

Inside ANEMIA of CKD: microsimulation modeling of the epidemiological burden of anemia of CKD in the USA



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1. Introduction

- Chronic kidney disease (CKD) is a debilitating condition that affects approximately 10% of the global population. CKD is linked to an increased risk of cardiovascular (CV) disease and all-cause mortality.¹
- Anemia is common in patients with CKD, occurring in approximately 15% of patients, and is associated with a high risk of complications and reduced quality of life.^{2,3}
- Patients with CKD in the more advanced stages are at the highest risk of developing anemia and CV complications.
- The number of patients in the USA who will be affected by anemia of CKD over the next 5 years and who will require treatment has not been reliably estimated.

2. Objective

- To project the epidemiological burden of anemia of CKD in the USA using the patient-level, microsimulation-based *Inside ANEMIA of CKD* model.

3. Methods

- Using an open-cohort analysis, a dynamic population-level microsimulation was developed to estimate the epidemiological burden of patients with anemia of CKD in the USA from 2021 to 2026 (Figure 1).
- The population model used national data sources (US Census Bureau, National Health and Nutrition Examination Survey [NHANES], Centers for Disease Control and Prevention) to inform parameters of population estimates and projections, fertility and birth rates (by the mother's age), and mortality. Virtual patients were categorized according to estimated glomerular filtration rate (eGFR) and albuminuria status using data obtained from the NHANES extrapolated to the US population.⁴
- CKD stages were defined as discrete health states in line with Kidney Disease Improving Global Outcomes (KDIGO) 2012 recommendations.⁵ Stage 5 CKD comprised patients with an eGFR < 15 mL/min/1.73 m² who were not undergoing dialysis, as well as those undergoing renal replacement therapy, which included dialysis (any modality) and renal transplant.

- eGFR slopes described in the literature were used in the model to determine the rate of CKD progression and the relative risk of developing complications according to an individual's clinical characteristics and comorbidities. Proportions of patients with fast or slow progression were derived from the literature.
- Severity of anemia was categorized as mild (hemoglobin [Hb] levels of 11.0–11.9 g/dL in women and 11.0–12.9 g/dL in men), moderate (Hb levels of 8.0–10.9 g/dL), or severe (Hb levels of < 8.0 g/dL for both women and men) in accordance with the World Health Organization (WHO) guidelines.⁶ Each time an individual reaches a specific CKD stage in the model, they have a probability of being assigned with one of the three anemia categories (none, mild and moderate-severe in accordance with the WHO categories) based on the severity of their CKD; probabilities were modeled on input from the NHANES (2017–2018).
- Incidence of CV complications, heart failure, myocardial infarction and stroke were drawn from literature sources appropriate to the US population.^{7,8} Data on the current treatment of anemia (treatment per level of anemia in patients with CKD) with erythropoiesis-stimulating agents (ESAs), red blood cell transfusions and intravenous iron were obtained from the literature.⁹
- Assumptions for this model included:
 - eGFR and albuminuria were independent predictors of CKD and related CV complications
 - individuals were randomly assigned a percentile in the albuminuria distribution (the assumed relative position was fixed throughout the simulation)
 - patients with CKD could die from CV complications or other causes.

4. Results

- The prevalence of stage 3a–5 CKD with anemia is projected to increase from 5.4 million cases in 2021 to 6.9 million cases in 2026.
 - The overall prevalence of anemia of stage 3a–5 CKD in the USA is projected to increase by approximately 30% by 2026; cases of mild anemia of stage 3a–5 CKD are projected to increase by approximately 25%, with a greater increase (41%) in the prevalence of moderate-severe anemia of CKD by 2026 (Figure 2).

Figure 2. Projected prevalence of mild and moderate-severe anemia in patients with CKD by disease stage in the USA from 2021 to 2026.

