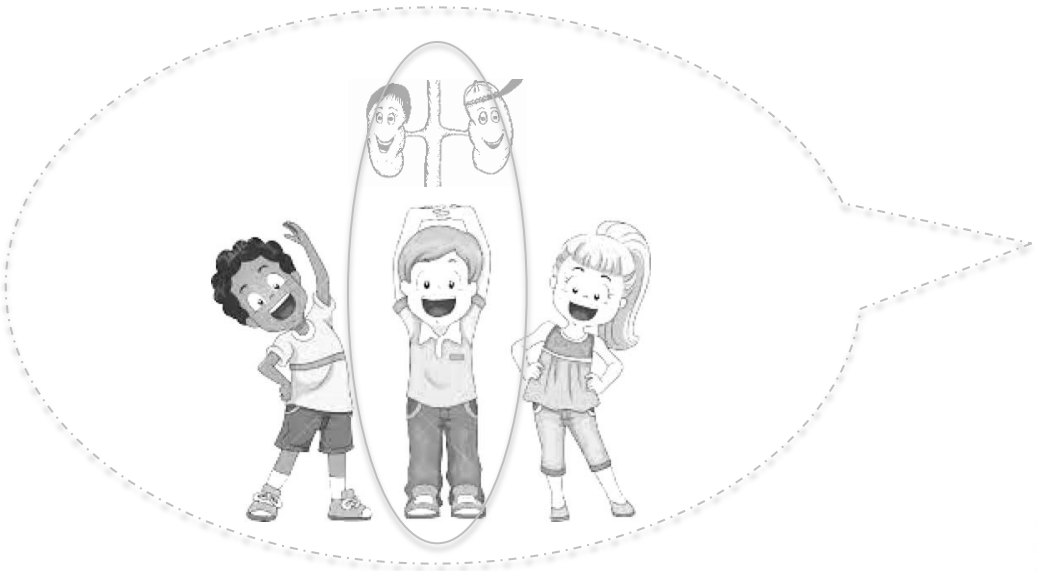
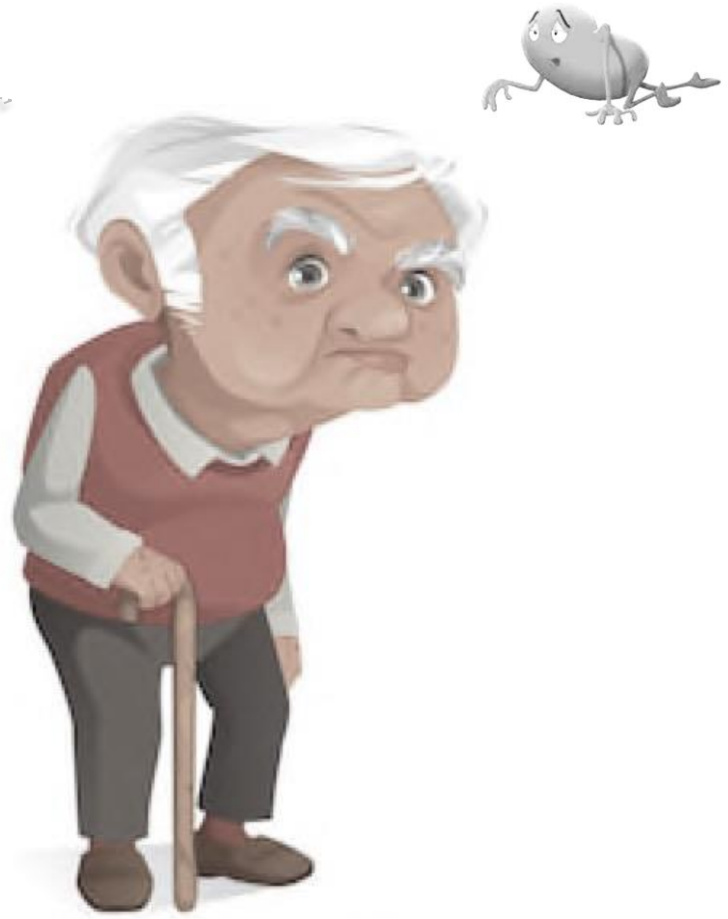
Παθοφυσιολογικές διαταραχές των παιδιών και εφήβων, που επηρεάζουν τους νεφρούς των ηλικιωμένων

Στέλλα Σταμπουλή
Επίκουρη Καθ. Παιδιατρικής ΑΠΘ
1η Παιδιατρική Κλινική
ΓΝΘ Θεσ/νικης Ιπποκράτειο



Could I have done better?



Υγιή παιδιά και εφήβους

Ποιοι παράγοντες κατά την παιδική ηλικία θα επιδράσουν βλαπτικά στη μακροχρόνια νεφρική λειτουργία?

Υποκείμενο νόσημα, αλλά φυσιολογική νεφρική λειτουργία

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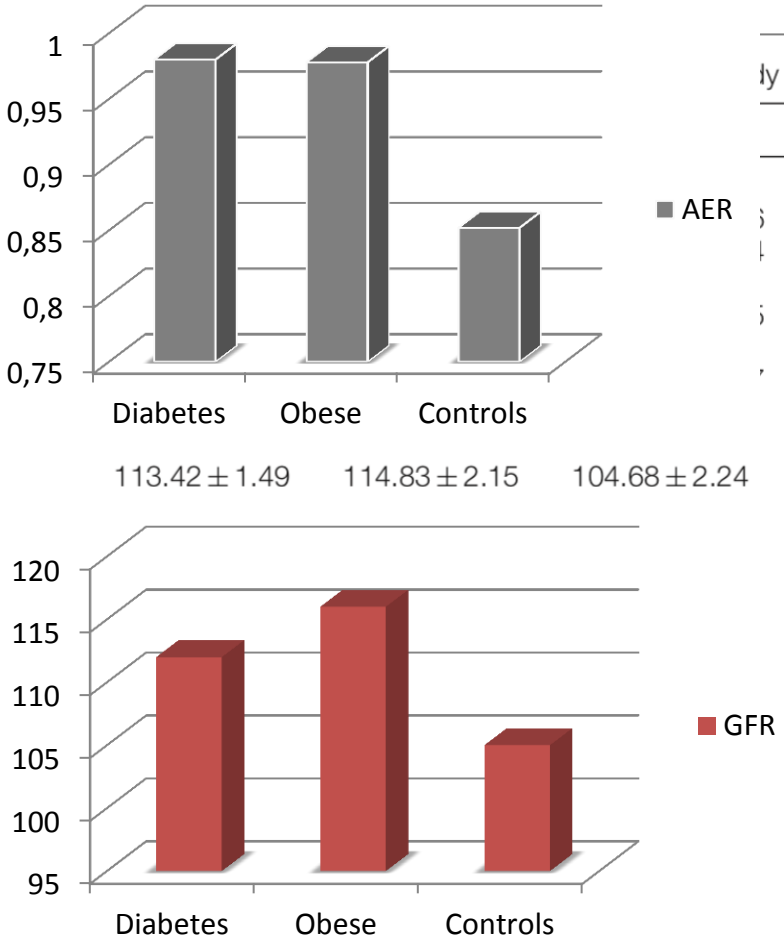
Επίδραση της παχυσαρκίας και του ΣΔ τύπου 1 στην νεφρική λειτουργία σε εφήβους

83 obese(age:11.6±3.0yr),164 non-obeseT1D(age: 12.4 ± 3.2 yr), and 71 non-obese control (age: 12.3 ± 3.2 yr) children

Table 2. Albumin excretion

				ly groups		
				P (1 vs. 2)	P (1 vs. 3)	P (2 vs. 3)
Log AER						
Unadjusted model				0.972	<0.001	0.014
Adjusted model 1: age, pubertal stage				1.000	<0.001	<0.001
Adjusted model 2: mode 1 + BMI z-score				0.434	<0.001	0.303
Adjusted model 3: mode 2 + log HbA1c				0.917	0.106	0.297
GFR						
Unadjusted model	113.42 ± 1.49	114.83 ± 2.15	104.68 ± 2.24	1.000	0.01	0.004
Adjusted model 1: age, pubertal stage				0.221	0.008	<0.001
Adjusted model 2: mode 1 + BMI z-score				1.000	0.009	0.21
Adjusted model 3: mode 2 + log HbA1c				1.000	0.474	0.210

BMI, body mass index; Hb
Data are least square mea

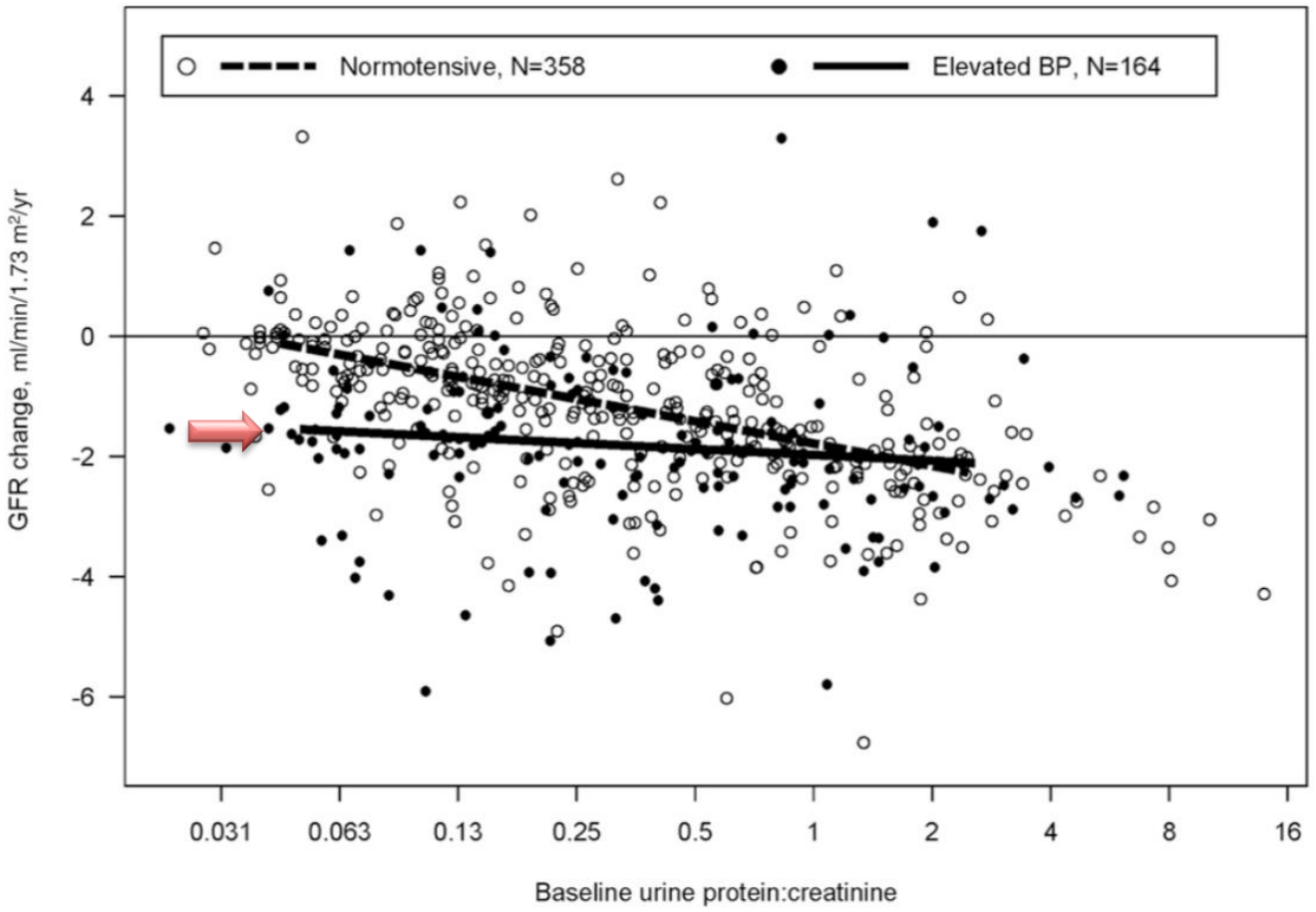


Franchini et al, Pediatric Diabetes 2015: 16: 427–433

Progression of Pediatric CKD of Nonglomerular Origin in the CKiD Cohort

522 children, median age 10 years with non-glomerular CKD were followed for a median of 4.4 years
The mean baseline GFR in the cohort was 52 ml/min per 1.73 m2

- A 1-unit hi
  decline of
- A 2-fold hi
  GFR declir



Fathallah-Shaykh et al, Clin J Am Soc Nephrol 10: 371–377, 2015

Long-Term Changes in Blood Pressure After Pediatric Kidney Transplantation

Stella Stabouli,[1] Nikoleta Printza,[1] John Dotis,[1] Chrysa Gkogka,[1] Konstantinos Kollios,[2] Vasilios Kotsis,[3] and Fotios Papachristou[1]

- 64 pediatric kidney recipients (median age 11 years)

- **For hypertension at 10 years post- Tx➔ HR of graft loss 8.079 (95% CI 1.561–41.807, P < 0.05).**

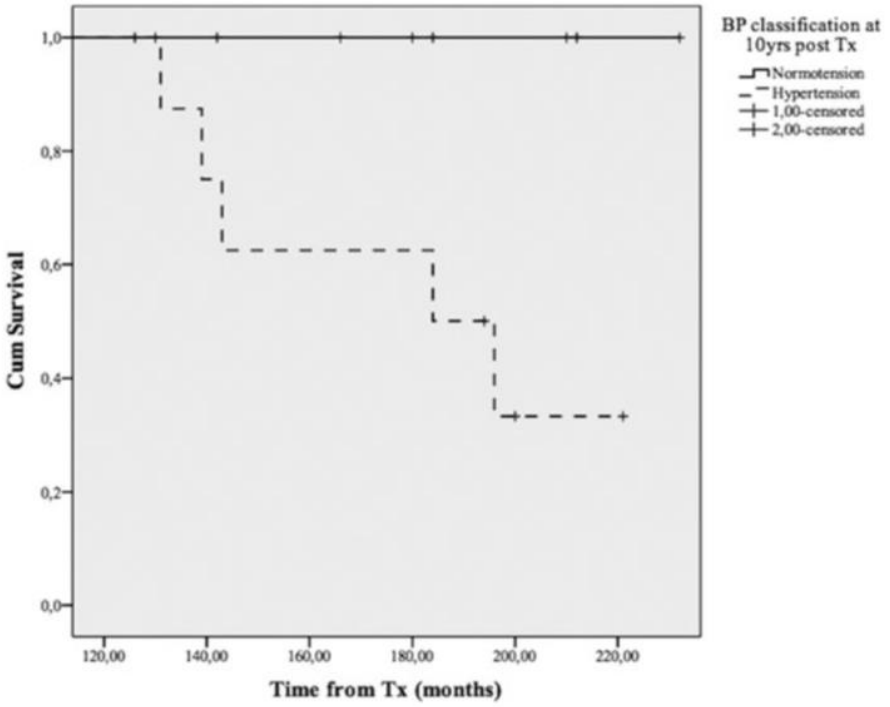


Figure 2. Twenty-years graft survival by BP classification in pediatric kidney recipients living with a functioning graft beyond 10 years after kidney Tx.

Am J Hypertens. 2016 Jul;29(7):860-5.

Υγιή παιδιά και εφήβους

Ποιοι παράγοντες κατά την παιδική ηλικία θα επιδράσουν βλαπτικά στη μακροχρόνια νεφρική λειτουργία?

Υποκείμενο νόσημα, αλλά φυσιολογική νεφρική λειτουργία

Χρόνια νεφρική νόσο

Original Article

Prehypertension amo
future risk for end-sta

Adi Leiba[a,b,c,d], Gilad Twig[b,c], Asaf
Dorit Tzur[b], Ehud Grossman[c], Rita D

Objective: Persistent hypertension in adulthood i
leading cause of end-stage renal disease (ESRD).
lower blood pressure (BP) values, in the range of
prehypertension, are also associated with future
occurrence of ESRD is unclear. Even less clear is t
potential risk of early prehypertension appearing
adolescence. To address this question, we examin
whether BP measurements in the prehypertensive
age 16–19 years predict adult ESRD.

Methods: Medical data on 2194 635 16–19-year
adolescents examined for medical fitness prior to
service from 1977 to 2013 were linked to the Isra
registry in this nationwide population-based cohor
Incident cases of ESRD were recorded. Survival m
were applied.

