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Timely Referral to Outpatient Nephrology Care Slows Progression and Reduces Treatment Costs of Chronic Kidney Diseases

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Introduction: We present a new approach to evaluate the importance of ambulatory nephrology care in patients with chronic kidney disease (CKD).

Methods: An anonymized health claims database of German insurance companies was searched in a retrospective analysis for patients with CKD using the codes of the International Classification of Diseases, 10th German modification. A total of 105,219 patients with CKD were identified. Patients were assigned to the group "timely referral," when nephrology care was present in the starting year 2009, or initiated during the following 3 years in CKD1–4. Using frequency matching for age and gender, 21,024 of the late referral group were matched with the equal number of patients in the timely referral group. Hospital admission rates, total treatment costs, and kidney function (change in CKD stages, start of dialysis, mortality) were documented each year during the 4-year follow-up.

Results: Hospital admission rates (110%–186%) and total treatment costs (119%–160%) were significantly higher ($P < 0.03$) in late referral compared with timely referral. In the timely referral group, significantly more patients did not change their CKD stage (65%–72.9% vs. 52%–64.6%, $P < 0.05$) compared with late referral. Starting in CKD3 more patients tended to start dialysis in 1 year in timely referral (1.9 ± 0.6 vs. 1.0 ± 0.4, $P = 0.1$). In contrast, death rates were significantly higher in the late referral group ($18.8 \pm 1.8\%$ vs. $6.7 \pm 0.4\%$, $P = 0.0001$).

Discussion: Timely referral to outpatient nephrology care is associated with slowed disease progression, less hospital admissions, reduced total treatment costs, and improved survival in patients with CKD.

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Chronic kidney disease (CKD) is an important risk factor of all-cause as well as cardiovascular mortality, the incidence of acute renal failure, and the progression to end-stage kidney disease in the need of renal replacement therapy. Similar to other industrialized countries such as Norway, Canada, and the USA, the prevalence of CKD3–5 (glomerular filtration rate < 60 ml/min per 1.73 m^2) in Germany is approximately 5% of the population.[1–3] Arterial hypertension, diabetes, and cardiovascular diseases are the main causes of progressive loss of kidney function. According to epidemiologic studies, patients with CKD3–5 in nonspecialized medical care lose approximately 5 ml/min per year of glomerular filtration rate.[4] Several studies suggest that the involvement of nephrologists in patient care starting at CKD3 (timely referral) results in a significant reduction of CKD progression to less than 2 ml/min per year.[5] Therefore, timely referral to nephrology care with optimized conservative and medical treatment prolongs the time until start of renal replacement therapy and may reduce significantly long-term treatment costs of CKD.

In this study, we choose a new approach to evaluate the importance of ambulatory nephrology care. Using the database of German health insurance companies, a cohort of patients was defined. Definition criteria were age, gender, CKD stage, and whether or not nephrology care had been introduced. We analyzed the association between outpatient nephrology care and (i) quality of disease coding, (ii) follow-up, (iii) rate of hospitalization,

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and (iv) mortality. Specifically, this paper evaluates the hypothesis that timely referral to nephrology care slows progression of CKD and reduces treatment costs.

METHODS

The study sample consisted of claims data from the German Health Risk Institute, which includes anonymized claims of approximately 80 different health insurance providers (of approximately 130 in Germany) and comprises the utilization of services on an anonymous patient-by-patient individual level. This research database comprises more than 3.3 million anonymized covered lives. The sample is representative for the German population in terms of age and gender.[6]

This database has been analyzed for the presence of CKD using the codes of the International Classification of Diseases, 10th German modification (ICD-10-GM). The ICD-10-GM allows us to identify the presence of CKD in general by the code N18.9. In addition, the CKD stages 1–5 can be indicated (N18.81, N18.82, N18.83, N18.84, N18.85 for the respective CKD stages until 2009; N18.1, N18.2, N18.3, N18.4, N18.5 for the respective CKD stages since 2010). Dialysis therapy in CKD5 can be indicated by adding codes Z49.*, Z99.2, EBM digits 40800–40808, 40812, 40813, 40820–40823, or OPS Code (ICPM) 8-854 to N18.5.

The inclusion criteria of this retrospective analysis were: (i) the presence of CKD stages 1–5 or dialysis therapy during the 4 years of observation from 2009 to 2012 in adults (age $>$ 18 years), (ii) at least one approved documentation of CKD stages 3–5 (N18.3, N18.4, N18.5) in ambulatory or inpatient care, and (iii) start of dialysis (Z49.*, Z99.2) in ambulatory or inpatient care. The exclusion criteria were: (i) loss of health insurance and (ii) loss of data during the observational period.

According to the inclusion criteria, all patients must have had at least once a documented CKD stage 3, 4, or 5 during the 4 years of observation. Using the pseudonyms, patients were tracked back to the first year of observation, 2009. Patients who had their first documentation of a CKD stage during the years 2010–2012 could have no CKD at all or no specified CKD stage in 2009.

To describe progression of CKD over time, the CKD stage had to be documented at least once a year. If different CKD stages were recorded in 1 year, the most advanced stage was used for analysis.

Timely versus late nephrology care was determined by documentation of care by a nephrologist during the 4-year study period. If nephrology care was received, the time point of first contact to a nephrologist was recorded.

Patients were assigned to group 1 "timely referral" (i) when information on CKD stage was available and nephrology care was present in 2009, or (ii) when during follow-up until 2012 start of nephrology care was documented in CKD1–3. Group 2 "late referral" included (i) all patients with a known CKD stage including clinical dialysis but without ambulatory nephrology care in 2009, (ii) no contact to a nephrologist throughout the study period, or (iii) start of ambulatory nephrology care in CKD5 or on dialysis in 2010–2012.

