

Prevalence of Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis and Patient Characteristics in a Large Managed Care Population

Michael Charlton¹; Ivy Tonnu-Mihara²; Chia-Chen Teng²; Rakesh Luthra³; Amy Artico⁴; Anthony Hoover⁴; Chioma Uzoigwe⁵

¹Department of Medicine, University of Chicago, Chicago, IL; ²Carelon Research, Wilmington, DE; ³Health Economics and Outcomes Research, Novo Nordisk Inc., Plainsboro, NJ; ⁴Medical Affairs, Novo Nordisk Inc., Plainsboro, NJ; ⁵Real World Evidence, Novo Nordisk Inc., Plainsboro, NJ.

Introduction

- Nonalcoholic fatty liver disease (NAFLD), a condition characterized by excessive fat accumulation in the liver, is the most common chronic liver disease in the US^{1,2}
- Nonalcoholic steatohepatitis (NASH) is the progressive form of NAFLD that may lead to cirrhosis or decompensated cirrhosis, liver failure, hepatocellular carcinoma, and the requirement for liver transplantation³
- A 2023 systematic review estimated the prevalence rates of NAFLD and NASH in North America to be 31% and 5%, respectively; however, there is a paucity of data from real-world settings (e.g., administrative claims from health care providers)¹
- This study aimed to estimate the annual prevalence rates of NAFLD and NASH from 2016 to 2020 and assess the demographic and clinical characteristics of patients diagnosed with NASH using real-world data from a large managed care population in the US

