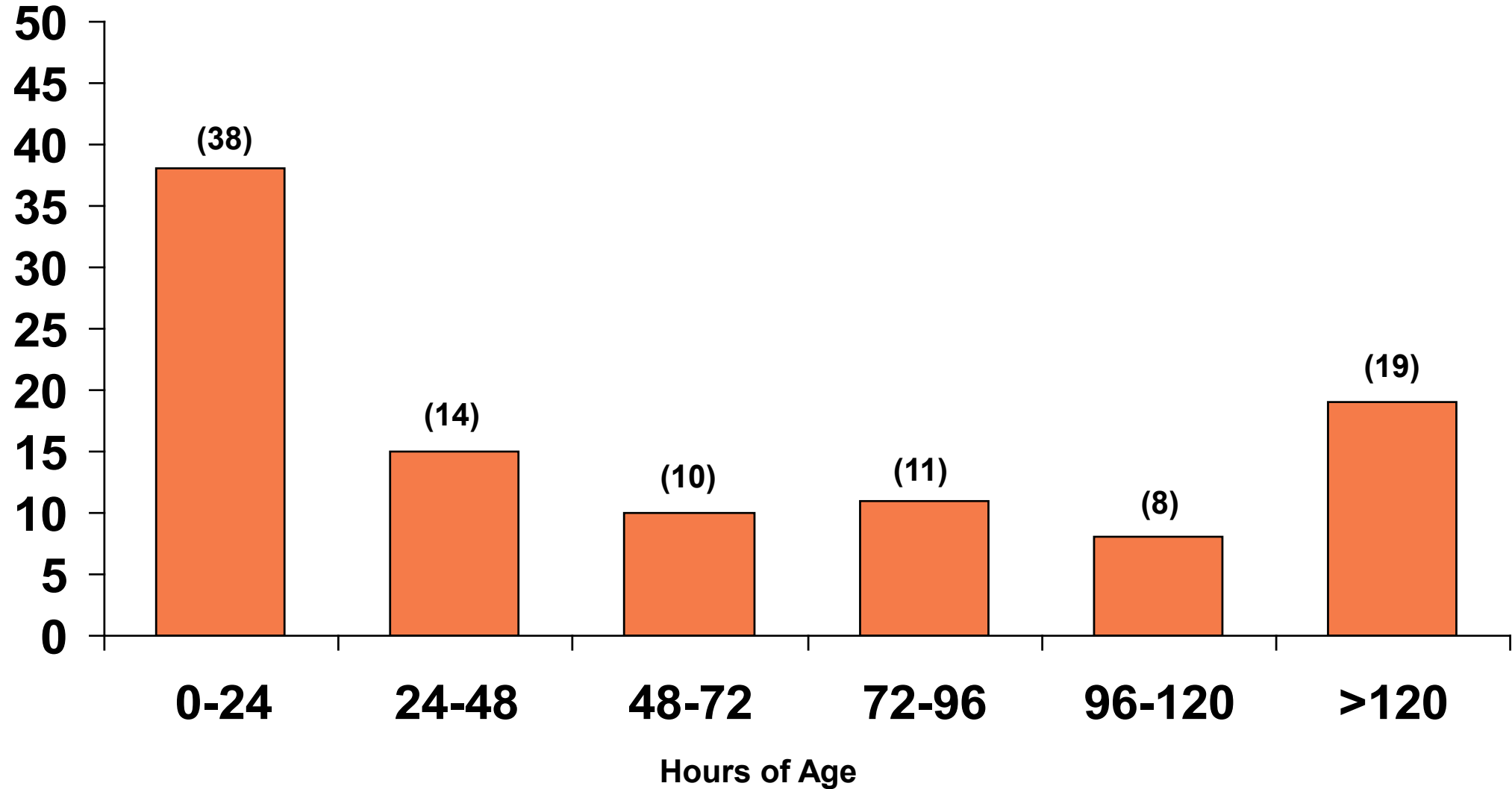


1995-1996

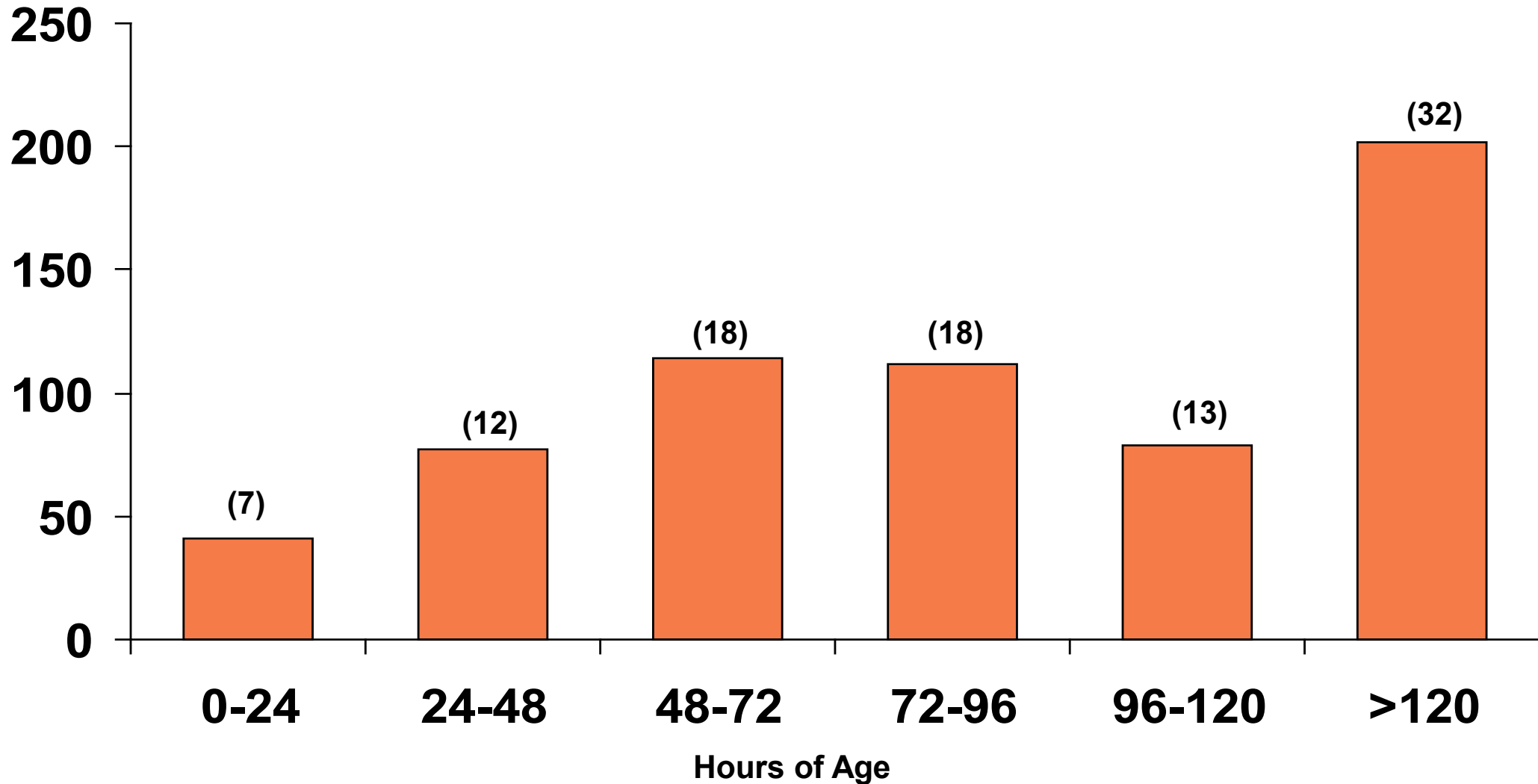


2017-2018

Timing of Operation (No ECMO)



