

Prematurità, IUGR e sviluppo renale

Dott.ssa Mariateresa Sinelli

UO Terapia Intensiva Neonatale e Neonatologia
Fondazione MBBM

Monza



La Nefrogenesi



Week 5
Nephrogenesis
commences

Week 9
Formation of
nephrons
begins

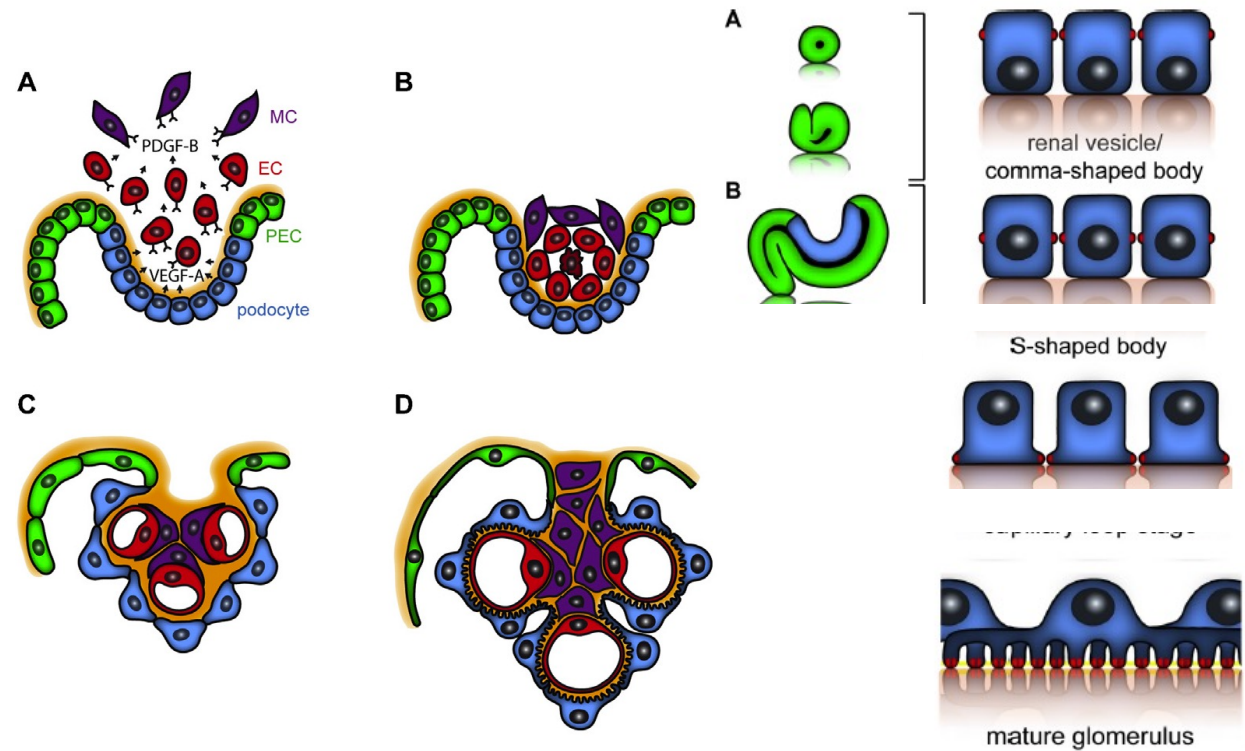
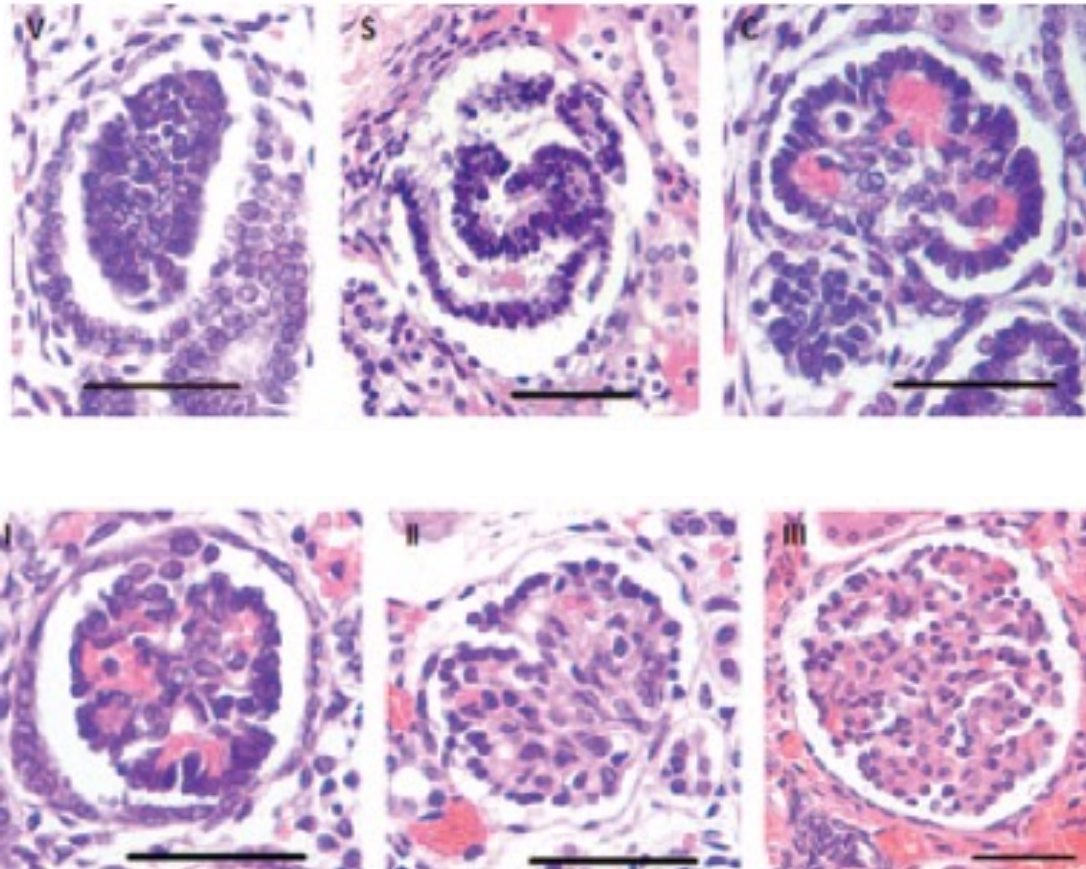
From ~Week 20
Nephrogenesis rapidly
on-going

Week 34-36
Nephrogenesis
is complete in
humans

No new
nephrons
formed after
this time point

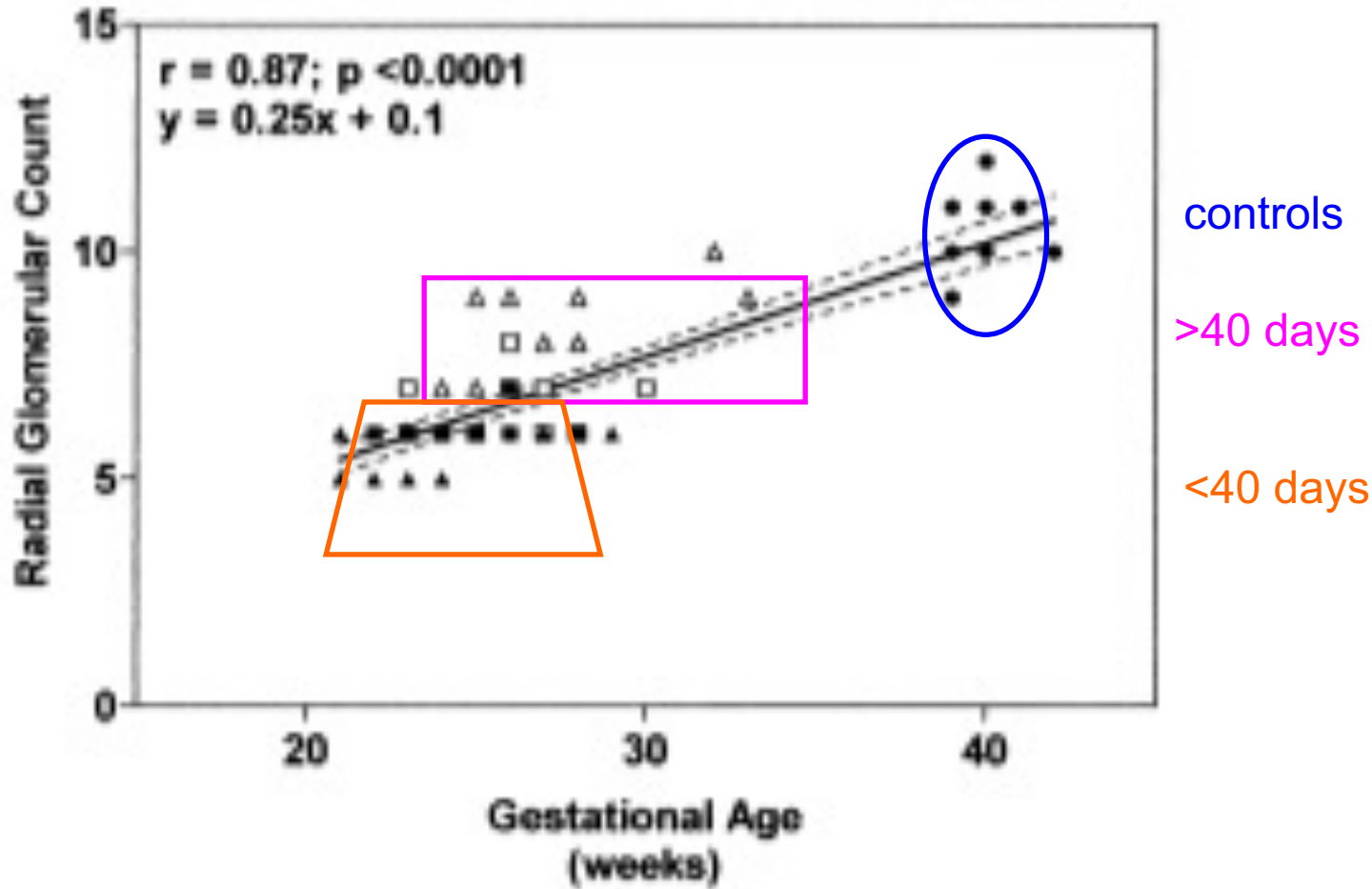
200.000-2.7 milioni
di nefroni

Stages of glomerular maturity in the developing human kidney

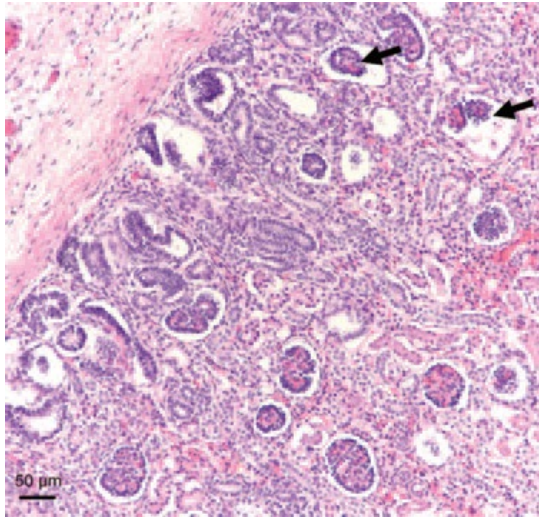


Histomorphometric Analysis of Postnatal Glomerulogenesis in Extremely Preterm Infants

