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Evaluation of health care utilisation and mortality in medical hospitalisations with multimorbidity and kidney disease, according to frailty: a nationwide cohort study

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Summary

INTRODUCTION: The impact of impaired kidney function on healthcare use among medical hospitalisations with multimorbidity and frailty is incompletely understood. In this study, we assessed the prevalence of acute kidney injury (AKI) and chronic kidney disease (CKD) among multimorbid medical hospitalisations in Switzerland and explored the associations of kidney disease with in-hospital outcomes across different frailty strata.

METHODS: This observational study analysed nationwide hospitalisation records from 1 January 2012 to 31 December 2020. We included adults (age ≥18 years) with underlying multimorbidity hospitalised in a medical ward. The study population consisted of hospitalisations with AKI, CKD or no kidney disease (reference group), and was stratified by three frailty levels (non-frail, pre-frail, frail). Main outcomes were in-hospital mortality, intensive care unit (ICU) treatment, length of stay (LOS) and all-cause 30-day readmission. We estimated multivariable adjusted odds ratios (OR) and changes in percentage of log-transformed continuous outcomes with 95% confidence intervals (CI).

RESULTS: Among 2,651,501 medical hospitalisations with multimorbidity, 198,870 had a diagnosis of AKI (7.5%), 452,990 a diagnosis of CKD (17.1%) and 1,999,641 (75.4%) no kidney disease. For the reference group, the risk of in-hospital mortality was 4.4%, for the AKI group 14.4% (adjusted odds ratio [aOR] 2.56 [95% CI 2.52–2.61]) and for the CKD group 5.9% (aOR 0.98 [95% CI 0.96–0.99]), while prevalence of ICU treatment was, respectively, 10.5%, 21.8% (aOR 2.39 [95% CI 2.36–2.43]) and 9.3% (aOR 1.01 [95% CI 1.00–1.02]). Median LOS was 5 days (interquartile range [IQR] 2.0–9.0) in hospitalisations without kidney disease, 9 days (IQR 5.0–15.0) (adjusted change [%] 67.13% [95% CI 66.18–68.08%]) in those with AKI and 7 days (IQR 4.0–12.0) (adjusted change [%] 18.94% [95% CI 18.52–19.36%]) in those with CKD. The prevalence of 30-day readmission was, respectively, 13.3%, 13.7% (aOR 1.21 [95% CI 1.19–1.23]) and 14.8% (aOR 1.26 [95% CI 1.25–1.28]). In general, the frequency of adverse outcomes increased with the severity of frailty.

CONCLUSION: In medical hospitalisations with multimorbidity, the presence of AKI or CKD was associated with substantial additional hospitalisations and healthcare utilisation across all frailty strata. This information is of major importance for cost estimates and should stimulate discussion on reimbursement.

Introduction

Kidney diseases have a major impact on global health and are a clinical challenge for healthcare providers worldwide [1]. In 2019, kidney diseases reached the 10th spot in the top ten causes of death in the global health study [2]. Acute kidney injury (AKI) and chronic kidney disease (CKD) are common in the ageing patient population with multimorbidity presenting to medical wards.

In a previous observational cohort study, we analysed hospitalisations to define associations between multimorbidity (two or more chronic diseases present in the same individual) and in-hospital outcome measures [3, 4]. In a dataset of 2,220,000 records from hospitalisations with a mean age of 68 years, about 80% fulfilled the criteria of multimorbidity with a median of four chronic conditions. While the percentage of hospitalisations with multimorbidity increased over the recent years, it was also associated with a higher likelihood of in-hospital mortality and other outcome parameters [3].

Kidney diseases are caused by many chronic conditions like diabetes or diseases from the cardiovascular spectrum and mirror an additional critical parameter in the complexity of multimorbid patients. However, it is still unclear to

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what extent the prevalence of a kidney disease is associated with additional resource use in the acute care setting.

In many countries, reimbursement is based on diagnosis-related groups (DRG). While the major part of a case-specific reimbursement is based on the main diagnosis and procedures performed during hospitalisation, additional diagnoses may increase the case mix index and reimbursement. However, it is debated whether this increase in reimbursement is sufficient given the additional multimorbidity-associated complexity in diagnostic and therapeutic work-up.

The aim of this study was to assess whether prevalence of AKI or CKD in medical hospitalisations is associated with additional resource use and a higher risk of mortality when compared to those without kidney disease.

Methods

Study design and data source

This was a nationwide retrospective observational cohort study in adult hospitalisations (≥18 years) hospitalised for a medical reason in Switzerland between 1 January 2012 and 31 December 2020. Hospitalisation data were obtained from population-based administrative claims data provided by the Federal Statistical Office (Bundesamt für Statistik, Neuchâtel, Switzerland). The database includes all Swiss hospitalisation records from acute care, general and specialty hospitals in Switzerland. Individual-level data on patient demographics, healthcare utilisation, hospital typology, medical diagnoses, diagnostic tests, clinical procedures and in-hospital patient outcomes were provided for all hospitalisations. The data were unidentifiable due to a multiple-step anonymisation procedure. Medical diagnoses were coded using International Classification of Diseases version 10, German Modification (ICD-10-GM) codes. While the coding process in Switzerland is primarily conducted for billing purposes, and the data may be susceptible to information bias, the definition of medical diagnoses is quite reliable. However, SwissDRG codes only one primary diagnosis, with the remaining diagnoses categorised as secondary. The order of these secondary diagnoses may not be specified. The ethical review board of Northwestern Switzerland (Ethikkommission Nordwest- und Zentralschweiz, EKNZ) declared that this study does not fall under the scope of the Human Research Act as data were anonymised before analysis (EKNZ Project-ID: Req-2021-01397). An authorisation from the ethical review board was therefore not required. A study protocol was not prepared for this analysis.

Study population

Eligible individuals included adult hospitalisations with underlying multimorbidity hospitalised for a medical condition. Hospitalisations with AKI were identified by applying the ICD-10-GM codes N17.0x, N17.1x, N17.2x, N17.8x, N17.9x and T86.10. AKI stages were not systematically recorded in the dataset before 2017 and were therefore not available before 1 January 2017. Hospitalisations with CKD were identified by applying the ICD-10-GM codes N18.1, N18.2, N18.3, N18.4, N18.5, N18.8x, N18.9, I12.0x, I13.1x, I13.2x, P96.0, T86.11, T86.12, T86.19 and Z94.0. Hospitalisations with codes for AKI and CKD were allocated to the AKI group. Acute-on-chronic kidney disease was categorised as an episode of AKI, based on the hypothesis that AKI may have a more significant effect on patient outcomes and hospital resources than CKD. Hospitalisations in need of dialysis were identified by applying the ICD-10-GM codes T82.4, T85.71, Z49.1, Z49.2 and Z99.2 and by applying the Swiss Operation Classification (CHOP) codes 38.95, 39.27, 39.42, 39.43, 39.95.1, 39.95.2, 39.95.3, 39.95.4, 39.95.I1, 39.95.I2 and 54.98. Hospitalisations in need of temporary haemodiafiltration were not included in the dialysis group. In prior investigations, the use of claims data to identify AKI has been validated against hospital records (with AKI defined as a ≥0.5-mg/dL increment of serum creatinine). It was found that an AKI discharge diagnosis in any position had a positive predictive value of 86% and a specificity of 97% [5]. For CKD, International Classification of Diseases (ICD)-10 based algorithms had a positive predictive value of >80% [6].

This study followed the Strengthening The Reporting of OBservational studies in Epidemiology (STROBE) reporting guideline [7].

Definition of "multimorbidity" and "chronic condition"

Multimorbidity was defined according to the World Health Organization (WHO) as the presence of at least two chronic conditions [8]. We applied the "Chronic Condition Indicator (CCI) for the ICD-10-CM" to distinguish between chronic and acute conditions based on ICD-10 codes. The CCI was developed as part of the Healthcare Cost and Utilization Project, a Federal/State/Industry partnership sponsored by the Agency for Healthcare Research and Quality in the USA [9]. It was designed to facilitate healthcare research using administrative data. It is publicly accessible and undergoes annual updates. For this analysis, the 2019.1 version was used. The CCI divides all ICD-10-CM codes into two categories: chronic or acute. To qualify as chronic, a condition has to last 12 months or longer and meet at least one of the following criteria: placing limitations on self-care, independent living and social interactions, and/or need for ongoing intervention with medical products, services or special equipment [9]. In case of an inconsistency between the ICD-10 codes of the CCI with the American ICD-10 coding standard and the Swiss database records, we chose the most representative code with the highest similarity to merge the ICD-10 codes of the CCI with the ICD-10 codes of the database records.

Measurement of frailty

Frailty was measured using a validated Hospital Frailty Risk Score derived from a broad set of ICD-10 codes, including measures of acuity. The Hospital Frailty Risk Score and its clinical application have been described in detail previously [10]. Using clinically meaningful cut points, we defined the status of non-frail as a score <5, pre-frail as a score of 5–15 and frail as a score >15.

Study outcomes

To assess the overall burden of healthcare utilisation among this medical inpatient population with multimorbidity, we defined the following outcomes: Main primary outcomes were all-cause in-hospital mortality, intensive care unit (ICU) treatment, length of hospital stay (LOS) and 30-day hospital readmission. Secondary outcomes encompassed length of ICU stay, need for mechanical ventilation, post-acute care facility discharge and 1-year hospital readmission. All outcome analyses were conducted at discharge record level. There were no missing data for the outcomes of interest.