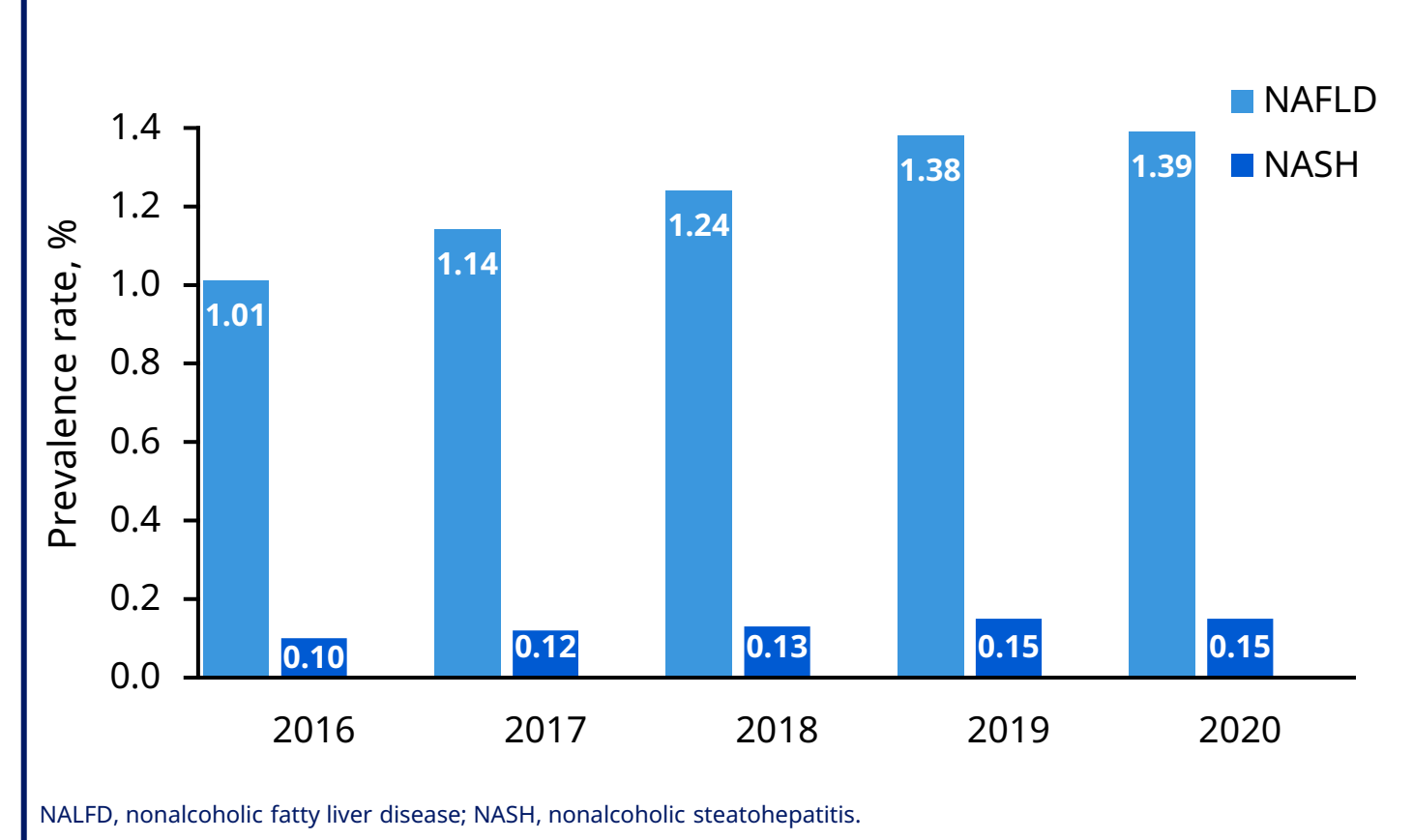
Methods

- This observational study used longitudinal medical and pharmacy claims data from the Healthcare Integrated Research Database (HIRD[®]) to identify patients with NAFLD and NASH, calculate the prevalence rates of NAFLD and NASH, and assess the demographic and clinical characteristics of patients with NASH
- Patients with ≥ 1 International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) claim for NAFLD (code K76.0) or NASH (code K75.81) between 1/1/2016 and 12/31/2020 were included to determine annual prevalence rates
 - Rates were calculated as the number of diagnosed cases divided by the person-years at risk in the given calendar year
- Patients with presence of any other liver-related diagnosis (e.g., other hepatitis-related diseases, alcoholic liver diseases, toxic liver diseases) during the study period were excluded
- Demographic and clinical characteristics and associated medication use were assessed by subgroups and included patients aged ≥ 18 years with a NASH diagnosis (≥ 2 entries for ICD-10-CM K75.81 between 10/1/2016 and 10/31/2020)
- Subgroups analyzed were newly diagnosed NASH, pre-existing NASH, NASH with cirrhosis (ICD-10-CM K71.7, K74.6), NASH without cirrhosis, and NASH with Fibrosis-4 Index (FIB-4) scores categorized into low (FIB-4 < 1.30), indeterminate ($1.30 \leq$ FIB-4 ≤ 2.67), and high (FIB-4 > 2.67) score groups
- Descriptive statistics were performed for all study measures

Results

- From 2016 to 2020, annual prevalence rates increased for NAFLD (from 1.01% to 1.39%) and NASH (from 0.10% to 0.15%; **Figure 1**)

Figure 1: NAFLD and NASH Prevalence Rates



NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

- The cohort used to assess baseline characteristics included a total of 11,876 patients, composed of 10,205 and 1,671 patients with new and existing NASH diagnoses, respectively (**Table 1**)
- Among those newly diagnosed with NASH, 1,104 (10.8%) had cirrhosis (**Table 1**), and 2,688 had calculated FIB-4 scores (low, n=1701; indeterminate, n=718; high, n=269; **Table 2**)
- Among those with a pre-existing NASH diagnosis, 277 (16.6%) had cirrhosis (**Table 1**), and 322 had calculated FIB-4 scores (low, n=174; indeterminate, n=108; high, n=40; **Table 2**)
- More females than males were diagnosed with NASH across all subgroups, with proportions ranging from 52.0% to 63.2% (**Tables 1 and 2**)
- Mean age was higher in patients with cirrhosis and in patients with high FIB-4 scores: 60.7 years for those newly diagnosed with NASH with cirrhosis, 62.0 years for those with a pre-existing NASH diagnosis with cirrhosis, 61.6 years for those newly diagnosed with NASH and a high FIB-4 score, and 61.4 years for those with a pre-existing NASH diagnosis and a high FIB-4 score
- Across all subgroups, antihypertensives were the most prescribed medications, with proportions ranging from 50.9% to 81.9%
- Hyperlipidemia, hypertension, obesity, sleep apnea, and type 2 diabetes (T2D) were the top 5 chronic conditions identified among patients with NASH. Hypertension and T2D were most prevalent in patients with cirrhosis; hypertension affected 82.2% and 80.9% of patients with cirrhosis with a new NASH diagnosis or pre-existing diagnosis, respectively, and T2D affected 72.3% and 76.2% of patients with cirrhosis with a new NASH diagnosis or existing diagnosis, respectively (**Figure 2**)