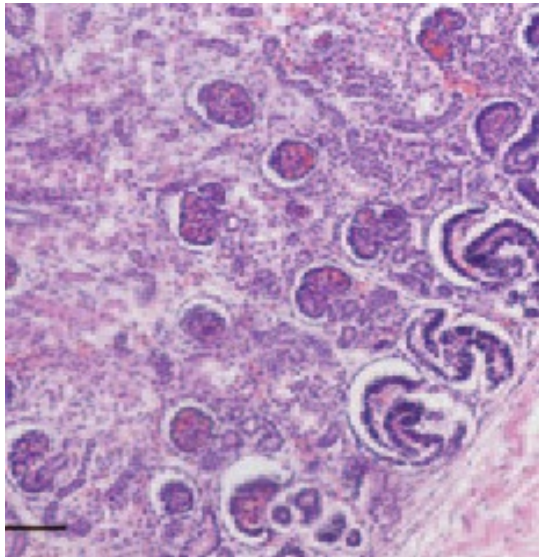
MARIA M. RODRÍGUEZ,^{1*} ALEXANDER H. GÓMEZ,¹ CAROLYN L. ABITBOL,²
JAYANTHI J. CHANDAR,² SHAHNAZ DUARA,³ AND GASTÓN E. ZILLERUELO²



Nefrogenesi e prematurità



Glomeruli a stadi
maturativi precoci



Zona nefrogenica
aumentata

Ridotto numero di glomeruli
rispetto a neonato a termine

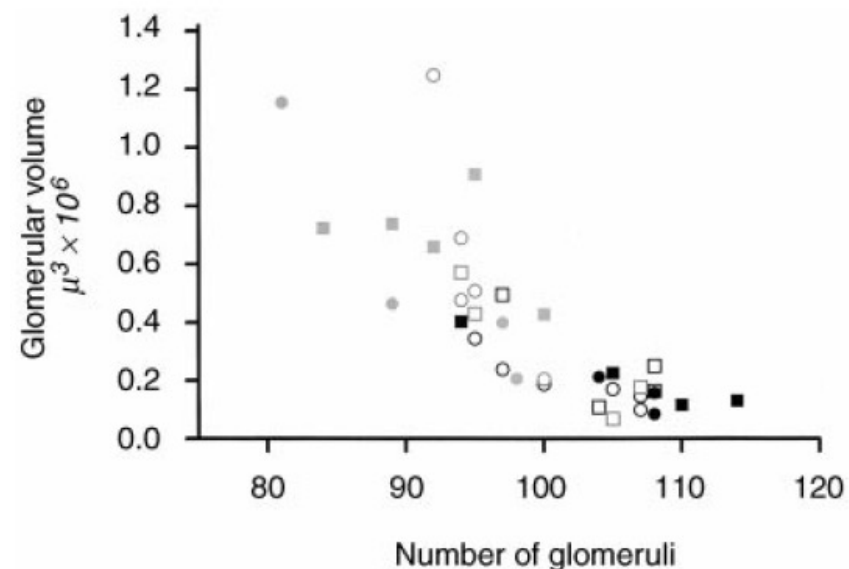
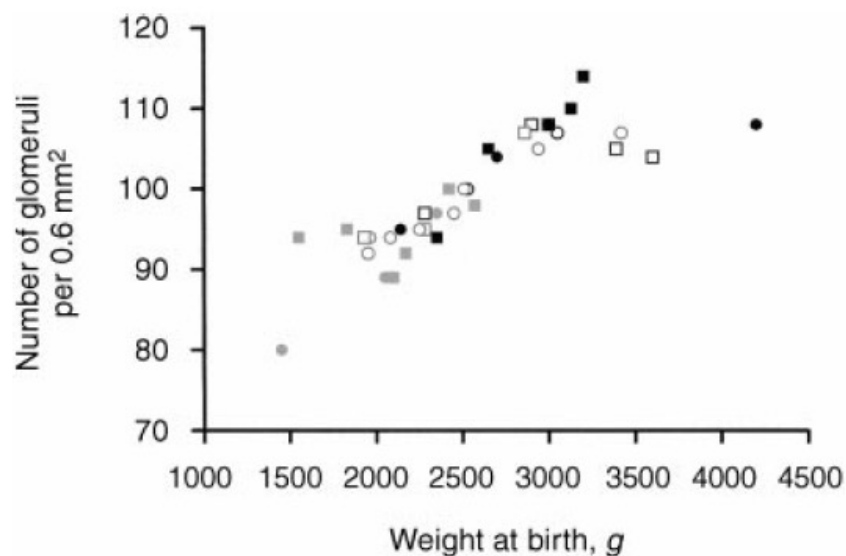
Glomeruli immaturi

Glomeruli poco funzionanti

Oligonephropathy of prematurity

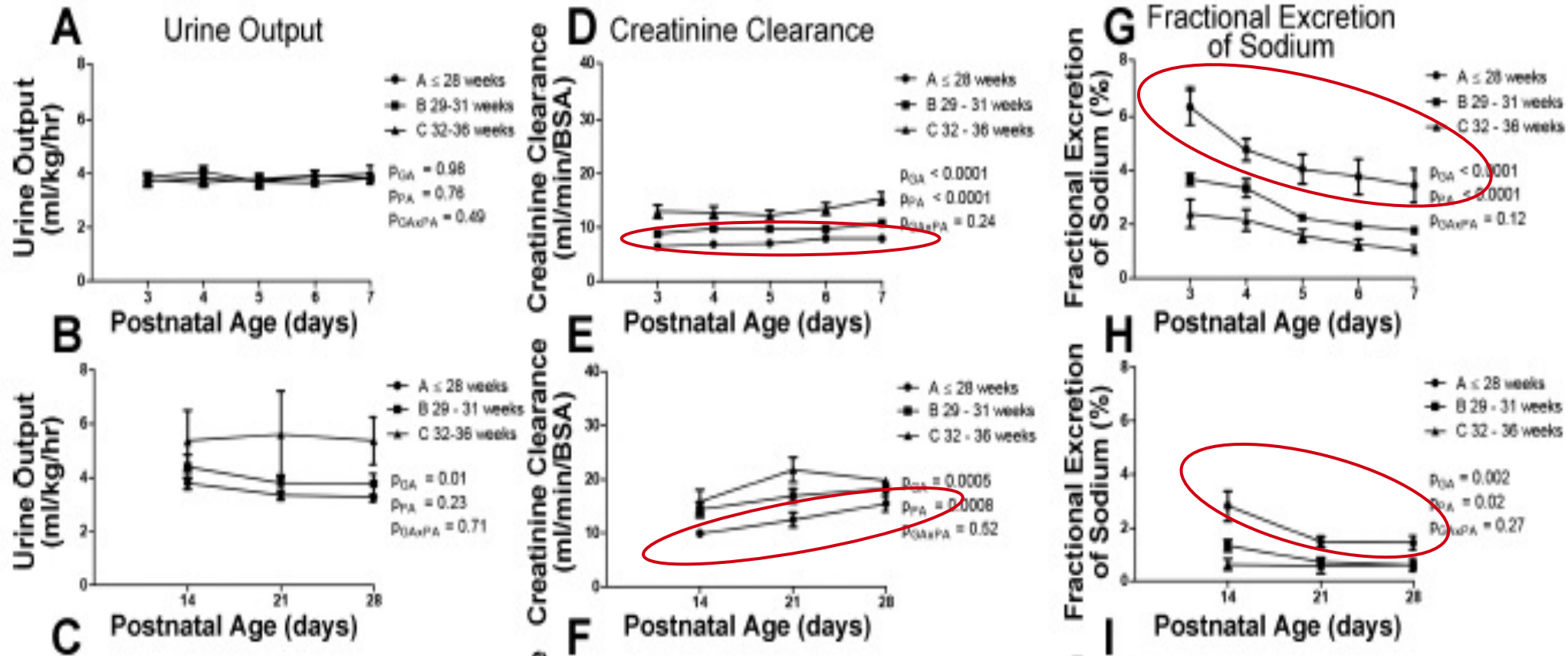
Relationship between weight at birth and the number and size of renal glomeruli in humans: A histomorphometric study

Pazienti arruolati
>36 settimane di eg
Deceduti in epoca neonatale



Assessment of renal functional maturation and injury in preterm neonates during the first month of life

Lina Gubhaju,^{1*} Megan R. Sutherland,^{2*} Rosemary S. C. Horne,³ Allson Medhurst,⁴ Allson L. Kent,⁵ Andrew Ramsden,⁴ Lynette Moore,⁶ Gurmeet Singh,⁷ Wendy E. Hoy,⁸ and M. Jane Black²



KDIGO Kidney Disease Improving Global Outcomes

PEDIATRICS Volume 136, number 2, August 2015

TABLE 1 Neonatal AKI KDIGO Classification

Stage	SCr	Urine Output
0	No change in SCr or rise <0.3 mg/dL	≥ 0.5 mL/kg/h
1	SCr rise ≥ 0.3 mg/dL within 48 h or SCr rise ≥1.5–1.9 × reference SCr ^a within 7 d	<0.5 mL/kg/h for 6 to 12 h
2	SCr rise ≥2.0–2.9 × reference SCr ^a	<0.5 mL/kg/h for ≥ 12 h
3	SCr rise ≥3 × reference SCr ^a or SCr ≥2.5 mg/dL ^b or Receipt of dialysis	<0.3 mL/kg/h for ≥24 h or anuria for ≥12 h

Differences between the proposed neonatal AKI definition and KDIGO include the following:

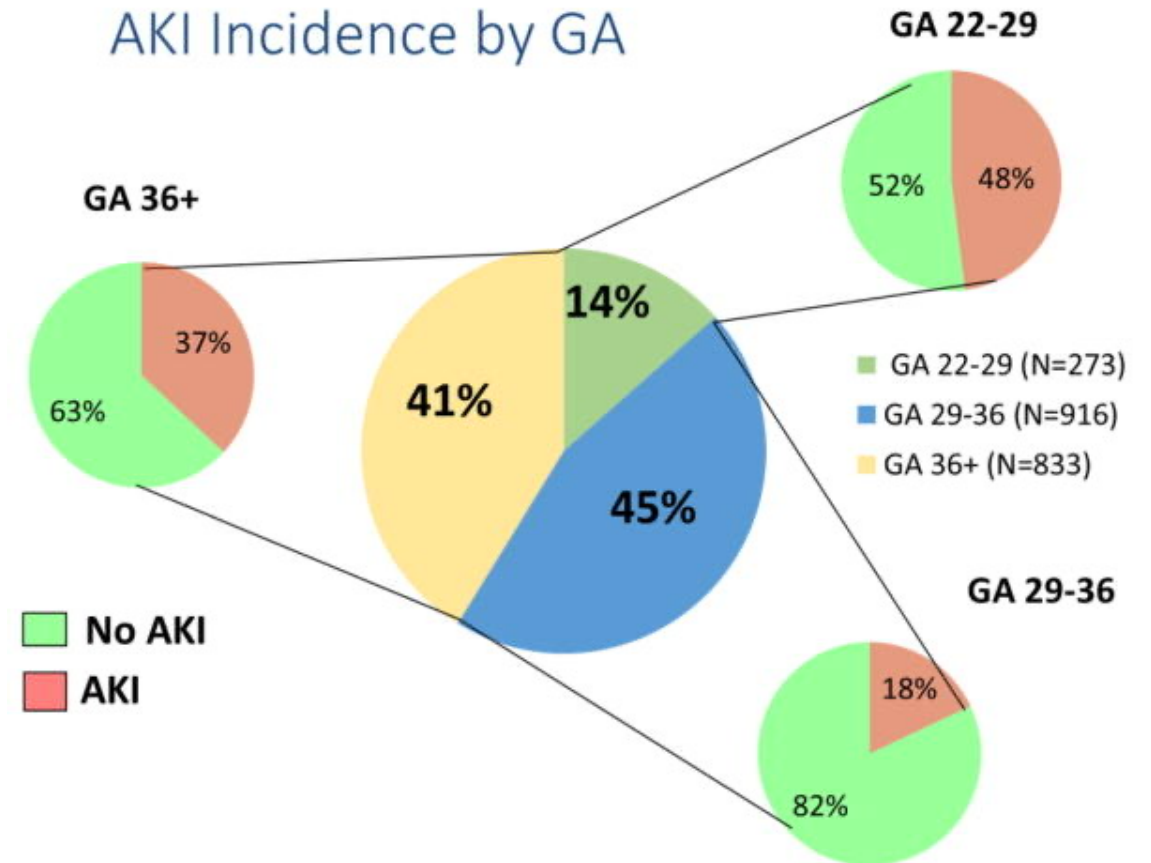
^a Reference SCr will be defined as the lowest previous SCr value.

^b SCr value of 2.5 mg/dL represents <10 mL/min/1.73m².

Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study

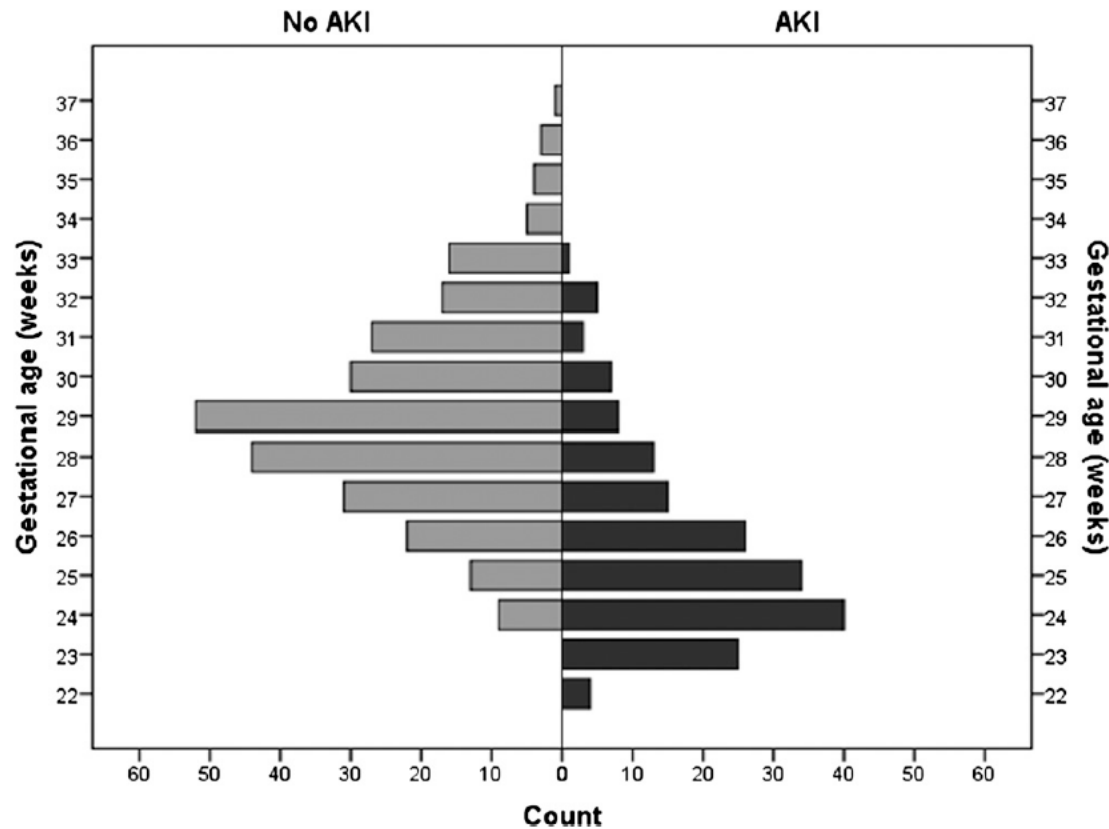
- 24 NICU (Australia, Canada, India, USA)
- 2022 neonati
- EG: 22-term

Al di sotto delle 29 settimane di età gestazionale quasi 1 neonato su 2 presenta un episodio di danno renale acuto



Recognition and Reporting of AKI in Very Low Birth Weight Infants

J. Bryan Carmody, Jonathan R. Swanson,[†] Erika T. Rhone,[‡] and Jennifer R. Charlton[‡]*

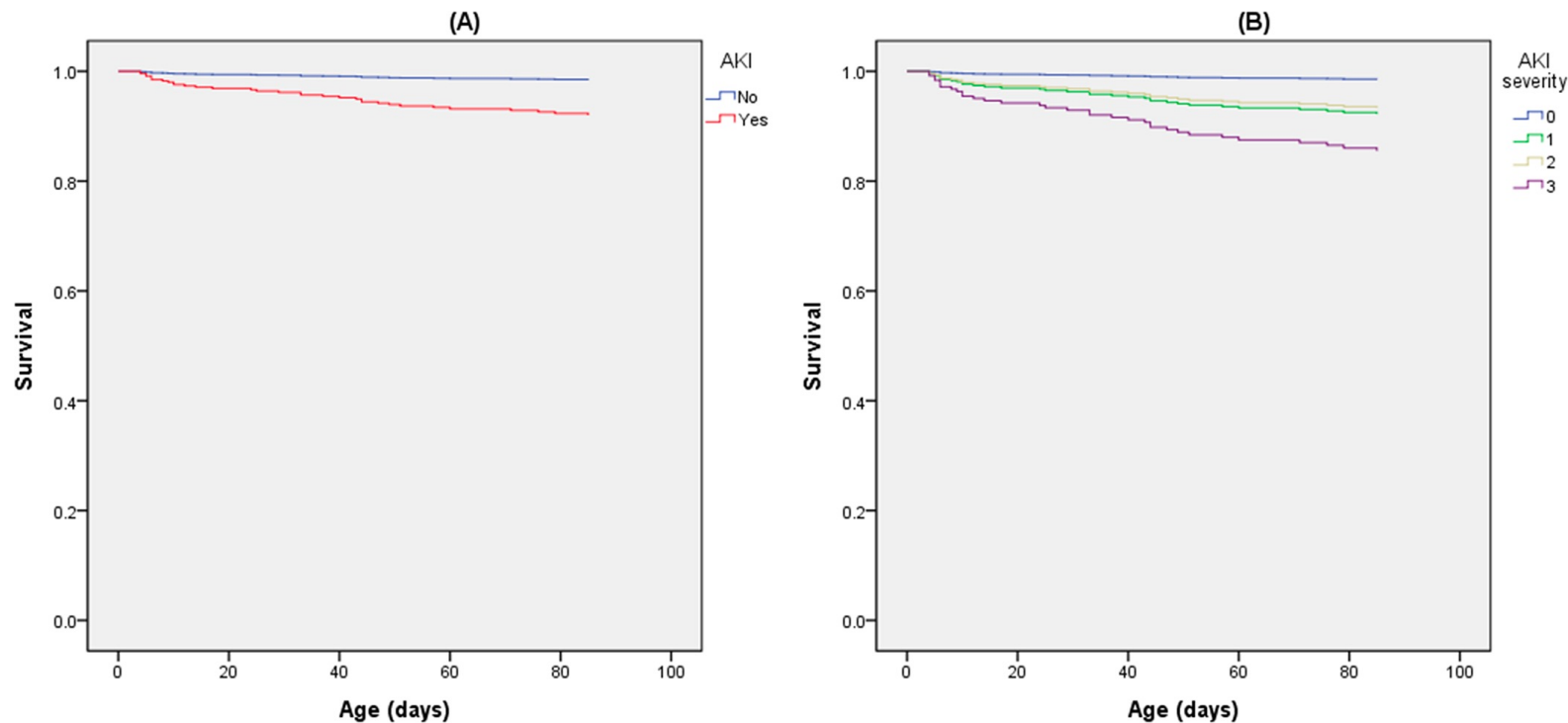


41% multiple episodes of AKI

13.5% reported AKI in discharge letter

Incidence and outcomes of acute kidney injury in extremely-low-birth-weight infants

Chien-Chung Lee^{1,2}, Oi-Wa Chan^{2,3}, Mei-Yin Lai¹, Kai-Hsiang Hsu^{1,2}, Tai-Wei Wu¹, Wai-Ho Lim¹, Yu-Cheng Wang⁴, Reyin Lien^{1*}



AKI aumenta il rischio di morte a 36 settimane di ec

Adjusted HR 10.60 (95% CI: 2.09-53.67, $p=0.004$) in AKI3

Studio Rene-IUGR: scopo dello studio

Valutare rischio di AKI secondo KDIGO nei nati <1500 grammi e/o < 32 settimane di eg

Valutare rischio di AKI in IUGR vs no IUGR

Valutare rischio di AKI in base a z-score del peso alla nascita (BW)

Consensus definition of fetal growth restriction: a Delphi procedure

S. J. GORDIJN*, I. M. BEUNE*, B. THILAGANATHAN†, A. PAPAGEORGHIU†,
A. A. BASCHAT‡, P. N. BAKER§, R. M. SILVER¶, K. WYNIA** and W. GANZEVOORT††

Ultrasound Obstet Gynecol 2016



PESO STIMATO < 10° centile
↻
SMALL FOR GESTATIONAL AGE
↻
LOW RISK PERINATAL OUTCOMES

FETAL GROWTH RESTRICTED



IUGR severo

IUGR moderato

Early FGR:
GA < 32 weeks, in absence of congenital anomalies
AC/EFW < 3rd centile or UA-AEDF

Or
1. AC/EFW < 10th centile combined with
2. UtA-PI > 95th centile and/or
3. UA-PI > 95th centile