Statistical analysis

Descriptive statistics were calculated by the presence of kidney disease for demographic information including age, sex, nationality, level of health care insurance, year of index admission, comorbidities and level of frailty. All baseline data are expressed as mean (standard deviation [SD], measuring the dispersion of a dataset relative to its mean, indicating how spread out the data points are), median (interquartile range [IQR]) or count (%).

Associations between the presence of kidney disease and binary outcomes were estimated using a multivariable logistic regression model adjusted for age, sex, level of healthcare insurance, year of admission, modality of admission (emergency versus planned) and level of hospital care. While LOS was right-skewed, we performed a multivariable generalised linear gamma regression analysis based on log-transformed values. In addition, we excluded hospitalisations with a LOS ≥100 days. Moreover, graphical illustration of odds ratios along increasing numbers of chronic conditions was performed using linear basis spline constructions (B-splines). B-splines are a type of smooth curve-fitting technique used to model and visualise trends across the number of chronic conditions, allowing for flexible data approximation and smoothness by combining several polynomial segments [11]. All analyses were performed within each frailty stratum. We used the Wald test for homogeneity to assess treatment heterogeneity across strata of AKI, CKD and frailty. Stratified analyses by strata of AKI were performed with data after 2016 only. Among hospitalisations for AKI, including those with acute-on-chronic kidney disease, outcomes were categorised solely by AKI stage and not further by CKD stages, as we assume CKD prevalence within the AKI group might be significantly underestimated. All tests were 2-sided, $p<0.05$ was considered significant and 95% confidence intervals (CIs) were reported for all effect estimates. Our analysis has not been adjusted for multiple testing. All statistical analyses were performed using STATA, version 17.1 (StataCorp LLC).

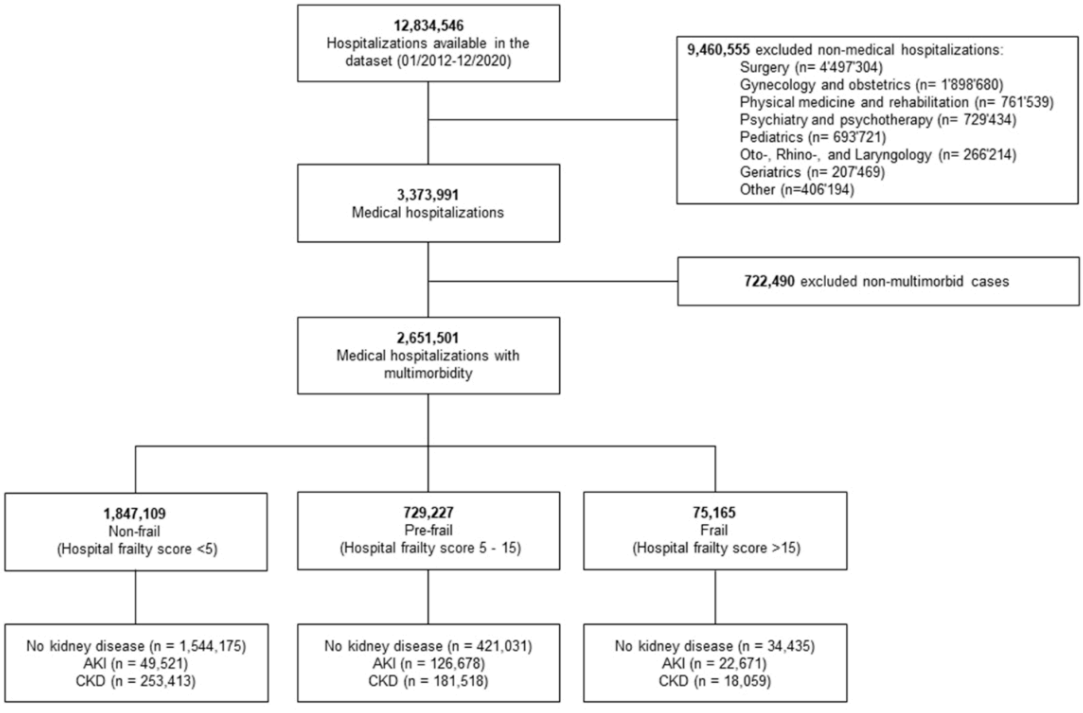
Results

Characteristics of the cohort

From 1 January 2012 to 31 December 2020, we identified a total of 2,651,501 medical hospitalisations meeting our inclusion criteria of multimorbidity (figure 1).

Baseline characteristics stratified by hospitalisations without kidney disease (n = 1,999,641; 75.4%), AKI (n = 198,870; 7.5%) and CKD (n = 452,990; 17.1%) are illustrated in table 1. Baseline characteristics stratified by level of frailty are applicable in the supplemental tables (tables S1 to S3). While hospitalisations without kidney disease had a median age of 71 years (IQR 59–80 years), hospitalisations with AKI or CKD were older with a median age of 78 years (IQR 69–85 years) and 81 years (IQR 73–86 years), respectively. The most prevalent comorbidities across all groups were hypertension (no kidney dis-

Figure 1: Study flowchart.



ease: 49.6%; AKI: 65.7%; CKD: 73.1%), coronary artery disease (no kidney disease: 25.3%; AKI: 29.5%; CKD: 35.9%) and gastrointestinal disorder (no kidney disease: 23.9%; AKI: 36.4%; CKD: 26.9%). Overall, when compared to hospitalisations without kidney disease (2.58 ± 1.61), those with AKI and CKD were sicker with a mean Elixhauser comorbidity index of 4.58 ± 2.10 and 4.51 ± 1.81. A relevant number of hospitalisations had six or more chronic conditions (no kidney disease: 27.7%; AKI: 61.3%; CKD: 66.6%).

Patient outcomes according to the presence of AKI and CKD

Crude patient outcomes stratified by the presence of AKI and CKD according to level of frailty are illustrated in table 2. In general, the number of events among hospitalisations with AKI and CKD was higher than in those without kidney disease. Moreover, except for hospital readmissions, number of adverse events was also increasing with the severity of frailty. Risk of 30-day and 1-year readmission was highest among non-frail hospitalisations and declined with increasing frailty.

Adjusted analysis of primary and secondary patient outcomes by AKI stages, according to level of frailty

More severe AKI stages were associated with a stepwise increase in relative risk of in-hospital mortality, ICU admission, need for intubation and discharge to a post-acute care facility (p for heterogeneity <0.001 for all variables). Similarly, we observed a longer length of ICU stay and hospital stay with more severe AKI stages (p for heterogeneity <0.001 for all variables). In more-frail people, however, the association of AKI and adverse outcome was attenuated. This was most obvious for the association of AKI stage 3 and in-hospital mortality (aOR of 9.92 among non-frail hospitalisations vs 3.52 among frail hospitalisations). Readmission rates did not relevantly change with more severe AKI stages or frailty levels. All results are summarised in table 3.

Adjusted analysis of primary and secondary patient outcomes by CKD stage, according to level of frailty

The multivariable regression models stratified by CKD stage (table 4) illustrate a more heterogeneous picture compared to hospitalisations with AKI. In general, more advanced CKD stages were associated with a stepwise increase in relative risk of in-hospital mortality, ICU admission and hospital readmission (p for heterogeneity <0.001, for all variables). In addition, more advanced CKD stages were associated with prolonged LOS and, mainly in individuals in need of dialysis, ICU LOS (p for heterogeneity <0.001, for all variables). The findings for the remaining outcomes did not consistently show a CKD stage-dependent increase in relative risk. More severe levels of frailty did not modify relative risk estimates in a clinically meaningful manner.

AKI and CKD associated with primary outcomes along prevalent chronic conditions

We aimed to assess the associations of AKI and CKD with primary outcomes across the continuous spectrum of prevalent chronic conditions, stratified by level of frailty. When compared to hospitalisations without a kidney disease, in those with AKI, we observed a consistently higher relative risk of all primary outcomes along the number of chronic conditions (figure 2). This finding was also consistent for all levels of frailty.

Along the number of chronic conditions, in hospitalisations with CKD, the relative risk of in-hospital mortality and ICU stay as well as hospital LOS was similar or even lower as compared to hospitalisations without kidney disease (figure 3). These findings were also consistent for all levels of frailty. Except for non-frail hospitalisations, the relative risk of intubation in pre-frail and frail hospitalisations with CKD was increased along the number of chronic conditions, when compared to those without kidney disease (figure 3).

Discussion

We performed a nationwide analysis of medical hospitalisations in Switzerland to explore associations of AKI and CKD with adverse in-hospital outcomes. The main findings of this study include the following aspects: First, estimates show that the number of events among multimorbid hospitalisations with AKI or CKD was higher than in those without kidney disease. Second, adverse outcomes were more common in more severe AKI stages and in more frail people. However, with increasing frailty, the association of AKI and adverse outcomes was attenuated. Third, hospitalisations with increasing severity of CKD had a higher risk of in-hospital mortality, ICU admission, hospital readmission and longer LOS than those without kidney disease. The presence of frailty did not modify this association in a clinically meaningful manner.