Results: During 35 007 506 person-years of follov
(median follow-up 16.8 years), there were 690 ES
with an overall incidence rate of 1.97 cases per 1
person-years. Examinees with elevated BP reading
prehypertensive range (BP between the 90th and
percentiles or between 120 and 139/80–89 mmH
increased incidence of ESRD with a hazard ratio o
(95% confidence interval, 1.11–1.58) adjusted for
birth, age at examination, sex, BMI, education,
socioeconomic status, and country of origin. Hype
(BP above the 95th percentile or above 140/90 mm
associated with a hazard ratio of 1.44 (95% confi
interval, 1.17–1.79). A spline model demonstrated
of risk at SBP values as low as 94 mmHg.

Conclusion: Asymptomatic, healthy adolescents v
prehypertension have a 32% increased risk for sut
ESRD, compared with adolescents with optimal BP

Keywords: adolescents, dialysis, end-stage renal
hypertension, prehypertension

Abbreviations: BP, blood pressure; ESRD, end-sta
disease; RRT, renal replacement therapy

INTRODUCTION

There is growing evidence that mildly elev
pressure (BP) is much more common a
dren and adolescents than was previous
[1]. Longitudinal studies have tracked BP ove
Abnormal BP during these ages frequently dev

ORIGINAL INVESTIGATION

Body Mass Index in 1.2 Million Adolescents and Risk for End-Stage Renal Disease

Asaf Vivante, MD; Eliezer Golan, MD; Dorit Tzur, MBA; Adi Leiba, MD; Amir Tirosh, MD, PhD; Karl Skorecki, MD; Ronit Calderon-Margalit, MD, MPH

Background: The relationship between adolescent body mass index (BMI) and future risk for end-stage renal disease (ESRD) is not fully understood, nor is it known the extent to which this association is limited to diabetic ESRD. We evaluated the association between BMI in adolescence and the risk for all-cause, diabetic, and nondiabetic ESRD.

Methods: Medical data about 1 194 704 adolescents aged 17 years who had been examined for fitness for military service between January 1, 1967, and December 31, 1997, were linked to the Israeli ESRD registry in this nationwide population-based retrospective cohort study. Incident cases of treated ESRD between January 1, 1980, and May 31, 2010, were included. Cox proportional hazards models were used to estimate the hazard ratio (HR) for treated ESRD among study participants for their BMI at age 17 years, defined in accord with the US Centers for Disease Control and Prevention BMI for age and sex classification.

Results: During 30 478 675 follow-up person-years (mean [SD], 25.51 [8.77] person-years), 874 participants (713 male and 161 female) developed treated ESRD, for an overall incidence rate of 2.87 cases per 100 000 person-years. Compared with adolescents of normal weight, overweight adolescents (85th to 95th percentiles of BMI) and obese adolescents (≥95th percentile of BMI) had an increased future risk for treated ESRD, with incidence rates of 6.08 and 13.40 cases per 100 000 person-years, respectively. In a multivariate model adjusted for sex, country of origin, systolic blood pressure, and period of enrollment in the study, overweight was associated with an HR of 3.00 (95% CI, 2.50-3.60) and obesity with an HR of 6.89 (95% CI, 5.52-8.59) for all-cause treated ESRD. Overweight (HR, 5.96; 95% CI, 4.41-8.06) and obesity (HR, 19.37; 95% CI, 14.13-26.55) were strong and independent risk factors for diabetic ESRD. Positive associations of overweight (HR, 2.17; 95% CI, 1.71-2.74) and obesity (HR, 3.41; 95% CI, 2.42-4.79) with nondiabetic ESRD were also documented.

Conclusions: Overweight and obesity in adolescents were associated with significantly increased risk for all-cause treated ESRD during a 25-year period. Elevated BMI constitutes a substantial risk factor for diabetic and nondiabetic ESRD.

Arch Intern Med. 2012;172(21):1644-1650.
Published online October 29, 2012.
doi:10.1001/2013.jamainternmed.85

OBESITY IS A GLOBAL HEALTH problem.[1,2] The high prevalence of overweight and obesity among children, adolescents, and adults is of great concern. Since 1980, the prevalence of obesity has tripled among US school-age children and adolescents, and it has remained high, at approximately 17%, from 1999 to the present.[3-6] Children and adolescents with high body mass index (BMI) often become obese adults,[7,8] and obese adults are at risk for many chronic conditions such as diabetes, which confers a future risk for chronic kidney disease (CKD) and end-stage renal disease (ESRD). The relationship between obesity and CKD is complex and not yet fully understood. Few studies[9-12] have examined the relationship between excess weight and risk for all-cause ESRD; although an association between BMI and ESRD in general has been documented, these studies did not determine whether such an association is limited to diabetic ESRD. In addition, previous investigations of the association between obesity and CKD or ESRD were conducted only among adults. It remains unclear whether a history of overweight and obesity during childhood or adolescence poses an additional risk.

See Invited Commentary at end of article

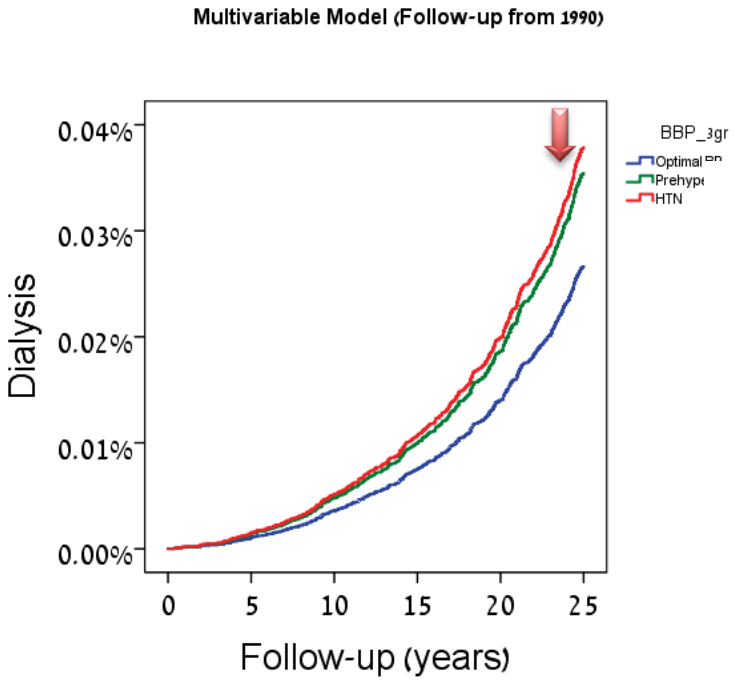
To address these issues, we conducted a nationwide population-based retrospective cohort study evaluating the association between BMI at age 17 years among almost 1.2 million adolescents and the fu-

Author Affiliations are listed at the end of this article.

Υγιείς έφηβοι 16-19 ετών στον Ισραηλινό στρατό

Follow up 16 και 25 έτη

Αρτηριακή πίεση στην εφηβεία και χρόνια νεφρική νόσος στην ενήλικη ζωή



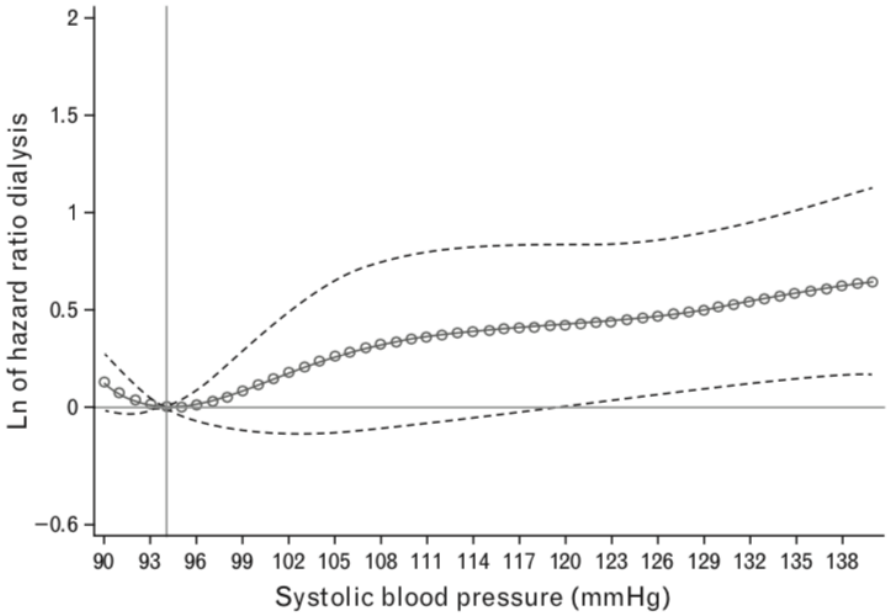
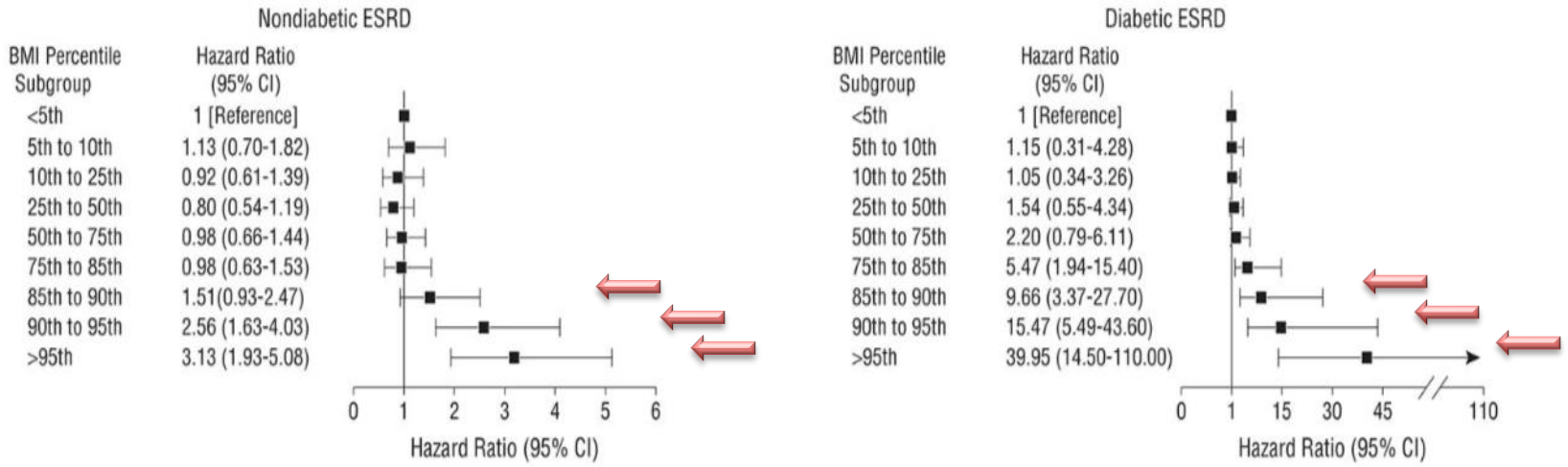


FIGURE 2 Spline model of Ln of hazard ratio of end-stage renal disease according to SBP.

Leiba et al, J Hypertens 2017, 35:1290–1296

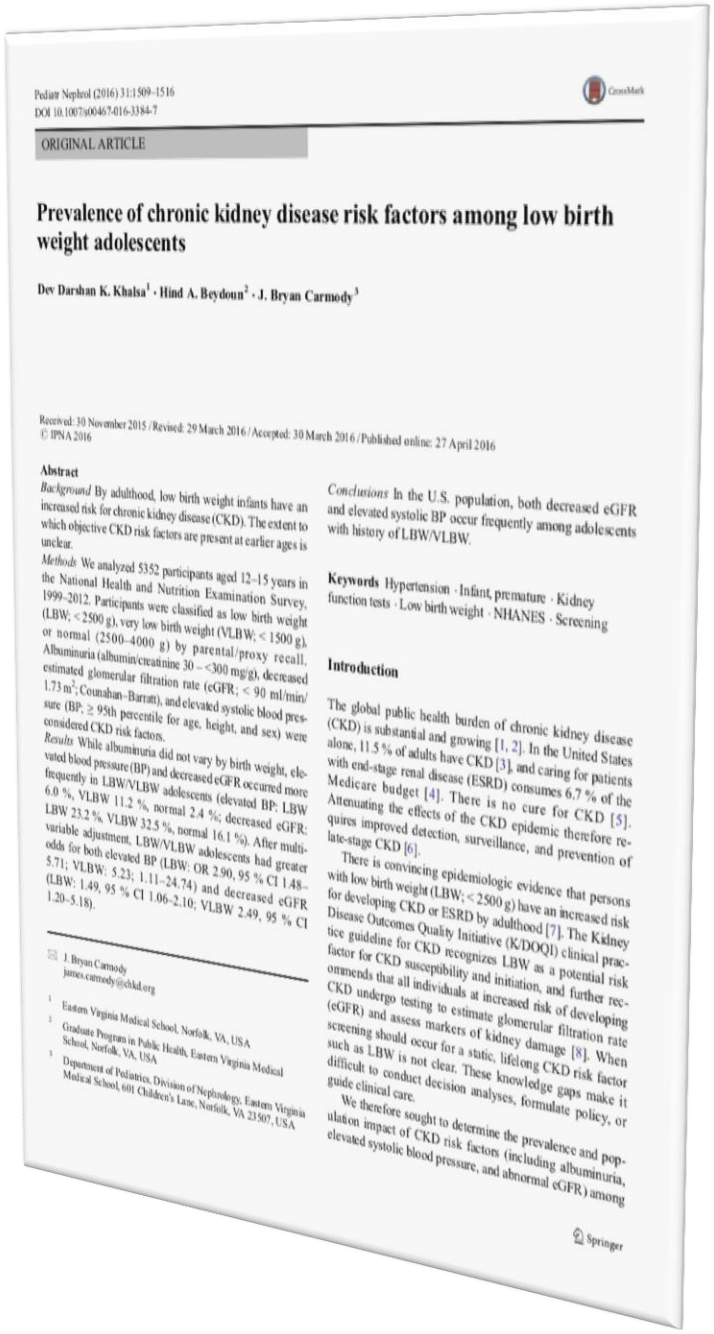
Παχυσαρκία στην εφηβεία και χρόνια νεφρική νόσος στην ενήλικη ζωή

Hazard ratios for diabetic and non-diabetic end-stage renal disease (ESRD) by body mass index (BMI) percentile subgroup. Black boxes indicate significant results ($P < .001$).



Vivante at al, Arch Intern Med. 2012 November 26; 172(21): 1644–1650

USA adolescents
National Health and Nutrition Examination Surveys



Pediatr Nephrol (2016) 31:1509–1516
DOI 10.1007/s00467-016-3384-7

ORIGINAL ARTICLE

Prevalence of chronic kidney disease risk factors among low birth weight adolescents

Dev Darshan K. Khalsa[1] · Hind A. Beydoun[2] · J. Bryan Carmody[3]

Received: 30 November 2015 / Revised: 29 March 2016 / Accepted: 30 March 2016 / Published online: 27 April 2016

Abstract
Background By adulthood, low birth weight infants have an increased risk for chronic kidney disease (CKD). The extent to which objective CKD risk factors are present at earlier ages is unclear.
Methods We analyzed 5352 participants aged 12–15 years in the National Health and Nutrition Examination Survey, 1999–2012. Participants were classified as low birth weight (LBW; < 2500 g), very low birth weight (VLBW; < 1500 g), or normal (2500–4000 g) by parental/proxy recall. Albuminuria (albumin/creatinine 30 – <300 mg/g), decreased estimated glomerular filtration rate (eGFR; < 90 ml/min/1.73 m^2; Counahan–Barratt), and elevated systolic blood pressure (BP; ≥ 95th percentile for age, height, and sex) were considered CKD risk factors.
Results While albuminuria did not vary by birth weight, elevated blood pressure (BP) and decreased eGFR occurred more frequently in LBW/VLBW adolescents (elevated BP: LBW 6.0 %, VLBW 11.2 %, normal 2.4 %; decreased eGFR: LBW 23.2 %, VLBW 32.5 %, normal 16.1 %). After multivariable adjustment, LBW/VLBW adolescents had greater odds for both elevated BP (LBW: OR 2.90, 95 % CI 1.48–5.71; VLBW: 5.23; 1.11–24.74) and decreased eGFR (LBW: 1.49, 95 % CI 1.06–2.10; VLBW 2.49, 95 % CI 1.20–5.18).
Conclusions In the U.S. population, both decreased eGFR and elevated systolic BP occur frequently among adolescents with history of LBW/VLBW.