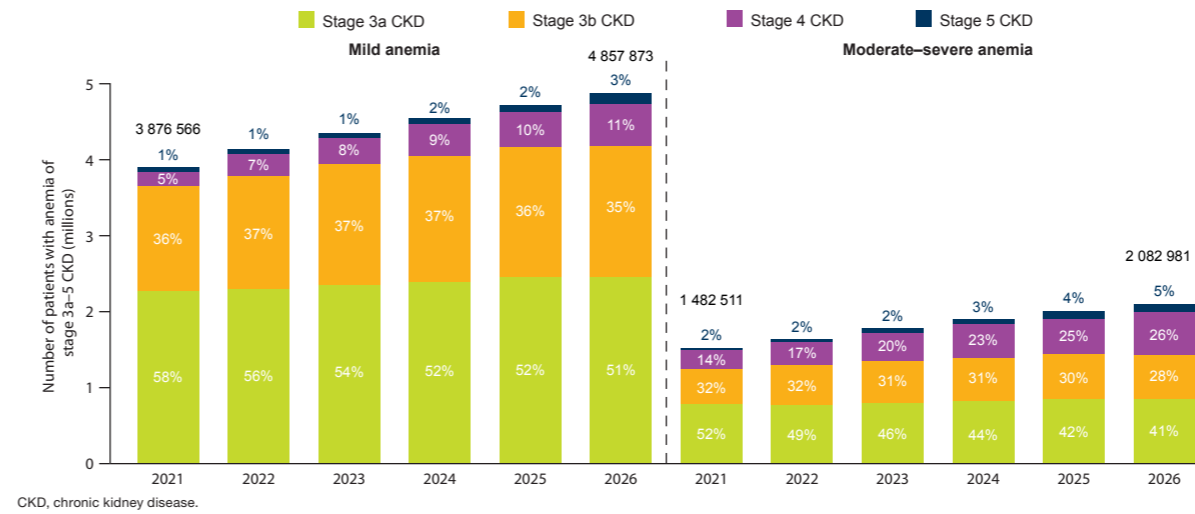


Figure 3. Projected incidence of cardiovascular complications in patients with anemia of CKD by disease stage in the USA from 2021 to 2026.

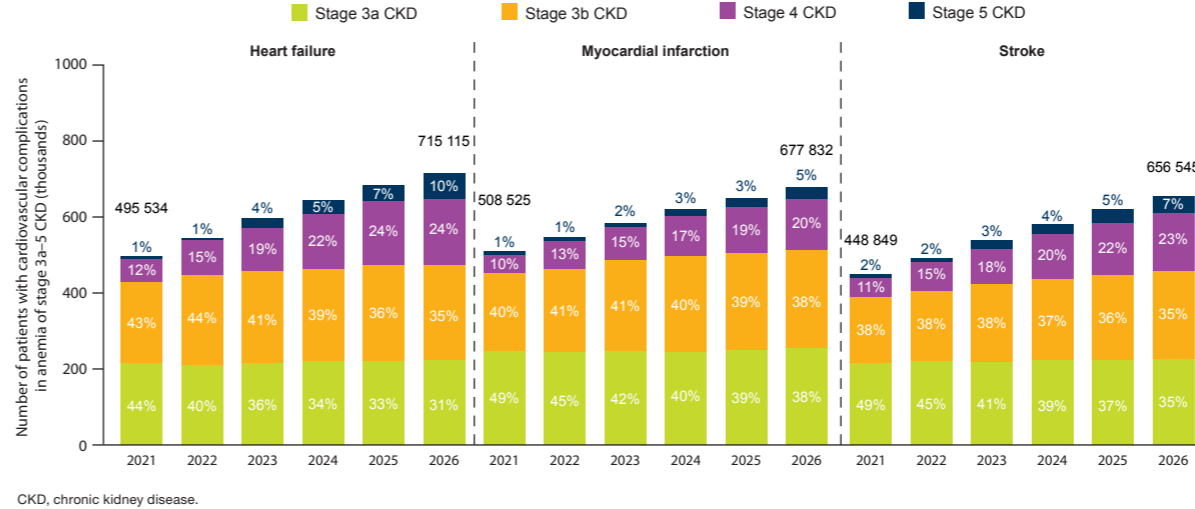


Figure 4. Projected changes in treatment of moderate-severe anemia in patients with stage 3a–5 CKD in the USA from 2021 to 2026.

