6-2024

Evaluation of Aluminum Exposure in Neonates Receiving Parenteral Nutrition

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IRB-Approved

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Background - Aluminum

- Metallic trace element associated with major toxicities
  - Bone and liver disease, cholestasis, anemia, and neurotoxicity
- Parenteral nutrition (PN) contaminants documented since the 1980s
- Recent changes in PN component manufacturing
  - Calcium and phosphate additives with less contaminant
  - Minimize use of glass vessels to reduce leaching
- High accumulation risk in premature neonates or poor renal function

1.Novak et al (1989), 2. Hall et al (2017), 3. Wier et al (2012),
4. Fanni et al (2014), 5. Huston et al (2015), 9. Klotz et al (2019)

Background

Lima Rogel et al (2016)

- Compared FDA-recommended limit to calculated exposure from PN component labeling
- Calculated mean aluminum intake: **11.8 mcg/kg/day**

Fortenberry et al (2017)

- Calculated exposure based on PN labeling
- Aluminum exposure in neonates with poor outcomes vs no poor outcomes: **78.8 mcg/kg/day vs 79.2 mcg/kg/day** (p = 0.87)

U.S. FDA (Dec 2022)

- Maximum recommended aluminum from PN additives: **5 mcg/kg/day**

6. United States Food and Drug Administration (2022),
7. Fortenberry et al (2017), 8. Lima-Rogel et al (2016)

Study Objectives

Primary Outcome

- Patients today versus patients in 2008

Secondary Outcome

- Aluminum exposure (mcg/kg/day) in PN compared to FDA recommendations

Methods

Inclusion Criteria

- Inpatient neonates at SFH NICU
- First course of parenteral nutrition
- At least 6 days of parenteral nutrition

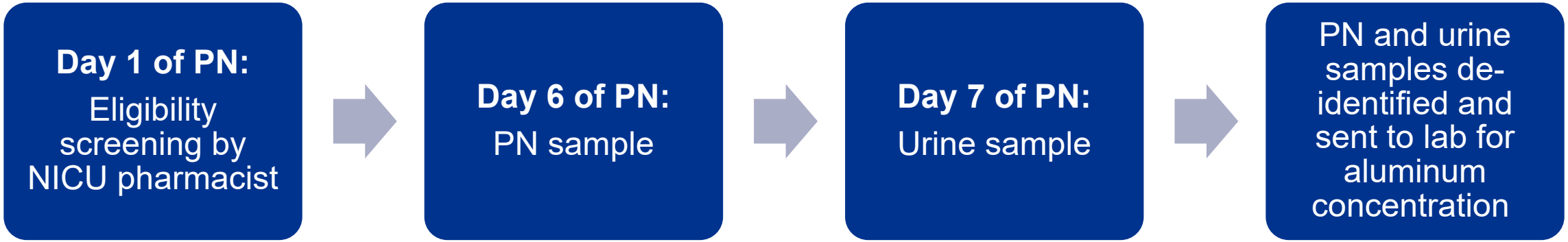
Exclusion Criteria

- Previous parenteral nutrition
- Poor baseline renal function
  - SCr > 1.2 mg/dL (if > 7 days)
  - SCr rise by ≥ 0.3 mg/dL within 48-hours
- Not viable or uncertain viability

Methods

Triple-arm prospective observational cohort

- Neonates in 2008 receiving standard PN
- Neonates in 2008 receiving low aluminum PN
- Neonates in 2024 receiving standard PN