Timing of Operation (No ECMO)



Publications

- **Data available only to CDHSG members**
- **Authored by writing committee on behalf of CDHSG**
- **55 publications**
- **Multiple studies in progress**

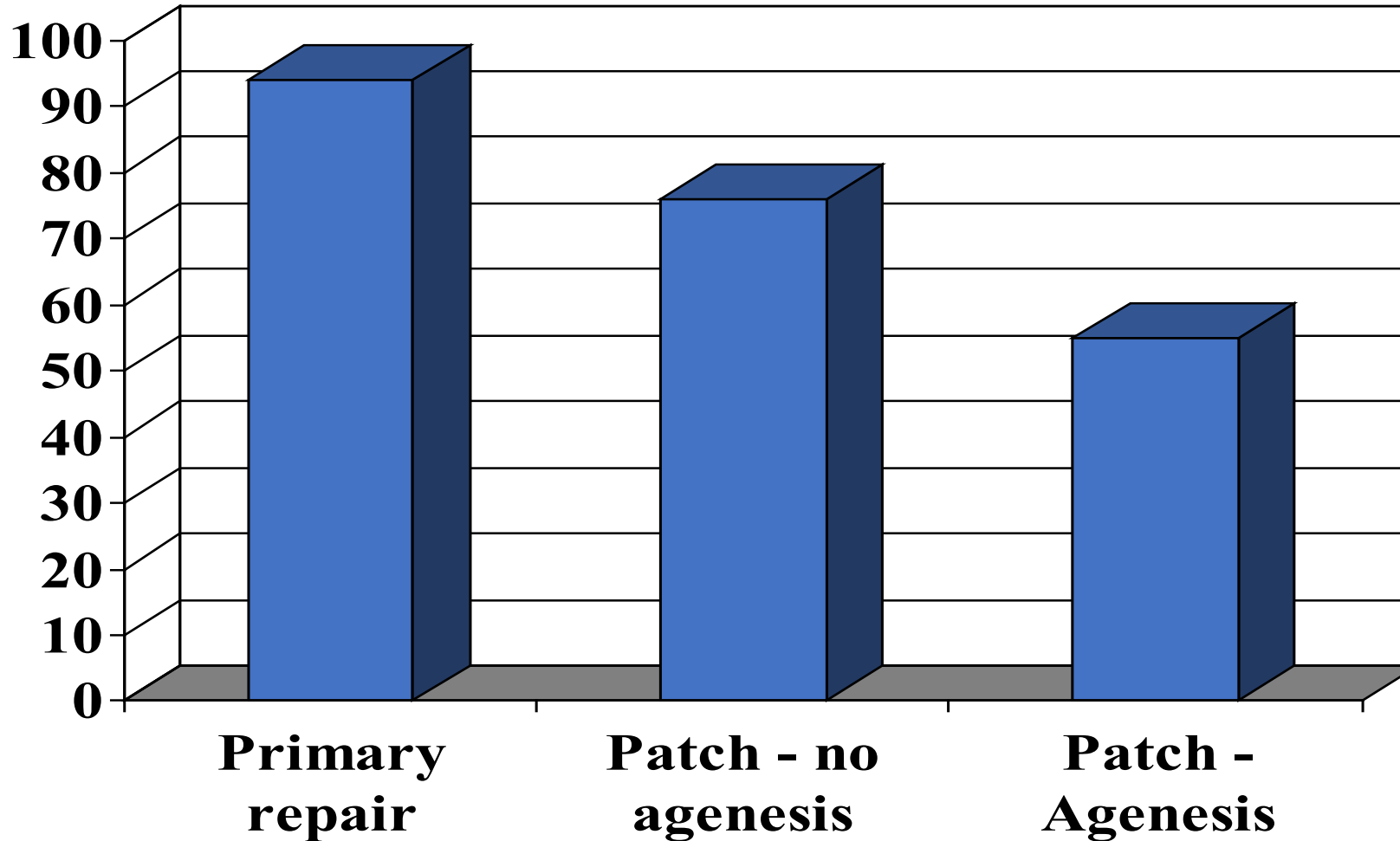
**Defect Size Determines Survival in Infants With Congenital Diaphragmatic
Hernia**

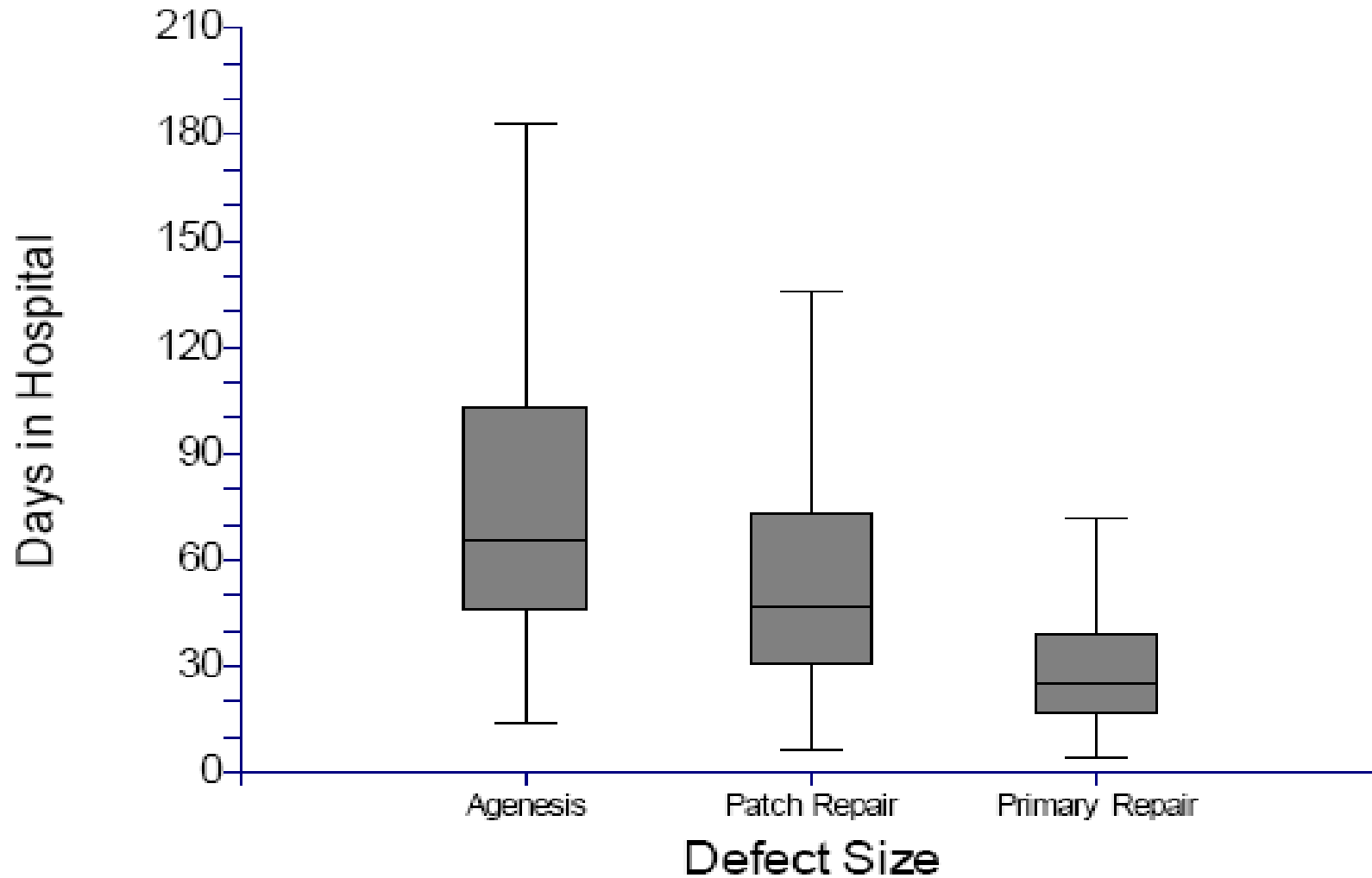
The Congenital Diaphragmatic Hernia Study Group