After the nationwide implementation of SwissDRG in 2012, in the context of increasing treatment complexity owing to changing demographics and a higher prevalence of multimorbidity and frailty, financial pressure has been growing and hospitals forced to improve the efficiency of their care. In recent years – and further accentuated through the COVID-19 pandemic – many Swiss hospitals have been heavily battling to cope with increasing financial pressure and current standardised reimbursements, as defined by SwissDRG, are no longer cost-covering [12]. While reimbursements are slanted towards the financially most lucrative cause of admission, disease complexity, the presence of chronic diseases and multimorbidity do not relevantly account for additional fees. Although it seems intuitive that underlying chronic conditions, such as kidney diseases, require more in-hospital resources, it is not yet correctly acknowledged by SwissDRG and payers [13]. Thus, this study aimed to assess whether the prevalence of AKI or CKD in medical hospitalisations with multimorbidity is associated with additional in-hospital resource use and a higher risk of mortality when compared to those without kidney disease.

AKI describes a rapid decrease in renal function and is characterised by an increase in serum creatinine [14]. Al-

Table 1:
Baseline characteristics among hospitalisations with AKI and CKD hospitalisations.

	Overall	No kidney disease	AKI	CKD
Hospitalisations, n	2,651,501	1,999,641	198,870	452,990
Patients, n	1,277,977	1,101,521	152,840	234,893
Demographics				
Age, median (IQR) [years]	73 (62–82)	71 (59–80)	78 (69–85)	81 (73–86)
Male sex, n (%)	1,412,459 (53.3)	1,062,210 (53.1)	110,326 (55.5)	239,923 (53.0)
Swiss nationality, n (%)	2,214,964 (83.5)	1,654,471 (82.7)	168,364 (84.7)	392,129 (86.6)
Supplementary insurance, n (%)	624,778 (23.6)	472,924 (23.7)	40,068 (20.1)	111,786 (24.7)
Admission data				
Year of admission, n (%)				
2012	258,185 (9.7)	208,566 (10.4)	7613 (3.8)	42,006 (9.3)
2013	266,840 (10.1)	215,319 (10.8)	5939 (3.0)	45,582 (10.1)
2014	278,746 (10.5)	222,293 (11.1)	5859 (2.9)	50,594 (11.2)
2015	290,680 (11.0)	230,631 (11.5)	6064 (3.0)	53,985 (11.9)
2016	300,982 (11.4)	236,936 (11.8)	5829 (2.9)	58,217 (12.9)
2017	305,059 (11.5)	220,105 (11.0)	37,897 (19.1)	47,057 (10.4)
2018	313,796 (11.8)	221,124 (11.1)	42,474 (21.4)	50,198 (11.1)
2019	323,664 (12.2)	226,806 (11.3)	43,526 (21.9)	53,332 (11.8)
2020	313,549 (11.8)	217,861 (10.9)	43,669 (22.0)	52,019 (11.5)
Emergency admission, n (%)	1,922,255 (72.5)	1,398,651 (69.9)	173,174 (87.1)	350,430 (77.4)
Admission from home, n (%)	2,258,473 (85.2)	1,723,173 (86.2)	158,344 (79.6)	376,956 (83.2)
Tertiary care hospital: University hospital	478,318 (18.0)	367,940 (18.4)	39,045 (19.6)	71,333 (15.7)
Tertiary care hospital: non-university hospital	1,566,306 (59.1)	1,159,366 (58.0)	124,827 (62.8)	282,113 (62.3)
Secondary care hospital	606,877 (22.9)	472,335 (23.6)	34,998 (17.6)	99,544 (22.0)
Comorbidities, n (%)				
Hypertension	1,453,650 (54.8)	991,661 (49.6)	130,732 (65.7)	331,257 (73.1)
Obesity	72,909 (2.7)	51,225 (2.6)	6923 (3.5)	14,761 (3.3)
Type 2 diabetes mellitus	515,830 (19.5)	318,939 (15.9)	58,122 (29.2)	138,769 (30.6)
Type 1 diabetes mellitus	15,840 (0.6)	11,156 (0.6)	1369 (0.7)	3315 (0.7)
Dyslipidaemia	556,385 (21.0)	412,191 (20.6)	40,151 (20.2)	104,043 (23.0)
Coronary artery disease	727,327 (27.4)	505,823 (25.3)	58,679 (29.5)	162,825 (35.9)
Myocardial infarction	158,508 (6.0)	123,868 (6.2)	12,206 (6.1)	22,434 (5.0)
Congestive heart failure	414,812 (15.6)	216,165 (10.8)	64,255 (32.3)	134,392 (29.7)
Atrial fibrillation	545,605 (20.6)	326,422 (16.3)	66,831 (33.6)	152,352 (33.6)
Peripheral arterial disease	143,042 (5.4)	81,018 (4.1)	15,011 (7.5)	47,013 (10.4)
Obstructive sleep apnoea syndrome	91,480 (3.5)	62,760 (3.1)	9523 (4.8)	19,197 (4.2)
Cerebrovascular disease	236,695 (8.9)	184,097 (9.2)	13,349 (6.7)	39,249 (8.7)
Ischaemic stroke	114,915 (4.3)	95,845 (4.8)	4524 (2.3)	14,546 (3.2)
Chronic obstructive pulmonary disease	264,633 (10.0)	186,241 (9.3)	24,302 (12.2)	54,090 (11.9)
Gastrointestinal disorder	672,853 (25.4)	478,554 (23.9)	72,302 (36.4)	121,997 (26.9)
Solid cancer	383,094 (14.4)	313,986 (15.7)	25,933 (13.0)	43,175 (9.5)
Haematological malignancy	89,766 (3.4)	67,981 (3.4)	8130 (4.1)	13,655 (3.0)
Musculoskeletal disorder	584,780 (22.1)	401,060 (20.1)	54,954 (27.6)	128,766 (28.4)
Mental disorder	784,397 (29.6)	596,705 (29.8)	68,772 (34.6)	118,920 (26.3)
Alcohol addiction	181,441 (6.8)	152,065 (7.6)	16,065 (8.1)	13,311 (2.9)
Elixhauser comorbidity index, mean (SD)	3.06 (1.88)	2.58 (1.61)	4.58 (2.10)	4.51 (1.81)
Hospital frailty score, n (%)				
<5 points	1,847,109 (69.7)	1,544,175 (77.2)	49,521 (24.9)	253,413 (55.9)
5-15 points	729,227 (27.5)	421,031 (21.1)	126,678 (63.7)	181,518 (40.1)
>15 points	75,165 (2.8)	34,435 (1.7)	22,671 (11.4)	18,059 (4.0)
Number of chronic comorbidities, n (%)				
2	443,338 (16.7)	415,325 (20.8)	13,362 (6.7)	14,651 (3.2)
3	451,620 (17.0)	402,820 (20.1)	18,202 (9.2)	30,598 (6.8)
4	422,380 (15.9)	352,964 (17.7)	21,983 (11.1)	47,433 (10.5)
5	356,980 (13.5)	274,949 (13.7)	23,338 (11.7)	58,693 (13.0)
≥6	977,183 (36.9)	553,583 (27.7)	121,985 (61.3)	301,615 (66.6)

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; IQR, interquartile range; SD, standard deviation.

though the three AKI stages were defined in 2012, only in 2017 was this acknowledged by SwissDRG and become relevant for reimbursement. Although ICD-10 codes for AKI have been reported to have low sensitivity resulting in underreporting of less severe hospitalisations [15–17], in this study we were able to identify a reasonable amount of multimorbid people with AKI. In addition, after the modification by SwissDRG in 2017, the number of people with

Table 2:
Crude outcomes among hospitalisations with AKI and CKD hospitalisations.

	Overall	Non-frail	Pre-frail	Frail
No kidney disease				
Hospitalisation, n	1,999,641	1,544,175	421,031	34,435
In-hospital mortality, n (%)	88,523 (4.4)	56,943 (3.7)	28,834 (6.8)	2746 (8.0)
ICU stay, n (%)	209,257 (10.5)	143,192 (9.3)	59,682 (14.2)	6383 (18.5)
ICU LOS, median (IQR) [days]	1.2 (0.8–2.5)	1.0 (0.8–1.9)	1.9 (1.0–4.0)	3.0 (1.3–7.5)
Need for intubation among ICU hospitalisations, n (%)	52,917 (25.3)	28,100 (19.6)	21,920 (36.7)	2897 (45.4)
Hospital LOS, median (IQR) [days]	5.0 (2.0–9.0)	4.0 (2.0–8.0)	8.0 (5.0–14.0)	12.0 (7.0–19.0)
Facility discharge, n (%)*	463,987 (24.3)	279,249 (18.8)	164,872 (42.0)	19,866 (62.7)
30-day all-cause rehospitalisation, n (%)*	254,024 (13.3)	207,150 (13.9)	44,104 (11.2)	2770 (8.7)
1-year all-cause rehospitalisation, n (%)*	689,280 (36.1)	554,842 (37.3)	126,750 (32.3)	7688 (24.3)
AKI**				
Hospitalisation, n	184,755	47,083	117,119	20,553
In-hospital mortality, n (%)	26,596 (14.4)	6050 (12.8)	17,367 (14.8)	3179 (15.5)
ICU stay, n (%)	40,365 (21.8)	7531 (16.0)	26,837 (22.9)	5997 (29.2)
ICU LOS, median (IQR) [days]	2.8 (1.2–6.1)	1.8 (0.9–3.5)	2.8 (1.3–6.2)	4.7 (2.0–11.6)
Need for intubation among ICU hospitalisations, n (%)	17,735 (43.9)	2408 (32.0)	12,137 (45.2)	3190 (53.2)
Hospital LOS, median (IQR) [days]	9.0 (5.0–15.0)	7.0 (4.0–11.0)	10.0 (6.0–16.0)	14.0 (9.0–24.0)
Facility discharge, n (%)*	59,843 (37.8)	9822 (23.9)	39,231 (39.3)	10,790 (62.1)
30-day all-cause rehospitalisation, n (%)*	21,737 (13.7)	6097 (14.9)	13,662 (13.7)	1978 (11.4)
1-year all-cause rehospitalisation, n (%)*	49,101 (31.0)	14,159 (34.5)	30,908 (31.0)	4034 (23.2)
CKD**				
Hospitalisation, n	395,665	222,317	158,191	15,157
In-hospital mortality, n (%)	23,376 (5.9)	9960 (4.5)	11,899 (7.5)	1517 (10.0)
ICU stay, n (%)	36,815 (9.3)	16,741 (7.5)	17,643 (11.2)	2431 (16.0)
ICU LOS, median (IQR) [days]	1.6 (0.8–3.0)	1.1 (0.7–2.0)	1.8 (1.0–3.8)	2.8 (1.2–6.4)
Need for intubation among ICU hospitalisations, n (%)	10,225 (27.8)	3229 (19.3)	6023 (34.1)	973 (40.0)
Hospital LOS, median (IQR) [days]	7.0 (4.0–12.0)	6.0 (3.0–9.0)	9.0 (5.0–14.0)	12.0 (7.0–19.0)
Facility discharge, n (%)*	101,691 (27.3)	39,853 (18.8)	54,115 (37.0)	7723 (56.6)
30-day all-cause rehospitalisation, n (%)*	54,976 (14.8)	32,416 (15.3)	20,982 (14.3)	1578 (11.6)
1-year all-cause rehospitalisation, n (%)*	163,308 (43.9)	99,359 (46.8)	59,766 (40.9)	4183 (30.7)