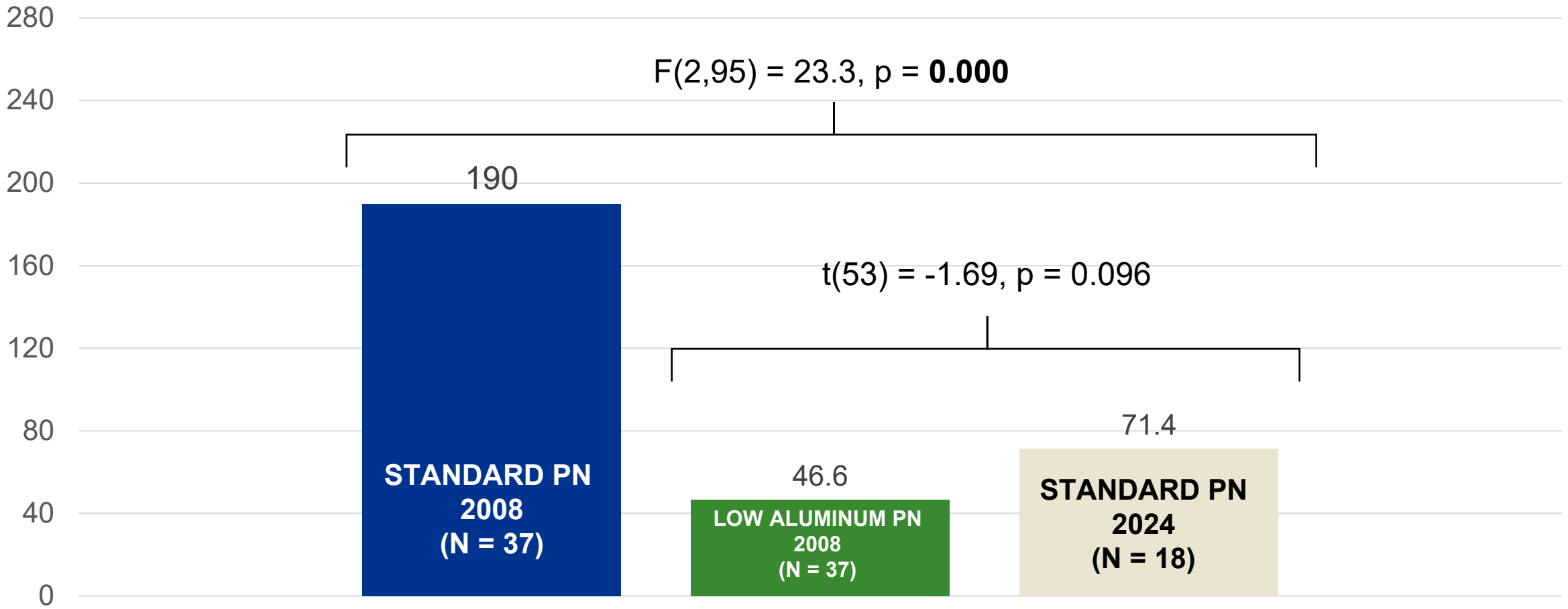


Baseline Characteristics

	Standard PN group from 2008 (n=37)	Low aluminum PN group from 2008 (n=37)	Standard PN group from 2024 (n=18)	F(2, 95)	p
Gestational age (days), mean [weeks + days] (SD)	210 [30 w] (24.7)	218 [31 w + 1 d] (18.6)	227 [32 w + 3 d] (26.8)	3.59	**0.032**
Length (cm), mean (SD)	37.8 (5.7)	40 (4.9)	40.4 (4.8)	2.25	0.112
Weight (kg), mean (SD)	1.29 (0.54)	1.48 (0.5)	1.56 (0.56)	1.96	0.147
24-hour urine output (mL/kg), mean (SD)	84.5 (25.8)	91.3 (27.5)	107.4 (32.1)	4.08	**0.021**
Serum creatinine (mg/dL), mean (SD)	0.84 (0.17)	0.69 (0.25)	0.61 (0.21)	8.43	**0.000**
Serum calcium (mg/dL), mean (SD)	8.4 (1.4)	8.8 (1.2)	9.7 (1.1)	5.42	**0.006**