Late FGR:
GA ≥ 32 weeks, in absence of congenital anomalies
AC/EFW < 3rd centile

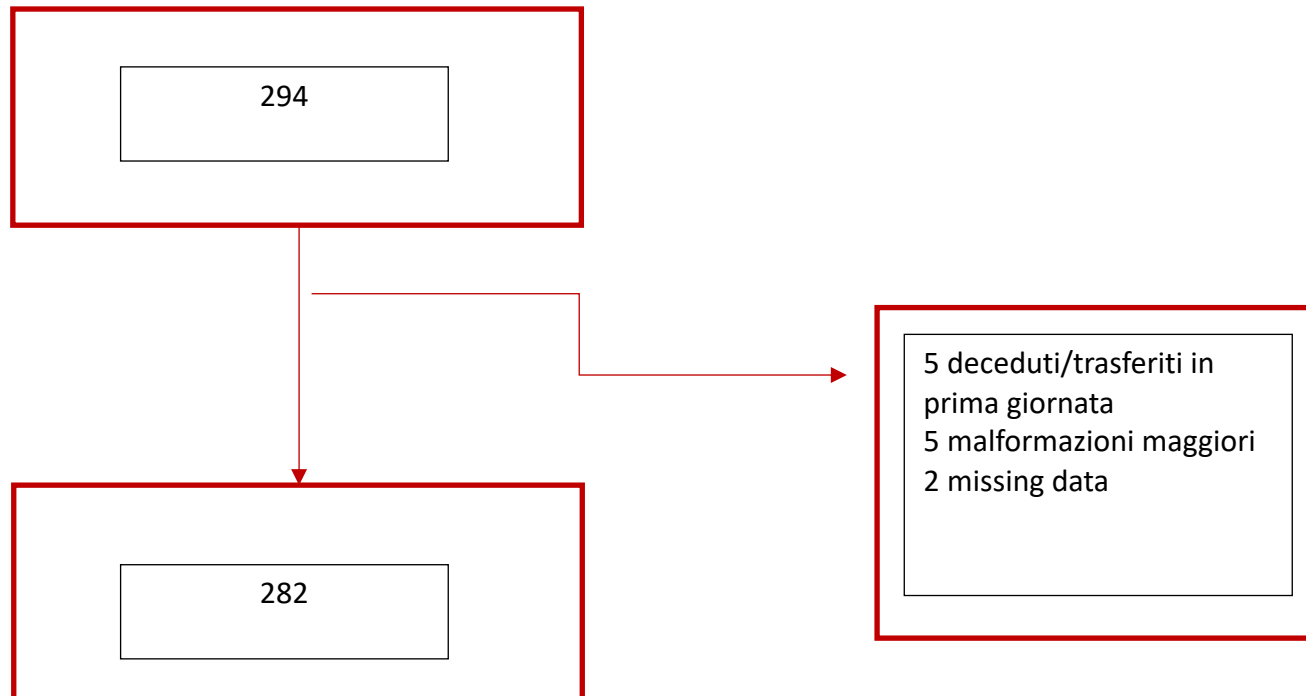
Or at least two out of three of the following
1. AC/EFW < 10th centile
2. AC/EFW crossing centiles > 2 quartiles on growth centiles*
3. CPR < 5th centile or UA-PI > 95th centile

Studio Rene-IUGR

Periodo di studio: 1 gennaio 2016-31 dicembre 2021

Criteri di inclusione: BW <1500 g e/o GA < 32 settimane

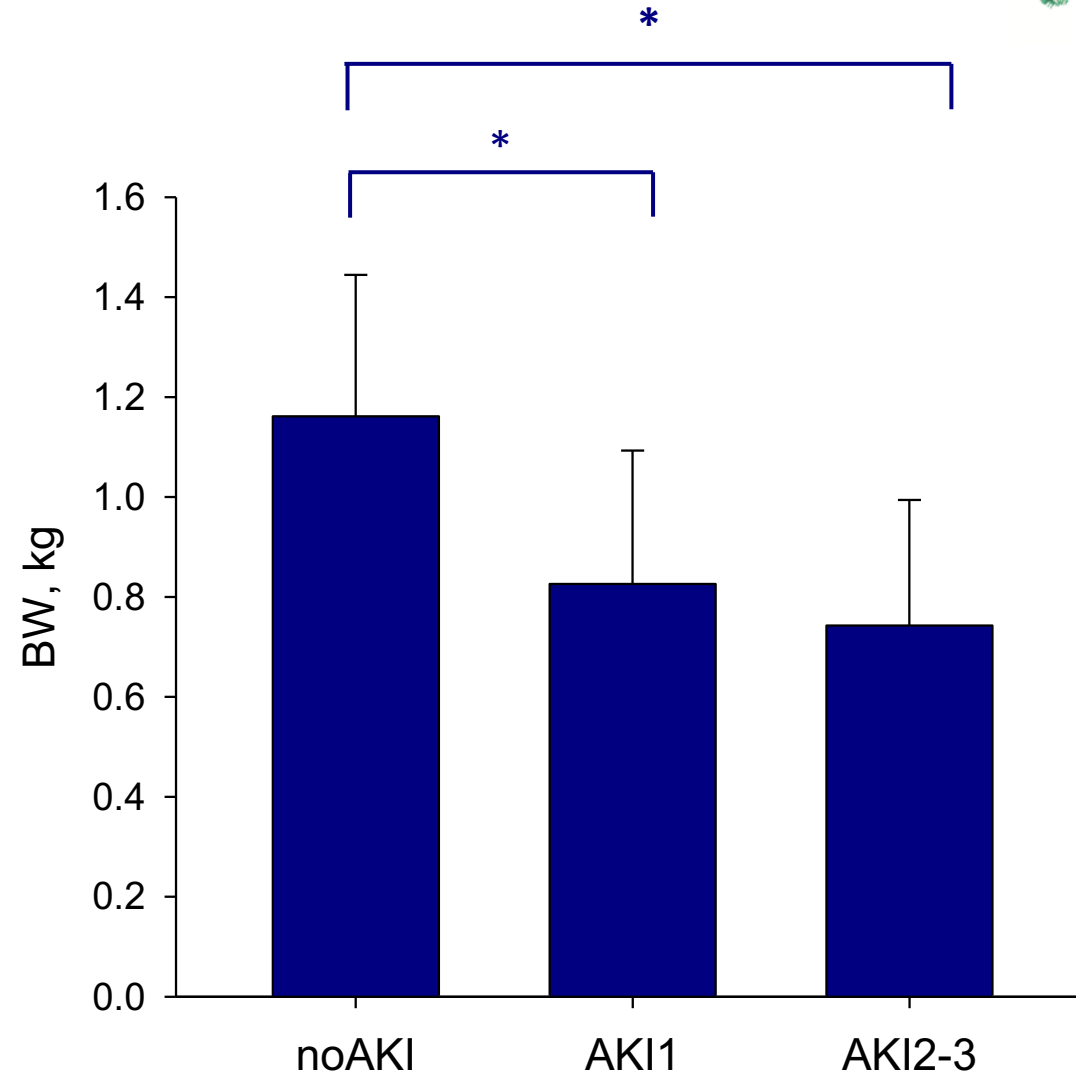
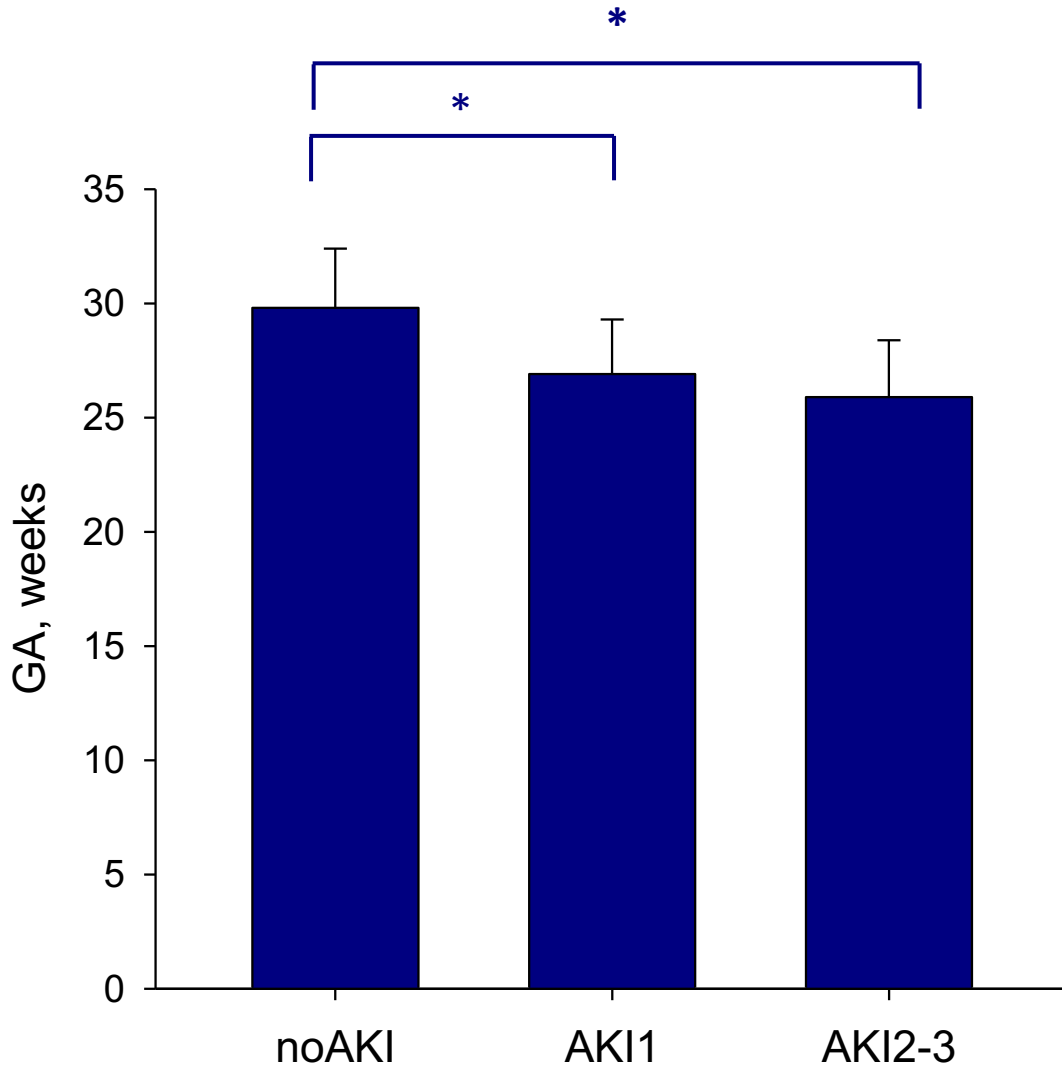
Criteri di esclusione: malformazioni maggiori, cromosomopatie, missing data



Studio Rene-IUGR

N	282
Male, n (%)	142 (50 %)
GA, weeks	29.4 (27.4, 31.3)
BW, g	1150 (870, 1360)
BW, z-score	-0.58 (-1.64, 0.25)
IUGR moderato, n (%)	108 (38 %)
IUGR severo, n (%)	85 (30 %)
PDA, n (%)	58 (21 %)
AKI, n (%)	36 (13 %)
AKI1, n (%)	23 (8 %)
AKI2, n (%)	9 (3 %)
AKI3, n (%)	4 (1 %)
Sepsi	110 (39 %)
NEC	23 (8 %)
BPD	80 (28 %)
Death	18 (6 %)

