Low Birth Weight Increases Risk for End-Stage Renal Disease

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ABSTRACT

Case-control studies have shown an association between low birth weight and risk for renal failure. The Medical Birth Registry of Norway, which comprises data on all births in Norway since 1967, and the Norwegian Renal Registry, which comprises data on all patients who have developed ESRD in Norway since 1980, were used to examine whether birth-related variables were associated with risk for ESRD. Of the 2,183,317 children born between 1967 and 2004, 526 were found in the ESRD registry. Compared with birth weight in the 10th to 90th percentiles, births <10th percentile had a relative risk (RR) for ESRD of 1.7 (95% confidence interval 1.4 to 2.2; $P < 0.001$). Births with a weight for gestational age <10th percentile had an RR of 1.5 (95% confidence interval 1.2 to 1.9; $P = 0.002$). These associations were virtually identical after adjustment for birth-related confounders such as congenital malformations, multiple delivery, maternal age at birth, and maternal preeclampsia. Low birth weight was more strongly associated with development of ESRD during the first 14 years of life than after age 15. Low birth weight and low birth weight for gestational age were similarly associated with multiple causes of ESRD. In conclusion, in this cohort study with a maximum follow-up of 38 years, low birth weight and intrauterine growth restriction were associated with increased risk for ESRD.

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Studies have shown that adults with a low birth weight face an increased risk for chronic diseases, including high BP, cardiovascular disease, and renal disease.[1–3] This increased risk might be transferred through generations and thus have important implications for future health.[4] During the past few decades, an epidemic of chronic renal failure has developed.[5] Thus, studies of the associations between intrauterine growth restriction and renal disease may be of major importance.

In the 1980s, Brenner and colleagues[6] hypothesized that intrauterine growth restriction might cause a low nephron number, which could predispose to hypertension and renal disease. Later, studies showed that low birth weight and intrauterine growth restriction were associated with mild to moderate elevations of BP,[2,7] a reduced number of compensatory hypertrophied glomeruli,[8–10] and lower GFR and higher urine albumin-to-creatinine ratio.[11,12] Furthermore, it has been shown that low birth weight is associated with more frequent re-

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lapses of nephrotic syndrome in children with minimal-change nephropathy and higher rates of progression in children with IgA nephropathy.[13,14] Two case-control studies have shown that birth weight <2.5 kg seems to be associated with a 40 to 60% increased risk for development of chronic renal failure.[3,15]

No cohort studies have investigated the association between birth weight and ESRD. In Norway, data on all births have been recorded in the Medical Birth Registry since 1967, and since 1980, data on all patients who have developed ESRD have been recorded in the Norwegian Renal Registry. We linked these two registries to investigate whether birth weight or other birth-related variables were associated with development of ESRD during adulthood. We also investigated whether birth weight was associated with specific causes of ESRD.

RESULTS

From 1967 to 2004, 2,183,317 children were included; from 1980 to 2005, 526 of these developed ESRD, and of these, 142 were due to congenital conditions. Of the 526 with ESRD, 314 (60%) were men and 212 (40%) were women. Mean age at the time of ESRD onset was 21.2 ± 8.9 yr (range 0.2 to 38.6 yr), and mean duration of follow-up of the entire population was 20.1 ± 11.2 yr (Table 1).

Risk Factors for ESRD, Total

At ages 10, 20, 30, and 38 yr, 0.004, 0.017, 0.044, and 0.078% of the individuals had developed ESRD. Men had a relative risk (RR) for ESRD of 1.4 (95% confidence interval [CI] 1.2 to 1.7) as compared with women (Figure 1). Birth weight <10th percentile was associated with an RR of 1.7 (95% CI 1.4 to 2.2) for ESRD (Table 2, Figure 2). Birth weight for gestational age <10th percentile was associated with an RR of 1.5 (95% CI 1.2 to 1.9), significant only for men and not for women. These associations were tested in an extensive adjustment model and found to be independent of other birth-related variables (Table 2). The analyses for birth weight were also adjusted for birth weight for gestational age, and *vice versa*. In these analyses, the effects of birth weight were hardly affected by adjustments for birth weight for gestational age, whereas the effects of birth weight for gestational age disappeared after adjustments for birth weight. As shown in Table 3, low birth weight was more strongly associated with ESRD during the first 14 yr of life than later. RR was 2.5 during the first 14 yr of life, 1.6 between the ages of 15 and 24 yr, and 1.4 between the ages of 25 and 38 yr. For the oldest age group, this was not statistically significant.

