Characterizing the Prevalence of Metabolic Dysfunction-Associated Steatohepatitis (MASH) Among Adults ≥65 Years of Age in the United States (US) Using Three Real-World Cohorts

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Background

- Metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), is characterized by a buildup of fat in the liver causing inflammation and hepatocellular damage that may lead to liver scarring.[1,2]
- Previous studies have found that between 1% to 6% of adults have MASH.[1]
- While MASH is considered common among people ≥65 years of age, the exact prevalence among this age group is unknown.

Objective

This analysis aimed to characterize the prevalence and incidence of MASH among adults ≥65 years in the US.

Methods

Data sources:

- Medicare 100% fee-for-service claims (**MCR**; 01Jan2016-31Dec2021) capturing >65 million patients.
- Optum's de-identified Clinformatics® Data Mart Database (**CDM**; 01Oct2015-31Dec2022) capturing >77 million patients.
- Veradigm's electronic health record (EHR)- linked to Komodo claims (**Veradigm**; 01Oct2015-31Dec2022) capturing ~50 million patients.

Study population:

- MASH was defined by ≥1 inpatient claim with a primary or secondary diagnosis of K75.81 (NASH) or ≥2 outpatient claims.
  - Within Veradigm, MASH could also have been identified by ≥1 EHR record with a NASH diagnosis resulting in a less specific definition than MCR and CDM.
  - In this analysis, data were restricted to the older adult population (≥65 years).

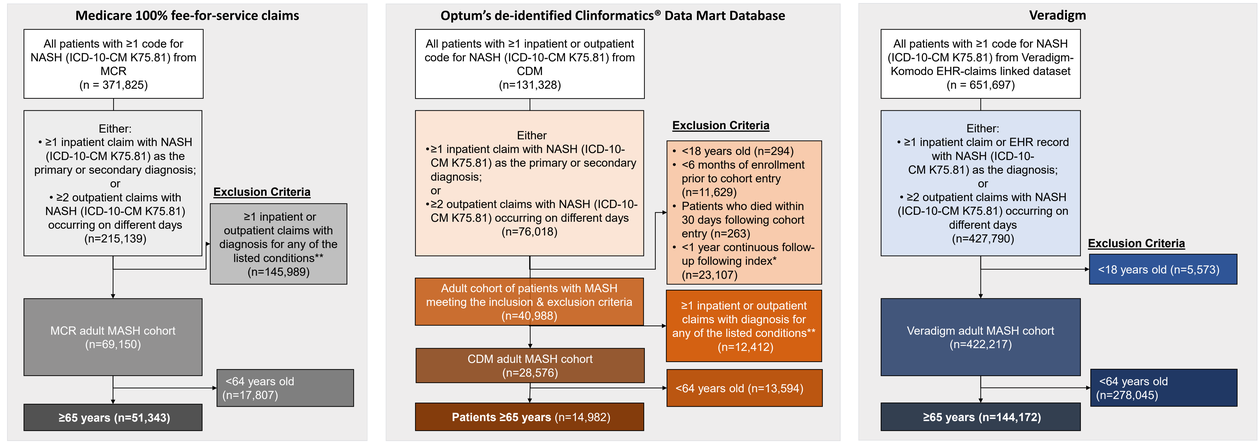
Outcomes & analyses:

- In addition to demographics and total MASH case counts, annual and period prevalence and annual incidence per 100,000 older adults were summarized.
  - The older adult population within each dataset was used as the denominator for each dataset.
  - Individuals with ≥6 months of baseline data (during which no NASH diagnosis was recorded) before the first NASH diagnosis within the study period were defined as incident patients.
  - Period prevalence was calculated in four ways to account for variations in follow-up time. Each method used the total number of MASH cases as the numerator; the denominator was estimated as the:
    1. Equivalent average annual number of older adults with 6 months of follow-up based on person-time
    2. Equivalent average annual number of older adults with 12 months of follow-up based on person-time
    3. The average annual number of older adults over the study period
    4. Number of older adults in the database in 2019 (mid-point)
- Prevalence estimates were scaled to 2021 by multiplying the annual MASH prevalence in 2021 by the total number of US adults in 2021 (55,892,014).[3]

Results

- There were 51,343 (MCR), 14,982 (CDM), and 144,172 (Veradigm) adults ≥65 years of age with MASH identified (**Figure 1**).