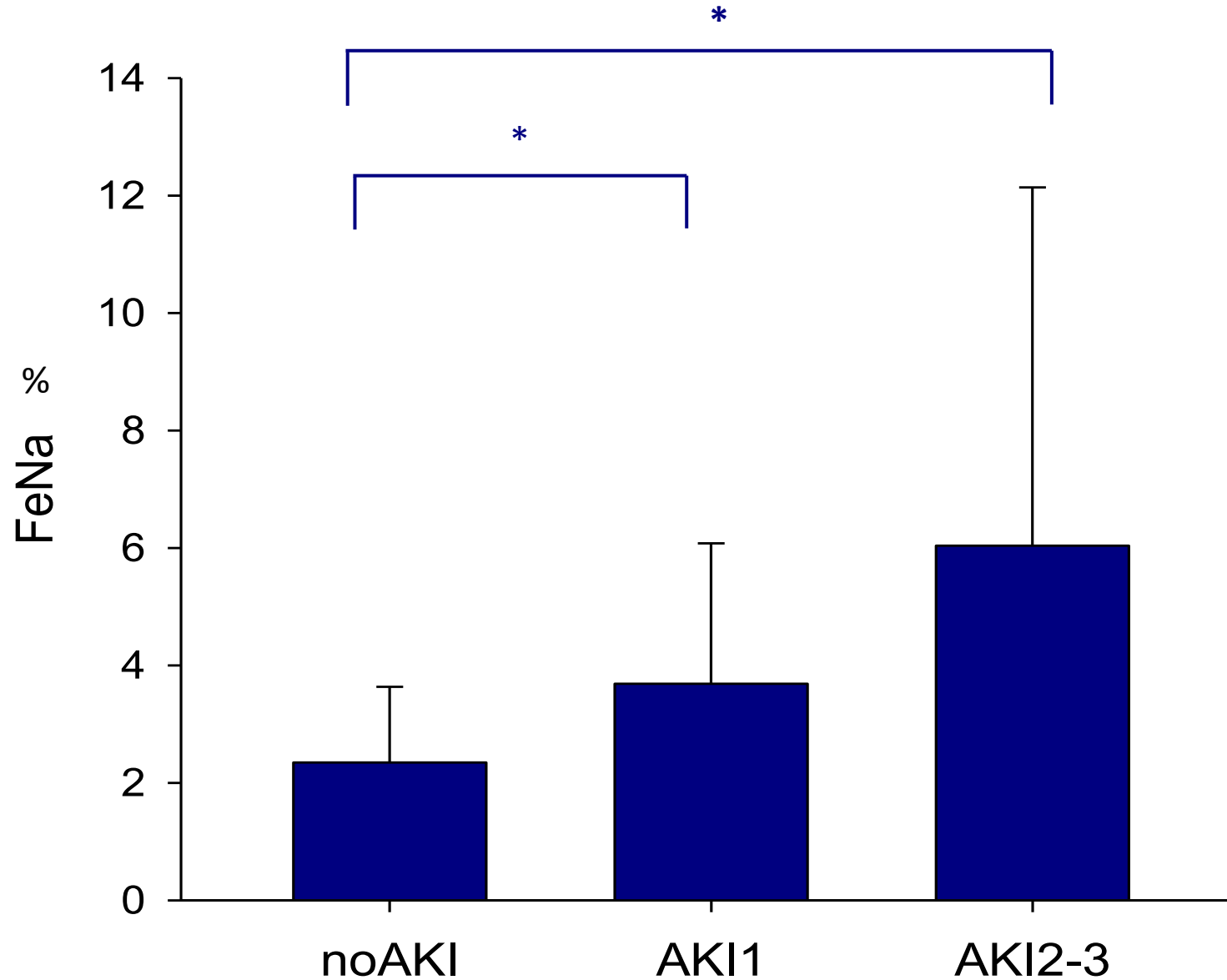
Rischio di AKI in base a età gestazionale e peso alla nascita



Risultati

	beta	std. err.	p-value
GA, weeks	-0,07	0,01	< 0.001
PDA	0,33	0,09	0,000
IUGR severo	0,16	0,07	0,029
GA, weeks	-0,06	0,01	< 0.001
PDA	0,34	0,09	0,000
IUGR moderato	0,13	0,07	0,067
GA, weeks	-0,07	0,01	< 0.001
PDA	0,30	0,08	< 0.001
BW, z-score	-0,08	0,03	0,003

Rischio di AKI in base a valutazione del FeNa nella prima settimana di vita



	Estimate	pValue
GA	-0,09	0,005
FeNa_2 days	0,04	< 0.001
GA	-0,03	0,212
FeNa_5-7 days	0,14	< 0.001

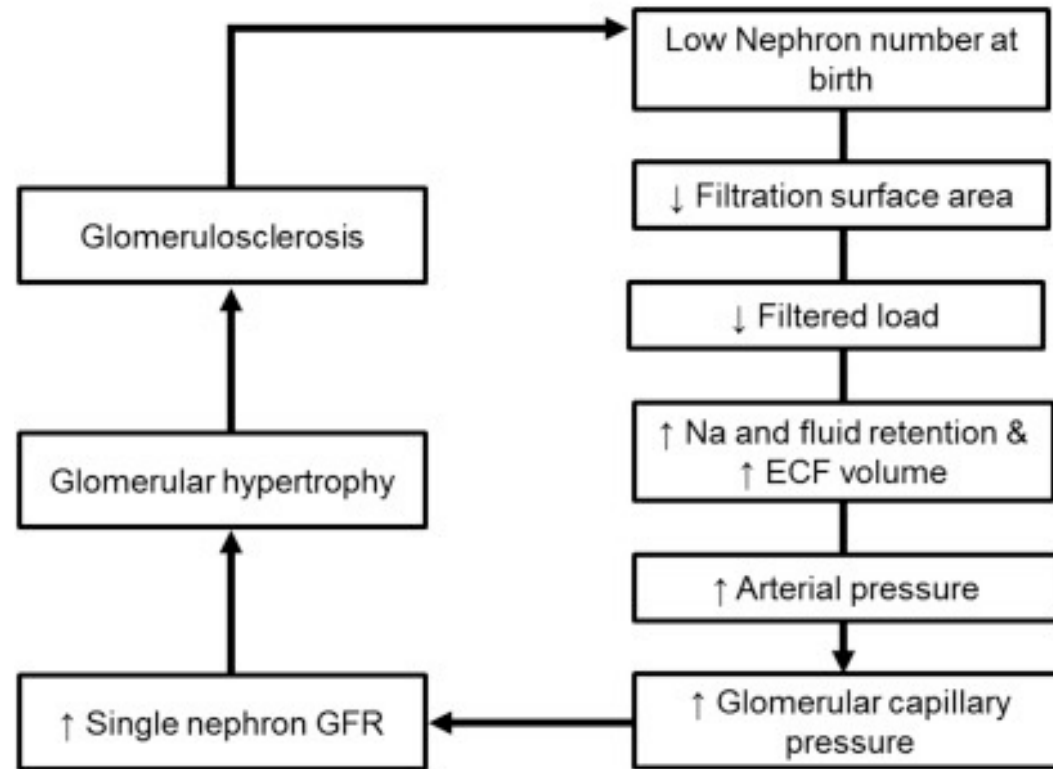
Conclusioni

- IUGR e basso BW z-score correla con AKI in maniera significativa
 - AKI risulta associato a IUGR e basso BW z-score anche dopo correzione con fattori potenzialmente confondenti
 - IUGR potrebbe rappresentare un ulteriore fattore aggiuntivo alla prematurità come fattore di rischio per danno renale acuto
-
- ❖ Necessità di ulteriori studi per confermare questi dati
 - ❖ Necessità di seguire con follow up a lungo termine questi bambini

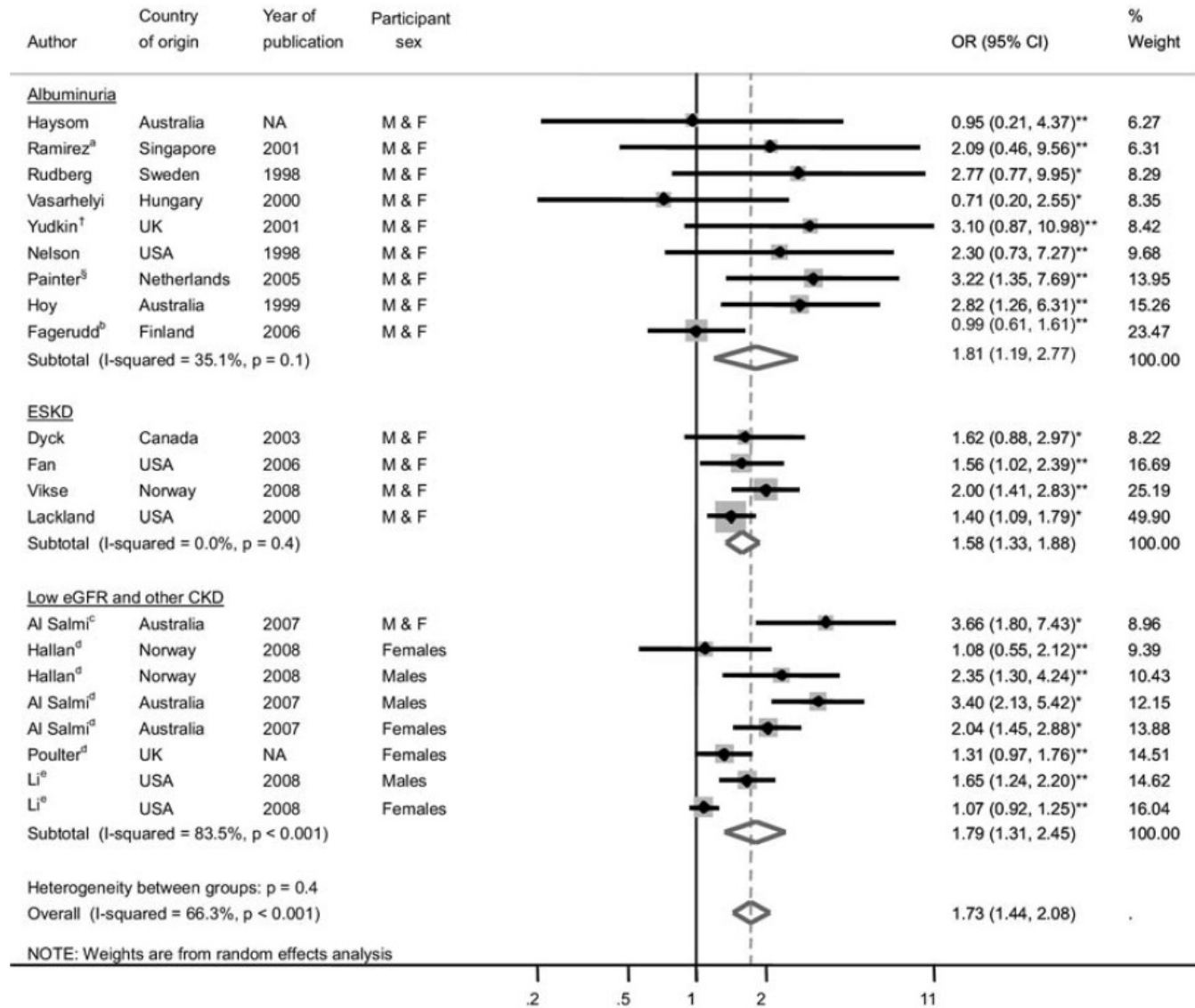
Fetal Programming



The etiology of adult hypertension and progressive renal injury: an hypothesis.

