Prevalence of Chronic Neutropenic Disorders in the United States: A Retrospective Analysis of a Large Claims Database

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INTRODUCTION

- Chronic neutropenia encompasses multiple blood disorders characterized by low levels of peripheral blood neutrophils, with absolute neutrophil count <1500/uL for >3 months[1]
- Primary chronic neutropenic (CN) disorders (Table 1) are associated with increased risk of infections and impaired quality of life in affected individuals[2-4]

Table 1. Causes of Chronic Neutropenia[1,2,4-9]

CN disorder	Characterized by	Commonly associated variants	ICD-10-CM code[a]
Congenital	Genetic variants	*ELANE*[b]	D70.0[6]
Cyclic	Recurrent neutropenia with episodes repeating typically every 3 weeks	*ELANE*	D70.4[7]
Chronic Idiopathic Neutropenia (CIN)	Persistent neutropenia of unknown underlying cause and may overlap with autoimmune neutropenia	Unknown	D70.8[8] D70.9[9]

CIN, chronic idiopathic neutropenia; CN, chronic neutropenic; ICD-10-CM, International Classification of Disease 10th Revision, Clinical Modification.

[a]ICD-10-CM diagnosis code D70, Neutropenia, encompasses: D70.0, Congenital agranulocytosis; D70.1 Agranulocytosis secondary to cancer chemotherapy; D70.2, Other drug-induced agranulocytosis; D70.3, Neutropenia due to infection; D70.4, Cyclic neutropenia; D70.8, Other neutropenia; D70.9, Neutropenia unspecified.

[b]Additional genetic variants include, but are not limited to, *CSF3R, CXCR2, G6PC3, GFI1, HAX1, JAGN1, and VPS45.*

- To our knowledge, the prevalence of chronic neutropenia in the United States has not been previously reported.[10,11] Determining the estimated projected prevalence of CN disorders in the United States is a key step to understanding the extent of existing unmet medical need for this patient population

AIM

This study aimed to examine the projected prevalence of primary CN disorders in the United States (congenital, cyclic, idiopathic neutropenia) using retrospective analysis of a large US claims database.

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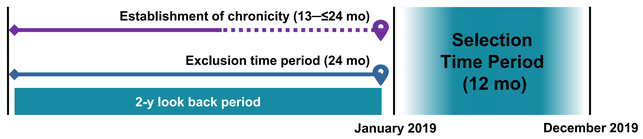
METHODS

- This is a retrospective analysis designed to project the prevalence of CN disorders based on US claims data for people with a diagnosis code for neutropenia during the calendar years 2018, 2019, and 2021
- The year 2020 was excluded from this analysis owing to anticipated reduced claims during the COVID-19 pandemic
- The analysis used longitudinal prescription data (Rx) and office-based claims data (Px) from IQVIA claims database that included 93% of retail Rx claims, 77% of mail-in Rx claims, and had >1.5 billion Px claims per year (includes >80% of active American Medical Association [AMA] office-based health care professionals [HCPs]) in the United States
- People diagnosed with congenital, cyclic, or chronic idiopathic neutropenia (CIN) were identified using the earliest relevant diagnosis claim based on International Classification of Disease 10th Revision, Clinical Modification (ICD-10-CM) codes in the calendar year of interest as index date (Table 1)
- A 13- to 24-month lookback period prior to index date was used to confirm chronic status, where ≥1 relevant neutropenia code (ICD-10-CM code 70.0, 70.4, 70.8 or 70.9) had to be found, or else that individual was excluded (Figure 1). For people who had multiple ICD-10-CM codes, a hierarchical order (cyclic>congenital>CIN) was established to avoid double counting
- People with a diagnostic, procedural, or product code for neutropenia resulting from secondary causes including chemotherapy, drug exposure, infection, solid organ transplantation, myelodysplastic syndrome, and end-stage renal disease within 24-month period prior to selection were excluded
- To ensure completeness of the data, all people in the study were required to meet stability and eligibility criteria (thereby ensuring continuous reporting)
- Results gathered were then projected at the national level by taking a sample of providers who were representative of the office-based universe. This sample was referred to as the projection panel. The projection panel was derived by testing within and between practitioners for both longitudinal and cross-sectional continuity. Projection factors were calculated as the universe of office-based practicing physicians (AMA) divided by the sample of office-based practice physicians. Projection factors were developed and applied at the market-based stratification of time and practitioner specialty or specialty group. The patient sample of interest projection factor results were summed to estimate the projected patient population
- Demographic data including age and sex were captured for all individuals based on diagnostic claims
- Because neutropenias other than CIN (eg, benign ethnic neutropenia and neutropenia due to irradiation) may be included in ICD-10-CM code 70.8, a sensitivity analysis was performed excluding people with the ICD-10-CM code 70.8 to determine the range of the projected CIN population

Figure 1. Approach for Patient Reporting Shown for 2019 as an Example



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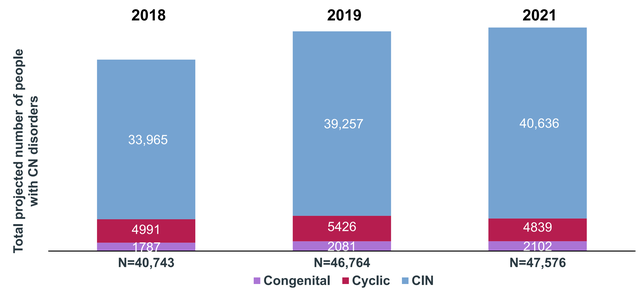
RESULTS