Table 1: Baseline Demographic and Clinical Characteristics by Cirrhosis Status

| | Newly diagnosed NASH n=10,205 | | Pre-existing NASH n=1,671 | |
|--------------------------------------|----------------------------------|------------------------------|------------------------------|------------------------------|
| | With cirrhosis n=1,104 | Without cirrhosis n=9,101 | With cirrhosis n=277 | Without cirrhosis n=1,394 |
| Sex, n (%) | | | | |
| Male | 434 (39.3) | 4,208 (46.2) | 102 (36.8) | 631 (45.3) |
| Female | 670 (60.7) | 4,893 (53.8) | 175 (63.2) | 763 (54.7) |
| Age, y | | | | |
| mean (SD) | 60.7 (10.9) | 51.7 (12.5) | 62 (10.2) | 53.4 (12.1) |
| Geographic region, n (%) | | | | |
| Northeast | 103 (9.3) | 1,235 (13.6) | 20 (7.2) | 163 (11.7) |
| Midwest | 345 (31.3) | 1,718 (18.9) | 73 (26.4) | 309 (22.2) |
| South | 463 (41.9) | 3,843 (42.2) | 119 (43) | 538 (38.6) |
| West | 151 (13.7) | 1,899 (20.9) | 39 (14.1) | 302 (21.7) |
| Unknown | 42 (3.8) | 406 (4.5) | 26 (9.4) | 82 (5.9) |
| QCI, n (%) | | | | |
| 0 | ≤ 10 | 3,246 (35.7) | 0 (0.0) | 604 (43.3) |
| 1 | ≤ 10 | 993 (10.9) | 0 (0.0) | 180 (12.9) |
| 2 | 272 (24.6) | 2,946 (32.4) | 47 (17) | 351 (25.2) |
| 3+ | 819 (74.2) | 1,916 (21.1) | 230 (83) | 259 (18.6) |
| Chronic medication use, n (%) | | | | |
| Glucose-lowering medications | 625 (56.6) | 2,973 (32.7) | 147 (53.1) | 536 (38.5) |
| Antihyperlipidemics | 546 (49.5) | 3,742 (41.1) | 137 (49.5) | 674 (48.4) |
| Antihypertensives | 860 (77.9) | 5,281 (58) | 227 (81.9) | 865 (62.1) |