Pediatrics 2007;120:e651-e657

DOI: 10.1542/peds.2006-3040

Defect Size





Size Does Matter!



Defect Size

It became apparent that not all CDH were created equal and that size of defect was important

Version III designed to quantitate size of defect

Standardized Reporting for Congenital Diaphragmatic Hernia An International Consensus

Methods

Factors Evaluated

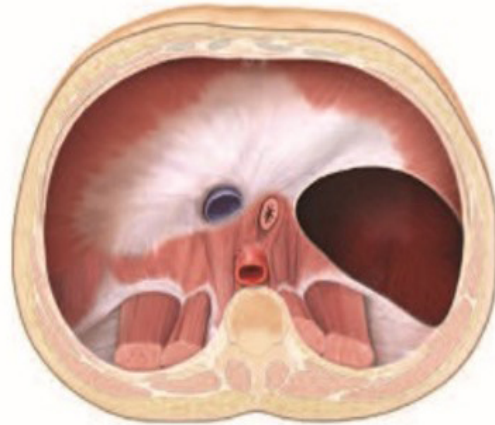
- **Defect class**
- **Cardiac anomalies**
- **Chromosomal anomalies**
- **Birthweight /Gestational age**
- **Apgar Scores**

CDHSG Staging

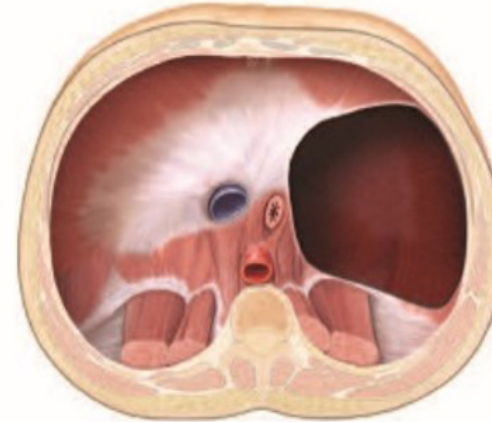
A



B



C



D



Frequency **13%**

Survival **99%**

44%

96%

30%

78%

13%

58%

Lally, et al, *J Pediatr Surg*, 2013



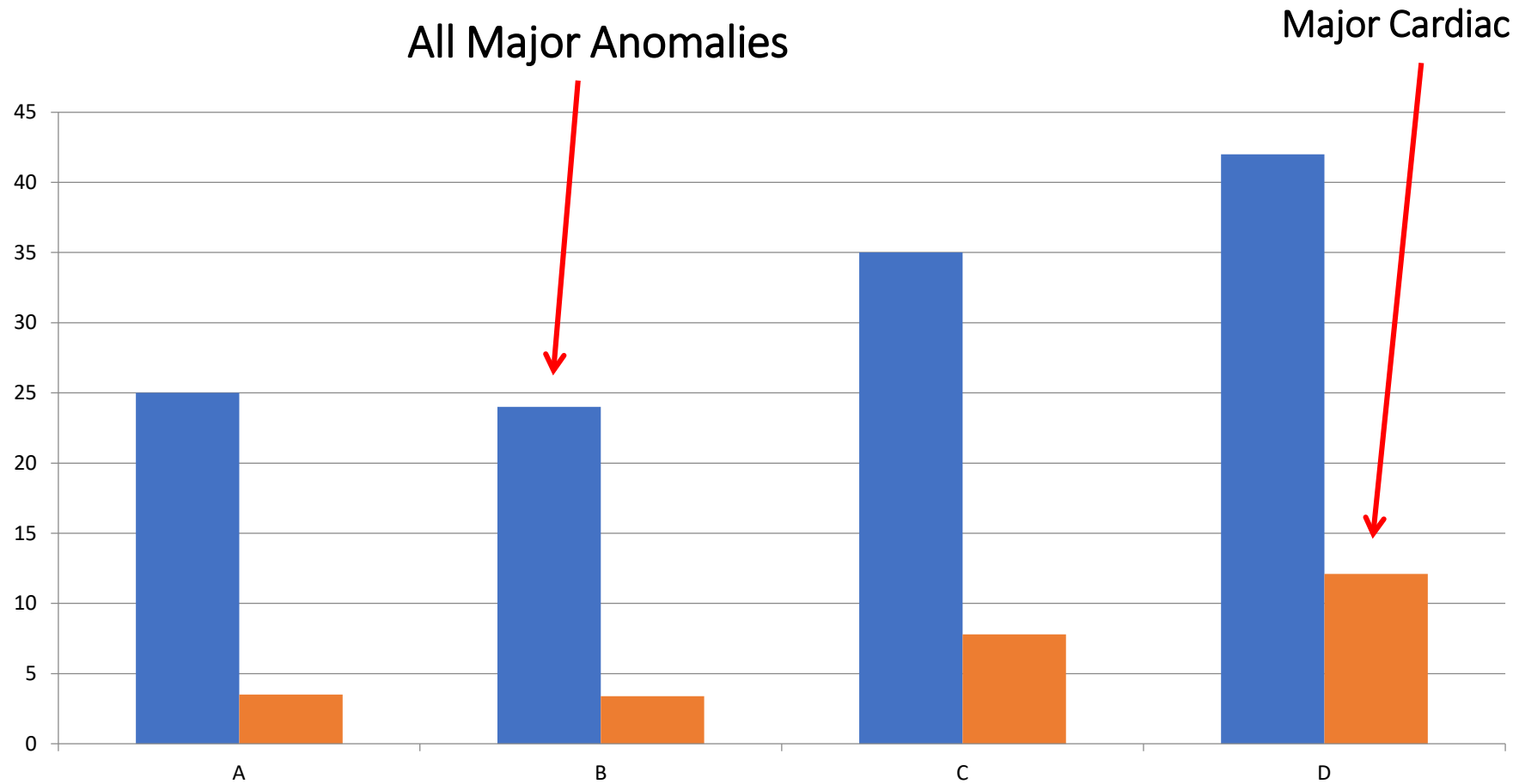
Congenital diaphragmatic hernia: Defect size correlates with developmental defect