* Patients who died during the hospitalisation were excluded from the calculation regarding facility discharge, 30-day and 1-year all-cause rehospitalisation. ** CKD stages 1 and 2 were not included in the calculation due to the high likelihood of underreporting using administrative data. Calculations refer to more clinically relevant stages (stages 3 to 5, dialysis and unspecified CKD stage). Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay.

AKI increased over time from 37,897 hospitalisations in 2017 to 43,669 hospitalisations in 2020. We found that the presence of AKI was associated with a higher use of in-hospital resources and a higher risk of mortality, with increased incidence in more advanced AKI stages. These results are also consistent with previous findings from Europe and United States linking the prevalence of ICD codes for AKI and the higher risk of short-term outcomes and mortality [15, 17, 18]. This association was even more pronounced in a recent study on COVID-19 patients showing a mortality risk of 50% in patients with AKI and 8% in controls without AKI [19].

In our study, the median LOS of all hospitalisations with AKI was 9 days (IQR 5–15 days) vs 5 days (IQR 2–9) in hospitalisations without kidney disease; the longest LOS (nearly 120% longer) was in hospitalisations with AKI stage 3. We did not find relevant differences in LOS between AKI stages 1 and 2, likely due to the retrospective use of ICD-10 codes, underestimating the number of hospitalisations admitted with AKI due to poor recognition of AKI, supporting the notion that AKI is underrecognised and underreported [20].

While – for many outcomes – we found consistent associations across the spectrum of frailty, the attenuation of relative risks in frailer hospitalisations is likely to be driven by a comparable baseline risk of adverse events in the control group, even without kidney disease. Whether the lower probability of hospital readmission among hospitalisations with AKI, as compared to kidney disease negative controls, is linked to closer outpatient monitoring with survival benefit or due to a higher likelihood of out-of-hospital mortality is unclear. However, results from a recent observational study indicate that – based on missing out-of-hospital mortality data and missing data from the outpatient setting – our results might be biased as Schulman et al. found AKI to be associated with higher rates of rehospitalisation (hazard ratio [HR] 1.62; 95% CI 1.60–1.65) [21]. To support the importance of AKI as a reason for higher in-hospital resource use, we found robust estimates across increasing numbers of chronic conditions with similar findings for all frailty levels. This further substantiates the hypothesis that already the presence of an even lower risk stage of AKI (stages 1 and 2) is a relevant cost driver in the setting of complex and multimorbid patients and seems not adequately addressed by current reimbursement. Given the number of hospitalisations with diagnoses of AKI 1 (83,718 hospitalisations; median LOS increased by 52% [to approximately 13.7 days]) and AKI 2 (27,829 hospitalisations; median LOS increased by 84% [to approximately 16.6 days]), and assuming conservative daily hospital costs of CHF 1000, the total hospital reimbursement shortfall would have exceeded CHF 600 million between 2017 and 2020.

Table 3:
Multivariable regression analyses of primary and secondary outcomes among hospitalisations with AKI, according to level of frailty.

	Overall	Non-frail	Pre-frail	Frail	p of heterogeneity
In-hospital mortality: OR (95% CI)*					
AKI overall	2.56 (2.52–2.61)	2.45 (2.36–2.54)	1.88 (1.83–1.93)	1.93 (1.80–2.07)	*<0.001*
AKI, stage 1	1.45 (1.41–1.49)	1.22 (1.15–1.30)	1.10 (1.06–1.14)	1.32 (1.21–1.45)	*<0.001*
AKI, stage 2	3.24 (3.13–3.36)	3.87 (3.58–4.18)	2.22 (2.12–2.32)	2.28 (2.06–2.53)	*<0.001*
AKI, stage 3	7.38 (7.15–7.61)	9.92 (9.26–10.62)	4.95 (4.76–5.15)	3.52 (3.19–3.87)	*<0.001*
AKI, unspecified	2.17 (2.09–2.25)	2.23 (2.06–2.40)	1.61 (1.53–1.69)	1.66 (1.47–1.86)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
ICU stay: OR (95% CI)*					
AKI overall	2.39 (2.36–2.43)	1.73 (1.67–1.78)	1.84 (1.80–1.87)	1.95 (1.84–2.06)	*<0.001*
AKI, stage 1	1.79 (1.75–1.82)	1.53 (1.47–1.59)	1.37 (1.33–1.41)	1.48 (1.38–1.59)	*<0.001*
AKI, stage 2	2.80 (2.72–2.89)	1.92 (1.78–2.06)	2.07 (2.00–2.16)	2.19 (2.01–2.39)	*0.003*
AKI, stage 3	5.86 (5.70–6.02)	3.35 (3.13–3.59)	4.23 (4.08–4.38)	4.15 (3.82–4.51)	*0.133*
AKI, unspecified	1.43 (1.38–1.48)	1.32 (1.23–1.42)	1.10 (1.05–1.15)	1.01 (0.90–1.12)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
ICU LOS: change in % (95% CI)**					
AKI overall	111.71 (106.97–116.55)	61.00 (55.03–67.19)	35.91 (32.28–39.64)	35.15 (26.34–44.57)	*<0.001*
AKI, stage 1	52.36 (47.46– 57.43)	29.60 (23.00–36.56)	3.83 (0.07–7.74)	3.17 (-5.33–12.43)	*<0.001*
AKI, stage 2	104.11 (95.16–113.48)	71.60 (56.57–88.08)	31.49 (25.38–37.89)	21.22 (9.66–34.00)	*0.255*
AKI, stage 3	211.04 (199.86–222.64)	152.49 (132.83–173.82)	83.67 (76.59–91.02)	81.32 (66.51–97.45)	*<0.001*
AKI, unspecified	64.16 (55.08–73.78)	33.25 (21.80–45.79)	13.39 (6.59–20.63)	11.66 (-2.89–28.40)	*0.119*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
Need for intubation: OR (95% CI)*					
AKI overall	2.22 (2.16–2.28)	1.87 (1.75–1.99)	1.34 (1.29–1.39)	1.31 (1.19–1.44)	*<0.001*
AKI, stage 1	1.71 (1.64–1.78)	1.40 (1.28–1.54)	1.10 (1.04–1.16)	1.10 (0.96–1.24)	*<0.001*
AKI, stage 2	2.16 (2.05–2.29)	2.06 (1.78–2.39)	1.24 (1.16–1.33)	1.25 (1.08–1.45)	*<0.001*
AKI, stage 3	3.20 (3.06–3.35)	3.13 (2.76–3.53)	1.78 (1.68–1.88)	1.67 (1.47–1.89)	*<0.001*
AKI, unspecified	1.97 (1.83–2.11)	1.87 (1.61–2.17)	1.26 (1.15–1.38)	1.12 (0.91–1.37)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
LOS: change in % (95% CI)**					
AKI overall	67.13 (66.18–68.08)	44.91 (43.33–46.51)	19.00 (18.25–19.75)	24.62 (22.71–26.55)	*0.001*
AKI, stage 1	52.07 (50.91–53.24)	38.61 (36.60–40.65)	11.34 (10.44–12.24)	14.95 (12.76–17.18)	*<0.001*
AKI, stage 2	84.41 (82.08–86.78)	62.31 (57.75–67.01)	27.29 (25.71–28.90)	31.87 (28.42–35.42)	*0.591*
AKI, stage 3	119.41 (116.48–122.39)	82.12 (76.41–88.01)	43.00 (41.13–44.89)	47.91 (43.94–51.99)	*<0.001*
AKI, unspecified	48.98 (47.19–50.79)	29.60 (26.59–32.68)	10.13 (8.78–11.50)	17.37 (14.21–20.61)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
Facility discharge: OR (95% CI)*					
AKI overall	1.48 (1.46–1.50)	1.15 (1.12–1.18)	0.79 (0.77–0.80)	0.93 (0.89–0.97)	*<0.001*
AKI, stage 1	1.30 (1.28–1.32)	1.03 (0.99–1.06)	0.72 (0.70–0.73)	0.87 (0.82–0.92)	*<0.001*
AKI, stage 2	1.72 (1.68–1.77)	1.35 (1.26–1.44)	0.88 (0.85–0.91)	1.03 (0.95–1.12)	*<0.001*
AKI, stage 3	2.26 (2.19–2.33)	1.82 (1.69–1.96)	1.11 (1.07–1.15)	1.11 (1.02–1.21)	*<0.001*
AKI, unspecified	1.35 (1.32–1.39)	1.11 (1.06–1.18)	0.72 (0.70–0.74)	0.85 (0.79–0.92)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
30-day rehospitalisation: OR (95% CI)*					
AKI overall	1.21 (1.19–1.23)	1.23 (1.19–1.27)	1.29 (1.26–1.32)	1.37 (1.27–1.47)	*0.065*
AKI, stage 1	1.22 (1.19–1.25)	1.25 (1.20–1.30)	1.29 (1.25–1.33)	1.39 (1.27–1.52)	*0.261*
AKI, stage 2	1.27 (1.22–1.31)	1.26 (1.17–1.37)	1.37 (1.30–1.43)	1.38 (1.22–1.56)	*0.415*
AKI, stage 3	1.19 (1.14–1.24)	1.26 (1.15–1.39)	1.25 (1.19–1.32)	1.36 (1.20–1.54)	*0.929*
AKI, unspecified	1.15 (1.11–1.20)	1.14 (1.06–1.21)	1.26 (1.20–1.32)	1.31 (1.16–1.49)	*0.108*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
1-year rehospitalisation: OR (95% CI)*					
AKI overall	1.15 (1.13–1.16)	1.23 (1.20–1.26)	1.29 (1.27–1.32)	1.26 (1.19–1.34)	*0.100*
AKI, stage 1	1.20 (1.18–1.23)	1.26 (1.22–1.30)	1.35 (1.32–1.39)	1.34 (1.25–1.44)	*0.703*
AKI, stage 2	1.12 (1.08–1.15)	1.20 (1.13–1.28)	1.25 (1.21–1.30)	1.25 (1.13–1.38)	*0.625*
AKI, stage 3	0.99 (0.96–1.03)	1.17 (1.08–1.26)	1.09 (1.04–1.14)	1.09 (0.98–1.21)	*0.021*
AKI, unspecified	1.14 (1.11–1.17)	1.20 (1.14–1.27)	1.31 (1.27–1.36)	1.25 (1.13–1.38)	*0.217*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	

