The Treatment of Iron Deficiency/Anaemia in Patients with Non-Dialysis Chronic Kidney Disease in Germany – A Claims Database Analysis

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BACKGROUND

- The prevalence of Iron Deficiency/Anaemia (ID/A) in chronic kidney disease (CKD) patients ranges from 8% to 53% depending on the respective CKD stage, also showing occurrence in chronic kidney disease patients who are not on dialysis (ND CKD).[1]
- If left untreated, ID/A is associated with reduced functional capacity, poor quality of life, and increased mortality.[2]
- In patients receiving haemodialysis, intravenous iron has been shown to be significantly more effective than oral iron for replenishing depleted iron stores and improving haemoglobin levels.[3] However, in patients with ND CKD, the evidence base supporting optimal iron management is not as strong.[4]

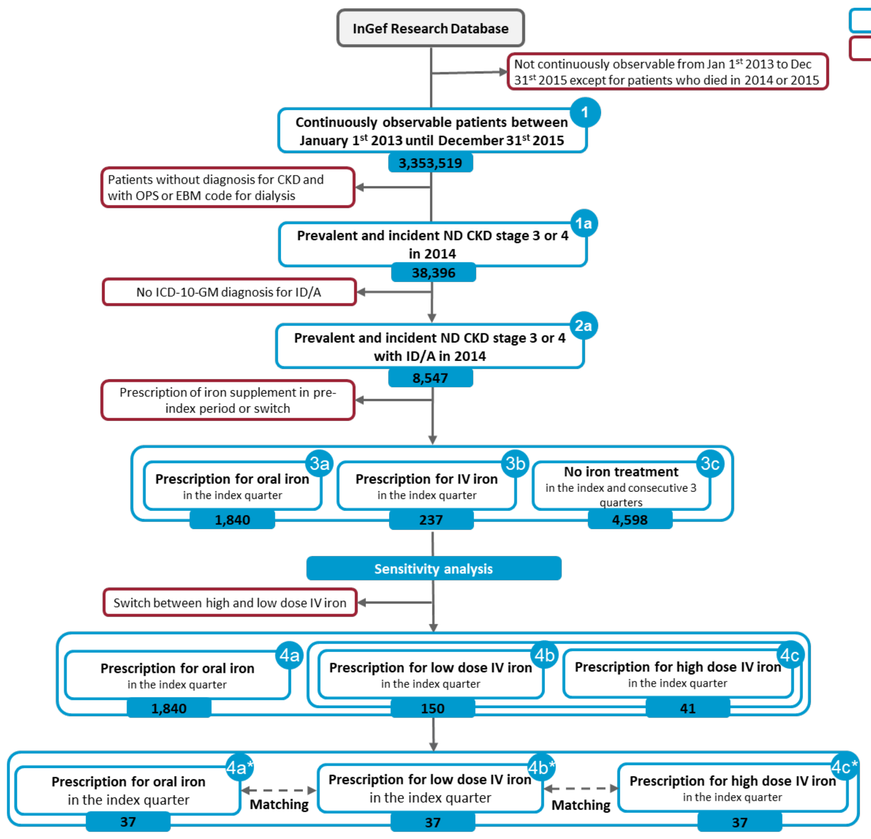
OBJECTIVE

- This study aimed at comparing health-related outcomes and healthcare costs of ND CKD patients with comorbid ID/A, who receive different types of iron treatment in Germany.

METHODS

- A retrospective claims database analysis was conducted using the “Institut für angewandte Gesundheitsforschung Berlin” (InGef) research database.
- The database comprises anonymized healthcare claims of approximately 4 million covered lives insured in the Statutory Health Insurance (SHI) in Germany.
- The sample represents about 4.8% of the German population and about 5.6% of the German SHI population and is structured to represent the German population in terms of age and gender (structure of age and gender according to the Federal Office of Statistics (DESTATIS)). It has also proven to have good external validity to the German population in terms of morbidity, mortality and drug use.[5]
- Data from January 1st, 2013 through September 30th, 2015 was used for this analysis.
- The enrolment period for the patient selection spanned from January 1st, 2014 through December 31st, 2014, to allow for an individual pre-index period of 4 quarters (Q1 2013 to Q3 2014) as well as an individual post-index period including the index quarter (defined as the first observable iron prescription in 2014) and 3 consecutive quarters (Q1 2014 to Q3 2015).
- ND CKD patients stages 3 and 4 with ID/A were identified by ICD-10-GM codes N18.3 and N18.4 for CKD and D50* (except D50.1), D63.8 and E61.1 for ID/A. Patients were excluded if they had any Operation and Procedure (OPS) code or any Practitioners' Fee Scale within the Statutory Health Insurance Scheme (EBM) code for dialysis from January 1st, 2014 through December 31st, 2014.
- Incident iron treatment which was identified based on Anatomical Therapeutic Chemical Classification (ATC) codes and Pharmacy Central Numbers (PZN) defined the index quarter in 2014.
- Iron treatment was stratified by oral iron, low dose (<1000mg per year) IV iron and high dose (≥1000mg per year) IV iron **(see Figure 1)**.