Figure 1: Patient flow diagram



*Note that index is defined as 30 days following cohort entry (first eligible NASH dx); this criteria is applied to all patients unless the patient had died during this time. **Viral hepatitis, Wilson's disease, Gaucher's disease, lysosomal acid lipase deficiency, alcoholism / alcoholic liver disease, primary biliary/sclerosing cholangitis, hemochromatosis, autoimmune hepatitis, human immunodeficiency virus, exposure to heavy metals. Diagnostic codes available upon request. Abbreviations: CDM, Optum's de-identified Clinformatics® Data Mart Database; ICD-10, International Classification of Diseases 10th revision; NASH, nonalcoholic steatohepatitis.

The majority of the populations within the MASH cohorts were female (MCR=62.2%, CDM=66.8%, Veradigm=63.1%).

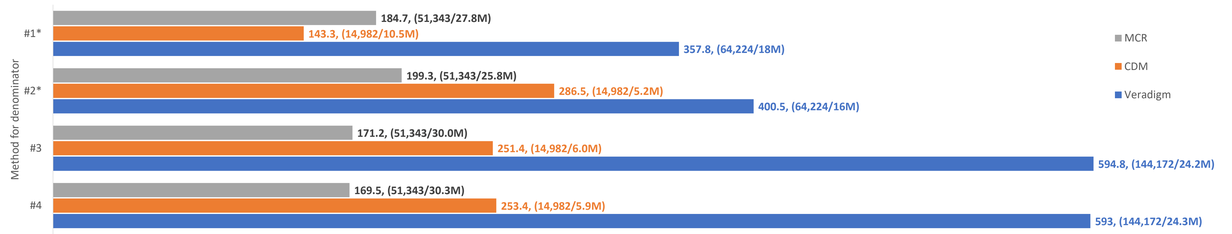
In MCR 81.7% of MASH patients were White; in CDM the population was predominantly White (67.8%) or Hispanic (16.3%); and in Veradigm, predominantly unknown (49.2%) or White (45.4%).

Mean age was 70 years in MCR and 72 years in both the CDM and Veradigm cohorts.

In MCR and Veradigm the majority of older MASH patients resided in California (7.9% and 10.5%, respectively) or Florida (7.7% and 11.3%, respectively), while in CDM most patients resided in Texas (12.8%) or Florida (9.0%).

- Period prevalence ranged from 143.3-286.5 per 100,000 adults ≥65 years in CDM, 169.5-199.3 per 100,000 adults ≥65 years in MCR, to 357.8-594.8 per 100,000 adults ≥65 years in Veradigm (**Figure 2**).

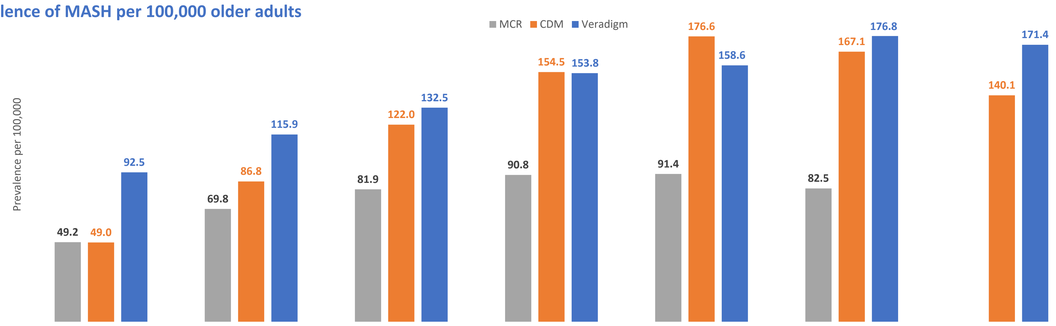
Figure 2: MASH period prevalence per 100,000 adults