Results for different AKI stages are based on data from 2017–2020 only, as AKI stages were not available (coding issue) in the dataset before 2017. Hospitalisations without kidney diseases served as the reference. Patients who died during the hospitalisation were excluded from the calculations for facility discharge, 30-day and 1-year all-cause rehospitalisation. * OR for binary outcomes calculated by a multivariable logistic model adjusted for age, sex, level of healthcare insurance, year of admission, month of admission, modality of admission (emergency vs planned) and level of hospital care; ** Changes in % for continuous outcomes calculated by a multivariable generalised linear gamma regression based on log-transformed values adjusted for age, sex, level of healthcare insurance, year of admission, month of admission, modality of admission (emergency vs planned) and level of hospital care. Abbreviations: AKI, acute kidney disease; CI, confidence interval; ICU, intensive care unit; LOS, length of stay; OR, odds ratio.

Table 4:
Multivariable regression analyses of primary and secondary outcomes among hospitalisations with CKD, according to level of frailty.

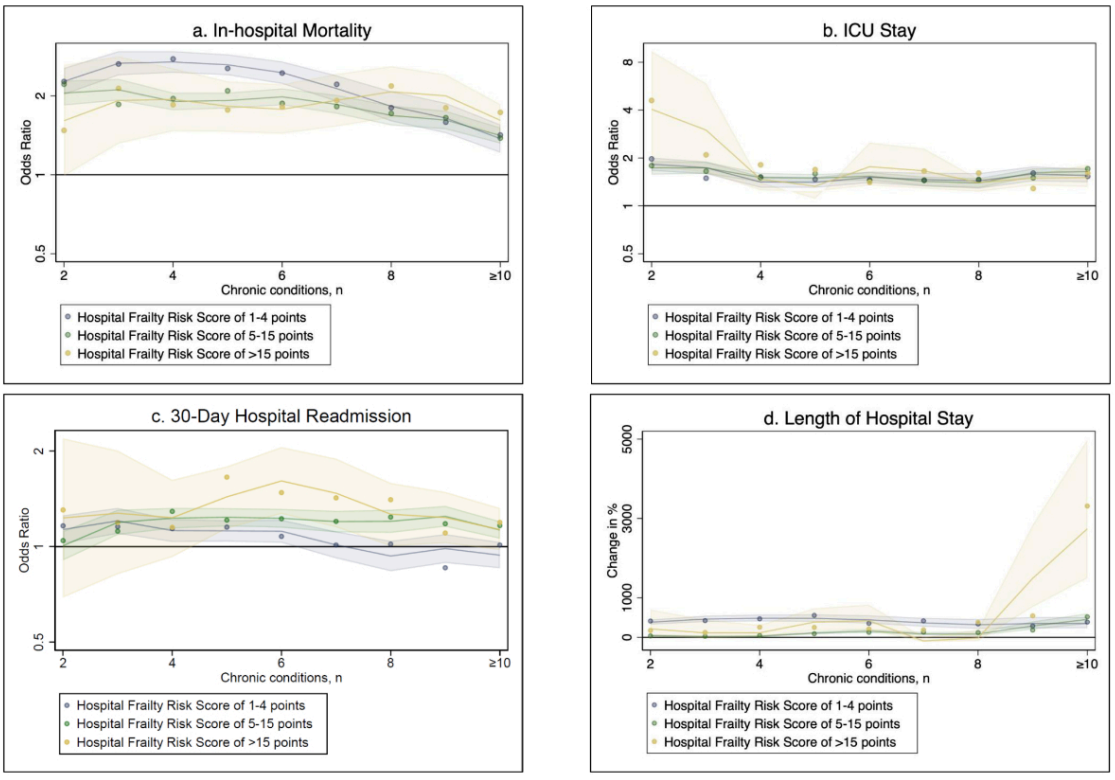
	Overall	Non-frail	Pre-frail	Frail	p of heterogeneity
In-hospital mortality: OR (95% CI)					
CKD overall	0.98 (0.96–0.99)	0.86 (0.84–0.88)	0.95 (0.93–0.97)	1.20 (1.12–1.28)	*0.123*
CKD, stage 3	0.76 (0.74–0.78)	0.64 (0.62–0.65)	0.77 (0.75–0.79)	1.04 (0.96–1.13)	*<0.001*
CKD, stage 4	1.38 (1.34–1.42)	1.31 (1.25–1.36)	1.29 (1.23–1.34)	1.55 (1.37–1.77)	*<0.001*
CKD, stage 5	2.95 (2.80–3.09)	3.06 (2.86–3.27)	2.45 (2.27–2.64)	2.86 (2.20–3.73)	*<0.001*
Dialysis	1.55 (1.48–1.61)	1.14 (1.07–1.22)	1.49 (1.41–1.58)	2.94 (2.44–3.55)	*<0.001*
CKD, unspecified	1.49 (1.42–1.56)	1.40 (1.30–1.50)	1.37 (1.28–1.46)	1.57 (1.28–1.93)	*0.009*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
ICU stay: OR (95% CI)*					
CKD overall	1.01 (1.00–1.02)	0.90 (0.88–0.91)	0.95 (0.93–0.96)	1.11 (1.05–1.17)	*<0.001*
CKD, stage 3	0.91 (0.89–0.92)	0.83 (0.81–0.85)	0.85 (0.83– 0.87)	1.02 (0.96– 1.09)	*<0.001*
CKD, stage 4	0.90 (0.87–0.92)	0.77 (0.74–0.81)	0.87 (0.83–0.90)	1.01 (0.90–1.14)	*0.001*
CKD, stage 5	1.21 (1.15–1.28)	1.23 (1.14–1.31)	0.98 (0.90–1.06)	1.31 (1.01–1.71)	*<0.001*
Dialysis	1.80 (1.75–1.85)	1.39 (1.34–1.45)	1.74 (1.67–1.82)	2.68 (2.27–3.15)	*<0.001*
CKD, unspecified	1.26 (1.21–1.32)	1.20 (1.13–1.27)	1.09 (1.02–1.16)	1.19 (1.00–1.42)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*0.338*	
ICU LOS: change in % (95% CI)**					
CKD overall	18.72 (16.47–21.01)	9.25 (6.92–11.62)	-4.57 (-6.86 – -2.21)	0.13 (-6.78 – 7.54)	*<0.001*
CKD, stage 3	5.99 (3.30–8.74)	0.21 (-2.65 – 3.15)	-12.33 (-15.11 – -9.45)	-11.09 (-18.83 – -2.61)	*<0.001*
CKD, stage 4	17.06 (11.45–22.95)	13.45 (6.94–20.35)	-6.99 (-12.19 – -1.49)	-2.08 (-17.55 – 16.30)	*<0.001*
CKD, stage 5	-0.72 (-8.96 – 8.26)	-6.65 (-14.78 – 2.26)	-12.48 (-21.88 – -1.96)	-19.03 (-42.80 – 14.60)	*0.002*
Dialysis	68.81 (61.23–76.75)	44.34 (36.80–52.29)	24.37 (17.77–31.34)	61.48 (35.51–92.43)	*<0.001*
CKD, unspecified	30.04 (21.37–39.32)	24.06 (14.77–34.10)	1.38 (-6.87 – 10.37)	27.93 (0.20–63.34)	*0.017*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*0.118*	
Need for intubation: OR (95% CI)*					
CKD overall	1.19 (1.16–1.22)	1.03 (0.99–1.07)	0.99 (0.96–1.03)	0.95 (0.86–1.05)	*<0.001*
CKD, stage 3	1.11 (1.07–1.15)	0.94 (0.89–0.99)	0.97 (0.92–1.01)	0.96 (0.85–1.08)	*<0.001*
CKD, stage 4	1.26 (1.19–1.34)	1.19 (1.07–1.32)	1.01 (0.93–1.10)	0.92 (0.73–1.16)	*<0.001*
CKD, stage 5	0.83 (0.73–0.93)	0.70 (0.58–0.84)	0.77 (0.65–0.91)	0.84 (0.52–1.34)	*0.604*
Dialysis	1.37 (1.30–1.45)	1.12 (1.02–1.23)	1.04 (0.96–1.12)	1.23 (0.97–1.56)	*0.957*
CKD, unspecified	1.61 (1.48–1.75)	1.52 (1.33–1.73)	1.28 (1.13–1.44)	1.39 (1.01–1.92)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*0.013*	*0.011*	
LOS: change in % (95% CI)**					
CKD overall	18.94 (18.52–19.36)	13.22 (12.70–13.75)	3.97 (3.49–4.46)	6.83 (5.35–8.34)	*<0.001*
CKD, stage 3	13.56 (13.06–14.07)	9.64 (8.99–10.29)	0.29 (-0.28 – 0.87)	2.55 (0.84–4.29)	*<0.001*
CKD, stage 4	25.28 (24.23–26.34)	22.90 (21.48–24.34)	7.65 (6.57–8.75)	12.65 (9.20–16.20)	*<0.001*
CKD, stage 5	18.59 (16.52–20.70)	11.22 (8.70–13.79)	6.67 (4.28–9.13)	14.23 (5.39–23.80)	*0.145*
Dialysis	46.43 (44.80–48.08)	27.76 (25.95–29.59)	28.35 (26.47–30.26)	56.46 (47.50–65.97)	*<0.001*
CKD, unspecified	26.41 (24.66–28.19)	20.31 (18.04–22.62)	7.23 (5.41–9.07)	15.62 (9.98–21.54)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
Facility discharge: OR (95% CI)*					
CKD overall	0.96 (0.95–0.96)	0.89 (0.88–0.90)	0.71 (0.70–0.72)	0.78 (0.75–0.82)	*<0.001*
CKD, stage 3	0.93 (0.93–0.94)	0.88 (0.86–0.89)	0.71 (0.70–0.72)	0.77 (0.74–0.81)	*<0.001*
CKD, stage 4	1.05 (1.04–1.07)	1.05 (1.02–1.08)	0.74 (0.73–0.76)	0.79 (0.72–0.86)	*<0.001*
CKD, stage 5	1.01 (0.97–1.05)	0.99 (0.93–1.05)	0.74 (0.70–0.79)	0.78 (0.62–1.00)	*<0.001*
Dialysis	0.80 (0.77–0.82)	0.74 (0.72–0.77)	0.58 (0.55–0.60)	0.67 (0.56–0.80)	*<0.001*
CKD, unspecified	1.28 (1.24–1.32)	1.23 (1.17–1.28)	0.90 (0.86–0.94)	1.09 (0.94–1.27)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
30-day rehospitalisation: OR (95% CI)*					
CKD overall	1.26 (1.25–1.28)	1.21 (1.19–1.22)	1.44 (1.41–1.46)	1.42 (1.34–1.52)	*<0.001*
CKD, stage 3	1.18 (1.17–1.20)	1.13 (1.11–1.15)	1.34 (1.32–1.37)	1.40 (1.30–1.51)	*<0.001*
CKD, stage 4	1.39 (1.36–1.43)	1.33 (1.29–1.37)	1.60 (1.54–1.65)	1.58 (1.39–1.81)	*<0.001*
CKD, stage 5	1.65 (1.57–1.72)	1.55 (1.46–1.64)	1.95 (1.80–2.10)	1.70 (1.21–2.39)	*<0.001*
Dialysis	1.74 (1.69–1.79)	1.63 (1.57–1.68)	2.04 (1.95–2.14)	2.13 (1.70–2.67)	*<0.001*
CKD, unspecified	1.08 (1.03–1.12)	1.07 (1.01–1.12)	1.21 (1.13–1.29)	0.97 (0.75–1.25)	*0.710*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	
1-year rehospitalisation: OR (95% CI)*					
CKD overall	1.45 (1.44–1.46)	1.48 (1.47–1.49)	1.53 (1.52–1.55)	1.39 (1.33–1.45)	*<0.001*
CKD, stage 3	1.36 (1.34–1.37)	1.36 (1.34–1.38)	1.47 (1.45–1.50)	1.38 (1.31–1.46)	*0.102*
CKD, stage 4	1.55 (1.52–1.58)	1.63 (1.59–1.67)	1.61 (1.57–1.66)	1.56 (1.42–1.71)	*<0.001*
CKD, stage 5	1.94 (1.87–2.01)	2.09 (1.99–2.19)	1.86 (1.75–1.98)	1.58 (1.23–2.03)	*<0.001*