Figure 1. Patient flow chart



- A 1:1:1 propensity score matching was performed for patients with oral, low dose IV, and high dose IV iron treatment using age, gender, Charlson Comorbidity Index (CCI), and baseline costs as matching parameters.
- ID/A-, cardiovascular- (CV), and ND CKD-related hospitalisations were analysed for the matched cohorts in the post-index period in terms of number of patients with hospitalisations, number of hospitalisations, and length of inpatient stays. The primary and secondary diagnoses were taken into account for the respective hospitalisation.
- Healthcare costs in the post-index period were assessed for inpatient care (all-cause) and stratified by hospitalisations due to ID/A, CV, and ND CKD (only taking those hospitalisations with the respective diagnoses in the primary position into account to avoid double counting of costs).
- Furthermore, all-cause mortality was determined for all patients.
- Differences between the matched cohorts were compared using McNemar’s test, Wilcoxon signed rank/rank-sum test, Fisher’s exact test, Chi-squared test or Paired t-test.

RESULTS

- In total, n=1,840 ND CKD patients with comorbid ID/A receiving oral iron treatment, n=150 low dose IV iron treatment, and n=41 high dose IV iron treatment were identified in the database in the enrolment period.
- Out of those patients with high dose IV iron treatment, all were treated with Ferric Carboxymaltose.
- After propensity score matching, 37 patients remained in each of the three treatment cohorts (4a* oral iron, 4b* low dose IV iron and 4c* high dose IV iron) **(see Tables 1 and 2)**.

Table 1. Matching parameters / baseline characteristics before matching – Groups 4a-4c

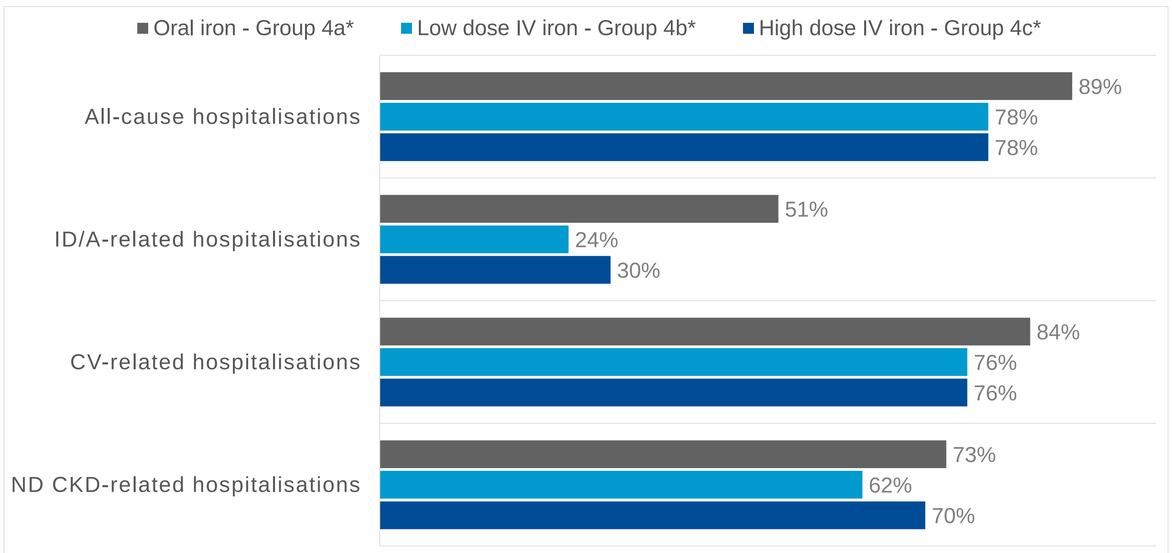
	Group 4a ND CKD stage 3 or 4 patients with ID/A and with oral iron prescription	Group 4b ND CKD stage 3 or 4 patients with ID/A and with low dose IV iron prescription	Group 4c ND CKD stage 3 or 4 patients with ID/A and with high dose IV iron prescription	Group 4a vs. 4b p-value	Group 4b vs. 4c p-value	Group 4a vs. 4c p-value
Age (mean, ± std)	78.99 ± 9.85	77.54 ± 10.44	75.2 ± 9.43	0.113[3]	0.073[3]	0.003[3]
Male (n, %)	860 (47%)	63 (42%)	23 (56%)	0.301[2]	0.152[2]	0.303[2]
Female (n, %)	980 (53%)	87 (58%)	18 (44%)	0.301[2]	0.152[2]	0.303[2]
CCI 0–<1 (n, %)	81 (4%)	<5	<5	0.018[1]	0.117[1]	0.702[1]
CCI 1–<2 (n, %)	140 (8%)	10 (7%)	<5	0.795[2]	1.000[2]	0.765[2]
CCI 2–<3 (n, %)	175 (10%)	11 (7%)	<5	0.462[2]	0.738[2]	0.424[2]
CCI 3–<4 (n, %)	293 (16%)	26 (17%)	12 (29%)	0.736[2]	0.140[2]	0.038[2]
CCI 4+ (n, %)	1151 (63%)	102 (68%)	23 (56%)	0.215[2]	0.217[2]	0.496[2]
Baseline costs (mean, ± std)	€13,287 ± €16,830	€15,079 ± €15,977	€14,851 ± €14,327	0.027[3]	0.663[3]	0.536[3]
Notation: [1]Fisher's exact test; [2]Chi-squared test; [3]Wilcoxon rank-sum test						

