

Glomerular filtration rate in former extreme low birth weight infants over the full pediatric age range a pooled analysis

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Background: Various cohort studies document a lower glomerular filtration rate (GFR) in former extremely low birth weight (ELBW, <1000 g) neonates throughout childhood when compared to term controls. The current aim is to pool these studies to describe the GFR pattern over the pediatric age range.

Methods: a systematic review on studies reporting on GFR measurements in former ELBW cases while GFR data of healthy age-matched controls included in these studies were co-collected.

Results:

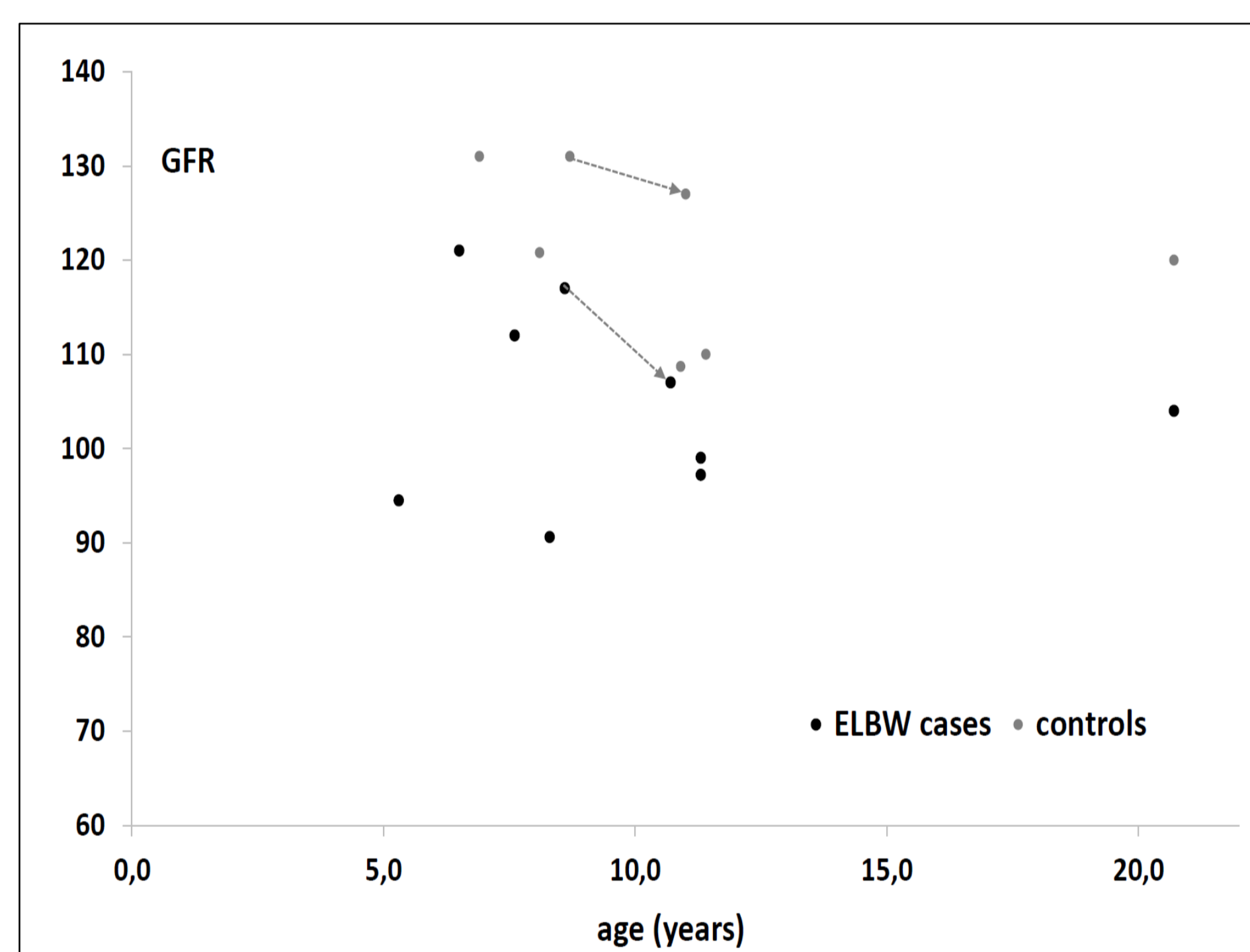
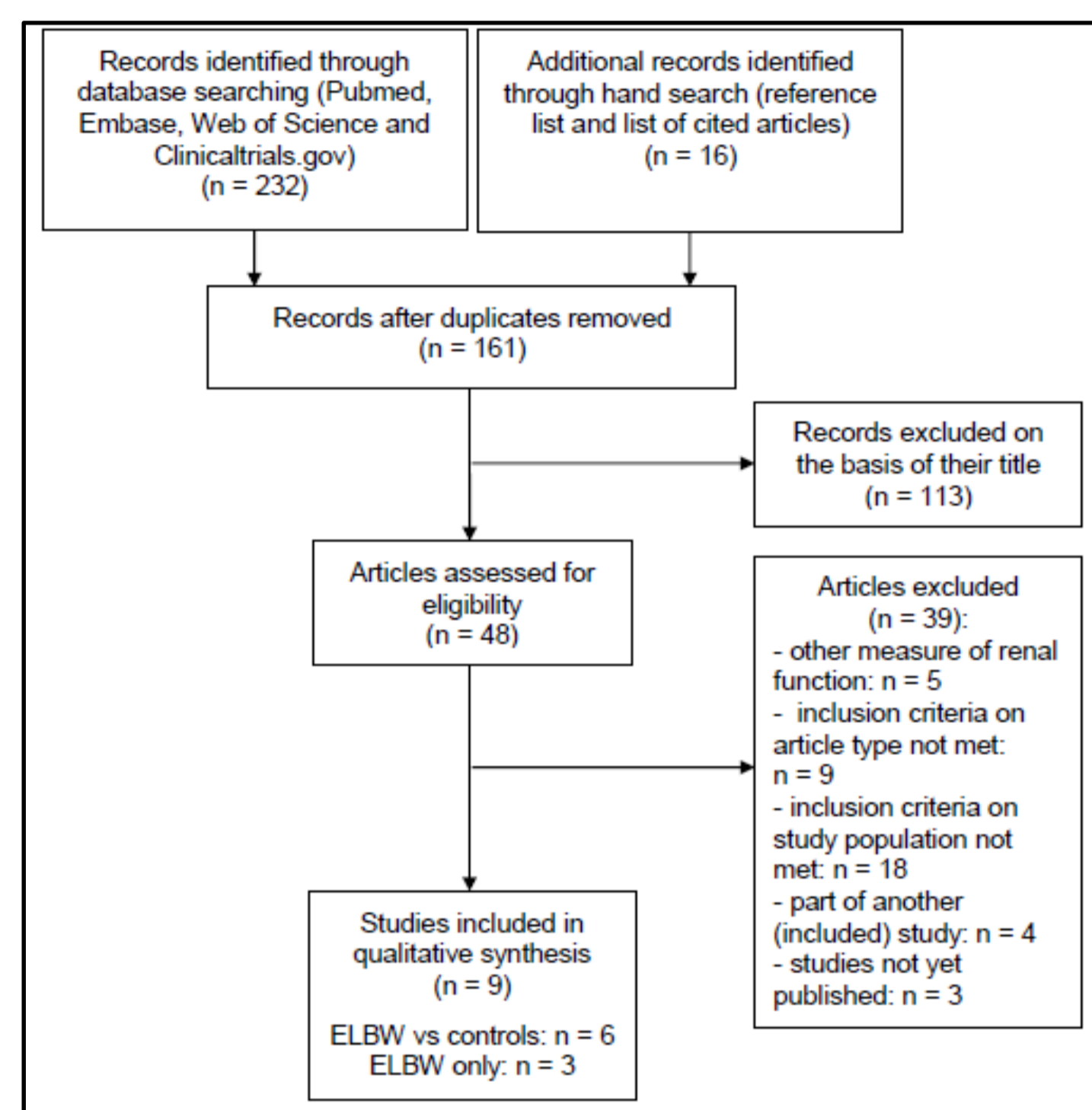