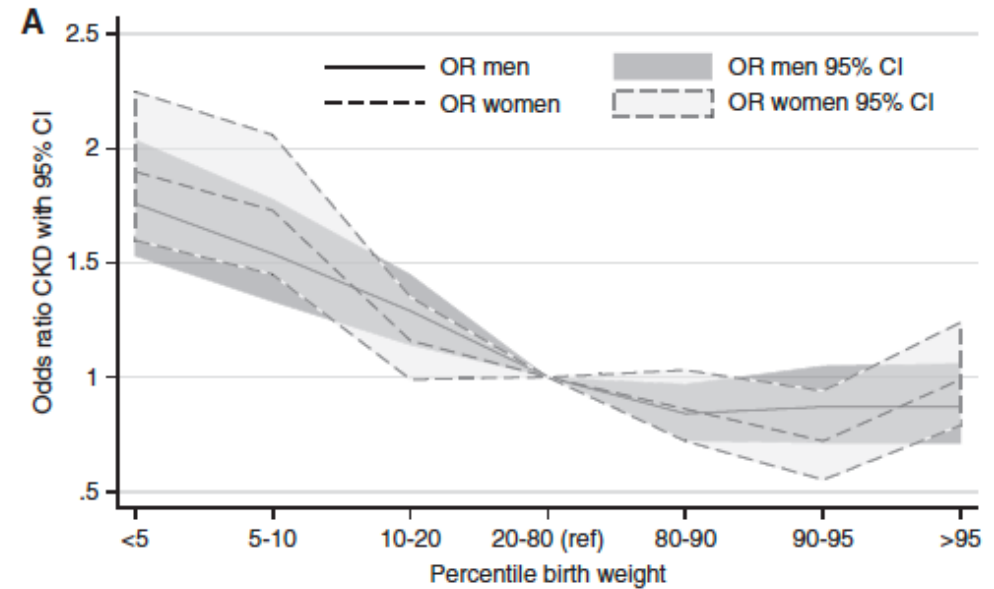
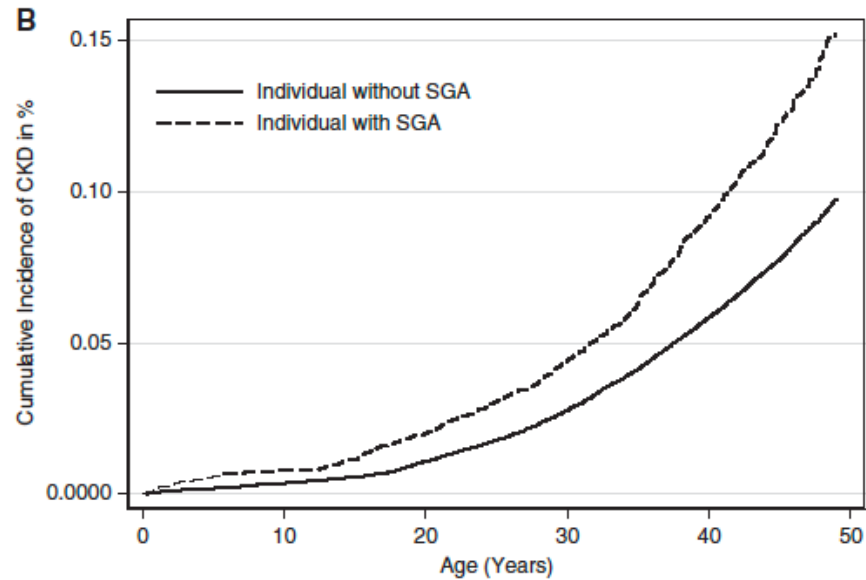
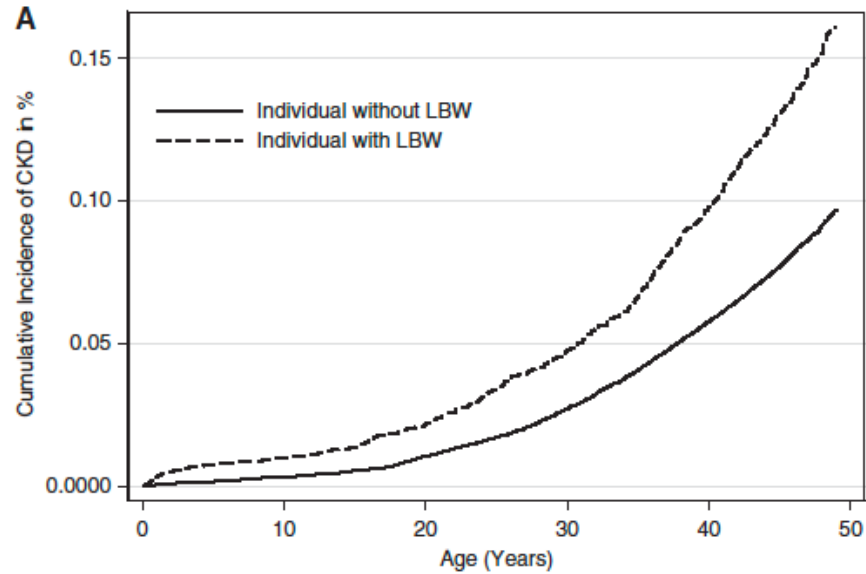


Is Low Birth Weight an Antecedent of CKD in Later Life? A Systematic Review of Observational Studies



Intrauterine Growth Restriction and Risk of Diverse Forms of Kidney Disease during the First 50 Years of Life

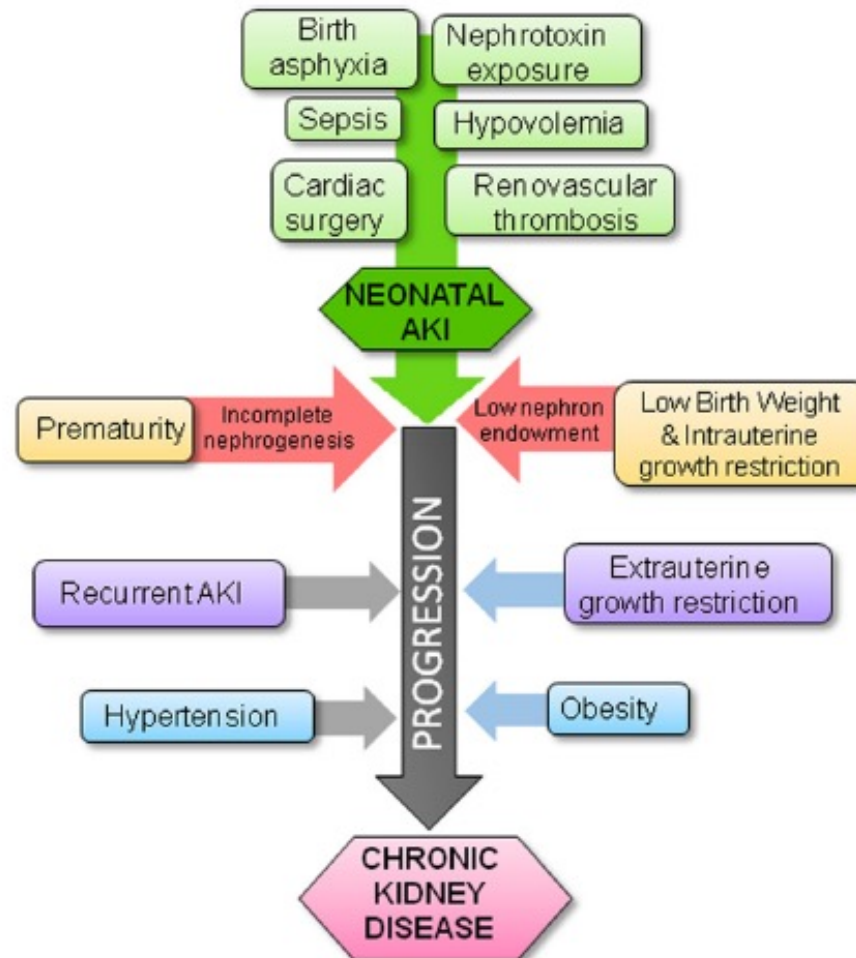
Anna Gjerde,^{1,2} Anna Varberg Reisæter,³ Rannveig Skrunes,^{2,4} Hans-Peter Marti,^{2,4} and Bjørn Egil Vikse^{1,2}



The path to chronic kidney disease following acute kidney injury: a neonatal perspective

Swasti Chaturvedi¹ • Kar Hui Ng^{1,2} • Cherry Mammen³

E se a danno
si somma
danno?

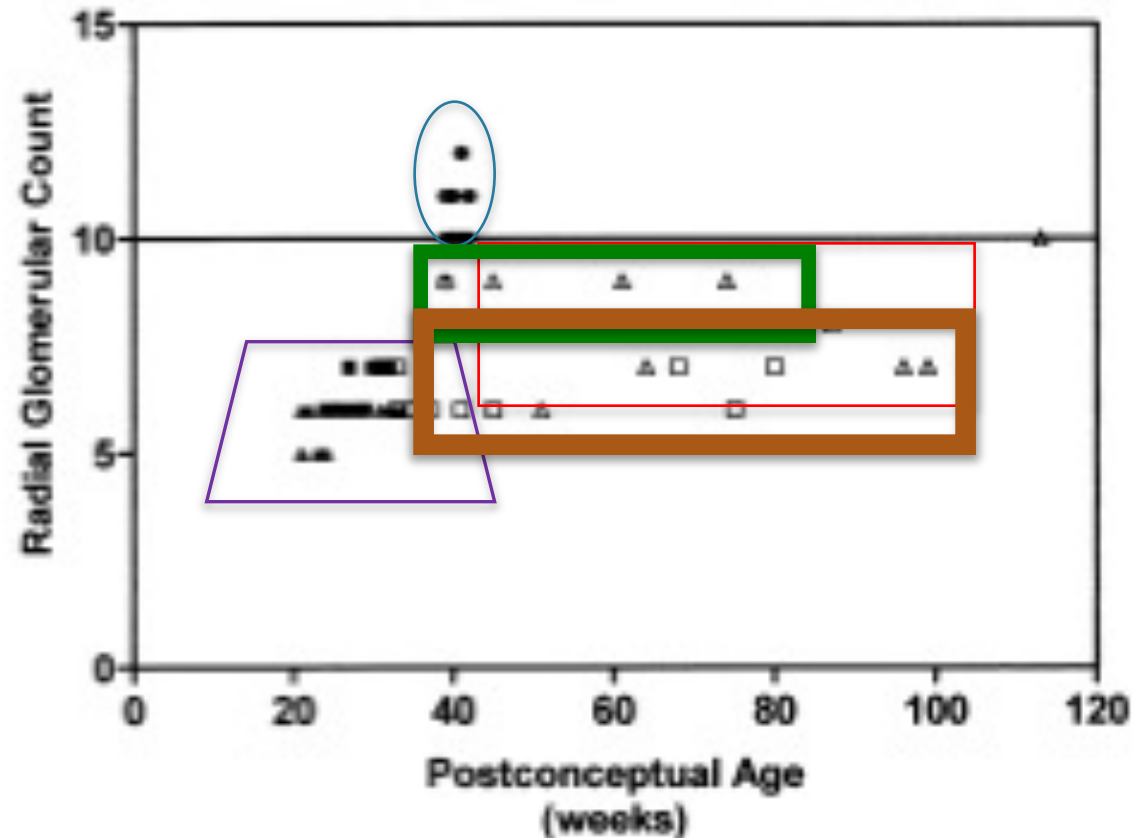




Il danno renale acuto non può più essere considerato un danno completamente reversibile...