The Congenital Diaphragmatic Hernia Study Group¹

Journal of Pediatric Surgery (2013) **48**, 1177–1182

Methods

- **V. 3 of Registry**
- **Grouped by defect size**
- **Compared for associated anomalies**



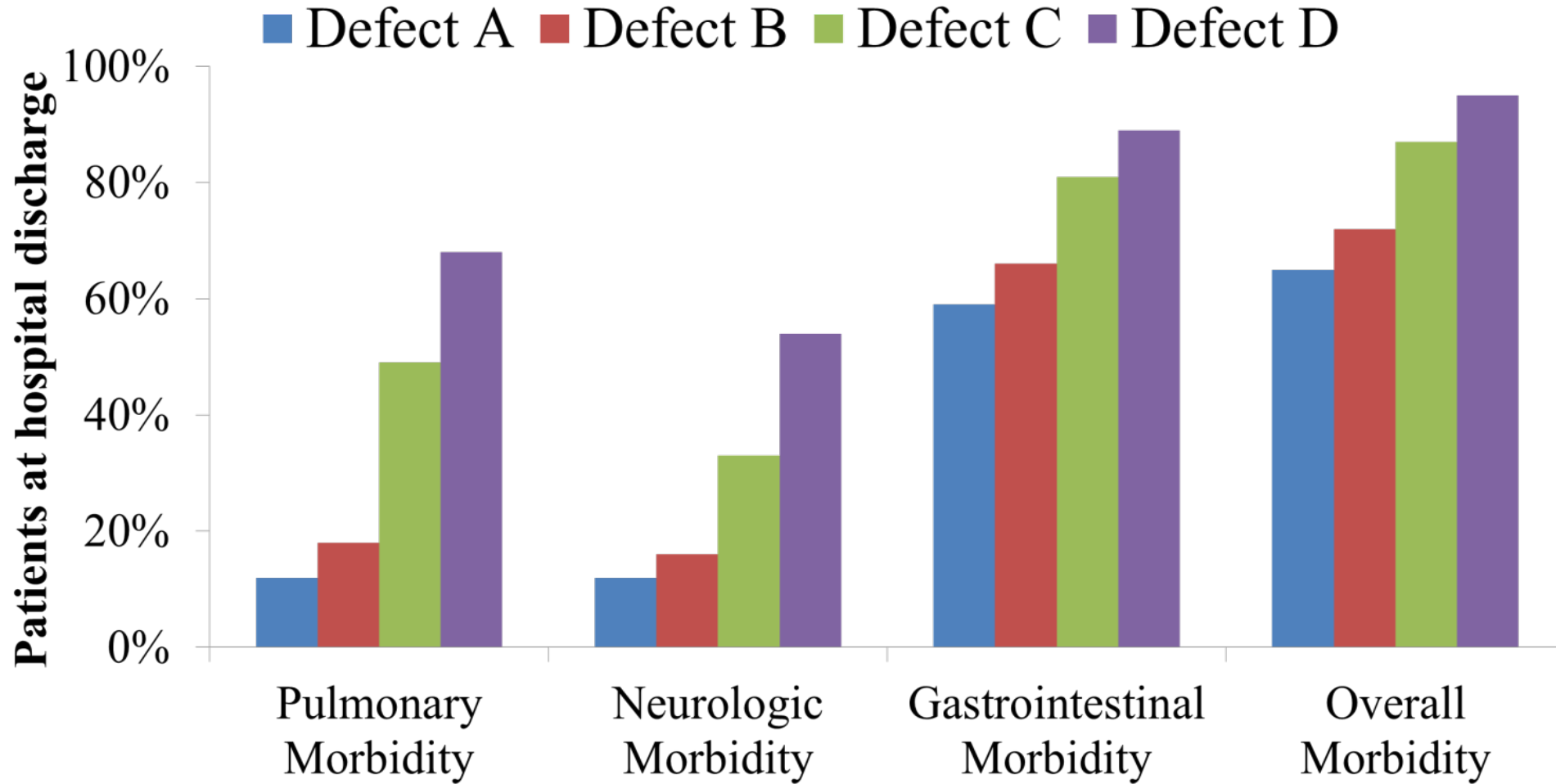
Congenital Diaphragmatic Hernia Defect Size and Infant Morbidity at Discharge

PEDIATRICS Volume 138: 2016:e2016204

Methods

- **V. 3 of Registry**
- **Evaluated recorded morbidity at d/c**
- **Correlated degree of morbidity to defect**
- **Analysis between groups and time**