Table 1. Key characteristics and findings of the 6 case-control cohort studies included.

Study	Number, Age	Assay, Formula	Results	Comments
Rodriguez-Soriano 2005	40 cases (8.6, 6.1-12.4), 43 controls (8.5, 5.2-13) y.	modified Jaffé crea, with subsequent eGFR Schwartz.	cases vs. controls: 117 (17, range 86-152) vs. 131 (17, range 97-173) mL/min/1.73m ²	single center, 40/75 ELBW cases included. Controls minor surgery cases.
Keijzer-Veen 2007	23/52 ELBW-SGA cases (20.7, SD 0.3); 30 controls (20.7, SD 0.8) y.	inulin clearance, at baseline and stimulated (protein rich lunch + low (2 µg/kg/min dopa).	cases vs. controls (baseline/stimulated): 104, SD 17/116, SD 27 vs. 120, SD 28 to 141, SD 34 mL/min; 107, SD 15 to 119, SD 23 vs. 112, SD 22, to 131, SD 26 mL/min/1.73m ²	cases recruited from a population follow-up study former preterms (the Netherlands); controls volunteers.
Kvintin 2011	78 cases, mean age 6.5; 38 controls (6.9) y.	Cys C, nephelometric assay (ref value 4-10 y 0.53-0.95 mg/l).	cases vs. controls (7 y): Cys C 0.64 (0.07) vs. 0.59 (0.07) mg/l. Using the Hoek formula, equal to 121 vs 131 mL/min/1.73m ² .	single center, 78/89 cases included, controls from general practitioners' offices.
Starzec 2016	64/78 cases re-studied at 10.7; 36/38 controls at 11 y.	Cys C + eGFR, based on Hoek formula; crea (assay ?)	cases vs. controls (11 y): Cys C 0.72 (SD 0.15) vs. 0.61 (SD 0.08) mg/l; eGFR 107.3 to 127.4 mL/min/1.73m ² ; crea 43.2, SD 7.7 vs. 46.3, SD 7.6 µmol/l)	single center, 64/78 cases retained, controls from general practitioner offices.
Yamamura-Miyazaki 2017	48 cases, mean age 8.3 y, and 48 controls, 8.1 y.	Cys C, latex turbidimetry; Cys-eGFR (Uemura formula); Crea enzymatic; Crea-eGFR (assay ?)	Cases vs. controls: Cys C 1.08 (0.17) vs. 0.82 (0.09) mg/l; Cys-eGFR 90.6 (15.5) vs. 120.8 (14.5) mL/min/1.73m ² ; crea 0.46 (0.09) vs. 0.37 (0.08) mg/dl; crea-eGFR 95.4 (15.5) vs. 123.9 (14.5) mL/min/1.73m ²	single center, 48/86 cases included; controls were outpatient clinics cases.
Raaijmakers 2017	59 cases (11.3, SD 1.4); 71 controls (10.9, SD 1.3) y.	Cys C (turbidimetry), Cys-eGFR (CAPA formula) Crea (enzymatic), Crea-eGFR (Schwartz).	Cases vs. controls: Cys C 0.96 (0.12) vs. 0.87 (0.11) mg/l; Cys-eGFR 97.2 (13.6) vs. 108.7 (15.3) mL/min/1.73m ² ; Crea 0.57 (0.1) vs. 0.56 (0.08) mg/dl; Crea-eGFR 111 (17) vs. 111 (15) mL/min/1.73m ² .	single center, 93/140 cases, but blood sampling in only 59 cases. Controls were volunteers.
Vollsaeter 2018	17 SGA cases (mean 11.3), and 45 controls (11.4) y.	Cys C (immuno-maldi); Crea (chromatography); eGFR Schwartz, Gao (crea), Zappitelli (crea+Cys C)	Cases vs. controls: Cys C 0.91 vs. 0.86 mg/l; Cys-GFR; Crea 53.6 vs. 51 µmol/l; GFR _{schw} 99 vs. 110; GFR _{gao} 98.4 vs. 105.6; GFR _{zpp} 95.1 vs. 104.8 mL/min/1.73m ² .	regional cohort with 17 SGA-ELBW cases. Controls volunteers from same maternity.

Table 2. Key characteristics of the 3 cohort studies included.

Study	Number, Age	Assay, Formula	Results	Comments
Bacchetta 2009	50 cases, 7.6 (range 5.8-10.3) y.	inulin clearance	average GFR 112 (range 91-158 mL/min/1.73m ²)	single center study, 50/143 with GFR in 46/50 cases, 39 ELBW cases
Zaffanello 2010	26 ELBW cases, 5.3 (95% CI 5.2-6.3) y.	Cys C assay (nephelometry); crea (modified Jaffé); Schwartz (crea, crea/Cys-C/BUN)	Median Cys C 0.67 mg/l; crea 0.42 mg/dl; Schwartz _{crea} 109 mL/min/1.73m ² ; Schwartz _{crea+cysc} 94.5 mL/min/1.73m ²	single center study, recruited 69/97 contacted cases, but 1000-1500 g birth weight cases also recruited.
Matsumura 2019	43 cases with follow-up, 7 (range 2-22) y.	Crea, assay unknown; eGFR Japanese children.	only qualitative reporting: 12 (28%) had low GFR (<90 mL/min/1.73m ²).	single center, retrospective, cross sectional study.

ELBW: extreme low birth weight; BUN: blood urea nitrogen; SGA: small for gestational age; eGFR: (estimated) glomerular filtration rate; Cys C: cystatin C; crea: creatinine; y: years.

Conclusions

- This pooled analysis confirms the pattern of reduced eGFR in former ELBW cases throughout childhood.
- Research should focus on perinatal risk factors for impaired GFR and long-term outcome (pharmacovigilance).
- This research is hampered by single center cohorts, study size and heterogeneity of GFR assessment tools.