Keywords Hypertension · Infant, premature · Kidney function tests · Low birth weight · NHANES · Screening

✉ J. Bryan Carmody
james.carmody@ehkd.org

1 Eastern Virginia Medical School, Norfolk, VA, USA
2 Graduate Program in Public Health, Eastern Virginia Medical School, Norfolk, VA, USA
3 Department of Pediatrics, Division of Nephrology, Eastern Virginia Medical School, 601 Children's Lane, Norfolk, VA 23507, USA

Introduction

The global public health burden of chronic kidney disease (CKD) is substantial and growing [1, 2]. In the United States alone, 11.5 % of adults have CKD [3], and caring for patients with end-stage renal disease (ESRD) consumes 6.7 % of the Medicare budget [4]. There is no cure for CKD [5]. Attenuating the effects of the CKD epidemic therefore requires improved detection, surveillance, and prevention of late-stage CKD [6].

There is convincing epidemiologic evidence that persons with low birth weight (LBW; < 2500 g) have an increased risk for developing CKD or ESRD by adulthood [7]. The Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guideline for CKD recognizes LBW as a potential risk factor for CKD susceptibility and initiation, and further recommends that all individuals at increased risk of developing CKD undergo testing to estimate glomerular filtration rate (eGFR) and assess markers of kidney damage [8]. When screening should occur for a static, lifelong CKD risk factor such as LBW is not clear. These knowledge gaps make it difficult to conduct decision analyses, formulate policy, or guide clinical care.

We therefore sought to determine the prevalence and population impact of CKD risk factors (including albuminuria, elevated systolic blood pressure, and abnormal eGFR) among

Επίπτωση παραγόντων κινδύνου για χρόνια νεφρική νόσο σε εφήβους με χαμηλό βάρος γέννησης

5352 participants aged 12–15 years in the National Health and Nutrition Examination Survey, 1999–2012

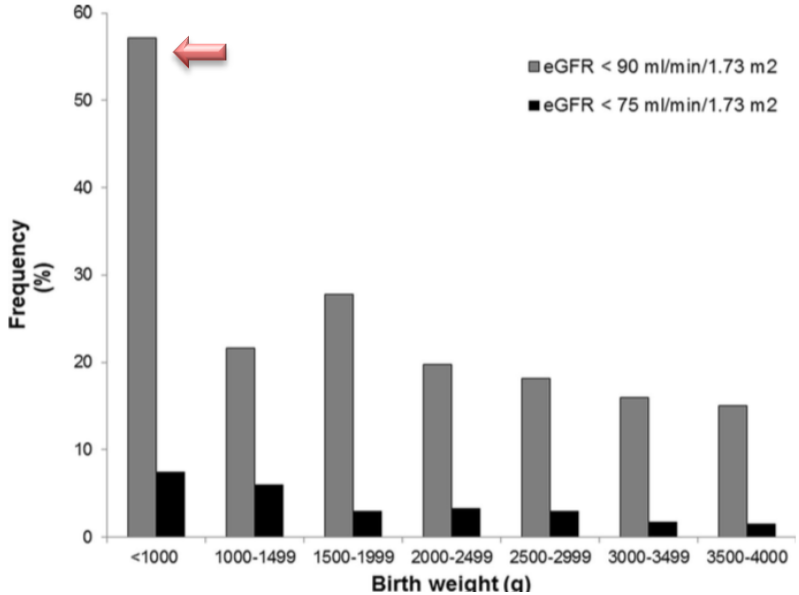


Table 3 Measures of exposure impact on adolescent CKD risk factors in U.S. adolescents, ages 12–15

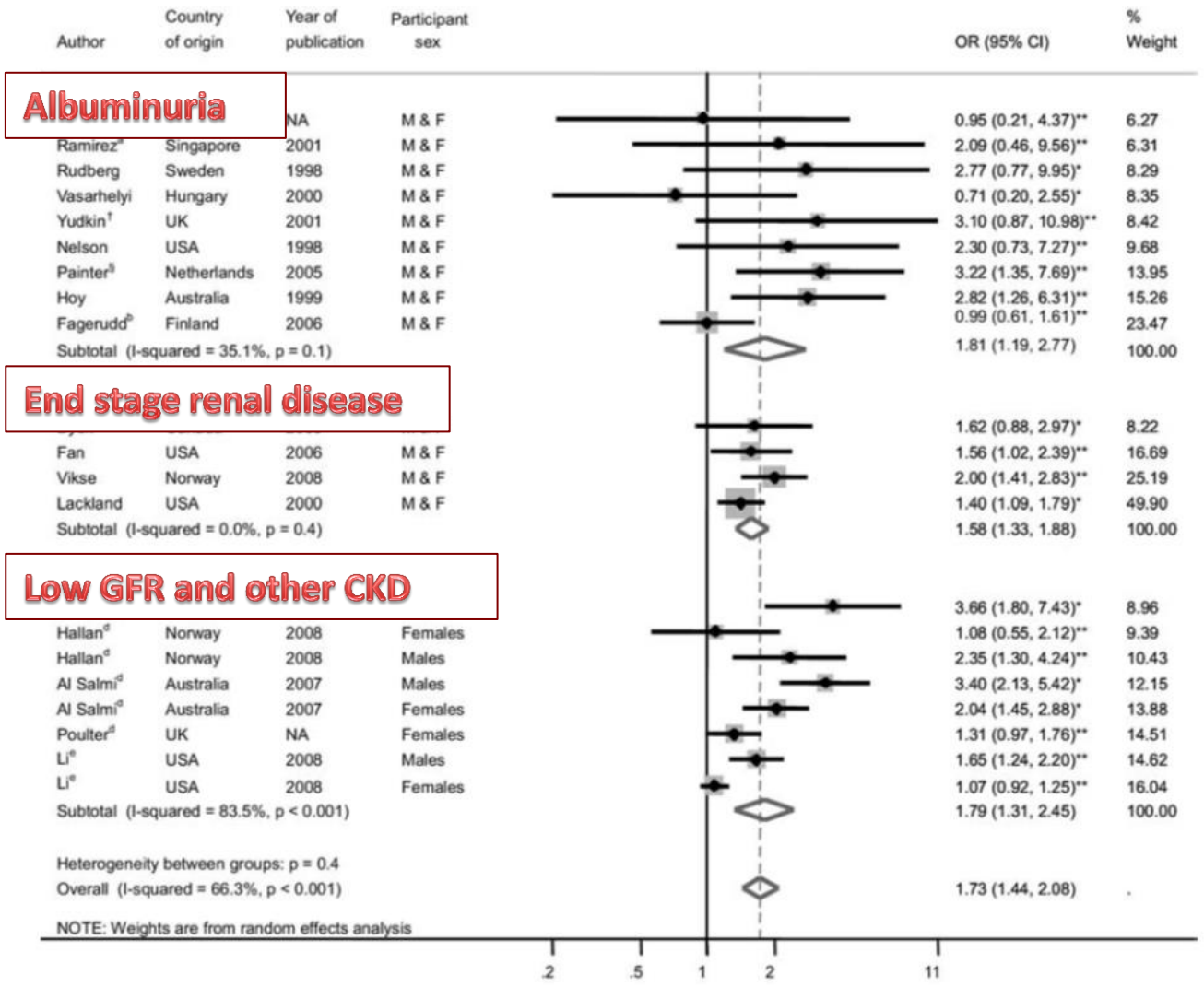
Factor	Low birth weight (<2500 g)			Very low birth weight (<1500 g)		
	Number needed to be exposed (NNE)	Population attributable risk (PAR)	Attributable population	Number needed to be exposed (NNE)	Population attributable risk (PAR)	Attributable population
↑ SBP		13.1%				
Elevated systolic blood pressure	23.5		47,581	11.1	4.2 %	15,371
eGFR <90		3.9%				
eGFR < 90 ml/min/1.73 m^2	16.3		79,448	6.2	1.5 %	29,541
eGFR <75		7.1%				
eGFR < 75 ml/min/1.73 m^2	62.7		17,551	23.1	2.8 %	6,934
↑ SBP and eGFR <90		5.2%				
Elevated systolic blood pressure and eGFR < 90 ml/min/1.73 m^2	12.7		119,204	5.1	1.8 %	40,838

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate

☞ **Non significant risk for albuminuria or proteinuria**

Kalsha et al, Pediatr Nephrol (2016) 31:1509–1516

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

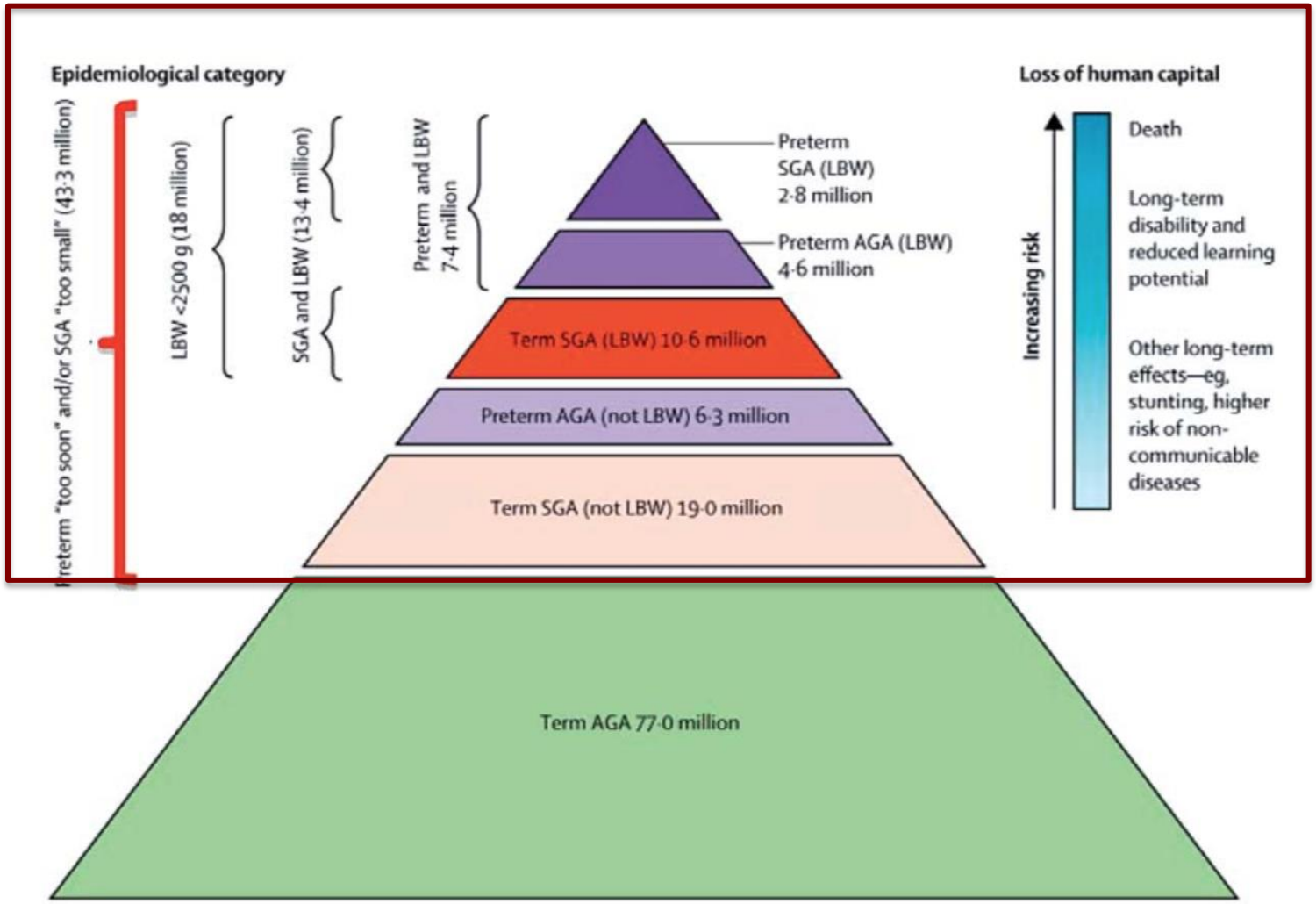


White et al, American Journal of Kidney Diseases 2009;54 (2): 248-261

Ορισμός πληθυσμού σε κίνδυνο

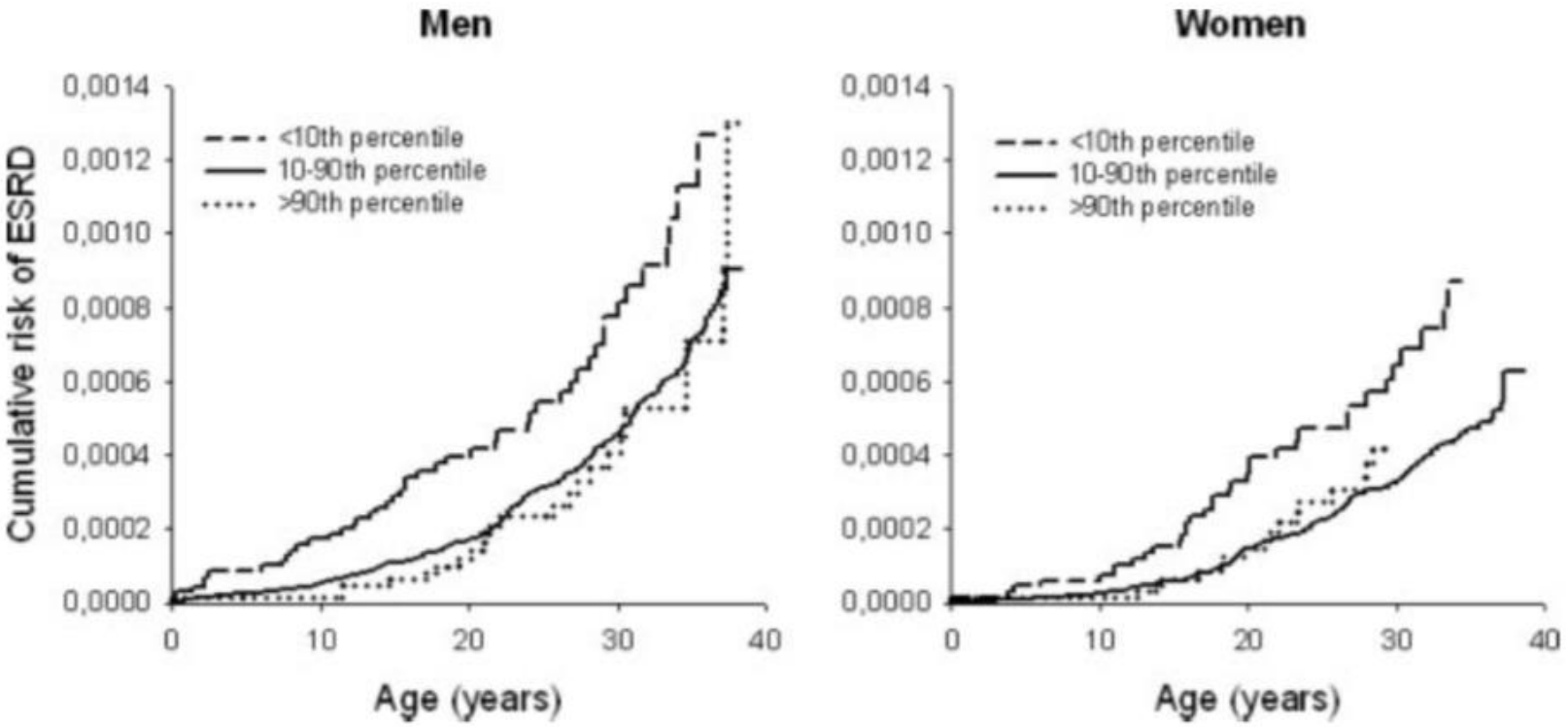
- **LBW: Χαμηλό βάρος γέννησης <2,500 gr**
- **Preterm: Προωρότητα < 37 εβδομάδες ηλικία κύησης**
- **SGA: Χαμηλό βάρος για την ηλικία κύησης < 2SD από το μέσο βάρος για την ηλικία κύησης**