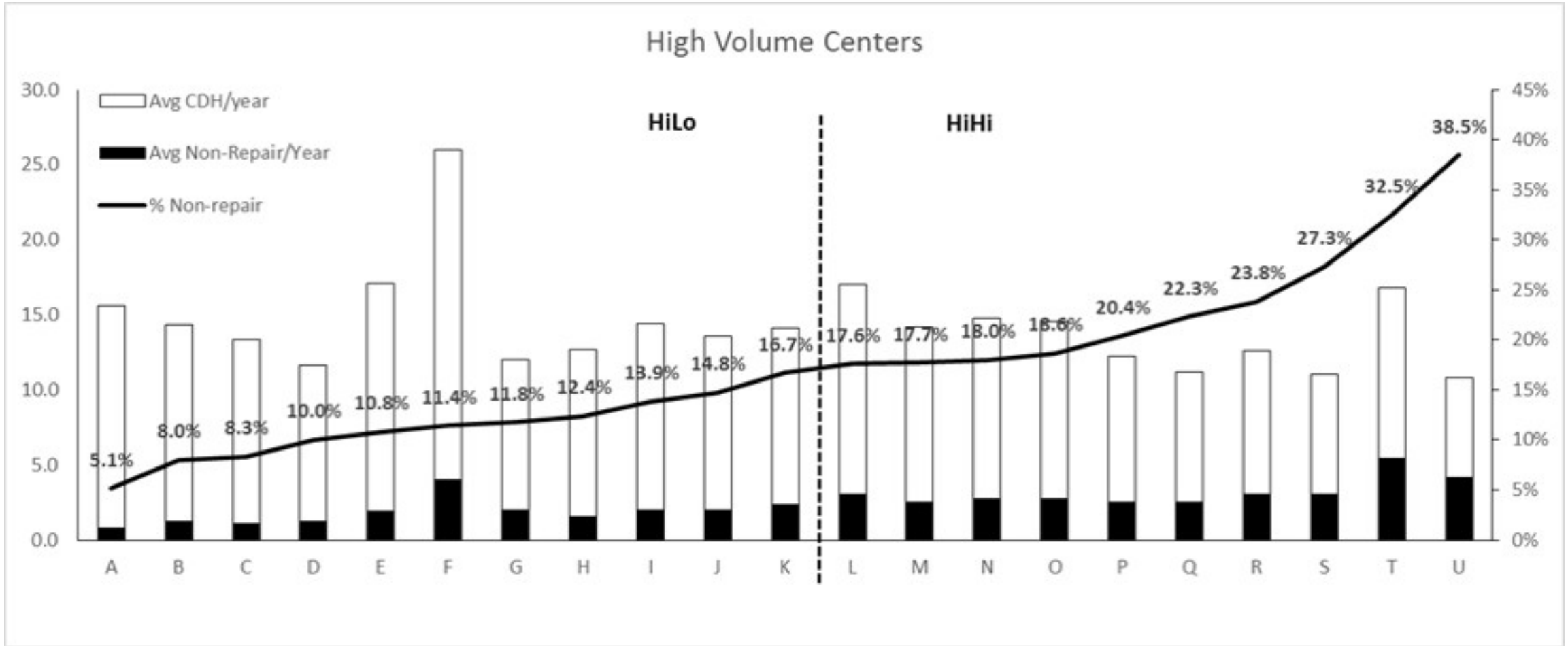
Morbidity by Defect Size



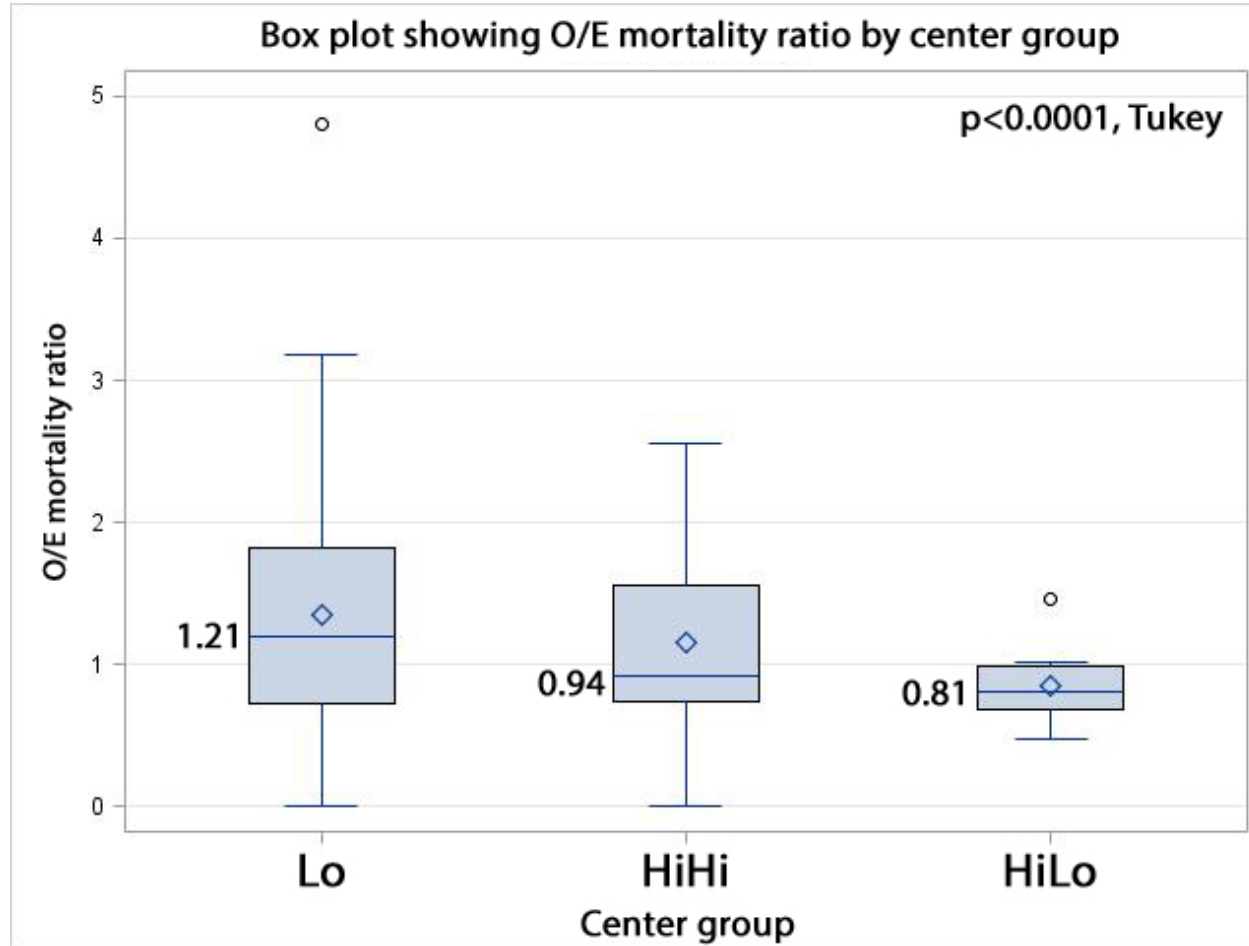
Conclusions

- **Defect correlated with morbidity as well as mortality**
- **Overall improving morbidity**
- **No major changes in large defect patients**

Is aggressive surgical management worth it?



Is aggressive surgical management worth it?



Conclusions

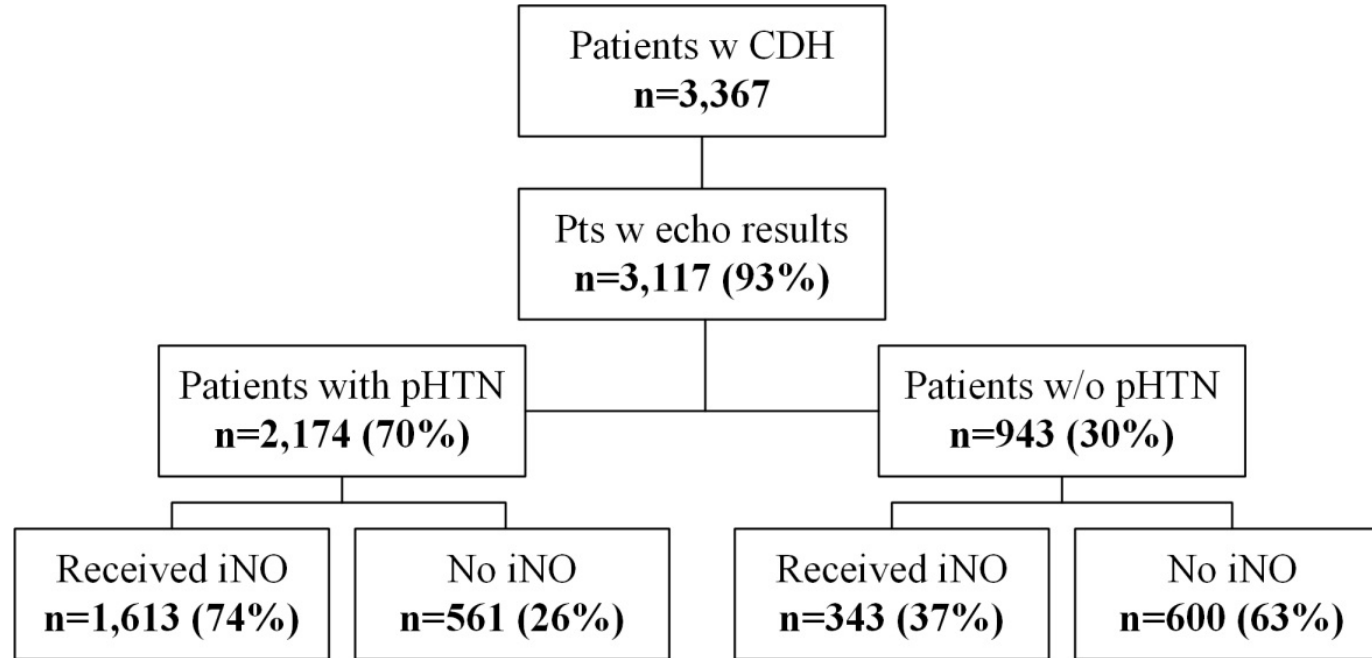
- **Aggressive approach leads to highest survival**
- **It is costly**
- **Morbidity is high**