Table 1. Births in Norway 1967 to 2004 according to birth-related variables and development of ESRD 1980 to 2005

Birth-Related Variables	Not Developed ESRD		Developed ESRD	
	n	%[a]	*n*	%[a]
Gender				
men	1,120,789	51	314	60
women	1,061,909	49	212	40
Birth weight				
<10th percentile	211,633	10	81	16
10 to 90th percentile	1,744,016	80	402	77
≥90th percentile	222,751	10	39	7.5
Gestational age (wk)				
<37	118,848	5.8	32	6.5
37 to 41	1,668,067	81	393	80
≥42	271,130	13	68	14
Birth weight for gestational age				
<10th percentile	217,067	11	81	17
10 to 90th percentile	1,627,085	80	369	76
≥90th percentile	200,788	9.8	38	7.8
Multiple delivery *versus* single				
multiple	53,037	2.4	9	1.7
single	2,129,753	98	517	98
Maternal preeclampsia during pregnancy				
yes	65,216	3.0	16	3.0
no	2,117,575	97	510	97
Congenital malformation of the kidney or urinary tract				
yes	1,729	0.08	12	2.3
no	2,181,062	99	514	97
Other congenital malformations				
yes	60,854	2.9	23	4.4
no	2,121,937	97	503	96

[a]Percentage within category of predictor variable.

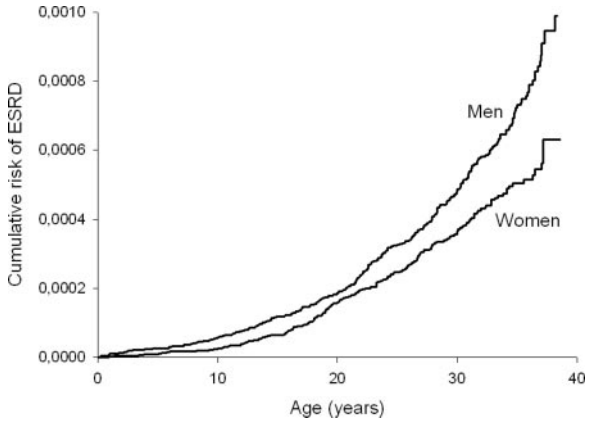

Figure 1. Cumulative risk for ESRD in men and women by age. Norway, births 1967 to 2004, ESRD 1980 to 2005.

Among individuals who developed ESRD during the first 15 yr of life, 32% developed ESRD as a result of glomerular disease, 6.2% as a result of interstitial disease, 56% as a result of congenital or inherited disease, 0% as a result of diabetic nephropathy, and 5.4% as a result of other causes; respective numbers for the oldest age group were 48, 6.7, 13, 19, and 13%.

Congenital urinary tract abnormalities were associated with increased risk for ESRD (RR 106; 95% CI 60 to 190), significant for both men and women. Other congenital abnormalities were also associated with an increased risk for ESRD (RR 2.1; 95% CI 1.4 to 3.2). Gestational age, multiple delivery, maternal age, birth order, maternal preeclampsia, maternal marital status, maternal kidney or urinary tract disease, maternal rheumatic disease, and maternal diabetes were not associated with later development of ESRD.

Analyses for birth weight were repeated using 2.5 and 4.5 kg as cutoffs. In these analyses, birth weight <2.5 kg had a RR of 2.0 (95% CI 1.4 to 2.8) for development of ESRD: RR 1.5 (95% CI 0.89 to 2.4) for men and 2.8 (95% CI 1.8 to 4.4) for women. Birth weight ≥4.5 kg was associated with ESRD for women but not for men: RR 2.3 (95% CI 1.2 to 4.5) for women and 0.48 (95% CI 0.22 to 1.1) for men (of the nine women with ESRD and birth weight ≥4.5 kg, five developed ESRD as a result of glomerular disease and two as a result of diabetic nephropathy).