Ορισμός πληθυσμού σε κίνδυνο



Χαμηλό βάρος γέννησης και αυξημένος κίνδυνος για χρόνια νεφρική νόσο

- Data on all births have been recorded in the Norwegian Medical Birth Registry since 1967
- Data on all patients who have developed ESRD have been recorded in the Norwegian Renal Registry since 1980



Vikse et al, J Am Soc Nephrol **19:** 151–157, 2008

Χαμηλό βάρος γέννησης και αυξημένος κίνδυνος για χρόνια νεφρική νόσο

Table 4. RR for different causes of ESRD according to birth weight: Births 1967 to 2004, ESRD 1980 to 2005, Norway

Birth Weight	ESRD as a Result of														
	Glomerular Disease			Interstitial Nephritis			Congenital or Inherited Causes			Diabetes			Other Causes		
	n	RR	*P*	*n*	RR	*P*	*n*	RR	*P*	*n*	RR	*P*	*n*	RR	*P*
All															
<10th percentile	32	1.5 (1.03 to 2.2)	0.04	7	1.6 (0.70 to 3.5)	0.3	30	2.5 (1.6 to 3.7)	<0.001	4	1.0 (0.36 to 2.9)	1.0	8	1.8 (0.85 to 3.9)	0.1
10 to 90th percentile	186	1.0		39	1.0		105	1.0		34	1.0		38	1.0	
≥90th percentile	20	0.97 (0.61 to 1.5)	0.9	5	1.1 (0.45 to 2.9)	0.8	6	0.49 (0.22 to 1.1)	0.09	4	1.1 (0.39 to 3.1)	0.9	4	0.95 (0.34 to 2.7)	0.9
Men															
<10th percentile	21	1.7 (1.1 to 2.8)	0.02	2	1.3 (0.29 to 5.5)	0.8	17	2.0 (1.2 to 3.4)	0.009	2	0.83 (0.20 to 3.5)	0.8	4	1.3 (0.45 to 3.7)	0.6
10 to 90th percentile	107	1.0		14	1.0		73	1.0		21	1.0		27	1.0	
≥90th percentile	12	1.0 (0.56 to 1.8)	1.0	2	1.3 (0.29 to 5.6)	0.8	5	0.59 (0.24 to 1.5)	0.3	2	0.89 (0.21 to 3.8)	0.9	1	0.33 (0.05 to 2.5)	0.3
Women															
<10th percentile	11	1.2 (0.63 to 2.2)	0.6	5	1.7 (0.66 to 4.5)	0.3	13	3.5 (1.8 to 6.6)	<0.001	2	1.3 (0.29 to 5.8)	0.7	4	3.1 (0.98 to 9.7)	0.05
10 to 90th percentile	79	1.0		25	1.0		32	1.0		13	1.0		11	1.0	
≥90th percentile	8	0.91 (0.44 to 1.9)	0.8	3	1.1 (0.33 to 3.6)	0.9	1	0.27 (0.04 to 2.0)	0.2	2	1.4 (0.33 to 6.4)	0.6	3	2.5 (0.68 to 8.8)	0.2

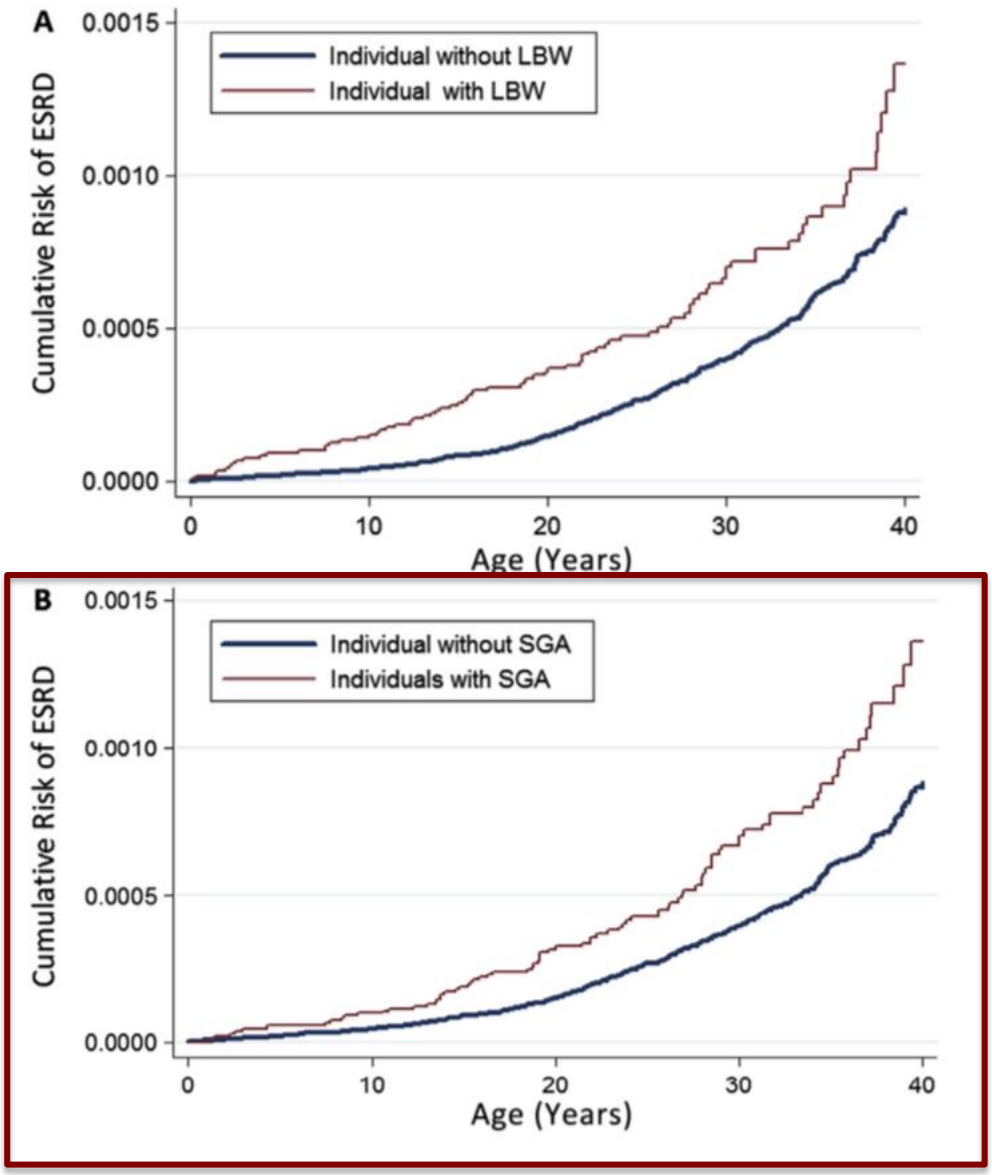
☞ **Low birth weight and ESRD was stronger during the first 15 yr of life while lost after the age of 24 yrs**

Vikse et al, J Am Soc Nephrol **19:** 151–157, 2008

Χαμηλό βάρος γέννησης ή SGA και κίνδυνος εμφάνισης χρόνιας νεφρικής νόσου στην ενήλικη ζωή

Since 1967, the Medical Birth Registry of Norway has recorded medical data for all births in the country

Of 1,852,080 included individuals, 527 developed ESRD



Ruggajo et al, Am J Kidney Dis. 2016;67(4):601-608

Χαμηλό βάρος γέννησης vs. SGA και κίνδυνος εμφάνισης χρόνιας νεφρικής νόσου στην ενήλικη ζωή

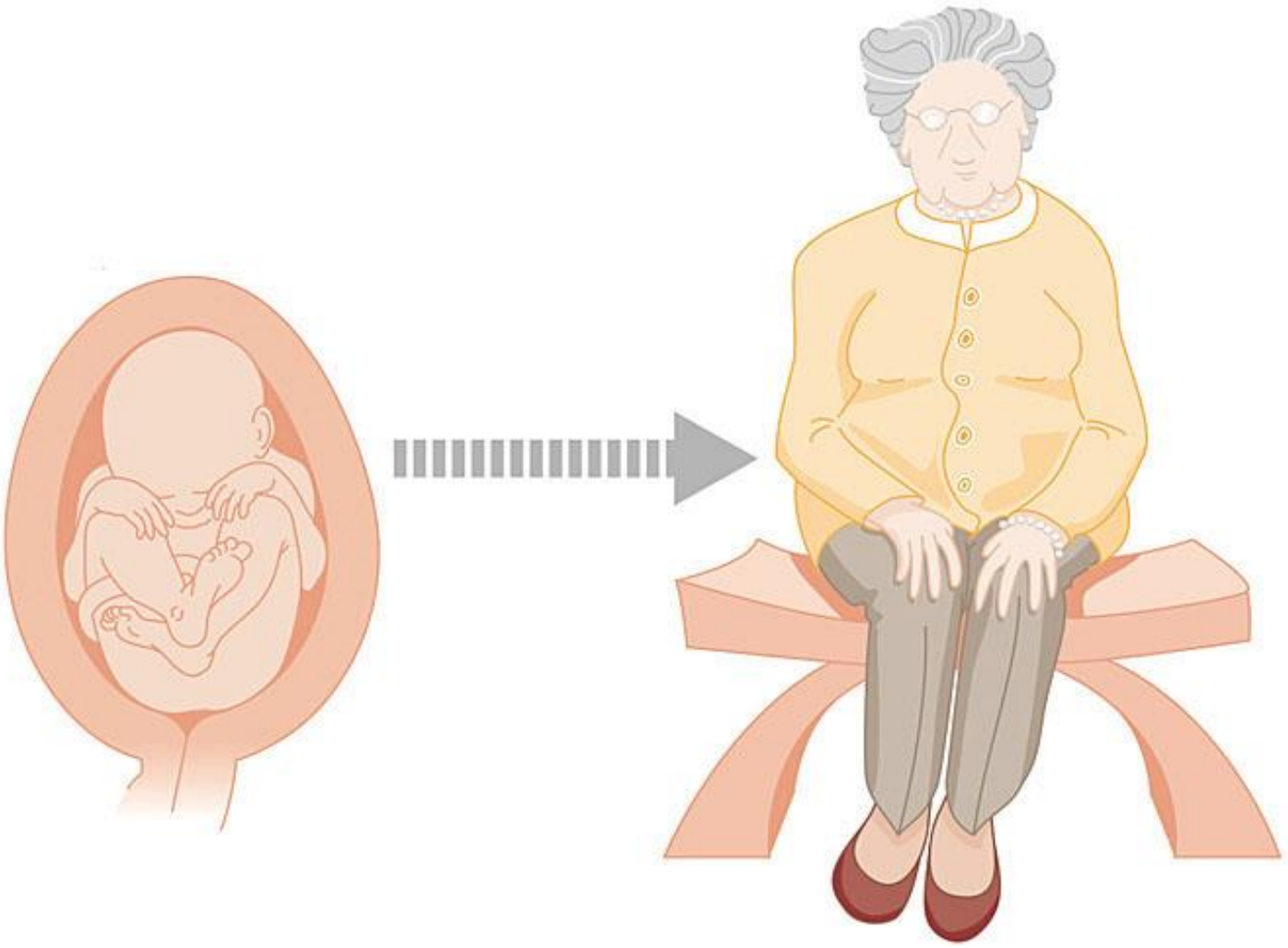
Table 4. HR for Different Causes of ESRD According to Birth Characteristic, Norway 1980-2009

		Glomerular Disease			Congenital or Inherited Disease			Diabetes			Other Causes		
Individual	Sibling	n	HR (95% CI)	*P*	n	HR (95% CI)	*P*	n	HR (95% CI)	*P*	n	HR (95% CI)	*P*
Not LBW	Not LBW	173	1.00 (reference)		101	1.00 (reference)		43	1.00 (reference)		70	1.00 (reference)	
	LBW											(0.77-2.62)	0.3
LBW	Not LBW	22	1.60 (1.03-2.50)									(0.47-2.49)	0.9
	LBW	10	1.17 (0.62-2.22)									(0.94-4.45)	0.07
Not SGA	Not SGA	150	1.00 (reference)		99	1.00 (reference)		34	1.00 (reference)		68	1.00 (reference)	
	SGA	20	1.05 (0.66-1.68)	0.8	13	1.07 (0.60-1.91)	0.8	1	0.23 (0.03-1.70)	0.2	10	1.18 (0.61-2.31)	0.6
SGA	Not SGA	28	2.08 (1.39-3.12)	<0.001	13	1.58 (0.88-2.82)	0.1	2	0.61 (0.14-2.54)	0.5	4	0.66 (0.24-1.81)	0.4
	SGA	13	1.59 (0.90-2.80)	0.1	10	1.99 (1.04-3.83)	0.04	6	3.07 (1.29-7.30)	0.01	4	1.09 (0.40-3.00)	0.9

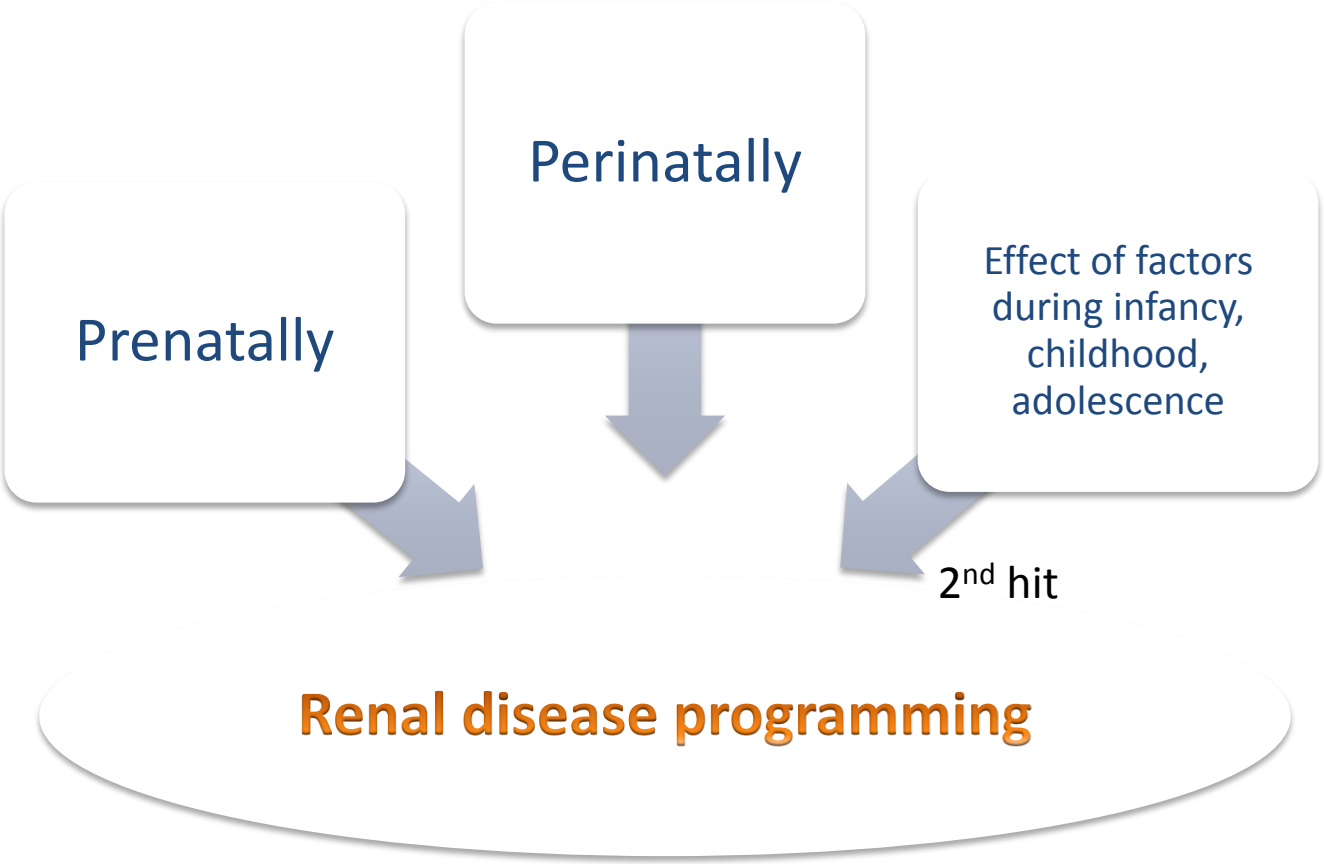
Abbreviations: CI, confidence interval; ESRD, end-stage renal disease; HR, hazard ratio; LBW, low birth weight; SGA, small for gestational age.