JAMA Pediatrics | Original Investigation

Evaluation of Variability in Inhaled Nitric Oxide Use and Pulmonary Hypertension in Patients With Congenital Diaphragmatic Hernia

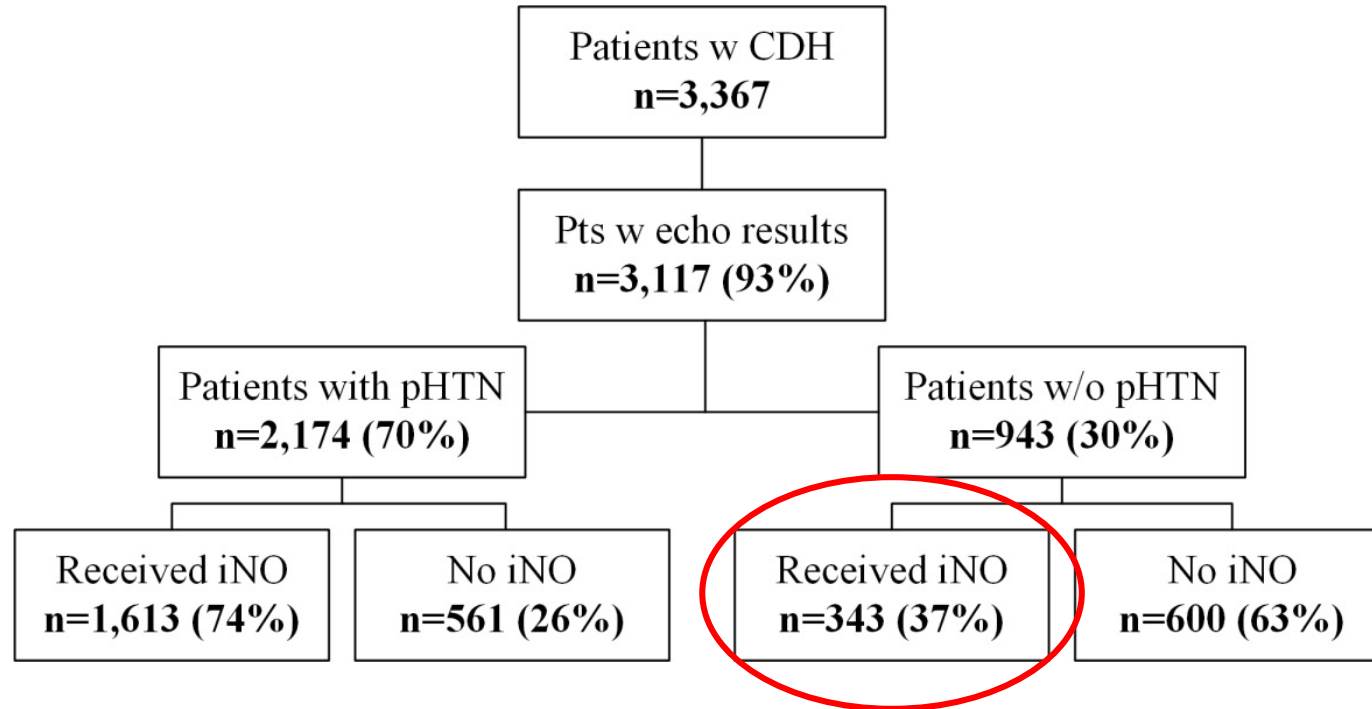
JAMA Pediatr. 2016;170(12):1188-1194. doi:10.1001/jamapediatrics.2016.2023
Published online October 10, 2016.

What about Nitric Oxide ?