From 1980 to 2005, complete registration of end points was obtained; we therefore performed separate analyses of this subgroup (including 1,417,036 children among whom 138 developed ESRD). These analyses yielded virtually identical results as those presented in the previous paragraph. Separate analyses of children without any congenital abnormalities registered at birth also yielded almost identical results as those presented in Table 2.

Risk Factors for ESRD, Noncongenital

There is a possibility that congenital urinary tract malformations and hereditary renal disease might be a cause of low birth weight. We therefore chose to analyze risk factors for noncongenital ESRD. In these analyses, we excluded 1741 individuals with recorded congenital urinary tract or kidney malformations at birth and 142 individuals who developed ESRD as a result of congenital urinary tract malformations and hereditary renal disease. Overall, risk factors for noncongenital ESRD were virtually identical with those for total ESRD with similar estimates of RR. Because of a lower number of outcomes, *P* values did, however, decrease in strength for most variables. Birth weight <10th percentile was associated with an RR of 1.5 (95% CI 1.1 to 2.0): 1.5 (95% CI 1.02 to 2.2) in men and 1.5 (0.93 to 2.3) in women. Birth weight for gestational age <10th percentile was associated with an RR of 1.5 (95% CI 1.1 to 1.9): 1.6 (95% CI 1.1 to 2.3) in men and 1.3 (95% CI 0.86 to 2.1) in women.

Risk Factors for ESRD, Specific Causes

Among the 526 who developed ESRD, 238 developed ESRD as a result of glomerular disease, 52 as a result of interstitial nephritis, 142 as a result of congenital or inherited causes, 42 as a result of diabetic nephropathy, and 52 as a result of other causes. Table 4 shows that low birth weight seems to be similarly associated with different causes of ESRD. The numbers of cases in several subgroups, however, were low with imprecise estimates of RR.

DISCUSSION

This study is the first cohort study to investigate the effect of birth weight on later risk for ESRD and confirms the hypoth-

Table 2. RR for ESRD according to birth-related variables, unadjusted and adjusted models: Childbirths 1967 to 2004, ESRD 1980 to 2005, Norway

Parameter	Unadjusted									Adjusted[a]			
	All			Men			Women			Men		Women	
	n	RR[b]	*P*	*n*	RR	*P*	*n*	RR	*P*	RR	*P*	RR	*P*
Birth weight													
<10th percentile	81	1.7 (1.4 to 2.2)	<0.001	46	1.7 (1.2 to 2.3)	0.001	35	1.9 (1.3 to 2.7)	<0.001	1.8 (1.3 to 2.4)	<0.001	1.8 (1.2 to 2.7)	0.002
10 to 90th percentile	402	1.0		242	1.0		160	1.0					
≥90th percentile	39	0.86 (0.62 to 1.2)	0.4	22	0.81 (0.52 to 1.3)	0.3	17	0.95 (0.58 to 1.6)	0.9	0.79 (0.51 to 1.2)	0.3	0.96 (0.58 to 1.6)	0.9
Birth weight for gestational age													
<10th percentile	81	1.5 (1.2 to 1.9)	0.002	50	1.6 (1.1 to 2.1)	0.005	31	1.4 (0.92 to 2.0)	0.1	1.6 (1.1 to 2.1)	0.006	1.3 (0.89 to 1.9)	0.2
10 to 90th percentile	369	1.0		216	1.0		152	1.0		1.0		1.0	
≥90th percentile	38	0.94 (0.67 to 1.3)	0.7	21	0.88 (0.56 to 1.4)	0.6	17	1.0 (0.62 to 1.7)	0.9	0.87 (0.55 to 1.4)	0.5	1.0 (0.62 to 1.7)	0.9

[a]Adjusted for birth year, maternal preeclampsia, any congenital malformation, multiple delivery, maternal age at birth, maternal marital status and birth order.
[b]Adjusted for gender.