Ενδομήτρια καθυστέρηση αύξησης παράγοντας κινδύνου για μη κληρονομικά/μη συγγενή αίτια ΧΝΝ

Ruggajo et al, Am J Kidney Dis. 2016;67(4):601-608



Renal disease programming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Effect of factors during infancy, childhood, adolescence
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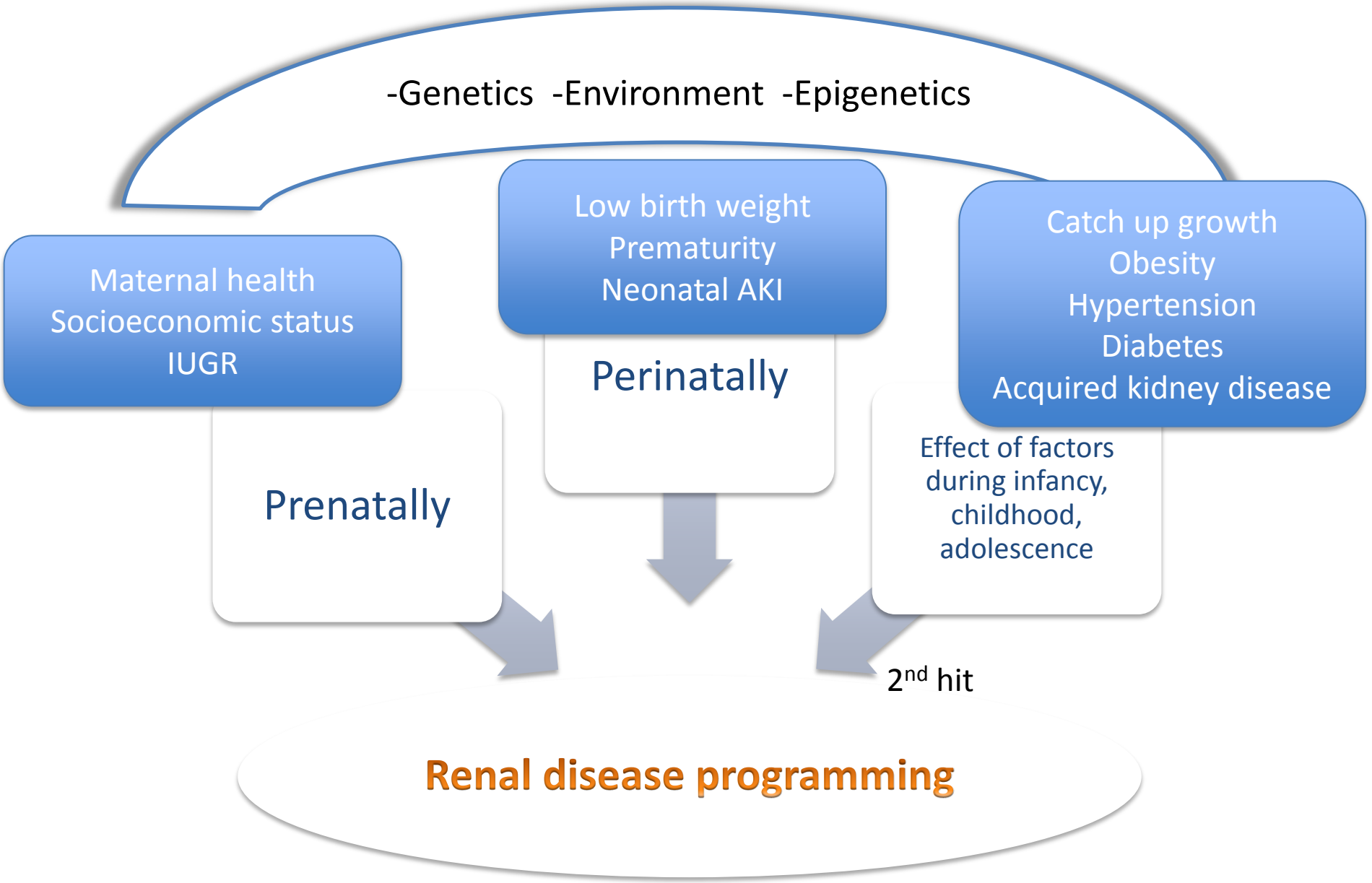
Renal disease programming


-Genetics -Environment -Epigenetics
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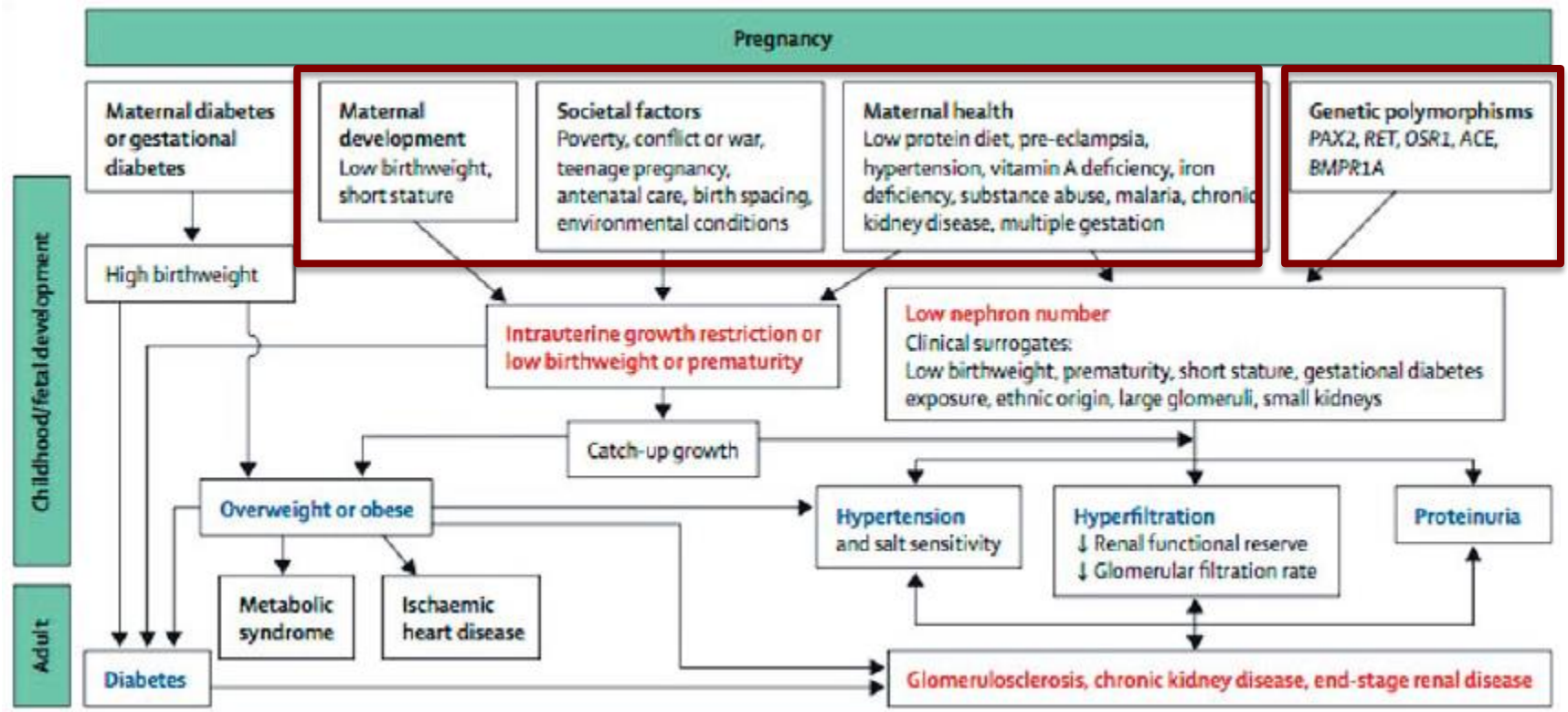
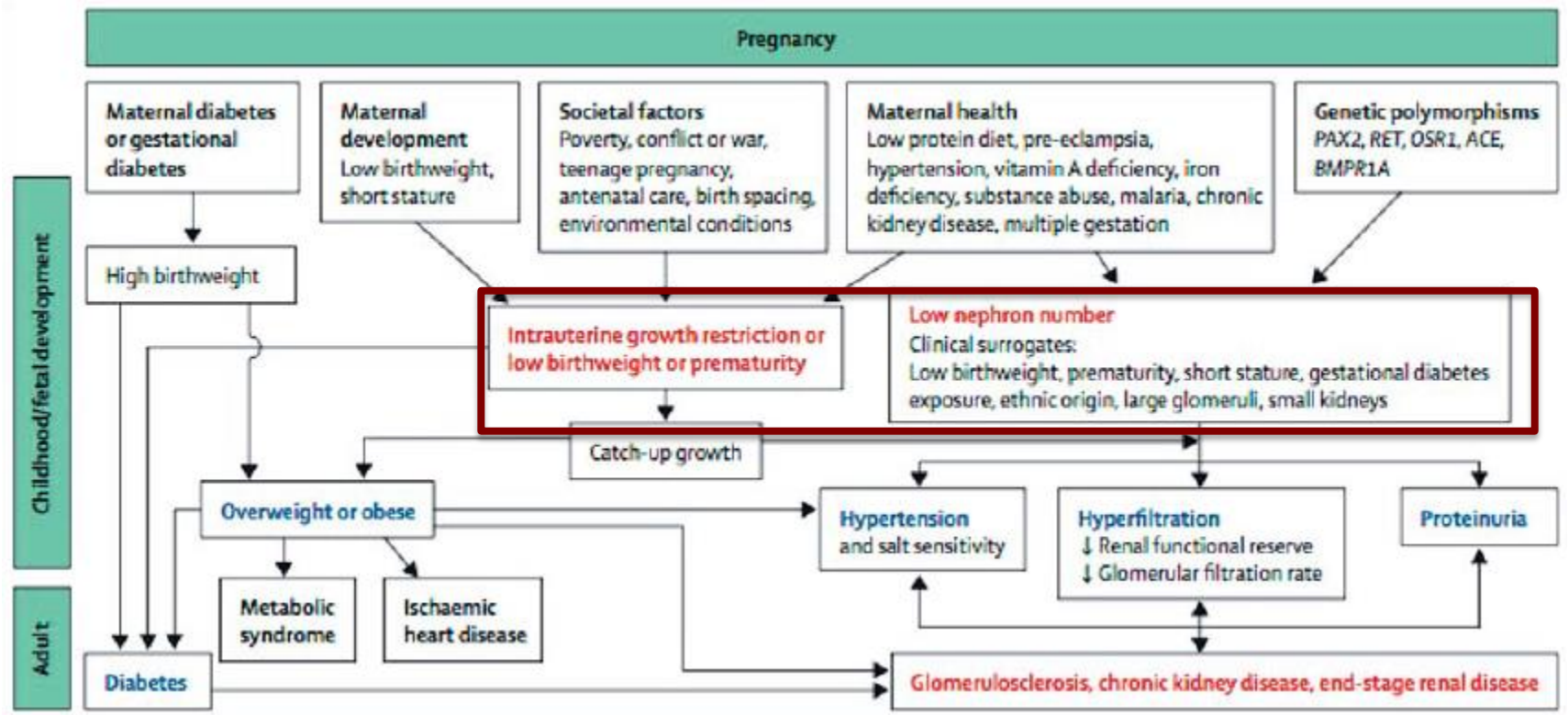
Socioeconomic status
IUGR
Low birth weight
Prematurity
Neonatal AKI
Catch up growth
Obesity
Hypertension
Diabetes
Acquired kidney disease
Prenatally
Perinatally
Effect of factors during infancy, childhood, adolescence
2nd hit
Renal disease programming

Multi-hit nature of renal disease programming



Luyckx et al, Lancet. 2013;382(9888):273-83.

Multi-hit nature of renal disease programming



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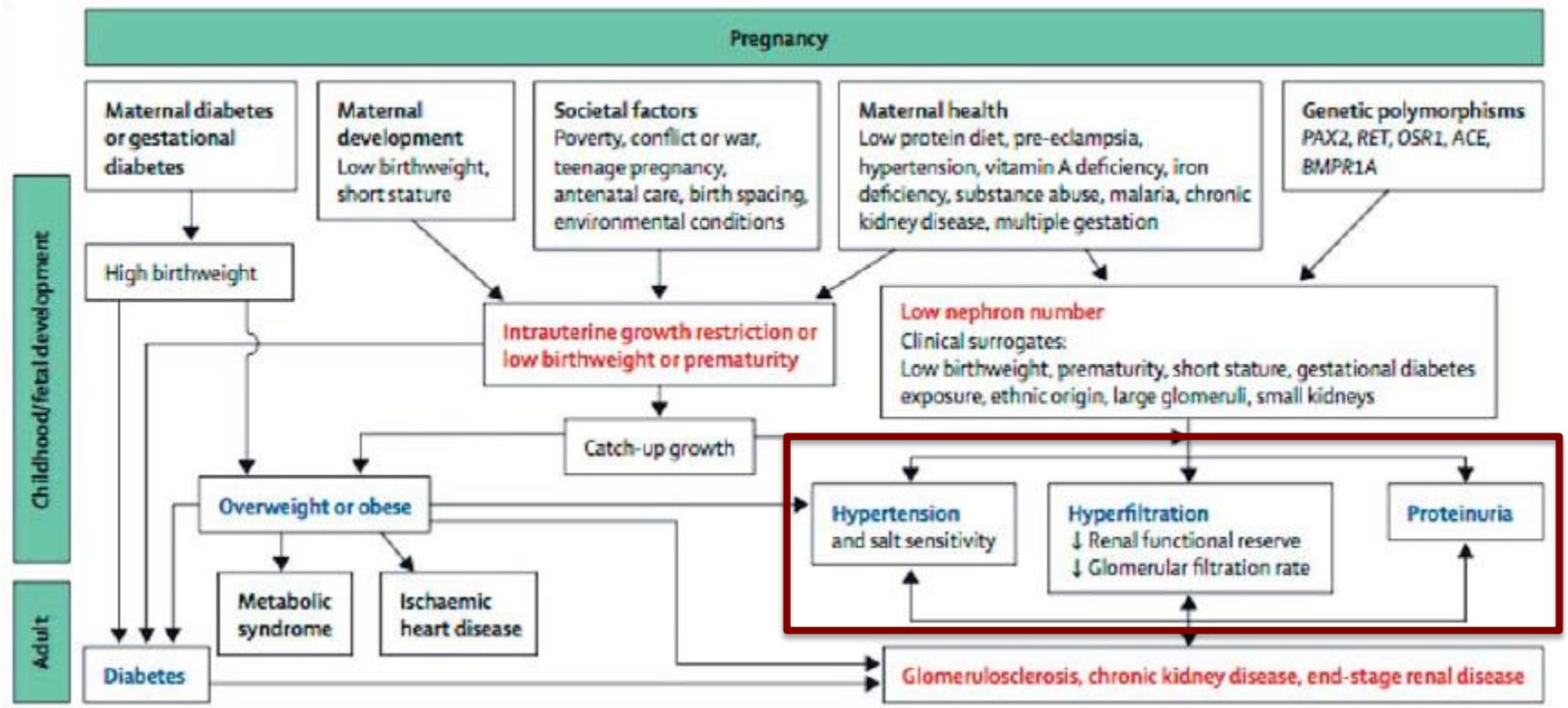
Multi-hit nature of renal disease programming



