Gastro Hep Advances 2024;3:965–972

ORIGINAL RESEARCH—CLINICAL

Projected Healthcare System Cost Burden of Metabolic Dysfunction-Associated Steatotic Liver Disease in Canada

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BACKGROUND AND AIMS: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common cause of chronic liver disease worldwide. The current and projected cost of treating individuals with MASLD in Canada remains unknown. Our objective was to calculate the projected liver-specific and total health-care costs for people living with MASLD in Canada from 2020 to 2050. **METHODS:** The health-care usage of a cohort of patients diagnosed with MASLD in Calgary, Alberta was calculated using administrative data. Liver-specific encounters were identified and the average costs per year per patient were calculated. Projected costs were calculated by multiplying the average cost per patient within each health state by the projected prevalence of each health state. **RESULTS:** There were 6358 patients in the cohort. The annual average liver-specific cost per patient was $7.02 for F0/F1, $35.30 for F2, $60.46 for F3, and $72.55 for F4. The projected Canada-wide liver-specific cost was $85.5 million in 2020 and was expected to increase by $51 million by 2050. The average annual total health-care cost per patient was $397.90 for F0/F1, $781.53 for F2, $2881.84 for F3, and $1598.82 for F4. Thus, the projected Canada-wide total health-care cost was $3.76 billion in 2020 and was expected to increase by almost $2 billion by 2050. **CONCLUSION:** These estimates underscore the need for a MASLD framework that focuses on both prevention and innovative care models to change the predicted trajectory of health-care costs.

Keywords: Nonalcoholic Fatty Liver Disease; Metabolic Dysfunction-Associated Steatotic Liver Disease; Health-care Cost; Prevalence

Introduction

The hallmark of metabolic dysfunction-associated steatotic liver disease (MASLD), previously referred to as nonalcoholic fatty liver disease, is the presence of excessive lipid accumulation in hepatocytes. It can present as simple hepatic steatosis or more seriously as cirrhosis, hepatocellular carcinoma (HCC), or chronic liver disease.[1] MASLD is the most common cause of chronic liver disease worldwide and the fastest-growing contributor to liver mortality and morbidity.[2,3] The international prevalence of MASLD is about 30%, having increased over 10% from 2005 to 2016,[4] and in the US, outpatient visits for the management of MASLD have doubled in recent years.[5] As MASLD is related to metabolic syndrome, it is highly associated with obesity, type 2 diabetes, dyslipidemia, and hypertension.[6]

The costs associated with the management of MASLD in Canada remain unknown but have been estimated as being very high. Specifically, in one study from the United States, the healthcare costs and utilization of those with MASLD was nearly double that of patients without MASLD but with similar health status.[7] This difference was largely due to increases in imaging, hospitalization, liver fibrosis assessment, laboratory tests, and outpatient visits. It has been projected that 64 million people in the US will have MASLD within 20 years, with annual direct medical costs of $103 billion, or $1613 per person.[8] The economic burden in Europe is similarly high, with MASLD costing up to €1163 per patient.[8]

Of additional concern, health-care costs and resource utilization associated with MASLD are expected to continue to increase.[9] As risk factors for MASLD, such as obesity and diabetes, increase, the prevalence of MASLD is also expected to increase. One Canadian model projected that the number of MASLD cases in Canada will increase by 20% between 2019 and 2030, with the biggest increase occurring in the most advanced stages.[10]

Abbreviations used in this paper: **CIHI, Canadian Institute of Health Information; DAD, discharge abstract database; HCC, hepatocellular carcinoma; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; LSM, liver stiffness measurements; MASLD, metabolic dysfunction-associated steatotic liver disease; NACRS, the National Ambulatory Care Reporting System; RIW, resource intensity weight.**

Most current article

2772-5723
https://doi.org/10.1016/j.gastha.2024.05.010

Currently to our knowledge, there are no Canadian estimates for the economic burden of MASLD. Thus, this work has 2 objectives: to (1) calculate the liver-specific and total health-care costs of people living with MASLD from 2018-2020, and (2) predict the liver-specific and total health-care costs of people living with MASLD from 2020 to 2050.