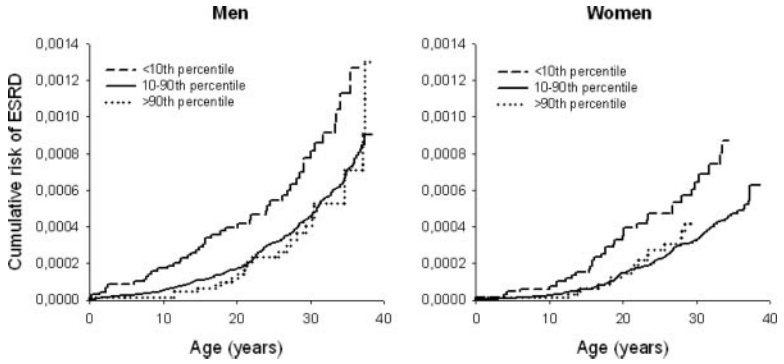

Figure 2. Cumulative risk for ESRD in men and women, by age and birth weight. Norway, births 1967 to 2004, ESRD 1980 to 2005.

esis of increased risk for renal failure associated with low birth weight.[6,16] It is a national registry–based study with complete inclusion and registration of end points. The study showed that low birth weight conferred a 70% increased risk for ESRD up to a maximum age of 38 yr. These findings were similar for men and women and persisted after adjustments for other birth-related variables. Further analyses showed that the association was stronger during the first 14 yr of life than after 15 yr of age. Low birth weight seemed to be similarly associated with different causes of ESRD.

Previous studies have shown that low birth weight is associated with a lower nephron number,[8–10] larger glomeruli,[8,10] mildly to moderately elevated BP,[2,7] lower GFR,[11] albuminuria,[11,12] and adverse clinical course of minimal-change nephropathy as well as IgA nephropathy.[13,14] In addition, two case-control studies showed a 40 to 60% increased risk for chronic renal failure in individuals with low birth weight.[3,15] The participants in these studies were older and more often black (70% *versus* none), and chronic renal failure was more often caused by hypertension or diabetes as compared with our study. Subanalyses of white individuals, however, showed similar findings as our study did.[3] Our study thus confirms previous findings in a cohort study of a white population up to a maximum age of 38 yr, showing a 70% increased risk for ESRD in low birth weight individuals, independent of other birth-related variables. Birth weight for gestational age <10th percentile was associated with a 50% increased risk for ESRD, significant for men but not for women. Comparing the predictors birth weight and birth weight for gestational age, birth weight was associated with somewhat higher RR, showed similar findings for men and women, and were more important in the adjustment analyses. In our study, birth weight therefore seems to be a more important predictor of ESRD than birth weight for gestational age. It has been argued that gestational age should be taken into account when analyzing effects of birth weight because low birth weight at short gestational age might be physiologically normal, whereas low birth weight at term probably reflects severe placental insufficiency. Our study suggests that birth weight *per se* might be more predictive for development of ESRD than birth weight for gestational age. Maternal preeclampsia is an important cause of low birth weight children and neonatal complications as well as an important risk factor for cardiovascular and renal disease in the mothers.[17,18] It is therefore interesting to note that data from this study indicated that maternal preeclampsia was not associated with development of ESRD for the children.

Further analyses showed that the association between low birth weight and ESRD was stronger during the first 14 yr of life

Table 3. RR for ESRD in different age groups according to gender and birth weight: Childbirths 1967 to 2004, ESRD 1980 to 2005, Norway

Birth Weight	Age 0 to 14 Yr			Age 15 to 24 Yr			Age 25 to 38 Yr		
	n	RR[a]	*P*	*n*	RR[a]	*P*	*n*	RR[a]	*P*
All									
<10th percentile	28	2.5 (1.6 to 3.8)	<0.001	28	1.6 (1.1 to 2.4)	0.03	25	1.4 (0.94 to 2.2)	0.1
10 to 90th percentile	96	1.0		155	1.0		151	1.0	
≥90th percentile	6	0.51 (0.23 to 1.2)	0.1	17	0.99 (0.60 to 1.6)	0.96	16	1.0 (0.60 to 1.7)	0.99
Men									
<10th percentile	19	2.6 (1.5 to 4.3)	<0.001	12	1.3 (0.69 to 2.3)	0.5	15	1.4 (0.83 to 2.5)	0.2
10 to 90th percentile	64	1.0		85	1.0		93	1.0	
≥90th percentile	3	0.38 (0.12 to 1.2)	0.1	8	0.85 (0.41 to 1.8)	0.7	11	1.1 (0.60 to 2.1)	0.7
Women									
<10th percentile	9	2.4 (1.1 to 5.0)	0.02	16	2.0 (1.1 to 3.4)	0.01	10	1.5 (0.74 to 2.8)	0.3
10 to 90th percentile	32	1.0		70	1.0		58	1.0	
≥90th percentile	3	0.78 (0.24 to 2.5)	0.7	9	1.2 (0.58 to 2.3)	0.7	5	0.81 (0.32 to 2.0)	0.6