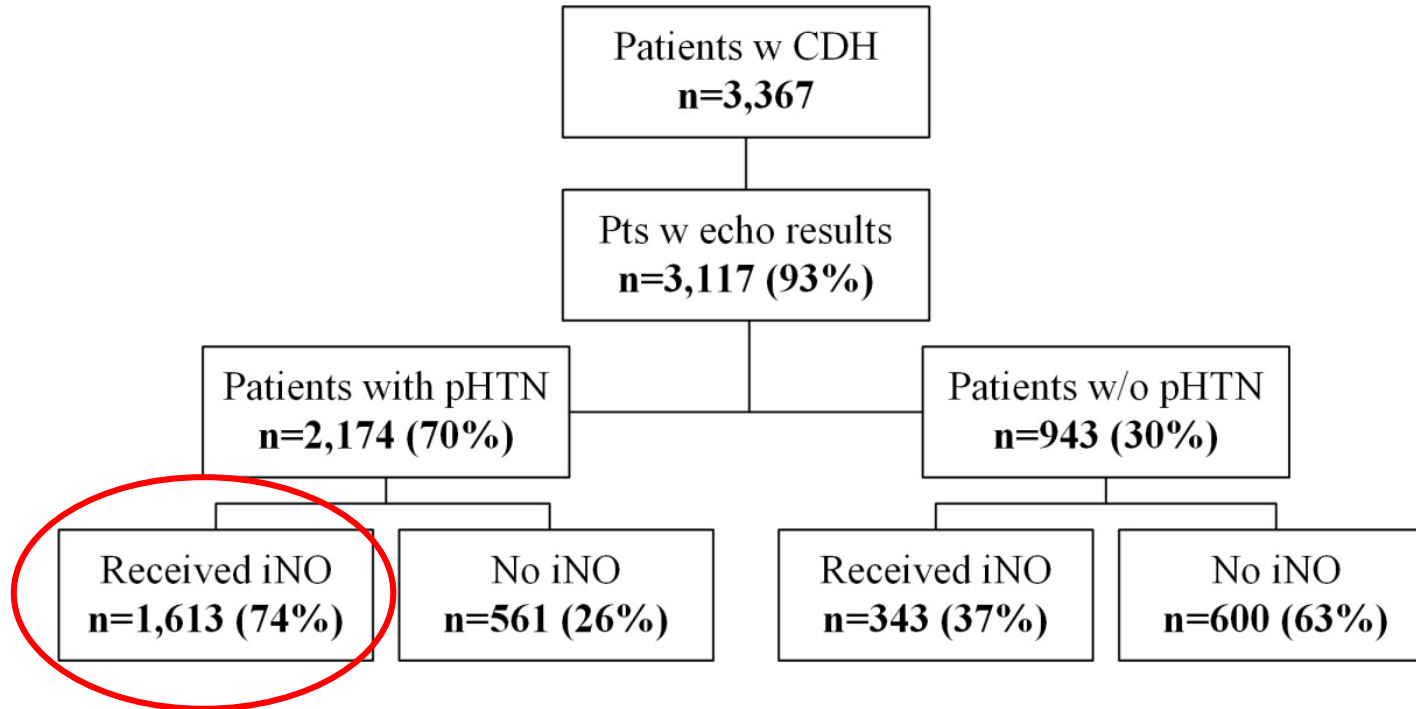
Putnam et al, *JAMA Pediatrics*, 2017

What about Nitric Oxide ?



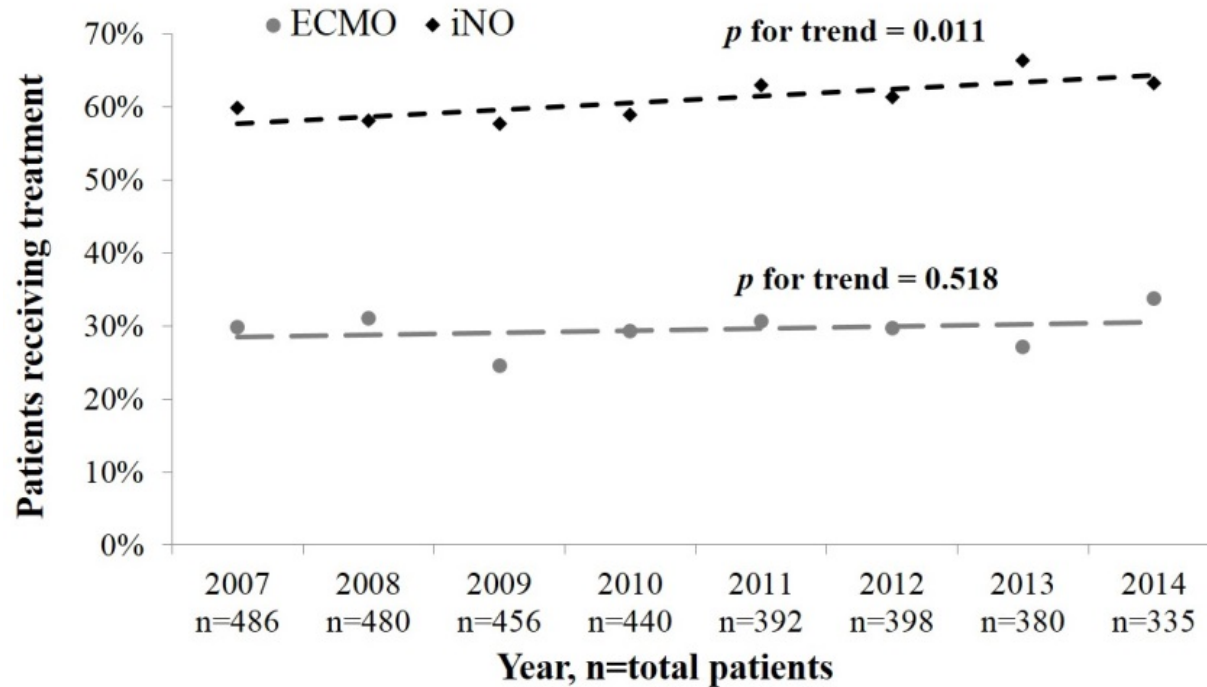
Putnam et al, *JAMA Pediatrics*, 2017

What about Nitric Oxide ?



Putnam et al, *JAMA Pediatrics*, 2017

What about Nitric Oxide ?



Putnam et al, *JAMA Pediatrics*, 2017

***Treatment with iNO was associated with a 15%
higher absolute mortality***

Conclusions

- **iNO use highly variable between centers**
- **> 1/3 patients w/o CDH-PHTN received iNO**
- **Little data to support iNO benefit in CDH**
- **iNO use is *associated* with worse outcome**
- **iNO use in patients with CDH needs re-evaluation**



TRADITION

JUST BECAUSE YOU'VE ALWAYS DONE IT THAT WAY
DOESN'T MEAN IT'S NOT INCREDIBLY STUPID.