Histomorphometric Analysis of Postnatal Glomerulogenesis in Extremely Preterm Infants

MARIA M. RODRÍGUEZ,^{1*} ALEXANDER H. GÓMEZ,¹ CAROLYN L. ABITBOL,²
JAYANTHI J. CHANDAR,² SHAHNAZ DUARA,³ AND GASTÓN E. ZILLERUELO²

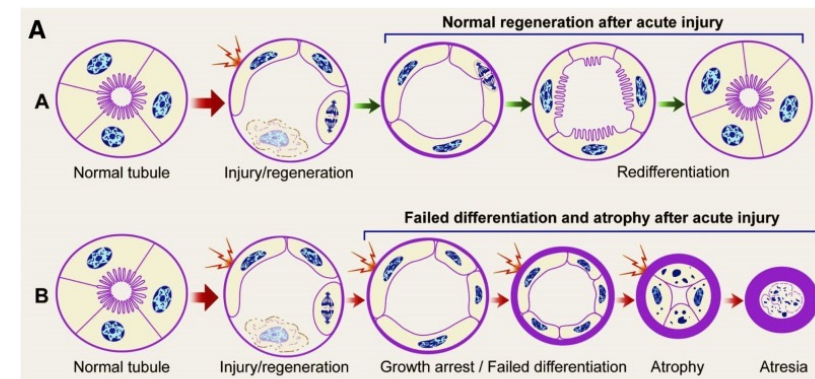
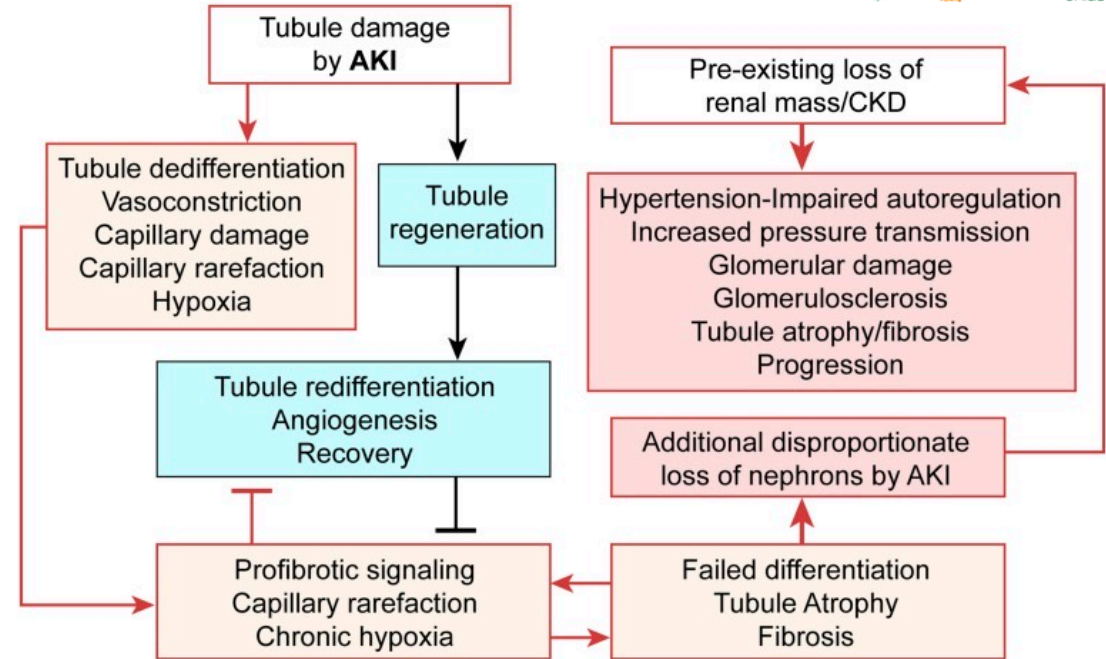
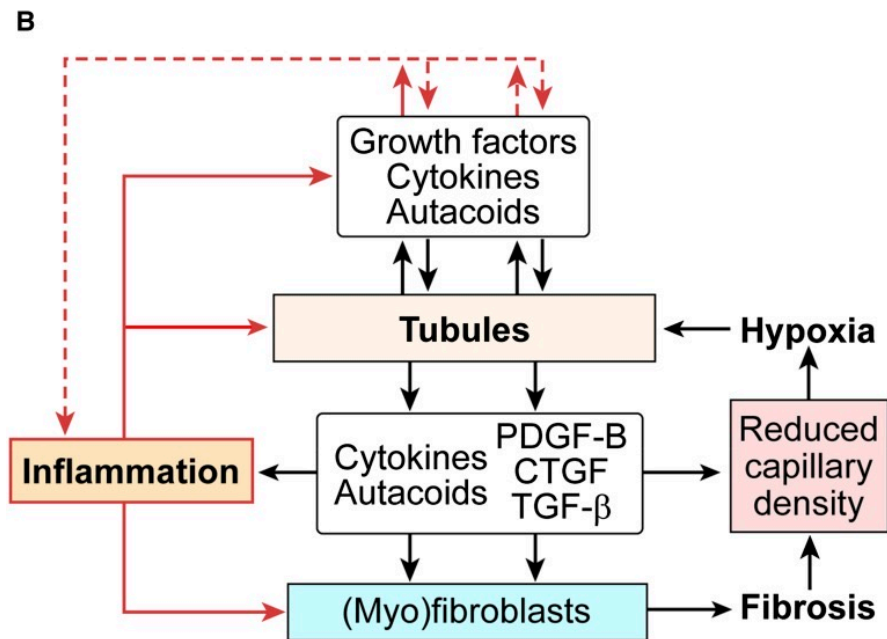
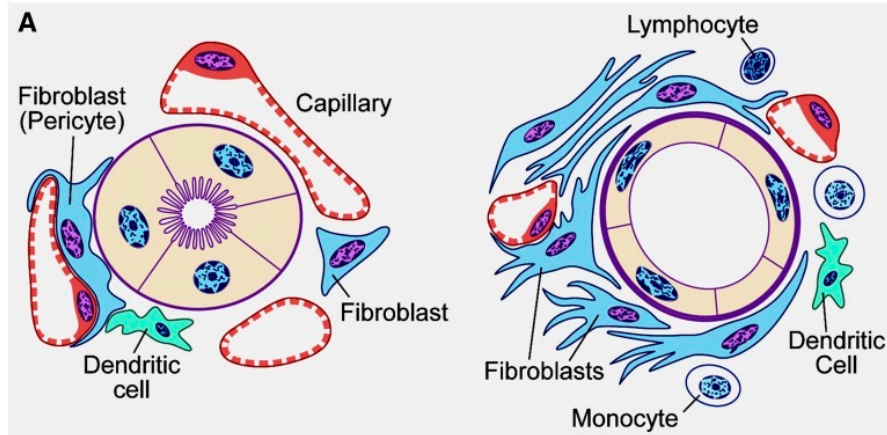