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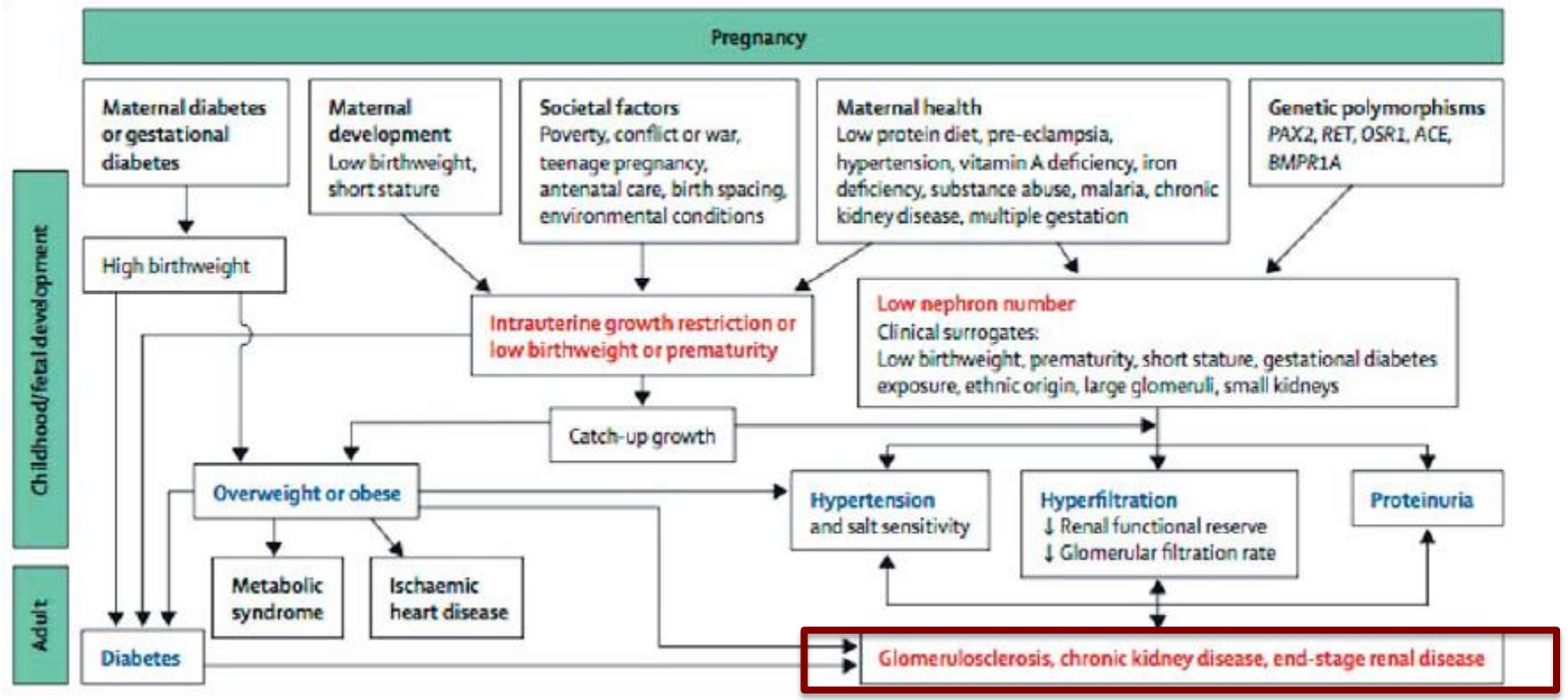
Multi-hit nature of renal disease programming



Luyckx et al, Lancet. 2013;382(9888):273-83.

Η υπόθεση του Brenner

- Εμβρυικός νεφρικός προγραμματισμός οδηγεί σε μειωμένο αριθμό νεφρώνων με αυξημένο κίνδυνο αρτηριακής υπέρτασης και ΧΝΝ

- Νεφροί με μειωμένο αριθμό νεφρώνων θα εμφανίζουν **σπειραματική υπερδιήθηση** και η σταδιακά επιδεινούμενη ΧΝΝ σηματοδοτείται από την εμφάνιση **πρωτεινουρίας**

Brenner BM et al, Am J Hypertens. 1988, Kidney International 1996

Ποιος ο αριθμός των ανθρώπινων νεφρώνων?

Από 7 νεκροτομικές μελέτες με περίπου 500 άτομα → μέσος αριθμός νεφρώνων ~ 1,000,000 ανά νεφρό

Ωστόσο υπάρχει σημαντική διακύμανση από 210.000 έως 2,700,000 → διαφορετικός κίνδυνος για υπέρταση και ΧΝΝ

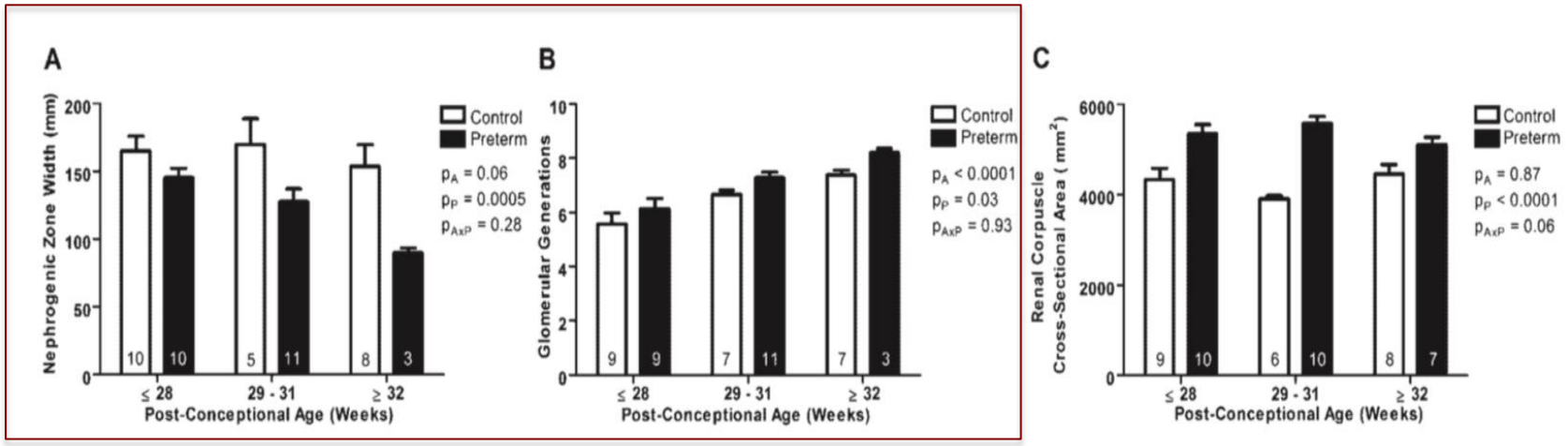
Περίπου 60% των νεφρώνων σχηματίζονται στο 3ο τρίμηνο της κύησης

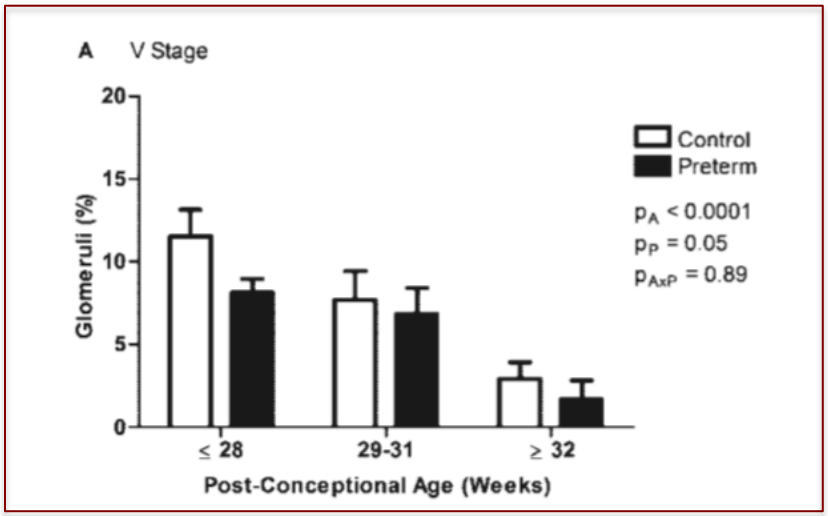
Νεφρώνες δημιουργούνται έως την 32η -34η εβδ.κύησης

Στα πρόωρα βρέφη η νεφρωνογένεση μπορεί να συνεχιστεί μέχρι και 40 ημέρες μετά τη γέννηση, αλλά μπορεί να είναι ανώμαλη

Nephron 2017;136:3–49

Νεφρωνογένεση σε πρόωρα νεογνά

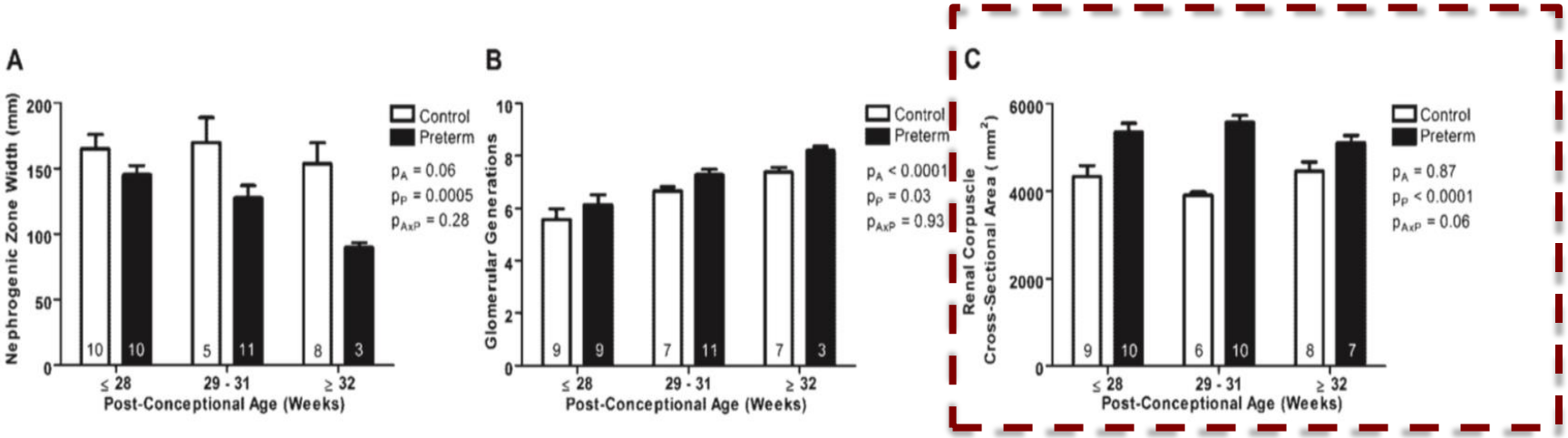


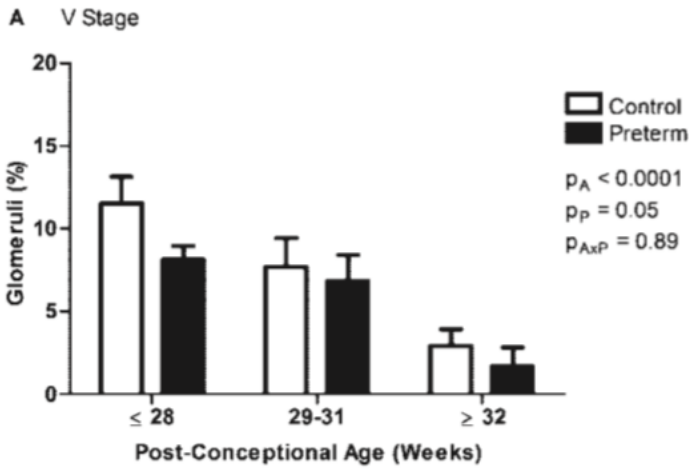


Autopsy from 28 kidneys from preterm neonates, whose postnatal survival ranged from 2 to 68 days

Sutherland et al, J Am Soc Nephrol 22:1365–1374, 2011

Νεφρωνογένεση σε πρόωρα νεογνά

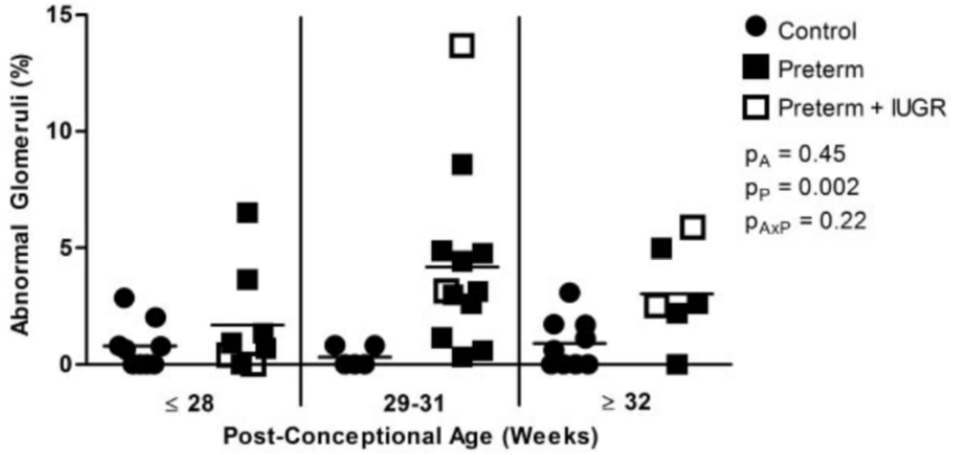


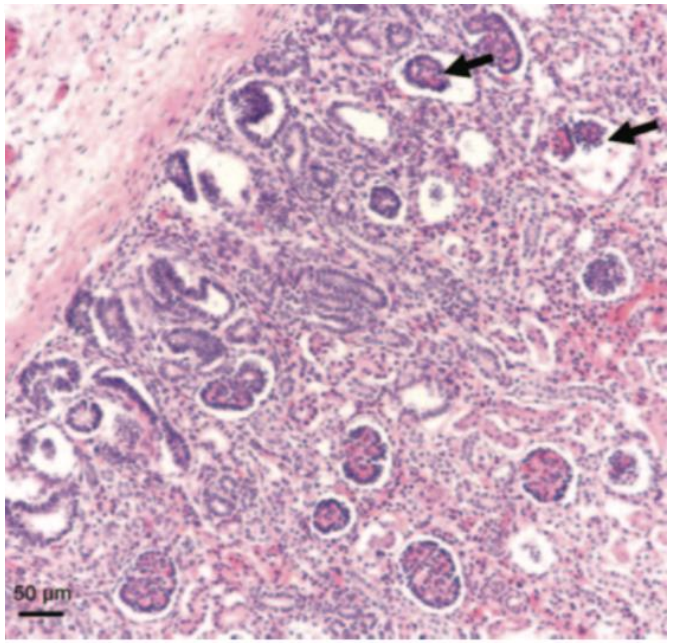


Autopsy from 28 kidneys from preterm neonates, whose postnatal survival ranged from 2 to 68 days

Sutherland et al, J Am Soc Nephrol 22:1365–1374, 2011

Accelerated Maturation and Abnormal Morphology in the Preterm Neonatal Kidney





Sutherland et al, J Am Soc Nephrol 22:1365–1374, 2011

Exposure to famines during pregnancy and BP: the nature's experiments

Among Dutch subjects at age 59 years

Among Biafran subjects at age 37–43 years

The effect of famine on blood pressure maybe accelerated in the African compared with the European populations

Περιγεννητικοί παράγοντες που συσχετίζονται με συγγενείς διαμαρτίες των νεφρών και ΧΝΝ

Table 6. Association of birth weight and maternal risk factors (maternal DM [PDM and GDM] and overweight/obesity) with development of renal dysplasia and aplasia

Risk Factor	*N*	Crude OR	95% CI
Low birth weight[a] (400–2499 g)	78	4.51	3.47 to 5.85
High birth weight[a] (>4000 g)	38	0.93	0.66 to 1.32
Maternal PDM[b]	11	7.52	3.97 to 14.24
Maternal GDM[b]	16	1.48	0.89 to 2.46
Maternal overweight[c]	44	1.02	0.71 to 1.45
Maternal obesity[c]	46	1.30	0.91 to 1.85

1994 cases ages <21 years with CKD-related hospitalizations during 1987–2008 and diagnosis of renal dysplasia/aplasia and obstructive uropathy

Hsu et al, J Am Soc Nephrol 25:2105–2111, 2014

Περιγεννητικοί παράγοντες που συσχετίζονται με συγγενείς διαμαρτίες των νεφρών και ΧΝΝ