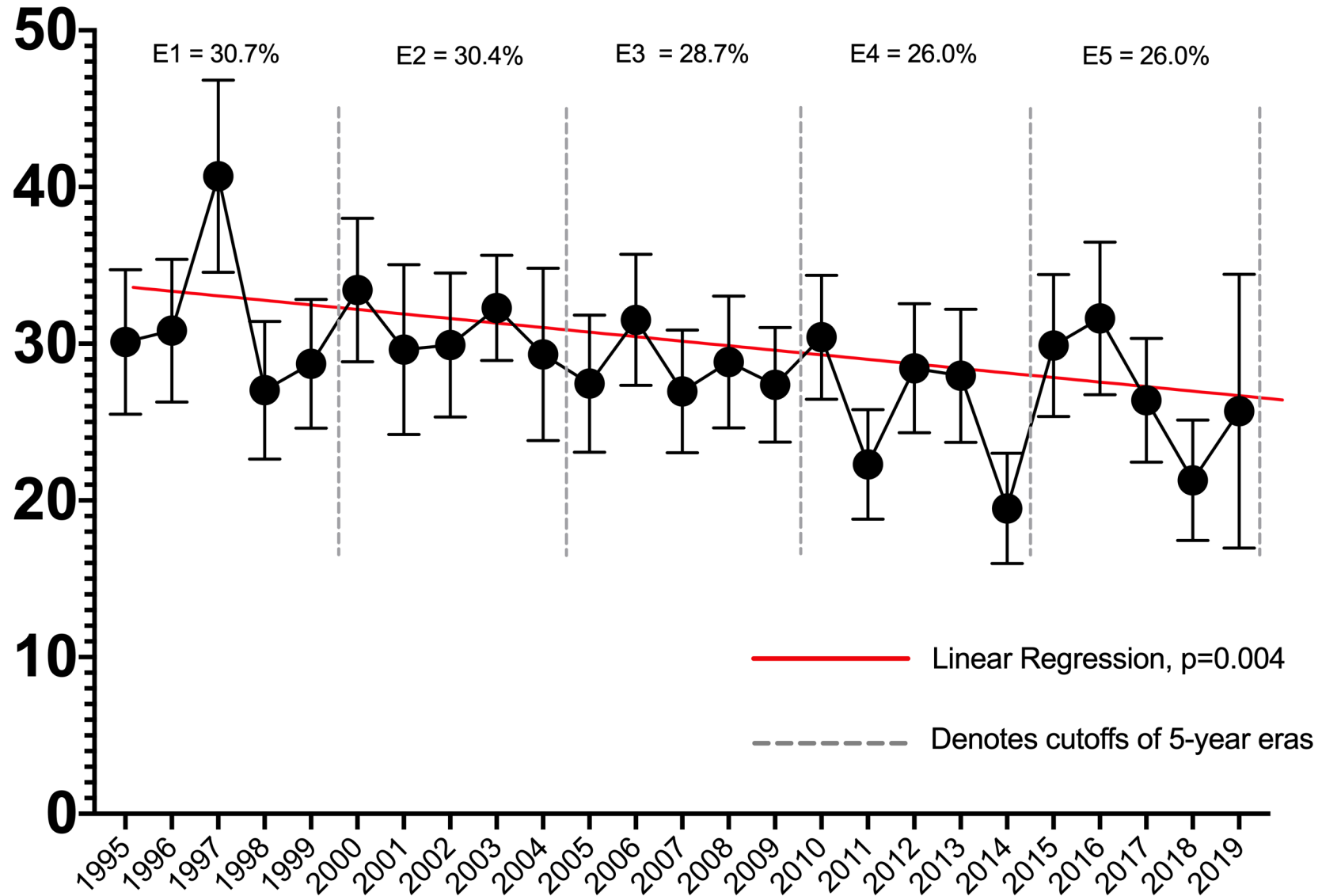
www.despair.com

25 Years – Any Progress?

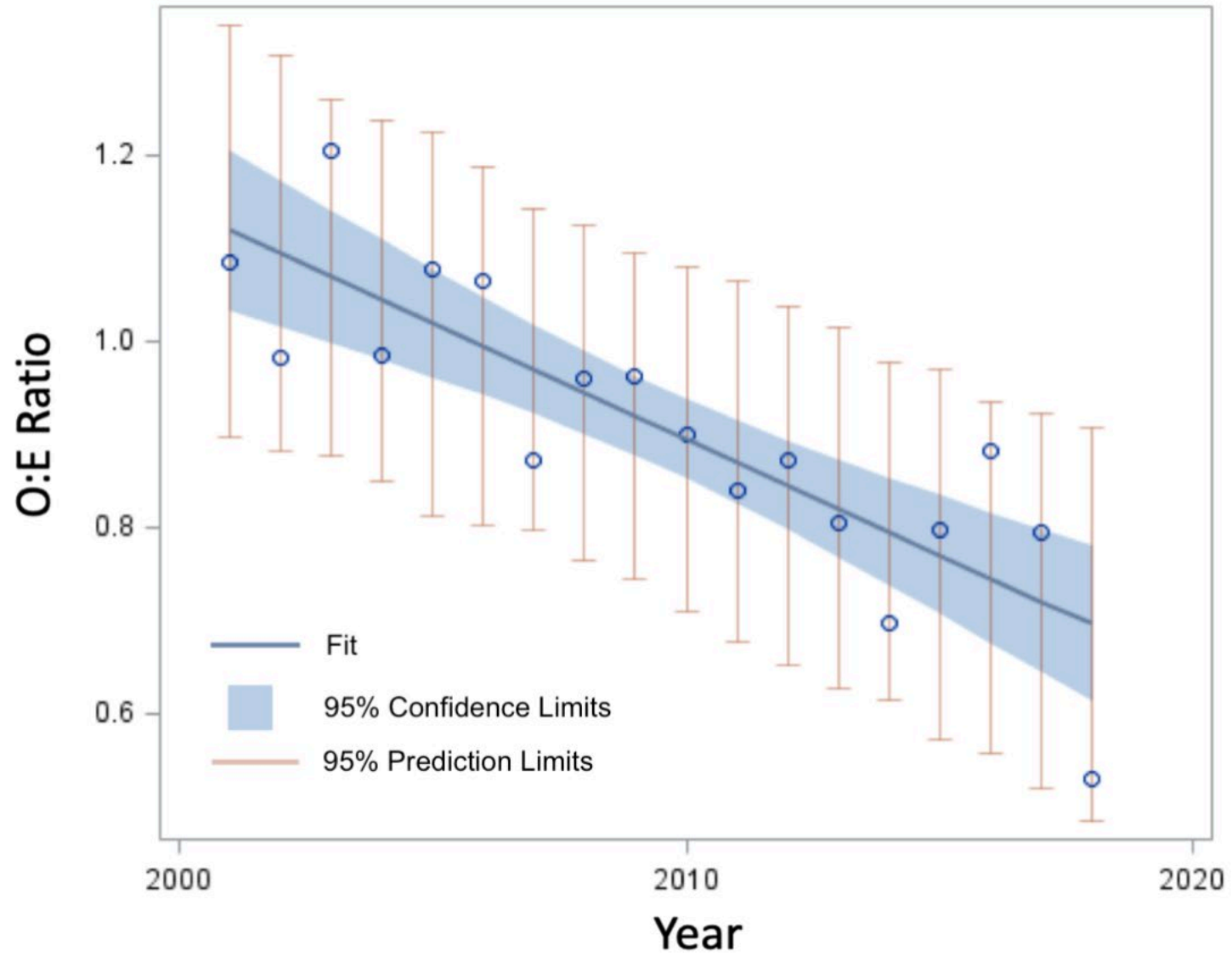
- **Centers with at least 22 years of continual participation**
- **Grouped by 5 year intervals**
- **Evaluated Overall Survival**
- **Looked at O:E survival**

Overall Mortality Rate

Average % Mortality at Long Term Contributing Centers



Fit Plot for Observed:Expected Mortality Ratio



25 Years – Any Progress?

- **Significant increase in survival over years**
- **Current overall survival is 73% for all comers**
- **Surgical survival is 85%**
- **Remains a large variation amongst centers**

The CDH Study Registry

PROs

- **Ability to study infrequent problems**
- **Data on very large number of patients**
- **Individual centers can compare themselves with others**
- **Demonstrate changes over time of management and outcome**

The CDH Study Registry

CONs

- **Observational data**
- **Inability to evaluate long-term sequelae**
- **Difficult to collect complicated information**
- **Wide spectrum of patients and treatment philosophies**



The “Gold Standard”

Randomized Clinical Trial

- **Expensive (\$500k-\$3 million+)**
- **Labor intensive**
- **Takes a long time (5-10 years)**
- **Requires consent / challenges of recruitment**
- **Requires multi-institutional cooperation**
- **Answers a single question**
- **Nearly impossible to achieve appropriate sample size in CDH**

The future of the CDHSG

- **Ongoing evolution of versions to address current questions**
 - **Version 5 – Breakout session this meeting**
- **Management standardization**
- **Long term data collection**
- **Novel statistical analysis**





Samford University
Commencement Ceremony
May 14, 2011







John Roesler – DOB 11/26/2019

The secret of enjoying a good wine:

1. Open the bottle to allow it to breathe.



2. If it does not look like it's breathing, give it mouth-to-mouth.