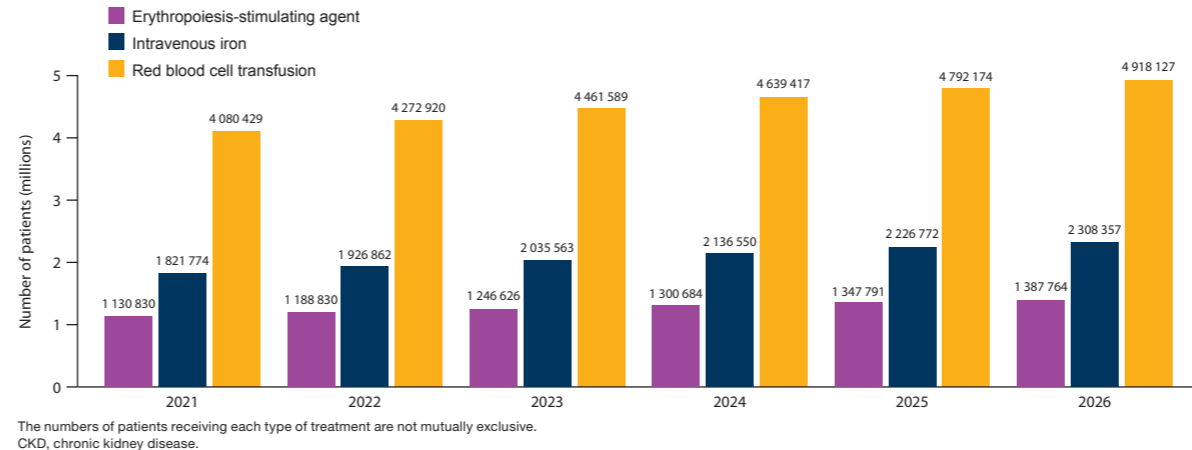
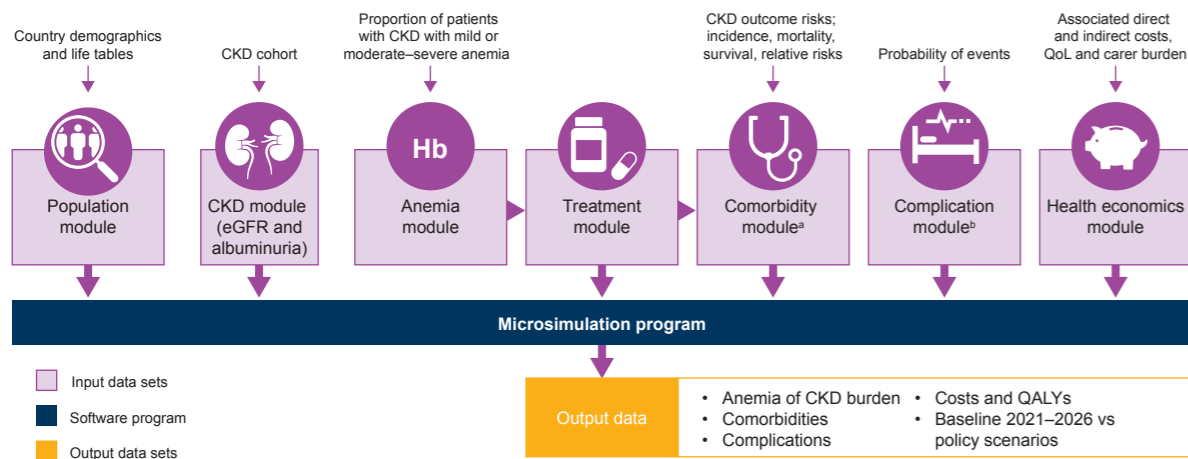


Figure 1. The flexible *Inside ANEMIA of CKD* microsimulation.



*Diabetes, hypertension, heart failure. [†]Myocardial infarction, heart failure, stroke. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; QALY, quality-adjusted life year; QoL, quality of life.