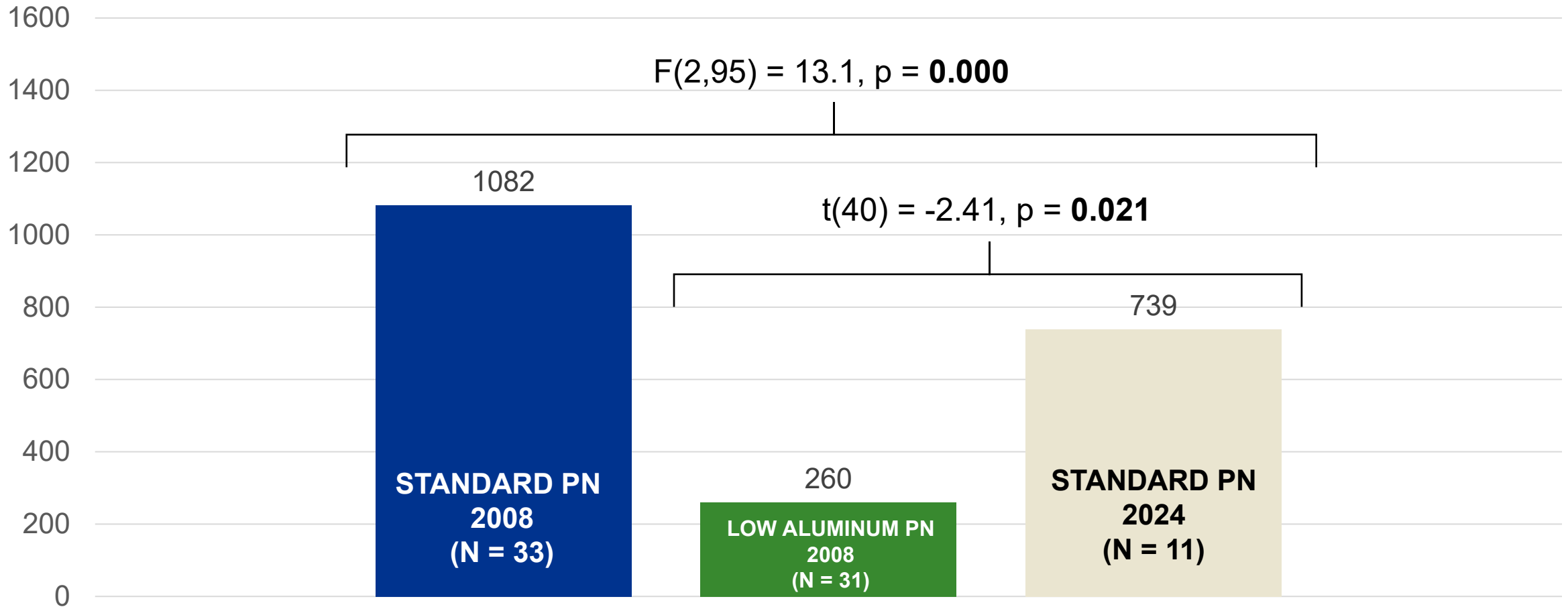
Primary Outcome

Urine Aluminum Concentration (mcg/L), mean



Primary Outcome

Urine Aluminum to Creatinine (mcg/g), mean



Smaller sample sizes as not all neonates had creatinine present in urine or a lab-reported urine aluminum to creatinine ratio

Discussion

Strengths

- Largest study assessing biological aluminum exposure during PN
- Low birth weight and young gestational age
  - Patients at high risk for overaccumulation

Limitations

- Relatively small patient population limits power
- Lack of non-PN control groups
- Limit ability to control for confounds
  - Correlational association only
- Baseline differences between arms due to changes in population over time

Conclusion

Primary outcome: urine aluminum concentration (mcg/L) and aluminum to creatinine ratio (mcg/g)

- Urine aluminum concentration was reduced with use of low aluminum products in 2008
- No difference in aluminum excretion between low aluminum group in 2008 and group in 2024, despite reported changes in manufacturing

Secondary outcome: aluminum exposure (mcg/kg/day)

- *Pending laboratory results*

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Thank You!

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