*Veradigm data for these calculations were limited to diagnoses in EHR or closed claims data where there were linked enrollment data to allow estimation of total member months of follow-up and thus yielded a lower estimate. CDM, Optum's de-identified Clinformatics® Data Mart Database; MASH, metabolic dysfunction-associated steatohepatitis; MCR, Medicare 100% fee-for-service claims.

Figure 3: Annual prevalence of MASH per 100,000 older adults

- Annual prevalence ranged from 49.2-91.4 per 100,000 adults ≥65 years in MCR, 49.0-176.6 per 100,000 adults ≥65 years in CDM, 92.5-176.8 per 100,000 adults ≥65 years in Veradigm (**Figure 3**).

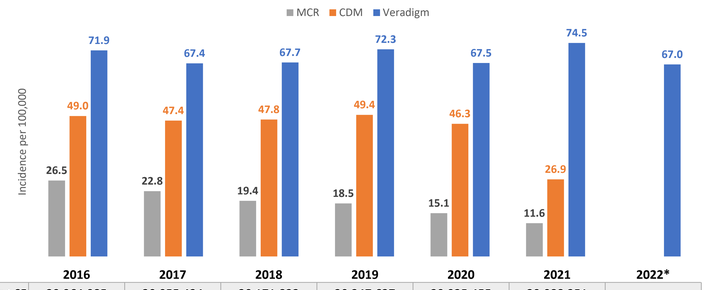


		2016	2017	2018	2019	2020	2021	2022
MCR	N adults ≥65	29,980,235	30,101,242	30,239,191	30,334,763	30,030,968	29,204,879	-
	n MASH ≥65	14,758	21,008	24,780	27,559	27,457	24,093	-
CDM	N adults ≥65	4,250,441	5,095,874	5,526,263	5,912,588	6,321,850	7,040,747	7,575,485
	n MASH ≥65	2,084	4,424	6,741	9,136	11,163	11,766	10,613
Veradigm	N adults ≥65	22,082,496	23,153,971	23,873,641	24,314,229	24,615,423	25,704,635	25,921,643
	n MASH ≥65	20,416	26,834	31,622	37,403	39,051	45,456	44,433

Abbreviations: CDM, Optum's de-identified Clinformatics® Data Mart Database; MASH, metabolic dysfunction-associated steatohepatitis; MCR, Medicare 100% fee-for-service claims

- Annual incidence ranged from 11.6-26.5 per 100,000 adults ≥65 years in the MCR, 26.9-49.4 per 100,000 adults ≥65 years in CDM, and 67.0-74.5 per 100,000 adults ≥65 years in Veradigm (**Figure 4**).

Figure 4: Annual incidence of MASH per 100,000 older adults



		2016	2017	2018	2019	2020	2021	2022*
MCR	N adults ≥65	29,964,985	30,055,424	30,171,832	30,247,637	29,925,455	29,088,251	
	n MASH ≥65	7,928	6,842	5,862	5,590	4,514	3,362	
CDM	N adults ≥65	4,250,441	5,095,874	5,526,263	5,912,588	6,321,850	7,040,747	
	n MASH ≥65	2,084	2,414	2,642	2,919	2,926	1,894	
Veradigm	N adults ≥65	22,082,496	23,153,971	23,873,641	24,314,229	24,615,423	25,704,635	25,921,643
	n MASH ≥65	15,886	15,601	16,161	17,587	16,626	19,146	17,378

*As MCR and CDM required ≥6 months of baseline data before first NASH diagnosis, incidence was not calculated for 2022 as follow-up was not long enough to capture a full year of patients.
Abbreviations: CDM, Optum's de-identified Clinformatics® Data Mart Database; MASH, metabolic dysfunction-associated steatohepatitis; MCR, Medicare 100% fee-for-service claims.