- The incidence of CV complications in patients with anemia of stage 3a–5 CKD is also projected to increase, with estimated increases of 219 581 cases for heart failure, 169 307 cases for myocardial infarction and 207 696 cases for stroke by 2026 (Figure 3).
- The number of patients with moderate-severe anemia of stage 3a–5 CKD requiring treatment is projected to increase by 22%, from 7.0 million in 2021 to 8.6 million in 2026, with a 23% increase in ESA treatment, a 27% increase in intravenous iron and a 21% increase in red blood cell transfusion (Figure 4), assuming no changes in treatment patterns over the 6-year period.
- Sensitivity analyses conducted using alternative eGFR slopes demonstrated similar projected prevalence of CKD.

5. Conclusions

- The *Inside ANEMIA of CKD* microsimulation is a novel model that projects the changes in epidemiology of anemia of CKD to increase disease awareness and inform healthcare policy.
- The prevalence of anemia of stage 3a–5 CKD in the USA is projected to increase by approximately 30% from 2021 to 2026, and the number of patients with mild anemia of stage 3a–5 CKD is projected to increase by 25%.
- The relatively large projected increase in prevalence of more moderate-severe anemia of stage 3a–5 CKD, and an increase in related CV complications, could put healthcare services under greater pressure.
- In fact, the number of patients with anemia of CKD requiring treatment is projected to increase by 22%. Nearly 5 million patients are projected to receive red blood cell transfusion in 2026, despite this treatment option being associated with adverse events¹⁰ and having a possible impact on future transplantation.¹¹ More than 1.3 million patients could receive ESA therapy, which is also associated with adverse events.¹²
- This microsimulation projects the likely burden of anemia of CKD over the next 5 years and demonstrates a need for healthcare policy in the USA to prepare to support this patient population.

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Disclosures

LR and LW are employees of HealthLumen. JJGS, CC, SG, NR, PB and JD are employees of AstraZeneca. LS, KHPY and RL are employees of FibroGen. NT and JBW received financial support to attend data review meetings.

Inside ANEMIA of CKD: quantifying the epidemiological burden of anemia of CKD in Canada via microsimulation modelling



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Introduction

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- Anemia is common in patients with CKD, occurring in approximately 15% of patients, and is associated with a high risk of complications and reduced quality of life.^{2,3}
- Patients with CKD in the more advanced stages are at the highest risk of developing anemia and CV complications.
- The number of patients in Canada who will be affected by anemia of CKD over the next 5 years and who will require treatment has not been reliably estimated.

Objective

- To project the epidemiological burden of anemia of CKD in Canada using the patient-level, microsimulation-based *Inside ANEMIA of CKD* model.