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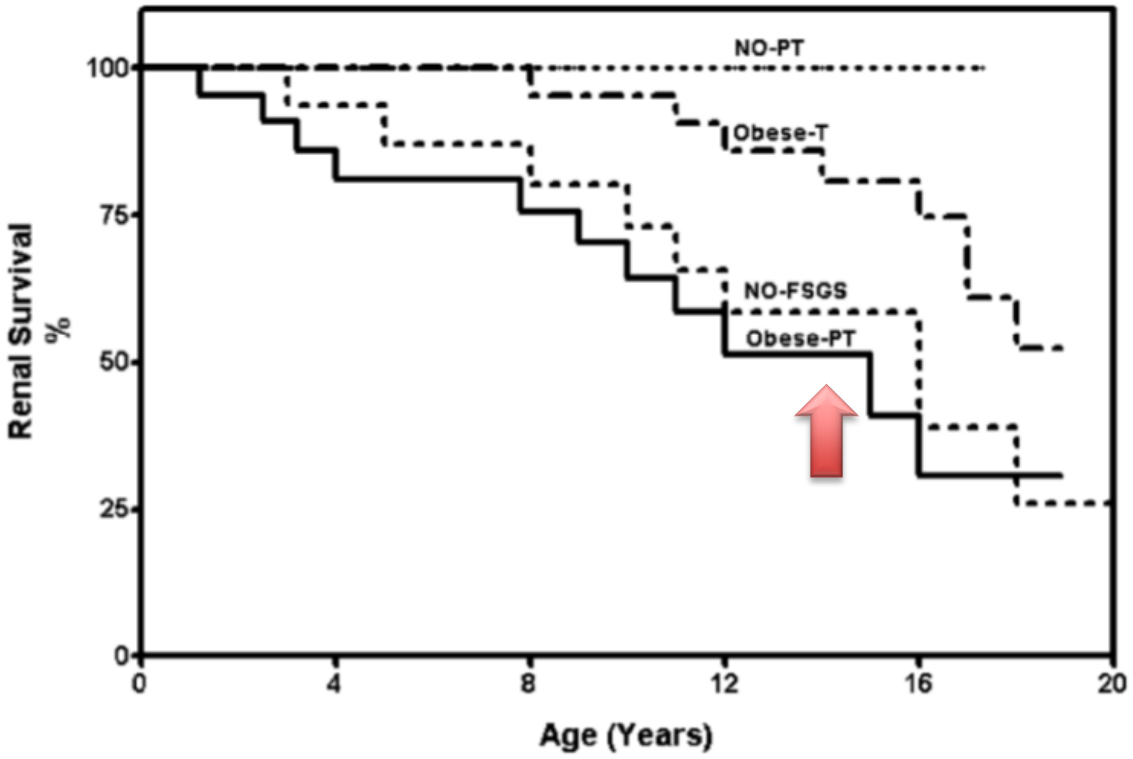
1994 cases ages <21 years with CKD-related hospitalizations during 1987–2008 and diagnosis of renal dysplasia/aplasia and obstructive uropathy

	Neonatal factors		Maternal factors			
	LBW	HBW	preexisting DM	GDM	overweight	obesity
Crude OR	2.41	1.17	1.97	1.40	1.19	1.27
95% CI	2.08–2.80	1.03–1.34	1.15–3.37	1.11–1.77	1.02–1.38	1.08–1.49
Adjusted OR[1]	2.88	0.97	1.12	1.54	1.24	1.26
95% CI	2.28–3.63	0.79–1.21	0.4–2.84	1.13–2.09	1.05–1.48	1.05–1.52

Hsu et al, J Am Soc Nephrol 25:2105–2111, 2014

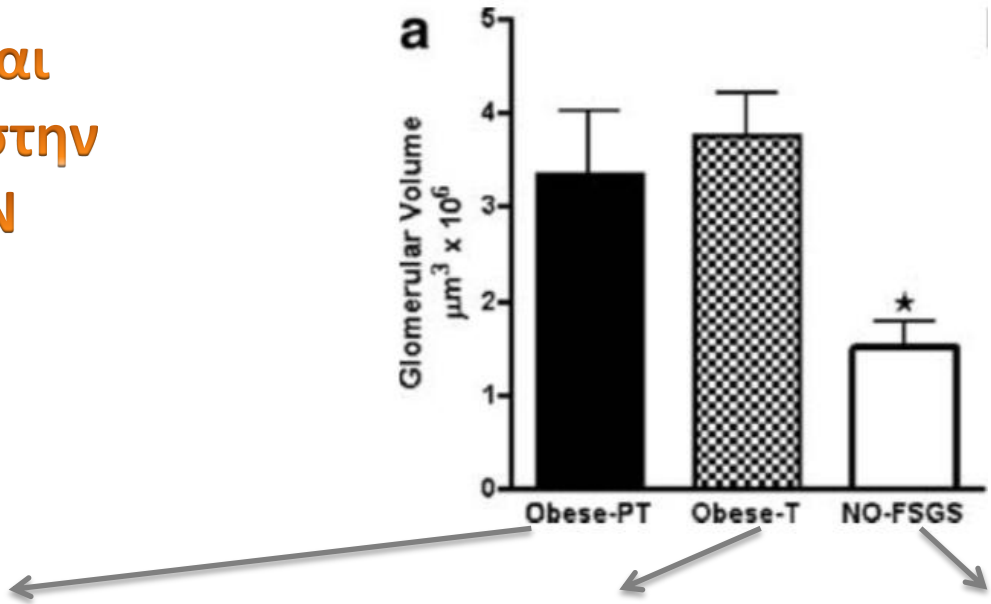
Επίδραση παχυσαρκίας και προωρότητας στην εξέλιξη της ΧΝΝ

80 children with non-diabetic kidney disease and proteinuria were identified for inclusion in this study



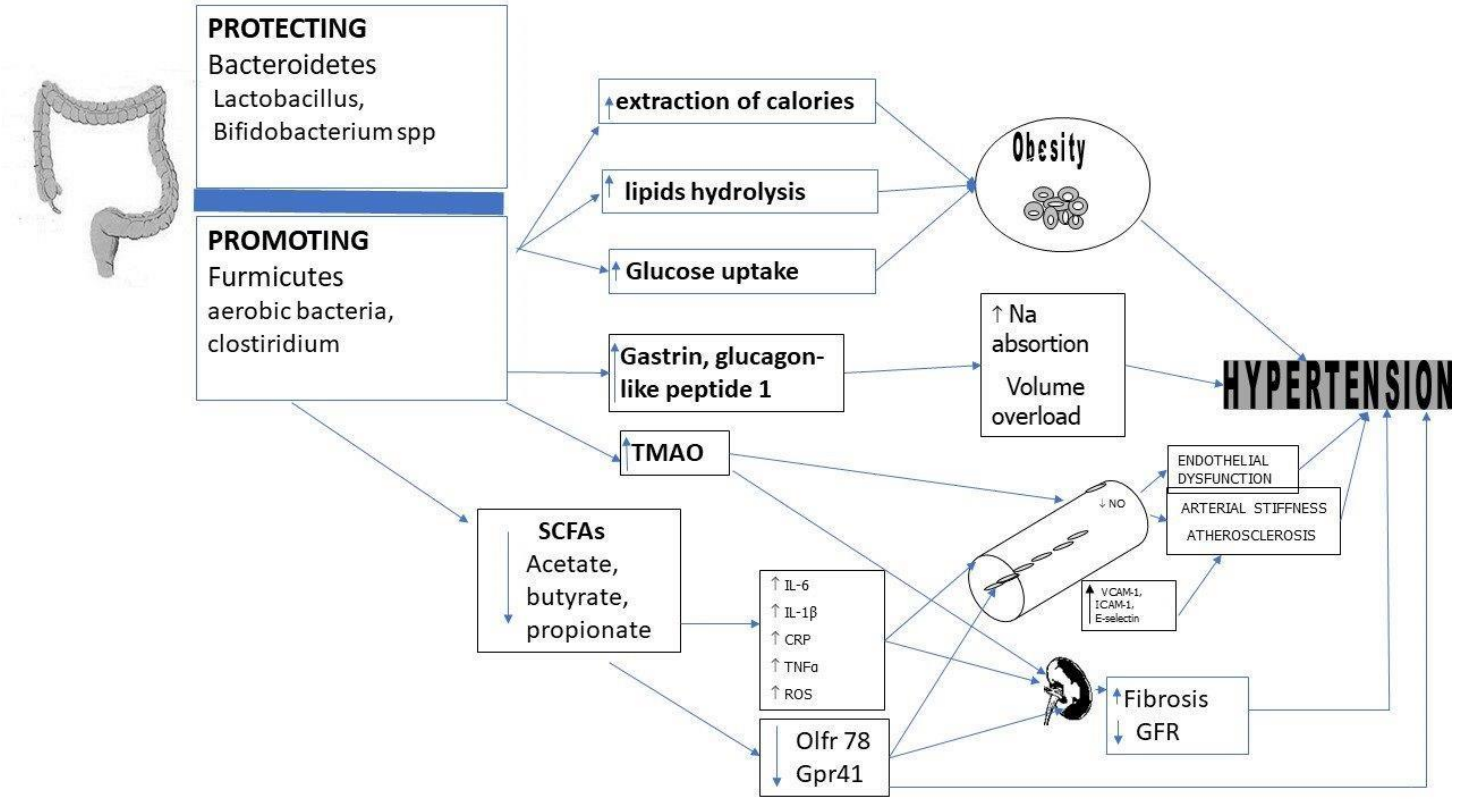
Arbitol et al, Pediatr Nephrol (2009) 24:1363–1370

Επίδραση παχυσαρκίας και προωρότητας στην εξέλιξη της ΧΝΝ



Arbitol et al, Pediatr Nephrol (2009) 24:1363–1370

Παίζει ρόλο το μικροβίωμα?



Antza C, Stabouli S, Kotsis V. Pharmacol Res. 2018 Apr;130:198-203.

Μετανάστευση στην παιδική και εφηβική ηλικία και υπέρταση

Original Article

Hypertension and childhood migration: a nationwide study of 2.7 million adolescents

Alon Peled[a,*], Barak Gordon[a,b,*], Gilad Twig[a,b,c,d], Ehud Grossman[a,e], Doraid Matani[a]
Estela Derazne[a,b], and Arnon Afek[a,f]

See editorial comment on page 680

Objectives: Immigration studies can shed light on hypertension development and reveal high-risk populations. To this end, we investigated the association between age at immigration and hypertension occurrence at adolescence among immigrants to Israel.

Methods: We analyzed cross-sectional data on 2 681 294 adolescents assessed for mandatory military service at approximately 17 years of age between 1967 and 2016. The study population constituted of 410 488 immigrants with origins in Ethiopia, Middle East and North Africa, Former USSR and Western Countries. Age at immigration was categorized into 0–5, 6–11 and 12–19 years. Odds ratios (ORs) for hypertension were calculated according to age at immigration with Israel-born participants as controls. Models were made to account for possible confounders. Additionally, the study population was stratified by country of origin and each immigrant group referenced to Israel-born participants of the same origin.

Results: In the fully-adjusted model, immigrants arriving until age 11 years had comparable ORs for hypertension to the Israeli-born reference group, whereas recent immigrants, arriving at age 12–19 years had a marked lower OR of 0.30 (95% CI 0.27–0.33; $P < 0.001$). The lower hypertension odds among recent immigrants persisted in all models and when the study sample was stratified by sex and origin, with all but those of Western origin showing a graded decrease with increasing age at migration categories.

Conclusion: Immigrants arriving earlier in childhood lose their protection against hypertension at adolescence relative to the Israeli-born, likely because of lifestyle acculturation. Prevention programs are needed, beginning upon arrival and placing emphasis on nutritional and physical activity habits.

Keywords: acculturation, adolescent, childhood, environment, ethnic groups, hypertension, immigration, lifestyle, pathogenesis, risk factors

Abbreviations: IDF, the Israeli Defense Forces; ME/NA, Middle East and North Africa; USSR, Union of Soviet Socialist Republics

INTRODUCTION

Immigration to developed countries is rising worldwide. In 2000, the estimated number of immigrants was 175 million. By 2015, that number was nearing 244 million, the majority of which are living in high-income countries [1]. Apart from its benefits, immigration can also bring with it substantial changes in cardiovascular risk factors in general and hypertension in particular [2–4]. While on average healthier than the

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Journal of Hypertensio

[a]Sackler Faculty of M
Forces, [b]Department
Medical Center, [c]Depa
Chaim Sheba Medical
Center, Tel Hashomer, Israel

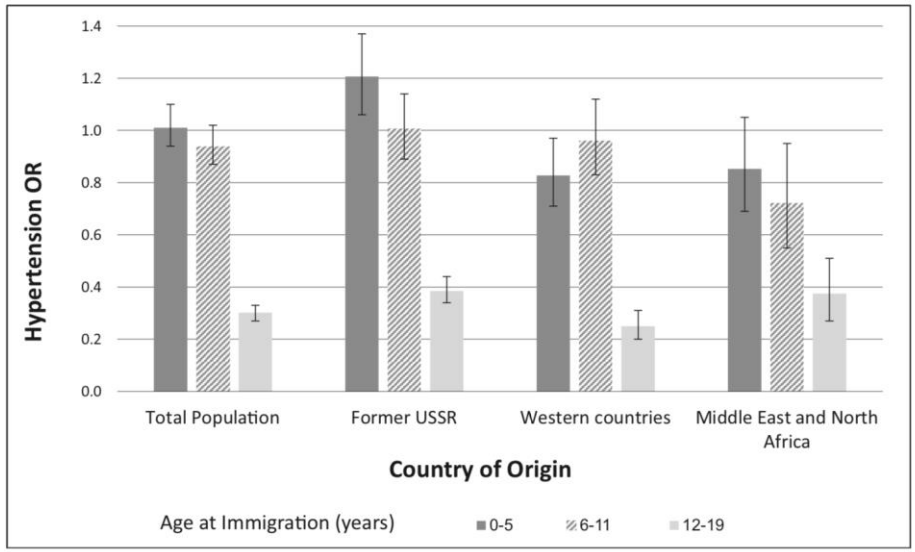
Correspondence to Alon Peled, Leshem 37, Rishon Lezion, Israel. Tel: +972 545820396; fax: +972 39510896; e-mail: Alon2313@gmail.com

*Alon Peled and Barak Gordon contributed equally to the manuscript.

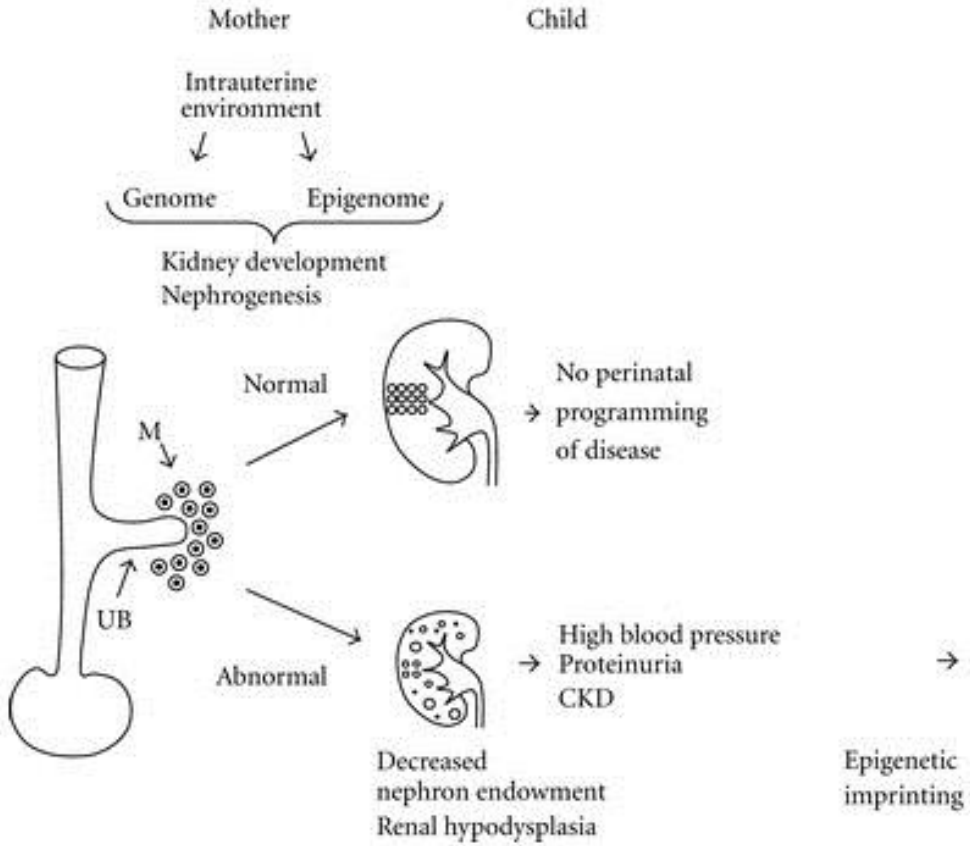
Received 16 May 2018 **Accepted** 5 September 2018

J Hypertens 37:702–709

DOI:10.1097/HJH.0000000000001957



Επιπτώσεις στις επόμενες γενεές?