Using these definitions, n = 105,219 patients fulfilled the inclusion criteria of our observation, n = 21,024 patients were assigned to timely referral and n = 84,195 patients to late referral. In the timely referral group, n = 8771 women, age (mean ± SD) 70.9 ± 12.1 years, and n = 12,253 men, age 68.9 ± 12.0 years, were included. Frequency matching for gender and age (5-year intervals) was performed to demographically adjust n = 21,024 patients of the late referral group to the timely referral cohort. We used the age when stage CKD3 or worse was documented for the first time (Figure 1).

After adjustment of the 2 cohorts, patients were grouped according to available information on the CKD stage.

As shown in Table 1, in the first year of observation (2009), the mean age and gender were comparable in both timely and late referral groups at all stages of CKD. The number of patients without specified information on the CKD stage ("no CKD" and "unknown") was higher in the late referral group (n = 12,213, 58.0%) than in the timely referral group (n = 8381, 39.9%). There were 4 times more patients on dialysis in the timely than in the late referral group.

As shown in Table 2, during the starting year 2009, considerable numbers of patients died before the end of 2009; for timely and late referral, n = 527 and n = 926, respectively. Only the surviving patients in the 2 groups, n = 20,515 (timely) and n = 20,098 (late), were included in the follow-up study.

During follow-up, changes in the CKD information were documented at 3 time points comparing 1-year periods 2009/2010, 2010/2011, and 2011/2012. In case the CKD stage changed during 1 year, the most advanced stage was used for analysis.

Table 3 shows the distribution of timely referral patients during the first transition from 2009 to 2010. For example, n = 5759 patients started in CKD3. Some patients lost detailed CKD information and were grouped in "no CKD" (n = 1007) or "unknown" (n = 818) in 2010, leading to n = 3934 patients who kept specific information on their CKD stage in 2010.

For subsequent analyses, only patients who started the year with a specified CKD stage (CKD1–5 or

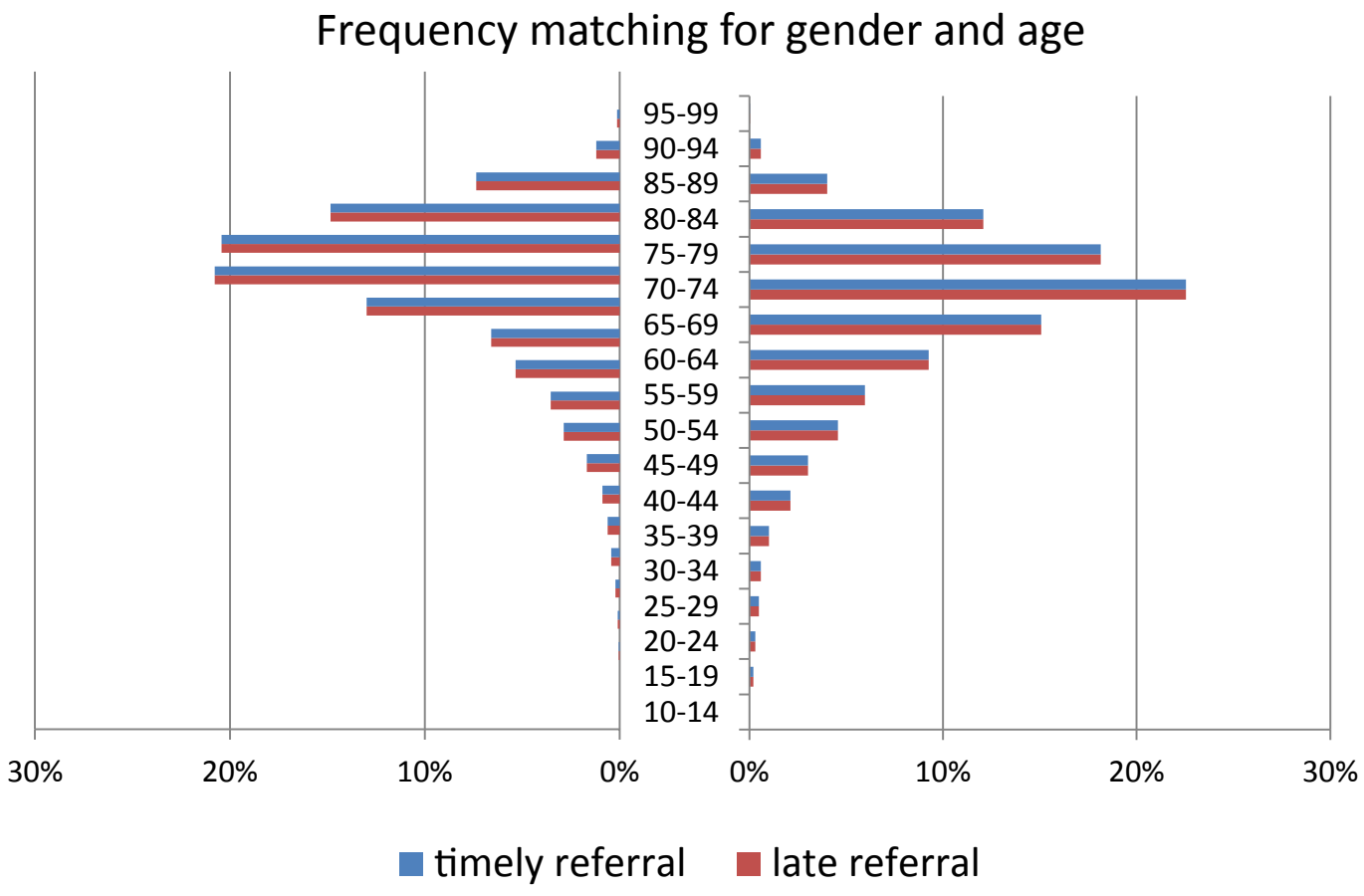


Figure 1. Frequency matching for gender and age using 5-year intervals. The paired bars represent the percentage of patients in the particular age group. Total numbers of women and men and mean ages ± SD are given.

dialysis) were included (highlighted box in Table 3). The total number of patients in the timely referral group in transition from 2009 to 2010 adds up to n = 9430 patients (Table 3).