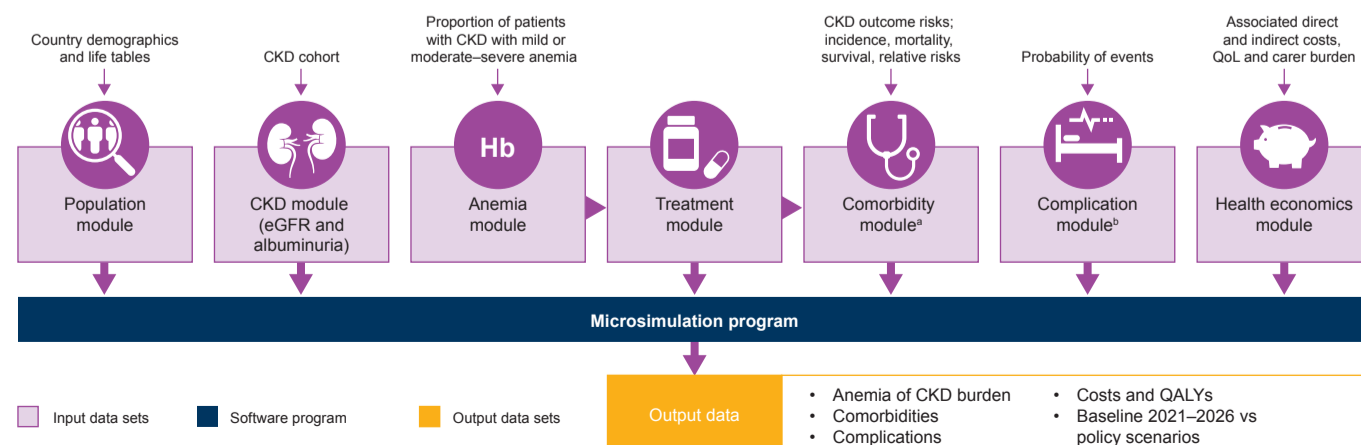
Methods

- Using an open-cohort analysis, a dynamic population-level microsimulation was developed to estimate the epidemiological burden of anemia in CKD in Canada from 2021 to 2026 (Figure 1).
- The population model used national data sources and a provincial renal database to inform parameters of population estimates and projections, fertility and birth rates (by the mother's age), and mortality.
- CKD stages were defined as discrete health states in line with Kidney Disease Improving Global Outcomes (KDIGO) 2012 recommendations.⁴ Stage 5 CKD comprised patients undergoing renal replacement therapy, which included dialysis (any modality) and renal transplant.
- Estimated glomerular filtration rate (eGFR) slopes described in the literature were used in the model to determine the rate of CKD progression and the relative risk of developing complications according to an individual's clinical characteristics and comorbidities. Proportions of patients with fast or slow progression were derived from the literature.
- Severity of anemia was categorized as mild (hemoglobin [Hb] levels of 11.0–11.9 g/dL in women and 11.0–12.9 g/dL in men), moderate (Hb levels of 8.0–10.9 g/dL), or severe (Hb levels of < 8.0 g/dL for both women and men) in accordance with the World Health Organization (WHO) guidelines.⁵ Each time an individual reaches a specific CKD stage in the model, they have a probability of being assigned with one of the three anemia categories (none, mild, and moderate–severe in accordance with the WHO categories) based on the severity of their CKD; probabilities were modelled on input from a provincial renal database.
- Incidence of CV complications, heart failure, myocardial infarction and stroke were drawn from literature sources appropriate to the Canadian population.^{6–10} Data on the current treatment of anemia (treatment per level of anemia in patients with CKD) with erythropoiesis-stimulating agents (ESAs) and intravenous iron were obtained from the literature, and proxy data for red blood cell transfusions were obtained from a US literature source.¹¹
- Assumptions for this model included:
 - eGFR and albuminuria were independent predictors of CKD and related CV complications
 - individuals were randomly assigned a percentile in the albuminuria distribution (the assumed relative position was fixed throughout the simulation)
 - patients with CKD could die from CV complications or other causes.