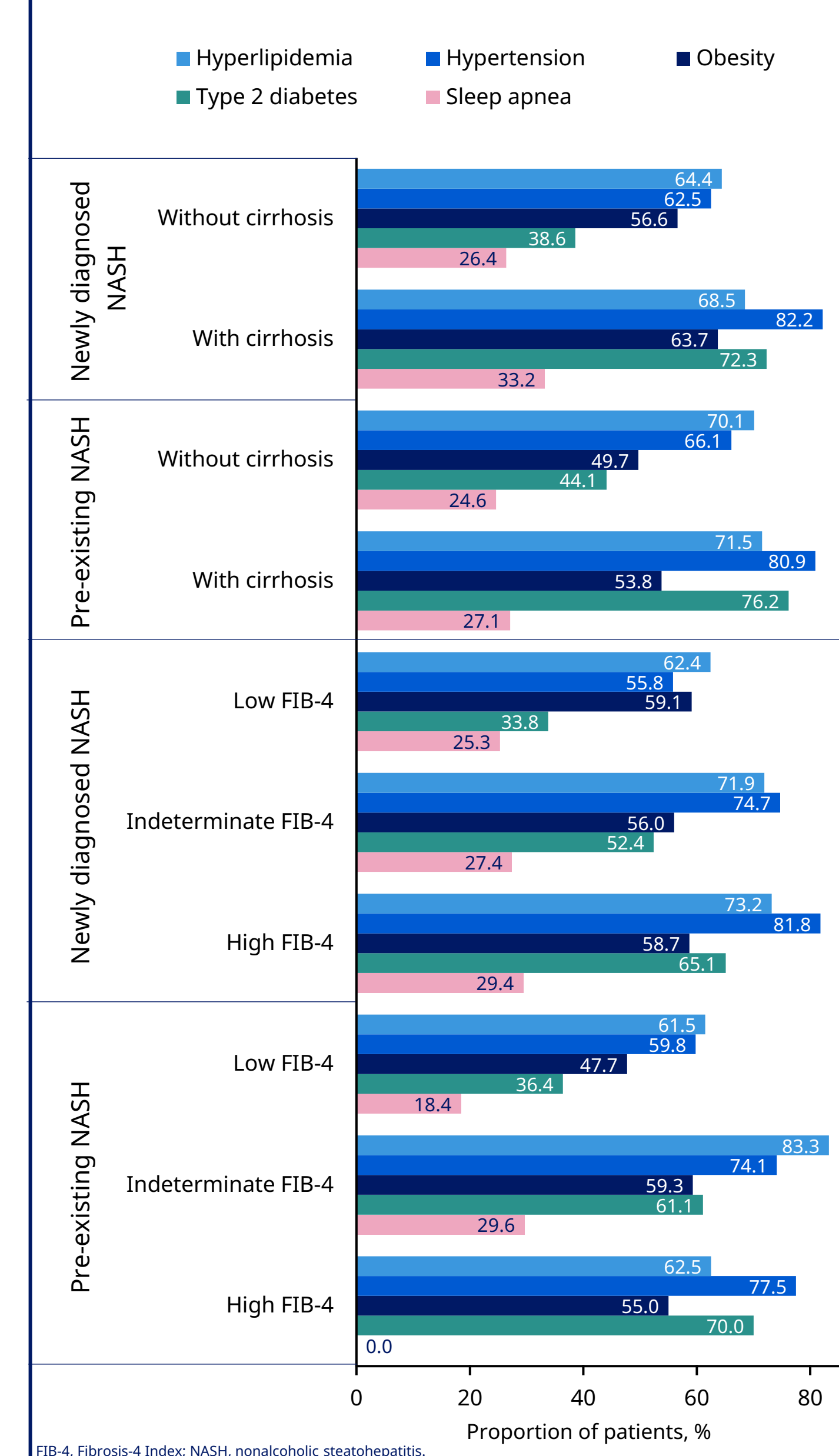
FIB-4, Fibrosis 4 Index; NASH, nonalcoholic steatohepatitis; QCI, Quan Charlson Comorbidity Index.

Table 2: Baseline Demographic and Clinical Characteristics by FIB-4 score

| | Newly diagnosed NASH n=2,688 | | | Pre-existing NASH n=322 | | |
|--------------------------------------|---------------------------------|---------------------------------|---------------------|----------------------------|---------------------------------|--------------------|
| | Low FIB-4 n=1,701 | Indeterminate FIB-4 n=718 | High FIB-4 n=269 | Low FIB-4 n=174 | Indeterminate FIB-4 n=108 | High FIB-4 n=40 |
| Sex, n (%) | | | | | | |
| Male | 740 (43.5) | 298 (41.5) | 129 (48.0) | 72 (41.4) | 43 (39.8) | 15 (37.5) |
| Female | 961 (56.5) | 420 (58.5) | 140 (52.0) | 102 (58.6) | 65 (60.2) | 25 (62.5) |
| Age, y | | | | | | |
| mean (SD) | 47.1 (11.3) | 58.1 (9.3) | 61.6 (8.6) | 48.9 (10.4) | 59.6 (8.8) | 61.4 (7.5) |
| Geographic region, n (%) | | | | | | |
| Northeast | 228 (13.4) | 91 (12.7) | 26 (9.7) | 16 (9.2) | 16 (14.8) | ≤ 10 |
| Midwest | 200 (11.8) | 112 (15.6) | 83 (30.9) | 17 (9.8) | 23 (21.3) | ≤ 10 |
| South | 712 (41.9) | 320 (44.6) | 105 (39.0) | 82 (47.1) | 42 (38.9) | 20 (50.0) |
| West | 492 (28.9) | 178 (24.8) | 50 (18.6) | 54 (31.0) | 25 (23.1) | ≤ 10 |
| Unknown | 69 (4.1) | 17 (2.4) | ≤ 10 | ≤ 10 | ≤ 10 | ≤ 10 |
| QCI, n (%) | | | | | | |
| 0 | 628 (36.9) | 190 (26.5) | 31 (11.5) | 69 (39.7) | 33 (30.6) | ≤ 10 |
| 1 | 173 (10.2) | 82 (11.4) | 14 (5.2) | 23 (13.2) | 12 (11.1) | 0 (0.0) |
| 2 | 528 (31.0) | 213 (29.7) | 66 (24.5) | 50 (28.7) | 33 (30.6) | ≤ 10 |
| 3+ | 372 (21.9) | 233 (32.5) | 158 (58.7) | 32 (18.4) | 30 (27.8) | 28 (70.0) |
| Chronic medication use, n (%) | | | | | | |
| Glucose-lowering medications | 498 (29.3) | 311 (43.3) | 137 (50.9) | 58 (33.3) | 55 (50.9) | 24 (60.0) |
| Antihyperlipidemics | 606 (35.6) | 371 (51.7) | 137 (50.9) | 63 (36.2) | 68 (63.0) | 18 (45.0) |
| Antihypertensives | 866 (50.9) | 513 (71.4) | 208 (77.3) | 97 (55.7) | 79 (73.1) | 31 (77.5) |