Table 1. Distribution of chronic kidney disease (CKD) stages in the 2 study groups in 2009

	Timely referral			Late referral		
CKD stage	Mean age (yr ± SD)	Female (%)	Patient number	Mean age (yr ± SD)	Female (%)	Patient number
No CKD	67.8 ± 11.4	43.0	7,084	67.6 ± 12.1	44.7	11,423
CKD stage not specified	69.6 ± 11.5	37.6	1,297	70.6 ± 10.8	35.4	790
CKD1	67.7 ± 12.2	40.9	237	69.9 ± 11.4	35.2	236
CKD2	69.5 ± 11.2	37.4	1,282	70.3 ± 10.6	35.1	972
CKD3	69.4 ± 11.3	40.8	5,849	69.4 ± 11.5	38.6	5,562
CKD4	72.1 ± 11.8	49.3	1,690	71.2 ± 12.3	44.8	946
CKD5	65.4 ± 14.4	43.5	580	64.3 ± 14.7	37.8	368
Dialysis	66.6 ± 14.3	39.6	3,005	61.1 ± 15.4	35.2	727
Total number			21,024			21,024

Stable kidney function is defined as the unchanged CKD stage in transition from one year to the next. In the first transition 2009/2010, the numbers of patients with stable function in CKD3, CKD4, and CKD5 are depicted in bold numbers (Table 3). These 3 numbers add up to 3723, which represents 65% of all patients with CKD3–5 in the timely referral group during the first transition (see Table 3). Similar tables

Table 2. Stages of chronic kidney disease (CKD) in the end of the starting year 2009

	Stage	Timely referral	Late referral
Last stage in 2009 (start year)	No CKD	7,084	11,423
	Unknown	1,297	790
	CKD1	237	236
	CKD2	1,282	972
	CKD3	5,759	5,017
	CKD4	1,595	728
	CKD5	548	316
	Dialysis	2,695	616
	Died	527	926
	Total	n = 21,024	n = 21,024

Table 3. Number of timely referral patients in the transition 2009/2010 with known chronic kidney disease (CKD) stage

		2010									
		No CKD	Unknown	CKD1	CKD2	CKD3	CKD4	CKD5	Dialysis	Died	Sum
2009	No CKD	4243	369	66	277	1868	116	13	54	78	
	Unknown	84	550	11	57	420	73	13	44	45	
	CKD1	45	38	42	20	80	5	1	3	3	154
	CKD2	228	142	23	288	462	66	12	22	39	912
	CKD3	1007	818	52	283	**2842**	347	40	102	268	3934
	CKD4	113	130	5	33	197	**697**	62	176	182	1352
	CKD5	68	42	4	18	60	62	**184**	77	33	438
	Dialysis	28	27	1	6	17	29	36	2167	384	2640
										Total	9430

Bold numbers add up to 3723, which represents 65% of all patients with CKD3–5 in the timely referral group during the first transition.

and calculations were produced for the transitions 2010/2011 and 2011/2012 in both groups (data not shown).

As shown in Table 4, compared with the timely referral group, twice as many patients in the late referral group lost specific CKD information during all 3 time periods. However, coding of CKD information improved during the following years resulting in lower numbers of patients with lost data in both groups, 12.5% and 27.8% in the timely and late referral groups, respectively.

Comorbidities were listed throughout the study period when CKD stage 3 or higher was coded for the first time.

Data on the hospital admission rates as well as the total costs for in-hospital care, outpatient care, and medication are expressed per patient per year. Total costs include all invoices issued by hospitals, ambulatory care, and pharmacies covered by the health insurance. In Germany, nonmedical costs for dialysis care (nursing, disposals) are covered by fixed prices per week that are excluded from these calculations. The results are expressed as median (min/max) of the 4 years, 2009 through 2012.

Statistics

Results are expressed as median (min/max) in Figures 2 and 3 or as means ± SD in Figure 5. To describe statistically significant differences, Student's *t*-test for paired observations was employed. A Kaplan-Meier analysis was done on the probability of survival in patients with CKD3 starting in 2009 (Figure 6).

RESULTS

Comorbidities

The predominant comorbidities were identified by ICD coding during the year when CKD3 or higher was coded for the first time (Table 5).

Chronic heart failure and disturbances of acid-base status and electrolyte plasma levels were more frequently noted in the late referral group. All other comorbidities were comparable in both the groups.