Results

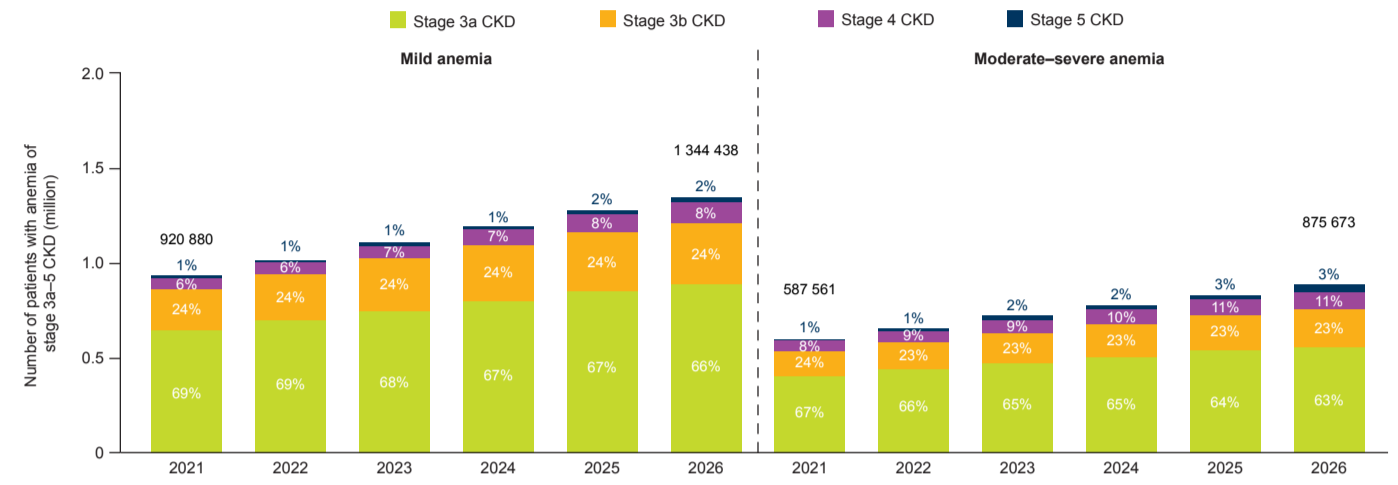
- The *Inside ANEMIA of CKD* microsimulation projects that the prevalence of anemia of stage 3a–5 CKD in Canada will increase from approximately 1.5 million patients in 2021 to 2.2 million patients in 2026.
- The proportions of patients with anemia of stage 3a–5 CKD are projected to increase markedly across all disease severities; with approximately 46% more patients with CKD having mild anemia and 49% more patients having moderate–severe anemia by 2026 (Figure 2).

Figure 1. The flexible *Inside ANEMIA of CKD* microsimulation.



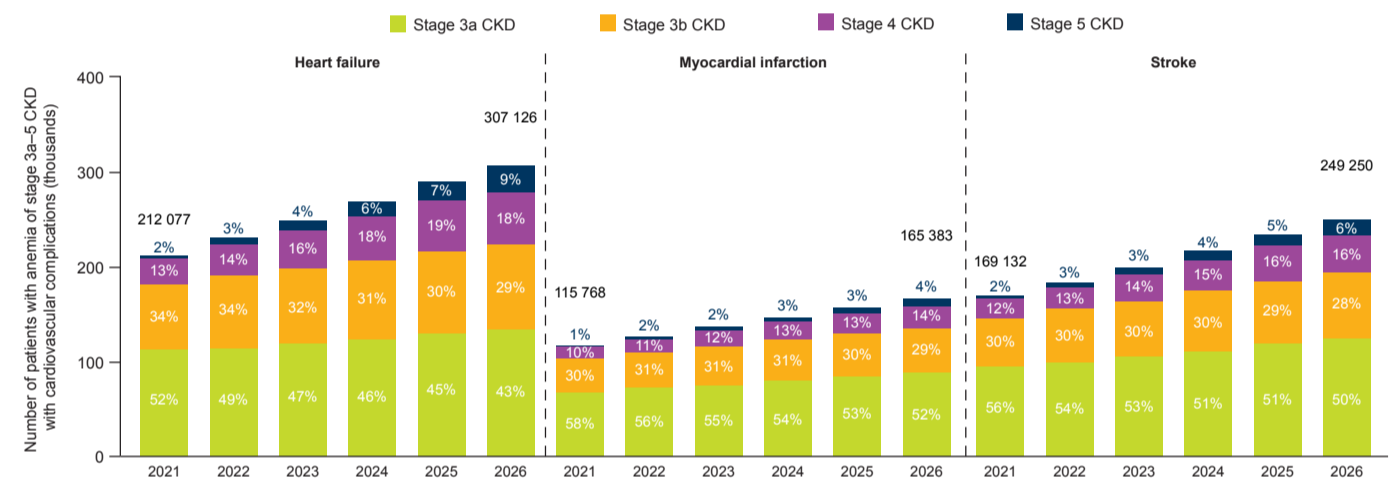
^{*}Diabetes, hypertension, heart failure; [†]myocardial infarction, heart failure, stroke. CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; QALY, quality-adjusted life year; QoL, quality of life.