Dialysis	2.57 (2.51–2.63)	2.68 (2.61–2.76)	2.55 (2.46–2.66)	1.93 (1.61–2.32)	*0.001*
CKD, unspecified	1.11 (1.08–1.14)	1.20 (1.16–1.25)	1.14 (1.09–1.20)	0.78 (0.66–0.92)	*<0.001*
p of heterogeneity	*<0.001*	*<0.001*	*<0.001*	*<0.001*	

Hospitalisations without kidney diseases served as the reference. Patients who died during the hospitalisation were excluded from the calculations for facility discharge, 30-day and 1-year all-cause rehospitalisation. * OR for binary outcomes calculated by a multivariable logistic model adjusted for age, sex, level of healthcare insurance, year of admission, month of admission, modality of admission (emergency vs planned) and level of hospital care; ** Changes in % for continuous outcomes calculated by a multivariable generalised linear gamma regression based on log-transformed values adjusted for age, sex, level of healthcare insurance, year of admission, month of admission, modality of admission (emergency vs planned) and level of hospital care. Abbreviations: CI, confidence interval; CKD, chronic kidney disease; ICU, intensive care unit; LOS, length of stay; OR, odds ratio.

CKD is diagnosed by the persistent elevation of urinary albumin excretion (albuminuria), low estimated glomerular filtration rate (eGFR) or other manifestations of kidney damage [22, 23]. According to the loss of renal function, CKD is divided into 7 stages (1 to 5, with additional stratification of stage 3 into 3a and 3b and stage 5 with or without dialysis) [22]. While there was a steep increase in prevalence of AKI codes between 2017 and 2020, hospitalisations with a code of CKD did not rise to the same extent. In detail, the percentage of CKD among the overall hospitalised medical population with multimorbidity rose from 9.5% in 2012 to 12.8% in 2016 and then plateaued (11.5% in 2020). This increase of about 2% is also consistent with previous literature assessing global dimensions of CKD [24]. Associations between CKD stages and adverse in-hospital outcomes were more heterogeneous than in hospitalisations with AKI. In particular, the risk of in-hospital mortality, ICU admission, hospital readmission and a longer LOS was increased in hospitalisations with CKD, with a certain "dose-dependent" effect – meaning that people with more-severe CKD stages were at a higher risk. These findings are comparable to previous studies showing a CKD stage-dependent association of in-hospital outcomes and resource use [25]. Interestingly, the CKD stage-dependent association was no longer observed in hospitalisations with dialysis, even though these hospitalisations carry a high burden of multimorbidity. It could be hypothesised that the decision not to start dialysis in hospitalisations with higher baseline mortality risk might explain this finding [26]. Like in hospitalisations with AKI, the presence of frailty in hospitalisations with CKD did not modify the relative risk estimates in a clinically meaningful manner. However, the absence of effect modification must be interpreted carefully as the development of frailty – a clinically detectable state of decreased physiological reserve and increased vulnerability to stressors and poor clinical outcomes [27, 28] – is also influenced by the presence of CKD by its effect on sarcopenia, mobility, cognitive impairment and exhaustion or through vascular complications [29, 30]. Multimorbidity, polypharmacy and unfavourable behavioural factors add to the complexity and challenges in the management of hospitalisations with kidney disease, which, again, is not yet adequately reimbursed. This is also further evidenced by a previous pop-

Figure 2: B-spline analysis of primary outcomes among hospitalisations with AKI by number of chronic conditions, according to frailty. a) In-hospital mortality, b) ICU stay, c) 30-day hospital readmission and d) length of hospital stay. Shaded regions denote 95% confidence intervals. Abbreviations: ICU, intensive care unit.



ulation-based cohort study of 2.5 million Canadian adults showing that patients seen by nephrologists were consistently more complex [31].