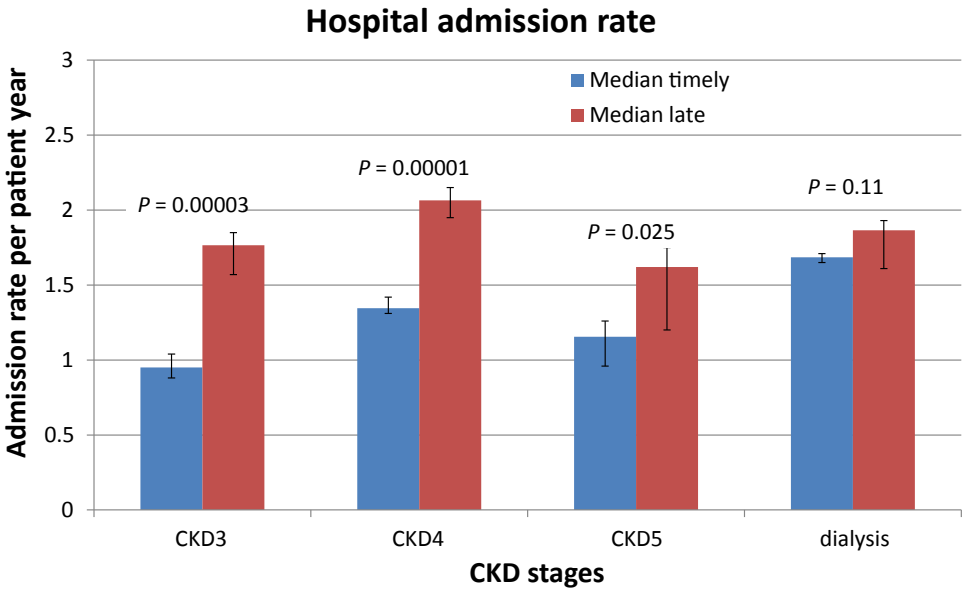


Figure 2. Hospital admission rates per patient per year. Bars represent the median (min/max) of n = 4 years (2009–2012) for patients with CKD3–5 and dialysis treatment. *P* values are given for comparison of the paired bars. The median (min/max) numbers of patients timely versus late were, for CKD3, n = 6724 (5759/8151) versus n = 5137 (4219/6128); for CKD4, n = 1682 (1395/1988) versus n = 1064 (728/1392); for CKD5, n = 447 (361/548) versus n = 259 (181/316); and for hemodialysis, n = 2593 (2521/2695) versus n = 778 (616/909). CKD, chronic kidney disease.

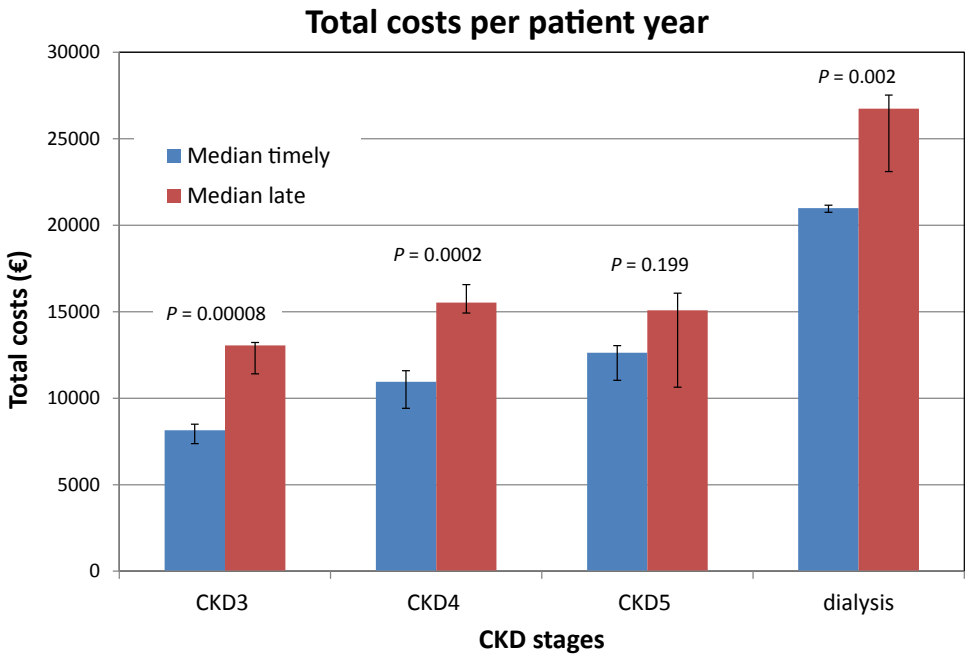


Figure 3. Total costs per patient per year in Euro (€). Bars represent the median (min/max) of n = 4 years (2009–2012) for patients with CKD3–5 and dialysis treatment. *P* values are given for comparison of the paired bars. For numbers of patients in the analyzed groups, see the legend of Figure 2. CKD, chronic kidney disease.

Hospital Admission Rates

The hospital admission rate per patient per year throughout the 4-year observation was significantly higher in the late referral group for all patients with CKD3–5 (Figure 2). Patients with CKD3 had a hospital admission rate of (median [min/max]) 0.95 (0.88/1.04) and 1.77 (1.57/1.85) ($P = 0.00003$) in the timely and late referral groups, respectively. In CKD4, the admission rates were 1.35 (1.31/1.42) versus 2.07 (1.95/2.15) ($P = 0.00001$); in CKD5, the admission rates were 1.16 (0.96/1.26) versus 1.62 (1.20/1.75) ($P = 0.025$) in favor of the timely referral group. For patients on dialysis treatment, the admission rate in the late referral group tended to be higher than in the timely referral group, 1.69 (1.65/1.71) versus 1.87 (1.61/1.93) without reaching statistical significance ($P = 0.11$).