FIB-4, Fibrosis 4 Index; NASH, nonalcoholic steatohepatitis; QCI, Quan Charlson Comorbidity Index.

Figure 2: Top 5 Most Prevalent Comorbidities Among Patients With NASH



FIB-4, Fibrosis 4 Index; NASH, nonalcoholic steatohepatitis.

Plain Language Summary

- Why does it matter?** Nonalcoholic steatohepatitis (NASH) is a serious liver disease that can lead to complications. NASH is becoming more common, and there is a need to understand the characteristics of patients with NASH
- How does it work?** This study used medical and pharmacy claims information to estimate the prevalence rate of NASH and to assess the characteristics of the NASH population
- What did we find?** The number of patients with NASH increased every year from 2016 to 2020. There were more females with NASH than males, and the average age ranged from 47 to 61 years. A large portion of the NASH population had other metabolic-related comorbidities

Conclusions

- This study demonstrated an increase in annual prevalence rates for NAFLD and NASH from 2016 to 2020; however, the rates calculated in this study are markedly lower than previously reported estimates in the US
 - Use of ICD-10-CM codes can underestimate the true presence of NASH due to the low use of these codes to report these diseases
- These findings may also suggest that NAFLD and NASH are underdiagnosed in a real-world managed care population in the US
 - Therefore, there is a need for increased awareness of NASH as a serious, progressive, metabolic liver disease that commonly exists together with other chronic disease states such as hyperlipidemia, hypertension, obesity, sleep apnea, and T2D
- The relatively high prevalence of cirrhosis at the time of diagnosis in this analysis highlights the need for refined diagnostics and treatments that can target this segment at the earlier stages of disease
- Consistent with previous studies, NASH was associated with many components of the metabolic syndrome, such as hyperlipidemia, hypertension, obesity, and T2D
- Overall, these results reiterate the need for early detection, diagnosis, and intervention to optimally manage patients with NAFLD and NASH

This study was sponsored by Novo Nordisk Inc. The authors acknowledge the medical writing assistance of Victoria Jeter, PhD, of PRECISIONscientia, Yardley, Pennsylvania. MC has consulted for Novo Nordisk, Pfizer, Madrigal, Sagimet, Ocelot, Novartis, Merck, Bristol Myers Squibb, 89Bio, and Intercept and received research support from NorthSea, Pfizer, and Madrigal. IT-M was an employee of Carelon Research at the time the study was conducted, and C-CT is an employee of Carelon Research, they received funding from Novo Nordisk Inc. to perform this research. RL, AA, AH, and CU are employees of Novo Nordisk Inc. Presented at the 18th annual Cardiometabolic Health Congress, October 18-21, 2023, Boston, Massachusetts.

References

- Younossi et al. *Hepatology*. 2023;77(4):1335-1347;
- Lindenmeyer et al. *Clin Liver Dis*. 2018;22(1):11-21;
- Alexander et al. *BMC Med*. 2019;17(1):95