This study has limitations. First, using administrative data is prone to information bias as hospitalisations were selected according to ICD-10 codes with the risk of misclassification and underreporting of diagnoses. Thus, we were not able to evaluate hospitalisations with unrecognised AKI or CKD. Due to this, AKI and CKD, particularly lower stages, may have been underreported in ICD-10 codes, which may underestimate admissions complicated by AKI and CKD [6, 15]. Second, hospitalisations with codes for both AKI and CKD were classified under the AKI group, based on the assumption that AKI was the primary medical condition. To avoid any potential misinterpretation, we conducted a sensitivity analysis that differentiated between hospitalisations for "AKI only" and those involving "acute-on-chronic kidney disease". This analysis revealed no clinically significant differences in the outcomes for all measured variables between the two groups (data not shown). Third, although we present longitudinal data, for hospitalisations with AKI not all years are represented, and the main analysis of this subpopulation was done with data from 2017 to 2020 only. Fourth, due to administrative restrictions, there was no information on out-of-hospital mortality available. Fifth, the study unit for this investigation was hospitalisations rather than patients. Consequently, hospitalisations could have been included more than once without opportunity for adjustment. Sixth, the non-experimental, observational design of our study limits the ability to draw a firm causal link. Seventh, we did not have information on treatment-level data, including clinical appearance, medication administration, and laboratory data.

Conclusion

This study provides evidence that the presence of kidney disease in hospitalisations with known multimorbidity is associated with additional risk of in-hospital adverse outcomes. Our data show that the presence of AKI entails a clinically relevant higher risk of adverse outcomes as compared to hospitalisations with the same level of frailty but no kidney disease. An accurate and thorough understanding of in-hospital resource utilisation can be of great value, as economic evaluations in the population with kidney disease were often generated using older healthcare resource use estimates or data not derived from real-world evidence.

Availability of data and materials

The availability of data generated or analysed during this study is subject to restrictions for reasons of patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

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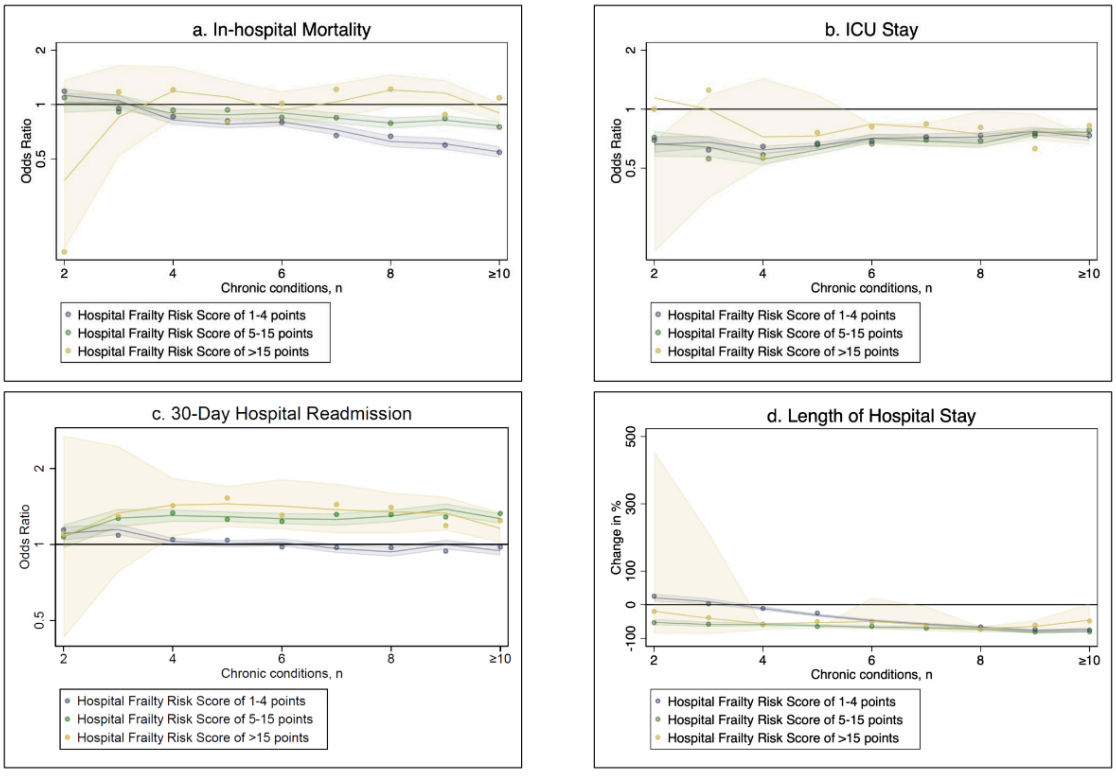
Figure 3: B-spline analysis of primary outcomes among hospitalisations with CKD by number of chronic conditions, according to frailty. a) In-hospital mortality, b) ICU stay, c) 30-day hospital readmission and d) length of hospital stay. Shaded regions denote 95% confidence intervals. Abbreviations: ICU, intensive care unit.



Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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Appendix

Table S1:
Baseline characteristics stratified by presence of kidney disease among non-frail hospitalisations.

	No kidney disease	AKI	CKD
Hospitalisations, n	1,544,175	49,521	253,413
Patients, n	920,620	44,848	151,753
Demographics			
Age, median (IQR) [years]	69 (57–78)	76 (67–84)	79 (71–85)
Male sex, n (%)	849,803 (55.0)	29,872 (60.3)	144,339 (57.0)
Female sex, n (%)	694,372 (45.0)	19,649 (39.7)	109,074 (43.0)
Swiss nationality, n (%)	1,262,958 (81.8)	41,162 (83.1)	216,622 (85.5)
Other nationality, n (%)	281,217 (18.2)	8359 (16.9)	36,791 (14.5)
Supplementary insurance, n (%)	371,045 (24.0)	10,489 (21.2)	64,217 (25.3)
Admission data			
Year of admission, n (%)			
2012	167,301 (10.8)	2653 (5.4)	25,227 (10.0)
2013	168,676 (10.9)	1580 (3.2)	26,166 (10.3)
2014	172,844 (11.2)	1521 (3.1)	28,481 (11.2)
2015	176,091 (11.4)	1384 (2.8)	29,215 (11.5)
2016	179,395 (11.6)	1211 (2.4)	29,187 (11.5)
2017	171,328 (11.1)	9784 (19.8)	27,140 (10.7)
2018	170,672 (11.1)	10,602 (21.4)	29,139 (11.5)
2019	173,752 (11.3)	10,504 (21.2)	30,493 (12.0)
2020	164,116 (10.6)	10,282 (20.8)	28,365 (11.2)
Emergency admission, n (%)	1,016,028 (65.8)	41,464 (83.7)	180,053 (71.1)
Admission from home, n (%)	1,367,643 (88.6)	42,144 (85.1)	220,975 (87.2)
Tertiary care hospital: University hospital	278,864 (18.1)	9202 (18.6)	42,920 (16.9)
Tertiary care hospital: non-university hospital	889,483 (57.6)	30,688 (62.0)	155,243 (61.3)
Secondary care hospital	375,828 (24.3)	9631 (19.4)	55,250 (21.8)
Comorbidities, n (%)			
Hypertension	745,929 (48.3)	31,054 (62.7)	184,210 (72.7)
Obesity	41,292 (2.7)	1404 (2.8)	8085 (3.2)
Type 2 diabetes mellitus	239,887 (15.5)	13,557 (27.4)	77,739 (30.7)
Type 1 diabetes mellitus	9307 (0.6)	409 (0.8)	2080 (0.8)
Dyslipidaemia	335,446 (21.7)	10,588 (21.4)	64,364 (25.4)
Coronary artery disease	428,147 (27.7)	15,568 (31.4)	99,855 (39.4)
Myocardial infarction	111,210 (7.2)	3793 (7.7)	14,210 (5.6)
Congestive heart failure	157,945 (10.2)	15,874 (32.1)	74,405 (29.4)
Atrial fibrillation	233,994 (15.2)	15,277 (30.8)	81,796 (32.3)
Peripheral arterial disease	64,198 (4.2)	3061 (6.2)	27,733 (10.9)
Obstructive sleep apnoea syndrome	49,634 (3.2)	2196 (4.4)	11,010 (4.3)
Cerebrovascular disease	77,270 (5.0)	983 (2.0)	9816 (3.9)
Ischaemic stroke	40,684 (2.6)	345 (0.7)	3619 (1.4)
Chronic obstructive pulmonary disease	140,061 (9.1)	5331 (10.8)	29,258 (11.5)
Gastrointestinal disorder	348,419 (22.6)	15,030 (30.4)	61,106 (24.1)
Solid cancer	255,989 (16.6)	7546 (15.2)	24,867 (9.8)
Haematological malignancy	55,958 (3.6)	2643 (5.3)	8569 (3.4)
Musculoskeletal disorder	275,431 (17.8)	9745 (19.7)	59,631 (23.5)
Mental disorder	378,659 (24.5)	7551 (15.2)	37,020 (14.6)
Alcohol addiction	109,516 (7.1)	2887 (5.8)	5638 (2.2)
Elixhauser comorbidity index, mean (SD)	2.35 (1.48)	3.68 (1.80)	4.197958 (1.68)
Number of chronic comorbidities, n (%)			
2	370,183 (24.0)	5677 (11.5)	10,349 (4.1)
3	340,295 (22.0)	6815 (13.8)	20,882 (8.2)
4	282,255 (18.3)	7278 (14.7)	31,032 (12.2)
5	206,298 (13.4)	6871 (13.9)	37,028 (14.6)
≥6	345,144 (22.4)	22,880 (46.2)	154,122 (60.8)

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; IQR, interquartile range; SD, standard deviation.