Total Treatment Costs

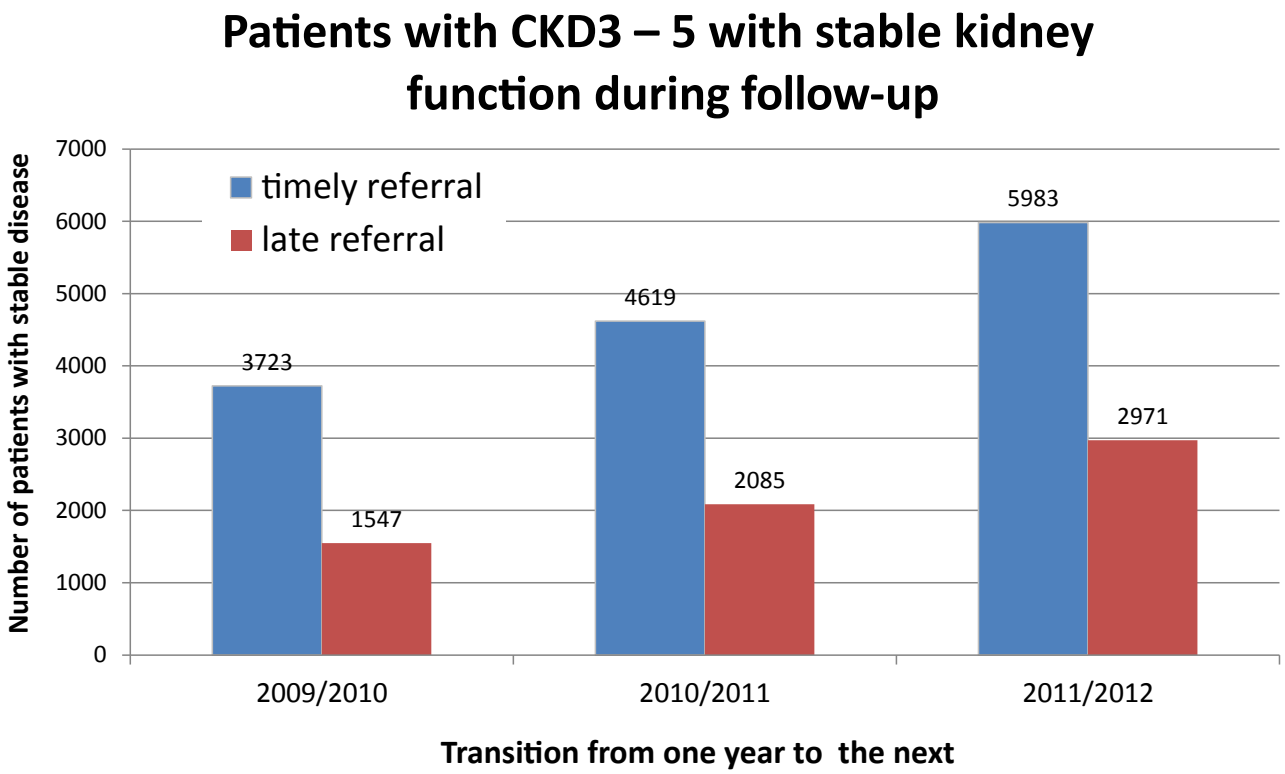
During the 4 years of observation, the expenses for hospital care, ambulatory care, and medication were added up to total costs per patient per year (Figure 3). In patients with CKD3, the median (min/max) costs in the timely referral group were 8149 (7375/8504) € versus 13,054 (11,409/13,223) € in the late referral group ($P = 0.00008$). For patients with CKD4, expenses increased and were significantly higher in the late referral group: 10,953 (9413/11,587) € (timely) versus 15,526 (14,922/16,563) € (late) ($P = 0.0002$). In patients with CKD5, the difference between the 2 groups was not significant: 12,634 (11,040/13,035) € versus 15,085 (10,633/16,069) € ($P = 0.199$). Interestingly, patients on hemodialysis in the late referral group caused significantly higher expenses for the health insurance companies: 20,991 (20,750/21,166) € (timely) versus 26,747 (23,105/27,526) € (late) ($P = 0.002$).

Patients With Stable CKD Stages

In patients with CKD3–5, the number of patients with stable disease was 8% to 13% higher in the timely than in the late referral group (Figure 4). In the transition period 2009/2010, 65% of patients in the timely referral group versus 52% in the late referral group kept their CKD stages. These differences persisted during the following years: 71.5% (timely) versus 60.3% (late) in 2010/2011 and 72.9% (timely) versus 64.6% (late) in 2011/2012 (Figure 4).

CKD Progression and Mortality

In patients with initial CKD3, timely referral to a nephrologist resulted in stability of their CKD stage (75.1 ± 2.6% in the timely referral vs. 63.0 ± 6.3% in the late referral, $P = 0.037$). As shown in Figure 5, the death rate was significantly higher in the late referral group than in the timely referral group (18.8 ± 1.8% vs. 6.7 ± 0.4%, $P = 0.0001$). The percentages of patients improving to CKD stage 1or 2 as well as those deteriorating to CKD stage 4 or 5 were low in both groups without significant differences (Figure 5). The percentage of patients starting dialysis tended to be higher in the timely referral group (1.9 ± 0.6 vs. 1.0 ± 0.4%, $P = 0.10$) without reaching significance.



	2009/2010			2010/2011			2011/2012		
	timely	late	*P* value	timely	late	*P* value	timely	late	*P* value
Stable patients (%)	65.0	52.0	0.009	71.5	60.3	0.049	72.9	64.6	0.006

Figure 4. Total number of patients with stable kidney function in transition from one year to the next. Mean percentages of patients with stable disease in the 2 groups are given in the table underneath. *P* values are depicted. CKD, chronic kidney disease.

Similar results were seen in CKD4 (not shown). More patients with timely referral maintained their stage compared with the late referral group (57.2 ± 5.0% vs. 46.6 ± 7.0%, $P = 0.1$). Also the death rate followed a similar pattern being significantly higher in the late referral group (23.1 ± 3.5% vs. 12.6 ± 0.5%, $P = 0.006$) and more patients started dialysis in the timely referral group (11.4 ± 2.0% vs. 6.4 ± 0.2%, $P = 0.013$).