controls

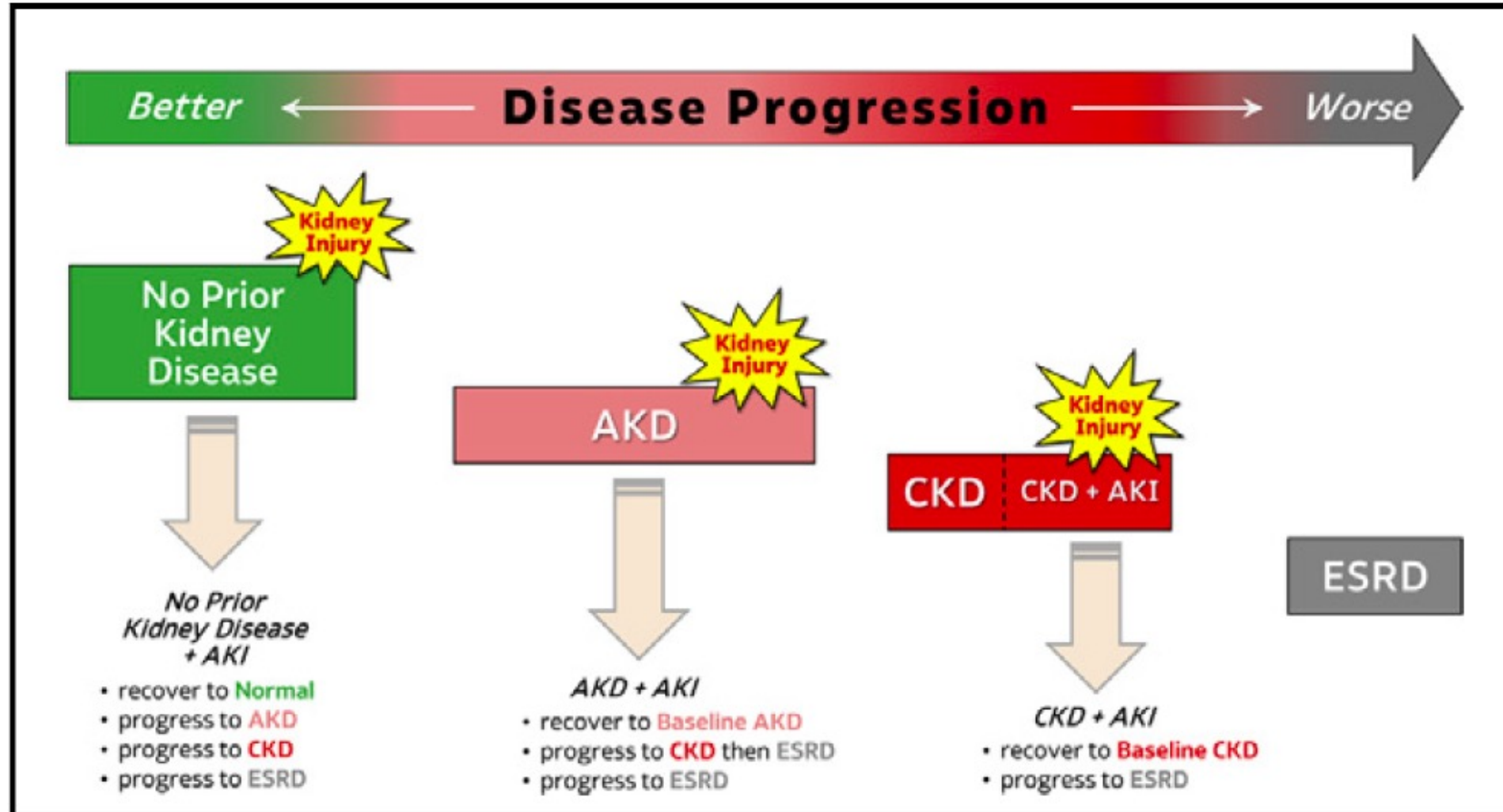
>40 d No AKI
 AKI

<40 d

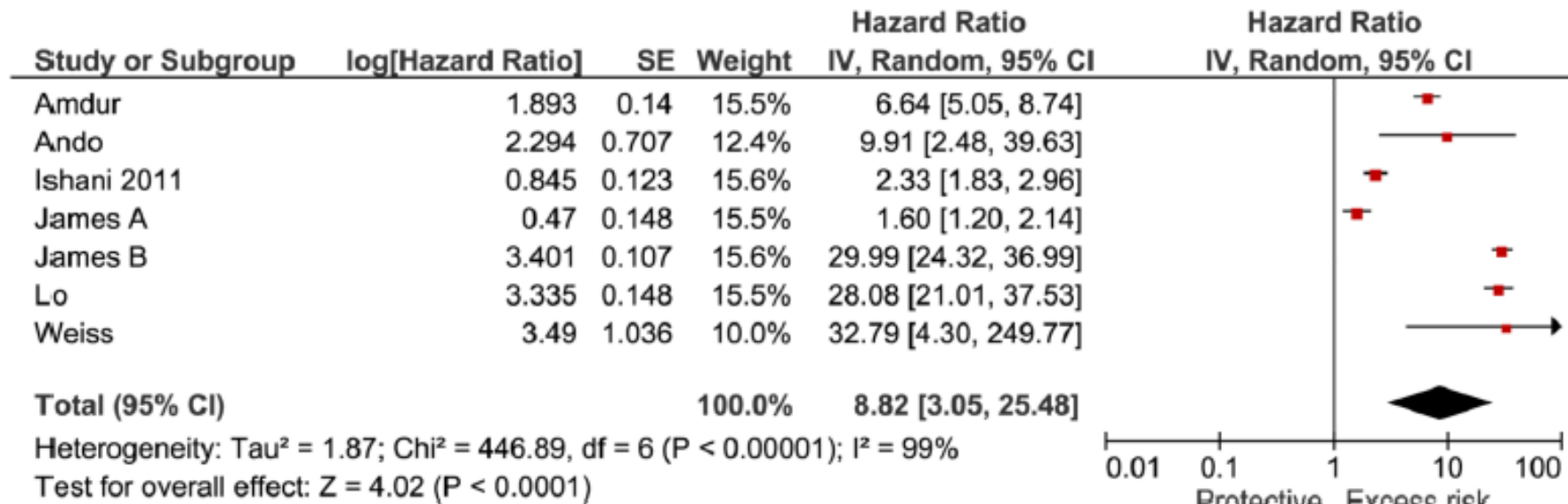
Riparazione del danno



Progressione del danno



Chronic Kidney Disease after Acute Kidney Injury: A Systematic Review and Meta-analysis



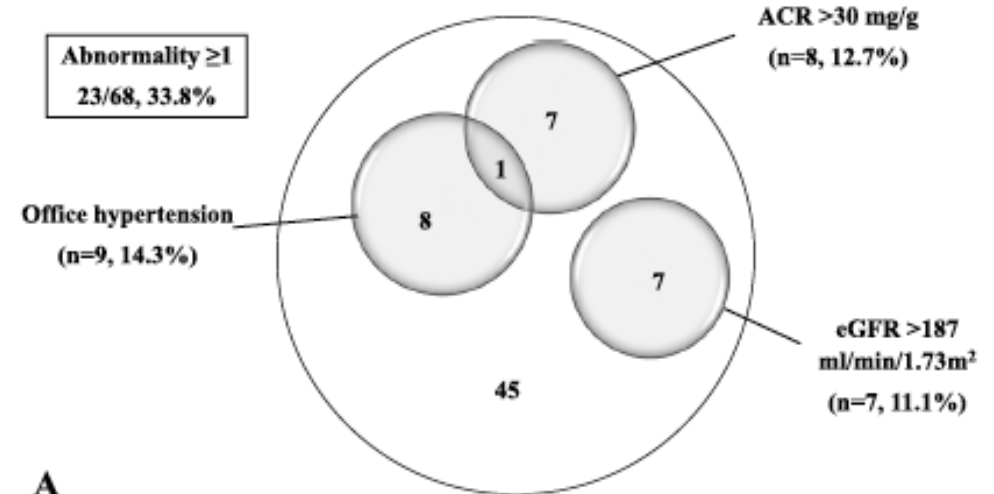
Long-term follow-up of patients after acute kidney injury in the neonatal period: abnormal ambulatory blood pressure findings



Gulsen Akkoc¹, Ali Duzova^{2*}, Ayse Korkmaz³, Berna Oguz⁴, Sule Yigit⁵ and Murat Yurdakok⁵

Akkoc et al. *BMC Nephrology* (2022) 23:116

Features	Results
Male/female, n/n (%/%)	46/26 (63.9/36.1)
Gestational age, n (%)	
24- < 28 weeks	6 (8.3)
28- < 32 weeks	17 (23.6)
32- < 36 weeks	12 (16.7)
36-42 weeks	37 (51.4)
Median age at AKI diagnosis (days)	5 (IQR 6)
0-3 days, n (%)	14 (19.4)
4-7 days, n (%)	36 (50.0)
8-14 days, n (%)	11 (15.3)
> 14 days, n (%)	11 (15.3)
eGFR (ml/min/1.73m ²)	152.3 ± 26.6
> 187 ml/min/1.73m ² , n (%)	7 (9.7)
> 150 ml/min/1.73m ² , n (%)	37 (51.3)
Median ACR (mg/g)	17.5 (IQR 17.3, range: 2.75 - 199.85)
0-30, n/N (%)	62/71 (87.3)
> 30, n/N (%)	9/71 (12.7)
Urinary	
TPR (%)	90.3 ± 3.6
TPR < 85%, n/N (%)	5/70 (7.1)
TmP/GFR (mg/dl)	4.39 ± 0.66
TmP/GFR > 6 mg/dl, n (%)	1/70 (1.4)



A Developmental Approach to the Prevention of Hypertension and Kidney Disease – a report from the Birth Weight and Nephron Number Working Group

Valerie A. Luyckx^{#1}, Norberto Perico^{#2}, Marco Somaschini³, Dario Manfellotto⁴, Herbert Valensise⁵, Irene Cetin⁶, Umberto Simeoni⁷, Karel Allegaert^{8,9}, Bjorn Egil Vikse^{10,11}, Eric A. Steegers¹², Dwomoa Adu¹³, Giovanni Montini¹⁴, Giuseppe Remuzzi^{15,16,17}, and Barry M. Brenner^{18,*} for the writing group of the Low Birth Weight and Nephron Number Working Group

Prima della nascita

- Ottimizzare cure pre-concezionali
- Screening e cura diabete gestazionale
- Evitare eccessivo aumento di peso, attenzione nutrizione e micronutrienti
- Evitare fumo e alcool
- Individuare ipertensione e alterazione flusso placentare

Alla nascita

- Individuare IUGR
- Individuare AKI
- Massimizzare sforzi per prevenzione AKI
- Migliorare nutrizione, attenzione farmaci..

Dopo la dimissione

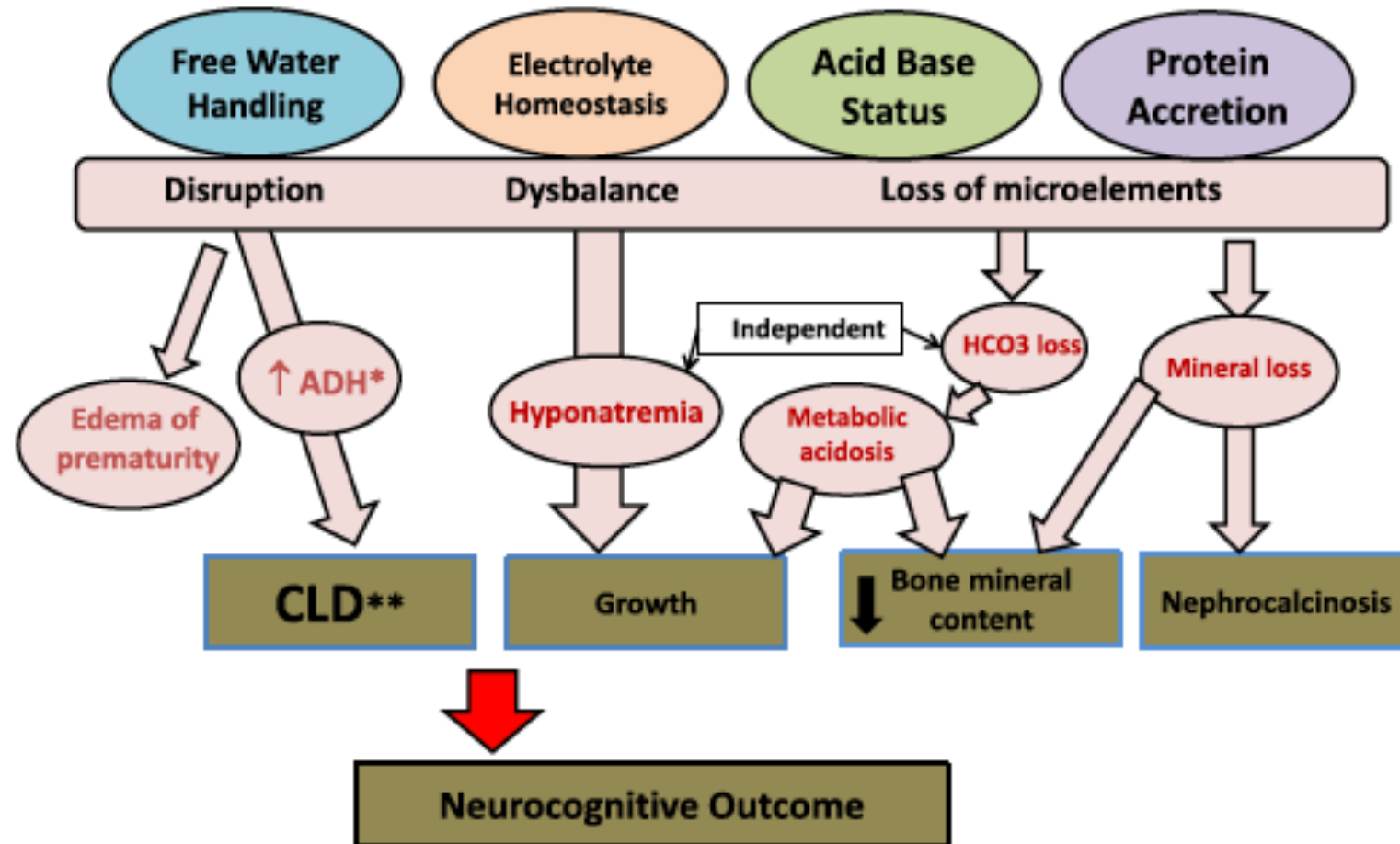
- Ottimizzare follow up
- Informare adeguatamente chi avrà in carico il bambino dei rischi renali e del monitoraggio adeguato
- Misura pressione arteriosa ed esami urine



Renal consequences of preterm birth

Amelie Stritzke^{1*}, Sumesh Thomas², Harish Amin³, Christoph Fusch^{4,5} and Abhay Lodha⁶

Only renal?



Grazie per l'attenzione