Chong et al, Int J Nephrol. 2012;2012:760580

Time for action

- **Healthy lifestyles** including exercise, healthy diet, tobacco control
- **Screening** for kidney diseases (e.g**. urine and blood tests**)
- **Screening of high risk individuals** and early diagnosis and treatment to prevent or delay end-stage kidney diseases
- Kidney patients receive basic health services e.g. **blood pressure, glucose, and cholesterol control**, essential medications to delay disease progression

Viewpoint

A developmental approach to the prevention of hy and kidney disease: a report from the Low Birth W Nephron Number Working Group

Valerie A Luyckx*, Norberto Perico*, Marco Somaschini, Dario Manfellotto, Herbert Valensise, Irene Cetin, Umberto Simo Björn Egil Vikse, Eric A Steegers, Dwomoa Adu, Giovanni Montini, Giuseppe Remuzzi, Barry M Brenner, for the writing gr Weight and Nephron Number Working Group†

Lancet 2017; 390: 424–28
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http://dx.doi.org/10.1016/S0140-6736(17)30576-7

*Contributed equally
†See appendix
Institute for Biomedical Ethics, University of Zürich, Zürich, Switzerland (V A Luyckx MBBCh); Clinical Research Center for Rare Diseases Aldo e Cele Daccò (N Perico MD, Prof G Remuzzi MD), and Centro Anna Maria Astori, Science and Technology Park Kilometro rosso (Prof G Remuzzi); IRCCS—Istituto di Ricerche Farmacologiche Mario Negri, Bergamo, Italy; Unit of Neonatology, Sant'Anna Clinic, Lugano, Switzerland (M Somaschini MD); Department of Internal Medicine, Afall Division, Fatebenefratelli Foundation, "San Giovanni Calibita" Fatebenefratelli Hospital, Isola Tiberina, Rome, Italy (Prof D Manfellotto MD); Department of Obstetrics and Gynecology, Tor Vergata University, Rome, Italy (Prof H Valensise MD); Unit of Obstetrics and Gynecology, Department of Biomedical and Clinical Sciences, Hospital "L Sacco", and Centre for Fetal Research Giorgio Pardi, University of Milan, Milan, Italy (Prof I Cetin MD); Service de Pédiatrie, Université de Lausanne, Lausanne, Switzerland (Prof U Simeoni MD); Intensive Care and Department of Pediatric Surgery, Erasmus Medical Center—Sophia Children's Hospital, Rotterdam, Netherlands (K Allegaert PhD); Department of Development and Regeneration KU Leuven, Leuven, Belgium (K Allegaert); Department of Medicine, Haugesund Hospital, Haugesund, Norway

Introduction

In 2008, the World Health Assembly endorsed WHO's Global Action Plan for the Prevention and Control of Non-Communicable Diseases (NCDs) 2013–2020,[1] based on the realisation that NCDs cause more deaths worldwide than do communicable diseases. This plan strongly advocates prevention as the most effective strategy to curb NCDs. Furthermore, the life-course approach, which was highlighted in the Minsk Declaration,[2] reflects increasing recognition that early development affects later-life health and disease.[3] Optimisation of early development offers the opportunity for true primary prevention of NCDs.

Developmental programming in the kidney has been recognised for more than two decades, but its contribution to the global burden of kidney diseases remains underappreciated by policy makers.[4] In view of the many factors known to affect fetal kidney development, including maternal health and nutrition, exposure to stress, poverty, pollutants, drugs, and infections during gestation,[5] a holistic strategy to prevent such programming effects is consistent with the life-course approach and aligns with the United Nations (UN) Sustainable Development Goals to foster health.[6]

Chronic kidney disease is an important contributor to the NCD burden that has been relatively neglected in WHO's Global Action Plan for the Prevention and Control of NCDs, despite chronic kidney disease being a major cause of hypertension and a major risk multiplier of cardiovascular disease.[7,8] Although the prevalence of chronic kidney disease in many low-income countries remains unknown, the disease is most prevalent among disadvantaged populations within industrialised nations—eg, African-Americans and Aboriginal Australians.[9] The number of people receiving dialysis or transplantation is projected to double, from 2·6 million in 2010 to 5·4 million in 2030.[9] In 2010, 2·3–7·1 million adults died from lack of access to dialysis and transplantation in low-income countries.[9] In view of the clinical outcomes and often prohibitively high costs of treatment, prevention and early detection are the only sustainable solutions to address this growing global burden.

To address the neglected issue of developmental programming of kidney disease and hypertension, a multidisciplinary working group was convened, including international expert obstetricians, neonatologists, and nephrologists (appendix). We argue Action Plan for the Prevention and C not adequately address the effect of c of NCDs, particularly in low-incom countries, where developmental ris burden of NCDs is growing fastest identified the need to raise aw of developmental programming in suggests locally adapted preven could have long-term benefits on h savings worldwide, integrating obs nephrology perspectives.

Gestational age, birthweight, n and kidney disease risk

Barker and colleagues[4] were the firs born at low birthweight (<2·5 kg) w of cardiovascular disease. Subsequ colleagues' proposed that developm in the kidney might reduce nephr could contribute to hypertension th sodium excretion because of a surface area, and could increase kidney disease by reducing renal further nephrons are lost through inj plausibly linked the observations th hypertension, and chronic kidney frequently in disadvantaged populatio form during the third trimester preterm birth or insults experienced might affect nephrogenesis and number.[5] Indeed, intrauterine growth affects the growth of splanchnic orga and low birthweight are all associated number as well as higher blood pres A lower nephron number is ass hypertension.[7] Findings of a meta-an low birthweight confers a 70% increa kidney disease—defined as albu glomerular filtration rate, or end-stag compared with normal birthweight. birth has also been associated with a filtration rate and higher album adulthood.[10] These findings support programming hypothesis.

In view of the challenges of m number in vivo, intrauterine growth r

nephron Clinical Practice

Clinical Practice: Consensus Statement

Nephron 2017;136:3–49
DOI: 10.1159/000457967

Published online: March 21, 2017

The Impact of Kidney Development on the Life Course: A Consensus Document for Action

The Low Birth Weight and Nephron Number Working Group

Keywords

Low birth weight · Nephron number · Intrauterine growth restriction · Small for gestational age · Preterm birth · Programmed risk of hypertension · Programmed risk of kidney disease · Maternal nutrition · Infant and child nutrition · Neonatal acute kidney injury

Abstract

Hypertension and chronic kidney disease (CKD) have a significant impact on global morbidity and mortality. The Low Birth Weight and Nephron Number Working Group has prepared a consensus document aimed to address the relatively neglected issue for the developmental programming of hypertension and CKD. It emerged from a workshop held on April 2, 2016, including eminent internationally recognized experts in the field of obstetrics, neonatology, and nephrology. Through multidisciplinary engagement, the goal of the workshop was to highlight the association between fetal and childhood development and an increased risk of adult diseases, focusing on hypertension and CKD, and to suggest possible practical solutions for the future. The recommendations for action of the consensus workshop are the results of combined clinical experience, shared research expertise, and a review of the literature. They highlight the need to act early to prevent CKD and other related noncommunicable diseases later in life by reducing low birth weight, small for gestational age, prematurity, and low nephron numbers at birth through coordinated interventions. Meeting the current unmet needs would help to define the most cost-effective strategies and to optimize interventions to limit or interrupt the developmental programming cycle of CKD later in life, especially in the poorest part of the world.

Preface

This consensus document aims to address the relatively neglected issue of the developmental programming of hypertension and chronic kidney disease (CKD). It emerged from a workshop, entitled The Fault Is Not in Our Stars but May Be in Our Embryos – Glomerular Number in Low Birth Weight Babies, held at the Clinical Research Center for Rare Diseases Aldo e Cele Daccò, IRCCS – Mario Negri Institute for Pharmacological Research, Bergamo, Italy, on April 2, 2016, including eminent internationally recognized experts in the field of

Participants of the Low Birth Weight and Nephron Number Working Group are listed in the Appendix.

Prof. Giuseppe Remuzzi
IRCCS – Istituto di Ricerche Farmacologiche Mario Negri
Centro Anna Maria Astori, Science and Technology Park Kilometro Rosso
Via Stezzano 87, IT–24126 Bergamo (Italy)
E-Mail giuseppe.remuzzi@marionegri.it

Dr. Valerie Luyckx
Institute for Biomedical Ethics
Winterthurerstrasse 30
CH–8006 Zurich (Switzerland)
E-Mail valerie.luyckx@uzh.ch

KARGER
E-Mail karger@karger.com
www.karger.com/nef

Regular monitoring of preterm and LBW individuals throughout life

Children

- Growth-restricted, preterm or LBW infants, exposed to preeclampsia or GDM undergo annual blood pressure measurement at least from age 3, with the addition of an annual urinalysis
- If other risk factors are present (high blood pressure, previous AKI, proteinuria, cardiovascular diseases, renal anomalies, obesity or diabetes) renal function evaluation, including proteinuria, should be performed at least every 2 years
- A baseline renal ultrasound should be performed to detect small kidneys, asymmetry or structural abnormalities
- Rapid catch-up growth should be avoided to prevent obesity-associated exacerbation of renal risk
- From childhood onwards a prudent dietary pattern (reduced sodium, carbohydrates and saturated fat) should be combined with enhanced physical activity and avoidance of smoking

Adults

- From 18 years onwards, blood pressure, BMI, and urinalysis should be monitored at least biannually until age forty and yearly thereafter
- Fasting blood sugar should be monitored in those with elevated BMI after age 30
- Any preterm or LBW women becoming pregnant should be closely monitored for gestational weight gain, fetal growth and preeclampsia

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

Lancet. 2017 July 22; 390(10092): 424–428.

Regular monitoring of preterm and LBW individuals throughout life

Children

- Growth-restricted, preterm or LBW infants, exposed to preeclampsia or GDM undergo annual blood pressure measurement at least

ΑΠ και γ.ούρων κάθε χρόνο από την ηλικία των 3 ετών

- If other risk factors are present (high blood pressure, previous AKI, proteinuria, cardiovascular diseases, renal anomalies, obesity or diabetes) renal function evaluation, including proteinuria, should be performed at

Αν συνυπάρχουν παράγοντες κινδύνου έλεγχος νεφρικής λειτουργίας και πρωτεινουρίας κάθε 2 χρόνια

- rapid catch up growth should be avoided to prevent obesity-associated exacerbation of renal risk
- From childhood onwards a prudent dietary pattern (reduced sodium, carbohydrates and saturated fat) should be combined with enhanced physical activity and avoidance of smoking

Adults

- From 18 years onwards, blood pressure, BMI,

ΑΠ, ΔΜΣ και γ. ούρων κάθε 1-2 έτη

Έλεγχος σακχάρου αν ↑ ΔΜΣ

- those with elevated BMI after age 30
- Any preterm or LBW women becoming pregnant should be closely monitored for gestational

Έλεγχος εγκύων για προεκλαμψία, ΣΔ κύησης

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

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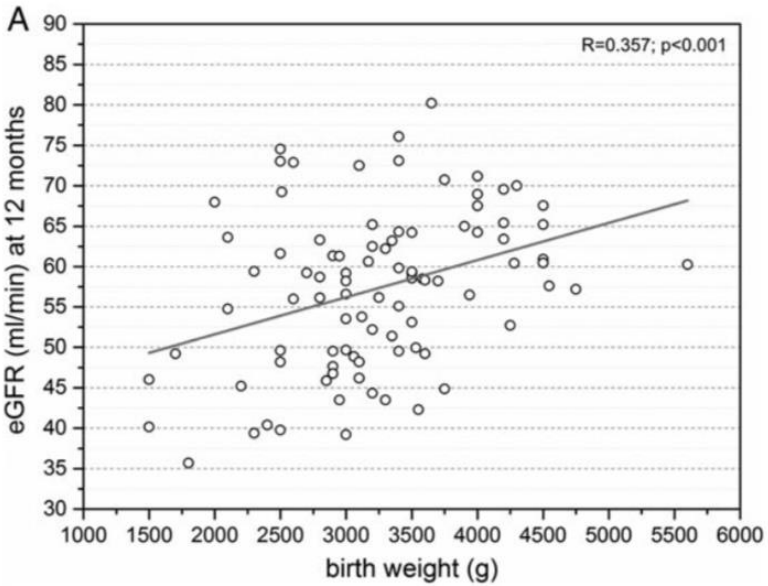
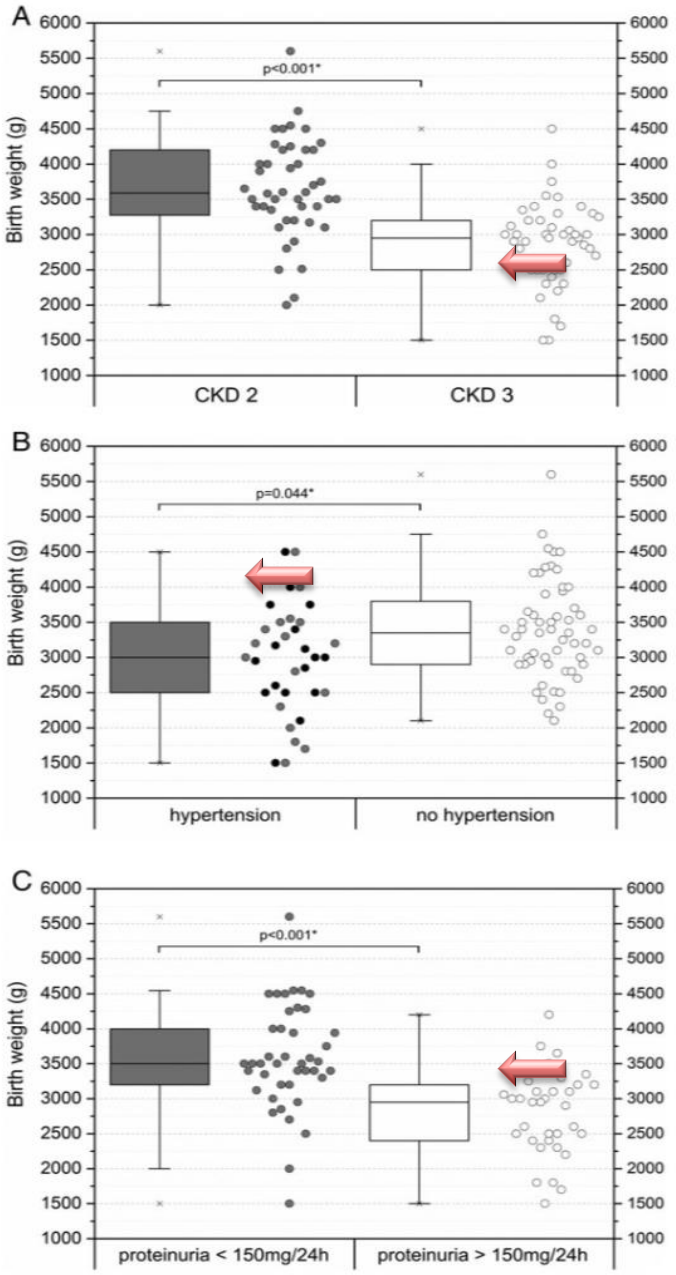
Κλινική σημασία του χαμηλού βάρους γέννησης στην έκβαση δότη νεφρικού μοσχεύματος





Schachtner et al, Nephrol Dial Transplant (2016) 31: 1523–1530

Συμπερασματικά

- Κλασσικοί παράγοντες κινδύνου για ΧΝΝ πρέπει να ελέγχονται στην παιδική και εφηβική ηλικία

- Το περιγεννητικό ιστορικό δίνει σημαντικές πληροφορίες σε άτομα υψηλού κινδύνου για υπέρταση και ΧΝΝ και καθορίζει πιθανόν την έκβαση σε νεφρικές παθήσεις στην πορεία της ενήλικης ζωής

Συμπερασματικά


. . . . . COULD BE WORSE