Figure 2. Projected prevalence of mild and moderate–severe anemia of stage 3a–5 CKD by disease stage in Canada from 2021 to 2026.



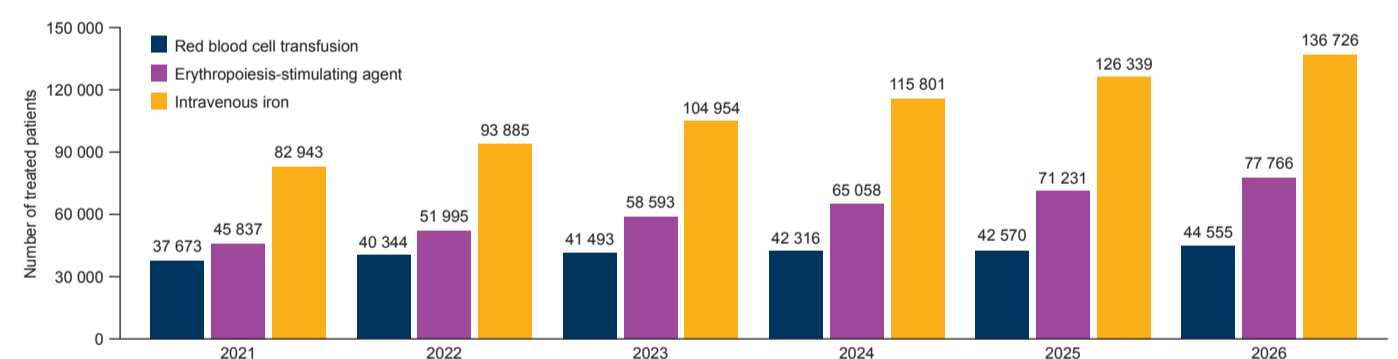
CKD, chronic kidney disease.

Figure 3. Projected prevalence of cardiovascular complications by disease stage in patients with anemia of stage 3a–5 CKD from 2021 to 2026.



CKD, chronic kidney disease.

Figure 4. Projected changes in treatment of moderate–severe anemia of stage 3a–5 CKD from 2021 to 2026.



The numbers of patients receiving each type of treatment are not mutually exclusive. CKD, chronic kidney disease.

- The prevalence of CV complications is also projected to increase by 45% overall in patients with anemia of stage 3a–5 CKD, with estimated increases of 95,049 cases of heart failure, 49,615 cases of myocardial infarction and 80,118 cases of stroke by 2026 (Figure 3).
- The number of patients with moderate–severe anemia of stage 3a–5 CKD requiring treatment is projected to increase by 53%, from 418,180 in 2021 to 640,756 in 2026, with an increase from 45,837 to 77,766 interventions with ESA therapy, an increase from 83,943 to 136,726 interventions with intravenous iron, and an increase from 37,673 to 44,555 in red blood cell transfusions (Figure 4), assuming no changes in treatment patterns over the 6-year period.
- Sensitivity analyses conducted using alternative eGFR slopes demonstrated similar projected prevalence of CKD.

Conclusions

- Inside ANEMIA of CKD* is the first microsimulation model to project the epidemiological burden of anemia attributable to CKD in Canada.
- The prevalence of anemia of stage 3a–5 CKD in Canada is projected to increase by approximately 46% from 2021 to 2026, and the number of patients with anemia of stage 3a–5 CKD is estimated to increase markedly across all disease severities.
- The projected increasing prevalence of advanced CKD and associated anemia, as well as the estimated increases in numbers of related CV events and patients who will require treatment, could put healthcare systems under greater pressure.
- Approximately 44,555 patients are projected to receive red blood cell transfusions in 2026, despite this treatment option being associated with adverse events¹² and having a possible impact on future kidney transplantation.¹³ More than 77,000 patients could receive ESA therapy, which is also associated with a serious adverse event profile.¹⁴
- This microsimulation projects the likely burden of anemia of CKD over the next 5 years and demonstrates a need for the Canadian health system to prepare to support this patient population.

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Acknowledgments and Disclosures

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