Using the calculated annual prevalence in 2021, the extrapolated 2021 US older adult population with MASH is estimated to range from 46,111 (MCR) to 93,396 (CDM) and 98,817 (Veradigm).

Discussion

- These data show the growing burden of MASH in older American adults, providing a range of estimates of contemporary MASH incidence and prevalence using claims and EHR-linked data.
  - Annual prevalence estimates highlight the substantial burden; in 2021, prevalence ranged from 82.5 to 176.8 per 100,000 adults ≥65 years of age.
- Prevalence estimates using MCR and CDM are generally lower; however, this may be driven by the follow-up requirements (≥1 year continuous follow-up & exclusion of those with death within 30 days of NASH diagnosis) and stricter case definitions (exclusion of non-NASH related liver disease).
- There are some important methodologic points to note
  - Across databases, the capture of MASH patients may be subject to under coding and/or miscoding, contributing to potential underestimation of prevalence.
  - It should also be noted that the Veradigm EHR-linked data includes open claims and therefore yielded a smaller subset of cohort when calculating period prevalence with methods #1 & #2.
- As with all studies relying on administrative health claims, estimates are dependent on the accuracy and completion of medical coding and the generalizability of databases.
  - CDM captures over 77 million patients enrolled in commercial or Medicare Advantage health plans in all 50 US states.[4]
  - Veradigm's EHR data linked to Komodo claims provides access to nearly 50 million private and public US patient records.[5]
  - MCR is the primary insurer for individuals older than 65 in the US. The program includes over 65 million beneficiaries, of which, nearly 34 million are enrolled in Medicare fee-for-service.[6]
- While these three data sources offer large coverage of US older adults, the findings may not be entirely generalizable to the US population. For example, CDM disproportionately samples certain states, capturing wealthier, older, more educated residents.[7] As a result, the range of estimates of this study may provide a better estimate of the overall prevalence in the US than any single data source alone.

Conclusions

- Data confirms the growing burden of MASH in older American adults, providing a range of estimates of contemporary MASH incidence and prevalence using claims and EHR-linked data.
- Annual prevalence ranged from 82.5 to 176.8 per 100,000 adults ≥65 years of age. However, prevalence estimates using MCR and CDM are generally lower due to the follow-up requirements (≥ 1-year continuous follow-up & exclusion of those with death within 30 days of NASH diagnosis) and stricter case definitions (exclusion of non-NASH related liver disease).
- While these three data sources combined would offer extensive coverage of US older adults, the findings from each individual data source may not be entirely generalizable to the US population due to the geographical variabilities; therefore, the range of estimates in this study may represent a better estimate of the overall prevalence in the US than any single data source alone.
- These findings demonstrate the substantial and increasing prevalence of MASH among adults 65 years of age and older.

References

1. Sheka AC, Adeyi O, Thompson J, et al. *JAMA*. 2020;323(12):1175-1183. 2.Estes C, Anstee QM, Arias-Loste MT, et al. *J Hepatol*. 2018;69(4):896-904. 3.US Census Bureau. https://data.census.gov/table?t=Age+and+Sex&g=010XX00US&y=2022. Accessed 26/09/2023. 4. Optum. https://www.optum.com/business/life-sciences/real-world-data/claims-data.html. Accessed 16/08/2023. 5. Veradigm. https://veradigm.com/veradigm-news/komodo-health-partnership-creates-largest-linked-ehr-claims-dataset-life-science-research. 6. Center for Medicare Advocacy. https://medicareadvocacy.org/medicare-enrollment-numbers/. 7. Dahlen A, et al. *JAMA Netw Open*. 2023;6(1):e2249804.

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