Probability of Patient Survival

A Kaplan-Meier analysis on the probability of survival was done in patients with CKD3 starting in 2009 (Figure 6). The numbers at risk were n = 5759 and n = 5017 for timely referral and late referral, respectively. The proportion of patients surviving in the 3-year follow-up was significantly higher in the timely referral group with a log rank of $P = 0.0001$ (Figure 6).

DISCUSSION

In this paper, we analyzed the anonymized database of German health insurance companies to describe the importance of timely outpatient nephrology care in patients with CKD with respect to hospitalization, treatment costs, progression of kidney disease, and mortality.

Table 4. Loss of specified chronic kidney disease (CKD) information during follow-up

	2009/2010		2010/2011		2011/2012	
	Timely referral	Late referral	Timely referral	Late referral	Timely referral	Late referral
Start with CKD information: total number of patients	12,116	7885	11,533	7033	13,237	8343
Loss of CKD information: number of patients (%)	2686 (22.17)	3597 (45.62)	1477 (12.80)	2183 (31.00)	1659 (12.53)	2323 (27.84)
Remaining number of patients for analysis (%)	9430 (77.83)	4288 (54.38)	10,056 (87.20)	4850 (69.00)	11,578 (87.47)	6020 (72.16)

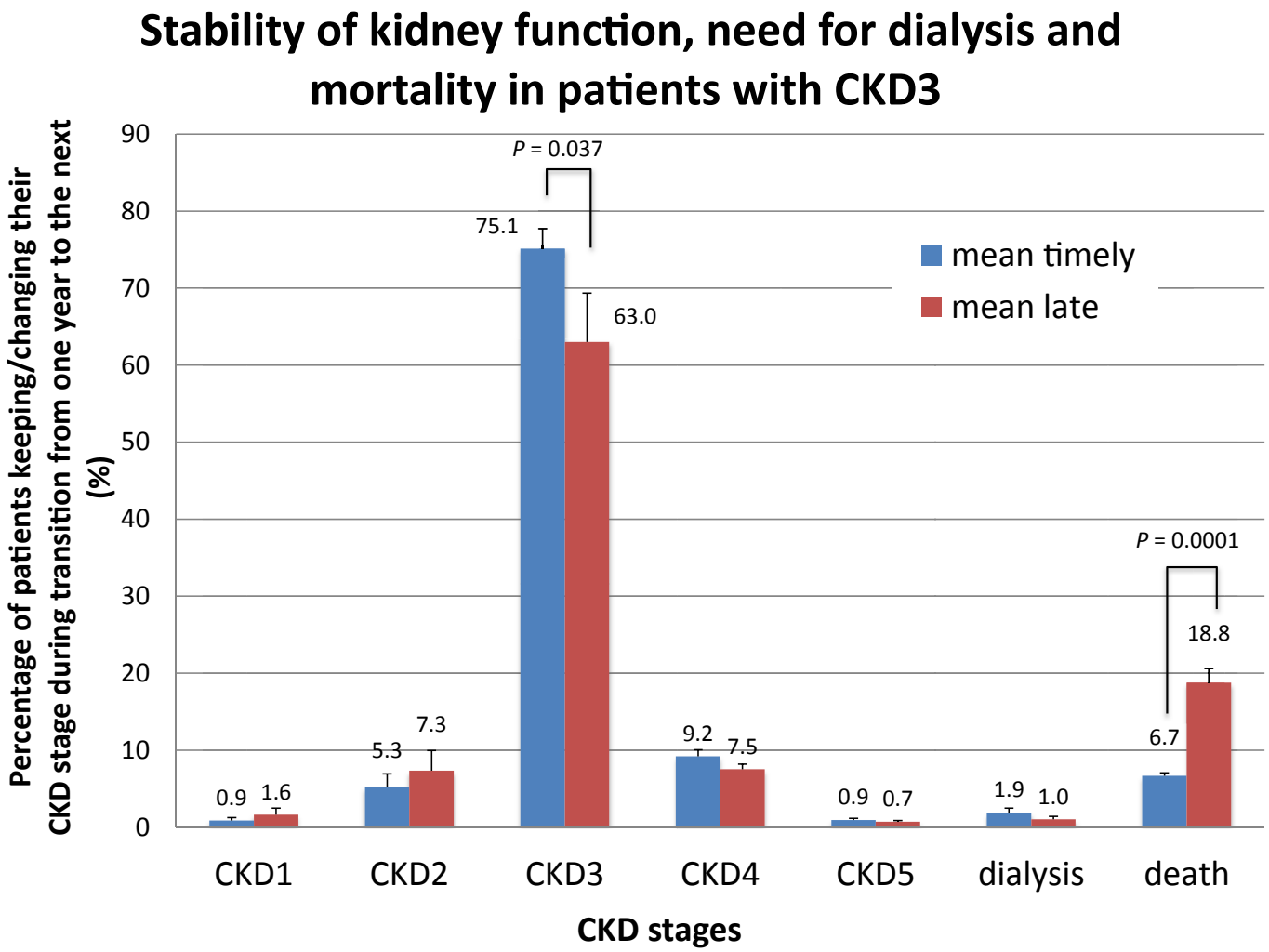
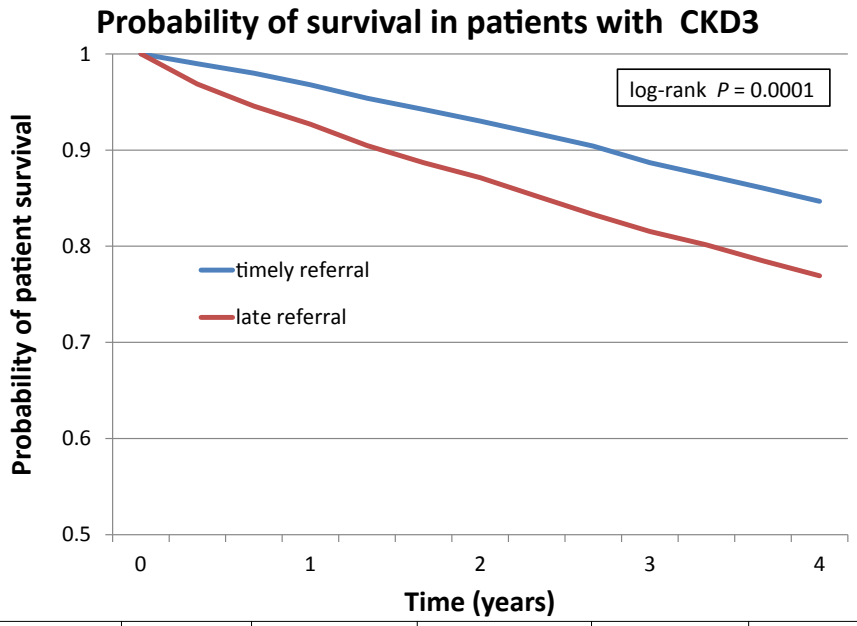