[a] Adjusted for gender in analyses of all subjects

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

than after 15 yr of age. This age-related difference may be explained by a stronger association between low birth weight and ESRD as a result of congenital or inherited causes that were more common during the first 14 yr of life. Another explanation might be confounding by unrecognized malformations of the kidney or urinary tract; this is also likely to be more important during the first 14 yr of life. Our main finding of increased ESRD risk associated with low birth weight, however, is unlikely to be explained by congenital malformations because low birth weight was significantly associated both with ESRD as a result of noncongenital causes and with ESRD as a result of glomerular disease. The latter is especially unlikely to be associated with congenital malformations. A possible interpretation might also be that a critical shortage of nephrons associated with low birth weight[8–10] manifests itself particularly strongly in the first 15 yr of life. The pathophysiologic background for an increased risk for glomerular and hypertensive nephropathy may be that low birth weight is associated with a decreased number of hypertrophied glomeruli[8–10] as well as mild to moderate elevations of BP.[2,7] We would thus expect a stronger effect with advanced age. Because this study had no data on glomeruli number and BP levels before development of renal disease and had follow-up data only up to a maximum age of 38 yr, these issues could not be investigated further.

In this study, birth weight ≥4.5 kg was associated with an increased risk for ESRD in women. Previous studies showed associations between high birth weight and later development of autoimmune diseases,[19–21] the metabolic syndrome,[22] and ESRD caused by diabetic nephropathy.[3] In the last study, birth weight ≥4.0 kg was significantly associated with development of ESRD as a result of diabetes. In this study, a similar association was found for birth weight ≥4.5 kg and seemed to be associated with an increased risk for both ESRD as a result of glomerular disease and diabetes. These differences might be explained by differences in study sample because the participants in the previous study were older and more often black (70% *versus* none), and diabetes was more common than in our study.[3] Our study also analyzed ESRD as a result of glomerulonephritis as a separate outcome, which was not done in the previous study.[3] The association between high birth weight and increased risk for renal failure should be investigated further.

This study included all children who were born between 1967 and 2004 in Norway and examined risk factors for development of ESRD in the period from 1980 to 2005. The major strength of our study is the complete national inclusion and registration of end points, yielding a large number of participants with prospective registration of birth related variables, allowing a cohort design of the study. Furthermore, the study used a hard outcome that is clinically useful and reliable. The main limitation is that it investigated risk factors for development of ESRD only up to a maximum age of 38 yr. Another limitation of the study is that ESRD is a rare end point, and despite the 2.2 million included individuals, only 314 men and 211 women developed ESRD. This is an adequate number for investigation of risk factors for our main outcome but too few to allow reliable analyses of risk factors for specific causes of ESRD. The previously mentioned study on low birth weight and ESRD, however, showed that low birth weight similarly predicted ESRD as a result of diabetes, hypertension, and other causes.[3] Together with the results from this study, it therefore seems as though birth weight is similarly associated with different causes of ESRD.

The study is also limited by the fact that individuals were included from 1967 to 2004, whereas outcomes were not registered until 1980. This limitation was compensated for by two approaches and is unlikely to have affected the results significantly. First, those born after 1980 were analyzed separately, yielding similar results as when the whole period was analyzed. Second, the statistical method that was used did not include patients in the analyses until an outcome can actually be registered. Some individuals who developed ESRD may have emigrated after birth; their development of ESRD would therefore not be registered in the Norwegian Renal Registry. Because the total emigration rate from Norway during the study period was only 0.1% (data from the Norwegian Population Registry), we

conclude that this is very unlikely to have affected the results. We therefore conclude that despite some limitations of this study, it has a robust design and the results are reliable.

This investigation is the first cohort study on birth weight and development of ESRD. We found that low birth weight was associated with a 70% increased risk for ESRD up to a maximum age of 38 yr. This confirms the hypothesis that low birth weight predisposes for renal failure, but the magnitude of RR is smaller than might be expected. Birth-related risk factors for different causes of ESRD seemed to be similar, but this finding should be confirmed in other studies including more individuals with ESRD.