US Projected Prevalence of Primary Chronic Neutropenic Disorders by Type and Years

- Among people diagnosed with a CN disorder, the majority were diagnosed as having CIN every calendar year analyzed, followed by cyclic and then congenital neutropenia (Figure 2)
- When patients with an ICD-10-CM code of 70.8 were excluded in a sensitivity analysis, the projected number of people with CIN in 2018, 2019, and 2021 decreased by 6578 (≈19%), 8946 (≈23%), and 10,287 (≈25%), respectively

Figure 2. Projected Prevalence of CN Disorders by Type of Neutropenia in 2018, 2019, and 2021

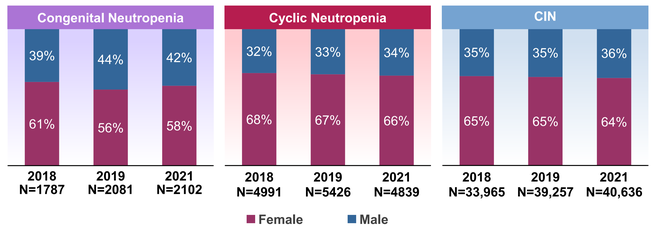


CIN, chronic idiopathic neutropenia; CN, chronic neutropenic.

Distribution of People Diagnosed With Primary Chronic Neutropenic Disorders by Sex

- Regardless of the type of neutropenia, people diagnosed with CN disorders were more likely to be female (Figure 3)

Figure 3. Distribution of CN Disorders by Sex in 2018, 2019, and 2021



CIN, chronic idiopathic neutropenia; CN, chronic neutropenic.

US Projected Prevalence of Primary Chronic Neutropenic Disorders by Age

- Across all 3 types of neutropenia, the majority of people who were diagnosed with a CN disorder were aged ≥18 years (≈92%), while a lower proportion of people were aged 12–17 years (≈3%) and <12 years (≈6%)
- Among people aged <12 years, a greater proportion were diagnosed with congenital neutropenia (13%–20%) compared with cyclic neutropenia (5%–8%) or CIN (5%–6%) (Table 2)

Table 2. Distribution of Projected Proportion of People With CN Disorders by Age in 2018, 2019, and 2021

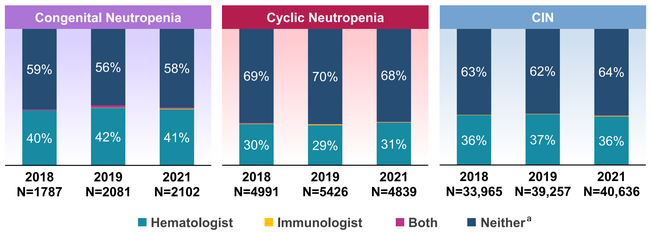
Years	Age, y	Congenital neutropenia,[a] %	Cyclic neutropenia,[a] %	CIN,[a] %
2018	<12	17	8	5
	12–17	6	3	2
	≥18	76	89	93
2019	<12	20	8	6
	12–17	3	4	2
	≥18	77	88	92
2021	<12	13	5	5
	12–17	4	7	2
	≥18	82	88	93

[a]Total projected proportion of people with primary CN disorder.
CIN, chronic idiopathic neutropenia; CN, chronic neutropenic.

Distribution of HCP Specialties That See People Diagnosed With Primary Chronic Neutropenic Disorders

- The majority of people diagnosed with CN disorders saw neither a hematologist nor an immunologist (Figure 4)

Figure 4. Type of HCP Specialists That Saw People With CN Disorders in 2018, 2019, and 2021



CIN, chronic idiopathic neutropenia; CN, chronic neutropenic; HCP, health care professional.
[a]The majority of specialists seen by people diagnosed with CN in the Neither category were Internal Medicine and Family Medicine HCPs.

CONCLUSIONS

- This retrospective analysis of large claims database projected that in 2021, between 37,000–48,000 people in the United States were living with a diagnosis of congenital, cyclic, or idiopathic neutropenia
  - Future analysis of the projected annual prevalence of CN over the next 5 years is required to understand if the growth seen in the CN population between 2018 and 2019 exceeds that of the annual estimated US population growth
- The most common type of primary CN disorder is CIN, followed by cyclic and congenital, with the majority of affected people being of adult age and female
  - The proportion of individuals with cyclic neutropenia in our analysis may have been elevated secondary to the hierarchal ranking used in our methodology and because ICD-10-CM code D70.4 may be used to diagnose non-ELANE cyclic neutropenias (eg, Shwachman–Diamond syndrome, neutropenia associated with autoimmune disease, neutropenia associated with gastrointestinal mucositis, neutropenia associated with nasal or oral mucositis, neutropenia associated with stomatitis, etc)
- In a sensitivity analysis, the projected number of people with CIN decreased by ≈19%–25% with exclusion of ICD-10-CM code 70.8. Future database analyses are needed to ensure non-CIN diagnoses (eg, benign ethnic neutropenia and neutropenia due to irradiation) are excluded from the CIN counts
- Further research is needed to characterize the severity of neutropenia, the number and severity of infections, and overall quality of life in people diagnosed with primary CN disorders in the United States

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