Figure 5. Stability of kidney function, start of dialysis, and mortality in patients starting with CKD stage 3. The bars represent the means ± SD of n = 3 transitions from one year to the next (2009/2010, 2010/2011, 2011/2012). *P* values for significant changes are given, for comparison of the paired bars. The numbers of patients timely versus late were 3934 versus 2337, 4830 versus 2600, and 6132 versus 3437 for the 3 time points. CKD, chronic kidney disease.

The severity of CKD was exclusively determined by the ICD-10 codes classifying the CKD stages. Laboratory data on kidney function, for example, according to the chronic kidney disease epidemiology collaboration formula, were not available. It became obvious that specific ICD coding of CKD stages was done much more thoroughly in the timely referral group (Table 1) resulting in 60.1% and 41.9% of patients in timely versus late referral with detailed information on the CKD stages in 2009. During the following 3 years of observation (2010–2012), coding of the CKD stage gradually improved resulting in decreased loss of CKD information (Table 4) increasing the sample size and thereby the power of the study. Explanations for these improvements remain speculative. Possibly, acceptance of detailed CKD coding improved with the modification of the ICD-10 system in 2010. This modification includes increasing reimbursements with higher specified CKD codes.

Continuous precise coding of the CKD stage as well as documentation of mortality is essential to obtain reliable longitudinal data sets. With respect to patients with CKD, this data documentation seems to be better done by nephrologists than by nonspecialists. Although the loss of specific CKD information during follow-up may weaken the value of the results, the analysis was carried out in 13,718 (2009/2010) to 17,598 (2011/2012) patients, which should result in a fairly powerful study.

After adjustment for gender and age, comorbidities were documented in the year when CKD stage 3 or worse was reached (Table 5). Almost all patients suffered from hypertension and 46% to 49% had diabetes. Interestingly, atrial fibrillation and disturbances of acid-base status and electrolytes appear to be more common in the late referral group. This may indicate that nephrologists pay more attention to these disturbances and treat metabolic acidosis by prescribing oral bicarbonate more often than nonspecialists. Taken together, the study cohort with a mean age of 70.0 ± 12.1 years, 42% females, and the distributed comorbidities represents the typical population with the risk of progressive CKD.[3]



Numbers at risk	start	1	2	3	4
Timely referral	5759	5574	5357	5108	4876
Late referral	5017	4650	4372	4091	3859

Figure 6. Kaplan-Meier analysis on the probability of patient survival in patients with CKD3 starting in 2009. The numbers at risk are depicted in the table underneath. The log rank is highly significant with $P = 0.0001$. CKD, chronic kidney disease.

Timely Referral Is Associated With Lower Hospital Admission Rates and Reduced Treatment Costs

The hospital admission rates for any medical reason as well as the total expenses for hospital care, outpatient care, and medication were compared per CKD stage and year in the 2 study groups (Figures 2 and 3). The hospital admission rate was significantly higher in the late referral group than in the timely referral. It remains unclear why in both groups the admission rate in CKD5 tended to be lower than in CKD4. The threshold between CKD4 and CKD5 is an estimated glomerular filtration rate of 15 ml/min. The frequency of hospital admissions may not be significantly different between CKD4 and nondialysis CKD5. Similarly, the total treatment costs were significantly higher when patients with CKD were in the late referral group. The health care costs for dialysis patients seem to be low. This is explained by the fact that expenses for nursing, overhead, and single-use dialysis material are not included. These results are in agreement with published retrospective analyses on the effect of timely referral to nephrology care on treatment costs.[7,8]

Those data strongly indicate that outpatient nephrology care should be initiated at the latest in patients with CKD stage 3 to reduce the need of hospital care and total treatment costs.

Table 5. Comorbidities in the 2 study groups

Diagnoses	Timely referral n = 20,962 (%)	Late referral n = 20,628 (%)
Hypertension	93	87
Hypertensive cardiac disease	24	23
Chronic heart failure	36	44
Chronic ischemic heart disease	45	46
Atrial fibrillation	24	30
Diabetes mellitus type 2	49	46
Disturbances of acid-base status and electrolytes	25	35
Adiposity	32	30
Lipid disorders	66	59

n, patient number.