Table 2. Matching parameters / baseline characteristics after matching – Groups 4a*-4c*

	Group 4a* ND CKD stage 3 or 4 patients with ID/A and with oral iron prescription	Group 4b* ND CKD stage 3 or 4 patients with ID/A and with low dose IV prescription	Group 4c* ND CKD stage 3 or 4 patients with ID/A and with high dose IV prescription	Group 4a* vs. 4b* p-value	Group 4b* vs. 4c* p-value	Group 4a* vs. 4c* p-value
Age (mean, ± std)	77.08 ± 8.39	75.95 ± 11.1	76.49 ± 7.84	0.263[3]	0.293[3]	0.437[3]
Male (n, %)	18 (49%)	19 (51%)	19 (51%)	0.625[1]	1.000[1]	0.500[1]
Female (n, %)	19 (51%)	18 (49%)	18 (49%)	0.625[1]	1.000[1]	0.500[1]
CCI 0–<1 (n, %)	0 (0%)	0 (0%)	0 (0%)	1.000[1]	1.000[1]	1.000[1]
CCI 1–<2 (n, %)	0 (0%)	<5	<5	1.000[1]	1.000[1]	1.000[1]
CCI 2–<3 (n, %)	<5	<5	<5	1.000[1]	1.000[1]	1.000[1]
CCI 3–<4 (n, %)	11 (30%)	10 (27%)	10 (27%)	1.000[1]	1.000[1]	1.000[1]
CCI 4+ (n, %)	23 (62%)	23 (62%)	23 (62%)	1.000[1]	1.000[1]	1.000[1]
Baseline costs (mean, ± std)	€13,460 ± €10,136	€13,038 ± €9,762	€15,301 ± €14,182	0.647[2]	0.185[2]	0.411[3]
Notation: [1]McNemar’s test (mid-p version); [2]Paired t-test; [3]Wilcoxon signed rank test						