CONCISE METHODS

Since 1967, medical data on all births in Norway (total population of 4.5 million) with a gestational age of at least 16 wk have, by compulsory notification, been forwarded to the Medical Birth Registry of Norway.[23] The registry notification form includes data on maternal disease, complications of delivery, and conditions of the newborn. The form is completed by the attending midwife and doctor and coded at the registry using the International Classification of Diseases (eighth revision for 1967 to 1998 and 10th revision from 1999). Since 1980, data on all patients in Norway starting chronic renal replacement therapy have been registered in the Norwegian Renal Registry (registering all cases with ESRD in Norway). The national Cause of Death Registry comprises data on all deaths in Norway since 1951, and these data were available until December 2004.

We included all children born alive in Norway between 1967 and 2004. Data on these children recorded in the Medical Birth Registry of Norway were linked with the Norwegian Renal Registry and the Cause of Death Registry using the national identification number. The outcome was development of ESRD, defined as starting long-term dialysis treatment or having a kidney transplantation. The study was approved by the regional ethics committee.

Exposure Variables

Birth weight was categorized into three categories using the gender-specific 10th and 90th percentiles (2.87 and 4.27 kg for men; 2.80 and 4.11 kg for women) as cutoffs. From 1967 through 1998, gestational age was based on the last menstrual period and from 1999 onward on routine ultrasonographic examination in gestational weeks 17 through 20. Gestational age was categorized into three categories: $<$37, 37 to 41, and $\geq$42 wk. Birth weight for gestational age was categorized into three categories ($<$10th percentile, 10 to 90th percentile, and $\geq$90th percentile) using previously published gender-specific reference values in Norway.[24,25] We used two categories of congenital disorders: Congenital malformation of the kidney or urinary tract (denoted as congenital urinary tract abnormalities in text) and any other congenital malformation.

Maternal age at time of birth was categorized into three groups using 25 and 30 yr as cutoffs. Marital status was recorded as either single (divorced or not living with partner) or not single (married or living with partner). Three categories of birth order were used: 1, 2, and $\geq$3. Preeclampsia was defined as increased BP after 20 wk gestation (BP $\geq$140/90 mmHg or increase by 30/15 mmHg from BP before 20 wk gestation) and proteinuria. Maternal diabetes (type 1 or 2), kidney disease (kidney or urinary tract disease), rheumatic disease (autoimmune connective tissue disease or inflammatory arthritides), and essential hypertension were recorded when present before pregnancy.

Outcome Variables

The outcome was development of ESRD, and onset was defined as the date of starting long-term dialysis treatment or undergoing renal transplantation. Causes of ESRD were divided into five categories: Glomerular disease (primary glomerulonephritis, inflammatory vascular disease, and systemic autoimmune disease), interstitial nephritis (upper urinary tract infections and nephropathy as a result of drugs or toxins), congenital disease (congenital kidney or urinary tract malformations, cystic kidney disease, and other heritable causes of renal disease), diabetic nephropathy, and other causes (renal vascular disease, amyloidosis, rare conditions, and idiopathic ESRD). Individuals who did not develop ESRD were followed until December 31, 2005, or date of death.

Statistical Analyses

Data were analyzed in a cohort design with birth-related variables as exposure and ESRD as outcome variables. RR estimates associated with selected risk factors for ESRD were obtained by Cox regression analyses. Because some analyses showed different results for men and women, analyses were stratified for gender. Analyses of the total cohort were adjusted for gender. Because development of ESRD had not been registered between 1967 and 1980, children who were born during this period were left truncated in the survival analyses before 1980. We therefore used the counting process formulation of proportional hazards.[26] This method did not include individuals in the analyses until an event could be registered (e.g., an individual who was born in 1975 would be included in the analyses at 5 yr of age and right-censored at 30 yr of age if the individual did not develop ESRD).

The analyses were performed with the statistical packages SPSS 14 (SPSS, Chicago, IL) and S-Plus 7.0 (Insightful Corp., Seattle, WA). Values are means $\pm$ SD or estimate (95% CI); $P < 0.05$ was considered statistically significant, and all tests were two tailed.

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DISCLOSURES

None.

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