Table S2:
Baseline characteristics stratified by presence of kidney disease among pre-frail hospitalisations.

	No kidney disease	**AKI**	**CKD**
Hospitalisations, n	421,031	126,678	181,518
Patients, n	314,819	103,911	124,812
Demographics			
Age, median (IQR) [years]	77 (66–84)	79 (70–85)	82 (75–87)
Male sex, n (%)	197,446 (46.9)	69,215 (54.6)	87,694 (48.3)
Female sex, n (%)	223,585 (53.1)	57,463 (45.4)	93,824 (51.7)
Swiss nationality, n (%)	361,537 (85.9)	107,848 (85.1)	159,523 (87.9)
Other nationality, n (%)	59,494 (14.1)	18,830 (14.9)	21,995 (12.1)
Supplementary insurance, n (%)	94,275 (22.4)	25,323 (20.0)	43,336 (23.9)
Admission data			
Year of admission, n (%)			
2012	38,835 (9.2)	4489 (3.5)	15,591 (8.6)
2013	43,706 (10.4)	3843 (3.0)	17,972 (9.9)
2014	46,175 (11.0)	3773 (3.0)	20,205 (11.1)
2015	50,453 (12.0)	3986 (3.1)	22,540 (12.4)
2016	53,164 (12.6)	3867 (3.1)	26,090 (14.4)
2017	45,058 (10.7)	24,227 (19.1)	18,223 (10.0)
2018	46,522 (11.0)	27,083 (21.4)	19,221 (10.6)
2019	48,579 (11.5)	27,814 (22.0)	20,680 (11.4)
2020	48,539 (11.5)	27,596 (21.8)	20,996 (11.6)
Emergency admission, n (%)	353,037 (83.9)	111,564 (88.1)	154,596 (85.2)
Admission from home, n (%)	332,375 (78.9)	100,672 (79.5)	143,668 (79.1)
Tertiary care hospital: University hospital	80,948 (19.2)	24,205 (19.1)	25,251 (13.9)
Tertiary care hospital: non-university hospital	249,559 (59.3)	80,186 (63.3)	115,354 (63.5)
Secondary care hospital	90,524 (21.5)	22,287 (17.6)	40,913 (22.5)
Comorbidities, n (%)			
Hypertension	225,920 (53.7)	83,920 (66.2)	133,538 (73.6)
Obesity	9250 (2.2)	4524 (3.6)	6093 (3.4)
Type 2 diabetes mellitus	72,799 (17.3)	37,712 (29.8)	55,495 (30.6)
Type 1 diabetes mellitus	1760 (0.4)	856 (0.7)	1143 (0.6)
Dyslipidaemia	71,049 (16.9)	25,095 (19.8)	36,194 (19.9)
Coronary artery disease	71,667 (17.0)	36,678 (29.0)	57,742 (31.8)
Myocardial infarction	11,697 (2.8)	7067 (5.6)	7501 (4.1)
Congestive heart failure	53,281 (12.7)	40,783 (32.2)	54,884 (30.2)
Atrial fibrillation	83,830 (19.9)	42,929 (33.9)	63,633 (35.1)
Peripheral arterial disease	15,444 (3.7)	9906 (7.8)	17,602 (9.7)
Obstructive sleep apnoea syndrome	12,246 (2.9)	6204 (4.9)	7557 (4.2)
Cerebrovascular disease	93,337 (22.2)	7610 (6.0)	23,442 (12.9)
Ischaemic stroke	50,142 (11.9)	2678 (2.1)	8982 (4.9)
Chronic obstructive pulmonary disease	43,571 (10.3)	16,278 (12.8)	23,024 (12.7)
Gastrointestinal disorder	119,462 (28.4)	47,379 (37.4)	54,874 (30.2)
Solid cancer	55,500 (13.2)	16,311 (12.9)	17,079 (9.4)
Haematological malignancy	11,522 (2.7)	4869 (3.8)	4779 (2.6)
Musculoskeletal disorder	114,337 (27.2)	36,364 (28.7)	61,734 (34.0)
Mental disorder	191,962 (45.6)	45,468 (35.9)	68,877 (37.9)
Alcohol addiction	39,607 (9.4)	10,945 (8.6)	6868 (3.8)
Elixhauser comorbidity index, mean (SD)	3.29 (1.75)	4.76 (2.05)	4.87 (1.87)
Number of chronic comorbidities, n (%)			
2	44,340 (10.5)	7355 (5.8)	4243 (2.3)
3	60,366 (14.3)	10,671 (8.4)	9462 (5.2)
4	67,230 (16.0)	13,509 (10.7)	15,715 (8.7)
5	64,392 (15.3)	14,773 (11.7)	20,481 (11.3)
≥6	184,703 (43.9)	80,370 (63.4)	131,617 (72.5)

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; IQR, interquartile range; SD, standard deviation.

Table S3:
Baseline characteristics stratified by presence of kidney disease among frail hospitalisations.

	No kidney disease	AKI	CKD
Hospitalisations, n	34,435	22,671	18,059
Patients, n	30,411	20,845	16,079
Demographics			
Age, median (IQR) [years]	81 (74–86)	81 (74–87)	84 (78–88)
Male sex, n (%)	14,961 (43.4)	11,239 (49.6)	7890 (43.7)
Female sex, n (%)	19,474 (56.6)	11,432 (50.4)	10,169 (56.3)
Swiss nationality, n (%)	29,976 (87.1)	19,354 (85.4)	15,984 (88.5)
Other nationality, n (%)	4459 (12.9)	3317 (14.6)	2075 (11.5)
Supplementary insurance, n (%)	7604 (22.1)	4256 (18.8)	4233 (23.4)
Admission data			
Year of admission, n (%)			
2012	2430 (7.1)	471 (2.1)	1188 (6.6)
2013	2937 (8.5)	516 (2.3)	1444 (8.0)
2014	3274 (9.5)	565 (2.5)	1908 (10.6)
2015	4087 (11.9)	694 (3.1)	2230 (12.3)
2016	4377 (12.7)	751 (3.3)	2940 (16.3)
2017	3719 (10.8)	3886 (17.1)	1694 (9.4)
2018	3930 (11.4)	4789 (21.1)	1838 (10.2)
2019	4475 (13.0)	5208 (23.0)	2159 (12.0)
2020	5206 (15.1)	5791 (25.5)	2658 (14.7)
Emergency admission, n (%)	29,586 (85.9)	20,146 (88.9)	15,781 (87.4)
Admission from home, n (%)	23,155 (67.2)	15,528 (68.5)	12,313 (68.2)
Tertiary care hospital: University hospital	8128 (23.6)	5638 (24.9)	3162 (17.5)
Tertiary care hospital: non-university hospital	20,324 (59.0)	13,953 (61.5)	11,516 (63.8)
Secondary care hospital	5983 (17.4)	3080 (13.6)	3381 (18.7)
Comorbidities, n (%)			
Hypertension	19,812 (57.5)	15,758 (69.5)	13,509 (74.8)
Obesity	683 (2.0)	995 (4.4)	583 (3.2)
Type 2 diabetes mellitus	6253 (18.2)	6853 (30.2)	5535 (30.6)
Type 1 diabetes mellitus	89 (0.3)	104 (0.5)	92 (0.5)
Dyslipidaemia	5696 (16.5)	4468 (19.7)	3485 (19.3)
Coronary artery disease	6009 (17.5)	6433 (28.4)	5228 (28.9)
Myocardial infarction	961 (2.8)	1346 (5.9)	723 (4.0)
Congestive heart failure	4939 (14.3)	7598 (33.5)	5103 (28.3)
Atrial fibrillation	8598 (25.0)	8625 (38.0)	6923 (38.3)
Peripheral arterial disease	1376 (4.0)	2044 (9.0)	1678 (9.3)
Obstructive sleep apnoea syndrome	880 (2.6)	1123 (5.0)	630 (3.5)
Cerebrovascular disease	13,490 (39.2)	4756 (21.0)	5991 (33.2)
Ischaemic stroke	5019 (14.6)	1501 (6.6)	1945 (10.8)
Chronic obstructive pulmonary disease	2609 (7.6)	2693 (11.9)	1808 (10.0)
Gastrointestinal disorder	10,673 (31.0)	9893 (43.6)	6017 (33.3)
Solid cancer	2497 (7.3)	2076 (9.2)	1229 (6.8)
Haematological malignancy	501 (1.5)	618 (2.7)	307 (1.7)
Musculoskeletal disorder	11,292 (32.8)	8845 (39.0)	7401 (41.0)
Mental disorder	26,084 (75.7)	15,753 (69.5)	13,023 (72.1)
Alcohol addiction	2942 (8.5)	2233 (9.8)	805 (4.5)
Elixhauser comorbidity index, mean (SD)	3.81 (2.05)	5.53 (2.29)	5.39 (2.09)
Number of chronic comorbidities, n (%)			
2	802 (2.3)	330 (1.5)	59 (0.3)
3	2159 (6.3)	716 (3.2)	254 (1.4)
4	3479 (10.1)	1196 (5.3)	686 (3.8)
5	4259 (12.4)	1694 (7.5)	1184 (6.6)
≥6	23,736 (68.9)	18,735 (82.6)	15,876 (87.9)

Abbreviations: AKI, acute kidney injury; CKD, chronic kidney disease; IQR, interquartile range; SD, standard deviation.