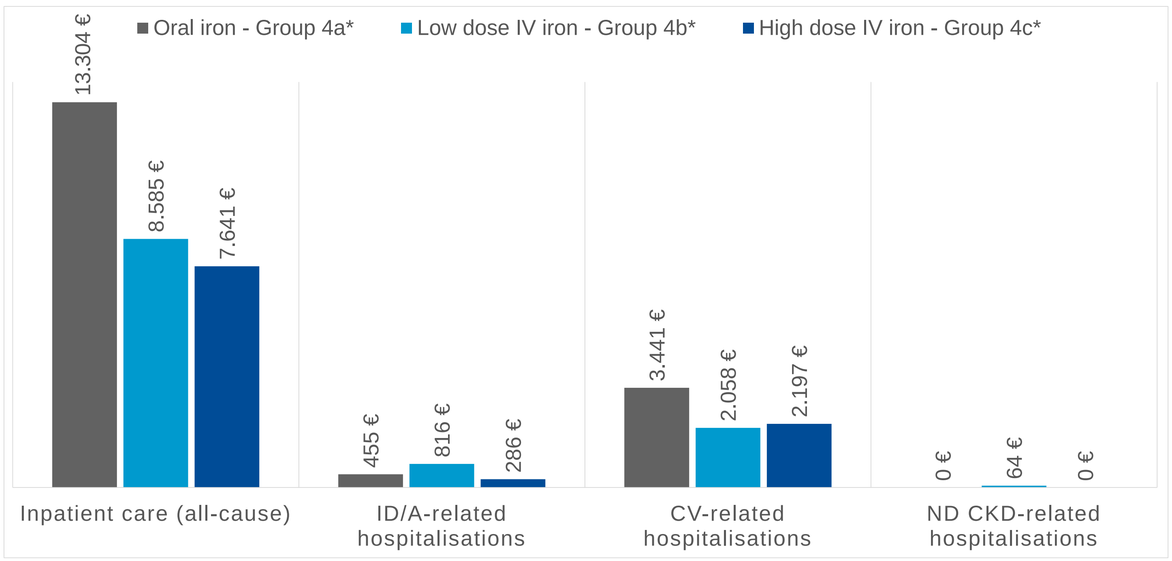
- Differences were observed concerning all-cause hospitalisations (oral iron vs. high dose IV iron (89.2% vs. 78.4%, p=0.227)). Furthermore, both CV-related and ND CKD-related hospitalisations were highest in the matched oral iron cohort (CV-related: oral iron vs. low dose IV iron (84% vs. 76%, p=0.424); ND CKD-related: oral iron vs. low dose IV iron (73% vs. 62%, p=0.359)) **(see Figure 2)**.
- ID/A-related hospitalisations (oral iron vs. low dose IV iron (51.4% vs. 24.3%, p=0.027) and oral iron vs. high dose IV iron (51.4% vs. 29.7%, p=0.049)) were significantly lower **(see Figure 2)**.

Figure 2. Patients with all-cause and disease-related hospitalisations



- Significant differences in the length of inpatient stays were observed for all-cause hospitalisations (1), CV-related hospitalisations (2) as well as for ND CKD-related hospitalisations (3):
  - **(1)** Group 4a* vs. 4b* (11.8 vs. 10.3 days, p=0.033),
    Group 4a* vs. 4c* (11.8 vs. 8.5 days, p=0.014),
    Group 4b* vs. 4c* (10.3 vs. 8.5 days, p=0.770).
  - **(2)** Group 4a* vs. 4b* (12.1 vs. 10.7 days, p=0.041),
    Group 4a* vs. 4c* (12.1 vs. 8.7 days, p=0.021),
    Group 4b* vs. 4c* (10.7 vs. 8.7 days, p=0.756).
  - **(3)** Group 4a* vs. 4b* (13.7 vs. 11.6 days, p=0.005),
    Group 4a* vs. 4c* (13.7 vs. 8.6 days, p=0.001),
    Group 4b* vs. 4c* (11.6 vs. 8.6 days, p=0.954).
- The cost comparison showed higher average CV-related hospitalisation costs for the oral iron cohort in comparison to the high dose and low dose IV iron cohorts in the post-index period **(see Figure 3)**.

Figure 3. Mean costs for all-cause and disease-related hospitalisations



Note: Cost differences were not significant across the compared cohorts (p>0.05).

- The oral iron cohort had the highest observable mortality compared to the low dose IV iron and high dose IV iron cohort (37.8% vs. <13.5% vs. 18.9%) and differed significantly to the matched cohorts treated with low dose IV iron (4a* vs. 4b* p=0.004) and with high dose IV iron (4a* vs. 4c* p=0.039).

CONCLUSIONS

- The results showed that the use of high dose IV iron treatment was associated with highest cost savings compared to oral and low dose IV iron.
- In general, claims data analyses are subject to limitations as they are primarily collected for accounting purposes, and therefore clinical parameters (e.g. severity grades, laboratory results), dosage and intake of medication, or additional information (e.g. quality of life) are not covered.

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