Timely Referral Is Associated With Reduced Disease Progression and Mortality in CKD

We also analyzed improvement, stabilization, and progression of CKD and mortality comparing the distribution of those parameters in the CKD stages from one year to the next. Starting with 2009, in all transitions, timely referral as compared with late referral resulted in approximately 13% more patients who remained in their CKD stages 3–5. In other words, patients in nephrology care had more often stable kidney function indicating slower progression of renal disease. Our data confirm results of the German CKD registry demonstrating that approximately 70% patients with

CKD3–4 in outpatient nephrology care had a stable CKD stage.[9]

Only a few patients improved to better CKD stages without significant differences between the 2 groups. In the timely referral cohorts, more patients started hemodialysis treatment, but death rates were significantly lower in the timely referral group. These data are supported by the Kaplan-Meier analysis on the probability of survival in patients starting in CKD3 in 2009. After 4 years of follow-up, approximately 85% of patients in the timely referral group versus only 77% in the late referral group survived (log rank, $P = 0.0001$). These data suggest that patients in outpatient nephrology care may survive longer, in part for the price of starting extracorporeal renal replacement therapy.

The strength of the presented retrospective analysis is based on the relatively high number of patients identified in an anonymized database of 80 health insurance providers. The study cohort including more than 42,000 patients seems to be representative for the German society in respect to age and gender distribution, because the CKD registry shows similar numbers.[9]

LIMITATIONS

This being an observational study, associations can be reported. Also the diagnostic performance of ICD-10 codes is not known, which may be a limitation. We pointed out that correct coding and the documentation of changes in CKD stages are improved but still not complete in nephrology care. Another limitation is the lack of data on proteinuria. Future studies should use the KDIGO classification instead of CKD coding only. A further disadvantage in analyzing an anonymized database is that longitudinal data are not available. Only changes in CKD stages in the defined study groups are documented with significant differences between the timely and late referral groups during the transition from one year to the next.

Keeping in mind that our analysis of a very large database of health insurance companies is a new approach to perform a retrospective study, our results are in agreement with retrospective clinical studies demonstrating that the early initiation of nephrology care slows down progression of CKD.[5,10,11] Mortality in incident dialysis patients is significantly reduced when outpatient nephrology care is initiated at least 3–12 months before the start of renal replacement therapy.[12,13] Improved mortality is, at least in part, due to a timely creation of a native arteriovenous fistula before the start of hemodialysis.[14,15] Although we did not study the role of vascular access on survival of hemodialysis patients, our data add evidence that timely referral to nephrology care improves survival of patients with CKD. In addition, the presented data suggest that hospital admission rates and total treatment costs are reduced as well when nephrology centers are involved in the treatment of patients with CKD stage 3 or worse.

DISCLOSURE

All the authors declared no competing interests.

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REFERENCES

1. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298:2038–2047.
2. Hallan SI, Coresh J, Astor BC, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *J Am Soc Nephrol*. 2006;17:2275–2284.
3. Vassalotti JA, Li S, Chen SC, Collins AJ. Screening populations at increased risk of CKD: the Kidney Early Evaluation Program (KEEP) and the public health problem. *Am J Kidney Dis*. 2009;53(Suppl 3):S107–S114.
4. Perkins RB, Bucaloiu ID, Kirchner HL, et al. GFR decline and mortality risk among patients with chronic kidney diseases. *Clin J Am Soc Nephrol*. 2011;6:1879–1886.
5. Jones C, Roderick P, Harris S, Rogerson M. Decline in kidney function before and after nephrology referral and the effect on survival in moderate to advanced chronic kidney disease. *Nephrol Dial Transplant*. 2006;21:2133–2143.
6. Anderson F, Walker J. Characteristics and external validity of the German Health Risk Institute (HRI) Database. *Pharmacoepidemiol Drug Saf*. 2016;25:106–109.
7. Fishbane S, Hazzan AD, Halinski C, Mathew AT. Challenges and opportunities in late-stage chronic kidney disease. *Clin Kidney J*. 2015;8:54–60.
8. Lee J, Lee JP, Park JI, et al. Early nephrology referral reduces the economic costs among patients who start renal replacement therapy: a prospective cohort study in Korea. *PLoS One*. 2014;9:e99460.
9. Kleophas W, Bieber B, Robinson BM, et al. Implementation and first results of a German chronic kidney disease registry. *Clin Nephrol*. 2013;79:184–191.
10. Smart NA, Titus TT. Outcomes of timely versus late nephrology referral in chronic kidney disease: a systemic review. *Am J Med*. 2011;124:1073–1080.
11. Hommel K, Madsen M, Kamper AL. The importance of timely referral for the treatment of chronic kidney disease: a Danish nationwide cohort study. *BMC Nephrol*. 2012;13:108.
12. Singhal R, Hux JE, Alibhai SM, Oliver MJ. Inadequate predialysis care and mortality after initiation of renal replacement therapy. *Kidney Int*. 2014;86:399–406.

13. Gillespe BW, Morgenstern H, Hedgeman E, et al. Nephrology care prior to end-stage renal disease and outcomes among new ESRD patients in the USA. *Clin Kidney J*. 2015;8:772–780.

14. Banerjee T, Kim SJ, Astor B, et al. Vascular access type, inflammatory markers, and mortality in incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. *Am J Kidney Dis*. 2014;64:954–961.

15. Rivara MB, Soohoo M, Streja E, et al. Association of vascular access type with mortality, hospitalization, and transfer to in-center hemodialysis in patients undergoing home hemodialysis. *Clin J Am Soc Nephrol*. 2016;11:298–307.