Methods

Cohort

To calculate health-care costs, a cohort of patients with confirmed MASLD were identified by their enrollment in the Calgary MASLD primary care Clinical Care Pathway[11] in Calgary, Alberta. Individuals within this cohort had their health-care usage analyzed by linking their unique health-care number to provincial administrative datasets.[11] The cohort was prospectively followed through administrative, laboratory and radiological databases with ongoing data capture starting in 2017.

The degree of liver fibrosis was estimated for each person within the cohort using liver stiffness measurements (LSM) as assessed by shear wave elastography.[11] Any LSM <7.0 kPa was considered to represent liver fibrosis scores of F0/F1, LSM between 7.0 and 9.2 kPa were considered to represent F2 fibrosis, LSM scores between 9.3 and 11.0 kPa were considered F3 fibrosis, and LSM scores >11.0 kPa were considered F4 fibrosis (ie, cirrhosis).[12,13] Decompensated cirrhosis, HCC, and liver transplants were determined based on International Classification of Diseases, Ninth Revision (ICD-9) and International Classifictaion of Diseases, Tenth Revision (ICD-10) coding (specific codes used are available in Appendix 1). LSM scores of F0 and F1 were combined as their management within the Calgary Clinical Care pathway is similar. Patients who had low liver LSM scores, but ICD-9 or ICD-10 codes for decompensated cirrhosis, HCC, or liver transplant, were classified as having F4 liver fibrosis. This was to account for any changes in disease progression that may have occurred between LSM scores being recorded and patients interacting with the health-care system.

Cost Calculations

Three provincial administrative databases were used to capture all health-care encounters within a calendar year. The Discharge Abstract Database (DAD) captures hospitalizations.[14] The National Ambulatory Care Reporting System (NACRS) database captures ambulatory care.[15] Last, the physician claims database captures all physician claims.[16] Cost information was extracted from each database, either using the Resource Intensity Weight (RIW) (DAD: RIW; NACRS: CACS_RIW) or the actual amount paid (claims: FRE_ACTUAL_PAID_AMT). Complete data were available for 2018, 2019, and 2020. Average annual costs were calculated in each of these 3 years and averaged to get the average overall cost.

Year-specific Cost per Standard Case from the Canadian Institute of Health Information was used to calculate the cost of hospitalization for the DAD database and ambulatory care for the NACRS database.[17] The RIW for the DAD and NACRS datasets was multiplied by the Canadian Institute of Health Information Cost per Standard Case to determine the cost of hospitalization or ambulatory care.

The total cost for each liver fibrosis state was calculated and divided by the total number of patients in that fibrosis stage in that year. Patients with no health-care encounters were coded as having zero costs and were included in the final cohort.

The cost of a liver transplant was calculated using Case Mix Groups + coding for liver, pancreas, and duodenum transplants.[18] The average cost for all cases (typical and atypical) was determined to be $120,636.69 2022 Canadian dollars. No out-of-hospital costs were included.

Analyses

All authors had access to the study data and have reviewed and approved the final manuscript. The primary analysis considered only liver-specific costs, and the databases were filtered for liver-specific encounters based on ICD-9 and ICD-10 codes, which were also used to identify encounters for the treatment of MASLD and related complications (Table 1). The claims database uses ICD-9 codes to classify interactions and both the DAD and NACRS databases use ICD-10 codes. ICD-9 and ICD-10 codes were provided by 2 hepatologists (co-authors MS and AS) and were based on the treatment pathway and typical treatment for a MASLD patient.[11] An event was defined as any liver-specific encounter with the health-care system.

The secondary analyses included determining the total health-care costs and most common comorbidities. All health-care encounters regardless of diagnosis codes were included in the analysis of total health-care costs. An event was defined as any encounter with the health-care system.

As only 3 years of data were used for this analysis, we were not able to complete a regression to predict how health-care costs would change over time. Instead, the average of the 3 available years was calculated to create an overall average cost per liver fibrosis stage. Prevalence estimates from Swain et al[10] were utilized to predict the number of patients expected in each treatment group. The projected cost was the observed average cost per person within each health state multiplied by the total projected prevalence of each liver fibrosis stage.

All values reported are in Canadian dollars. Costs were calculated based on the observation year and were not standardized to a specific year. As such, there were no inflation adjustments.

To determine the common reasons MASLD patients might be seeing physicians, the most common physician claims were identified for each liver fibrosis stage group. Claims were grouped into general categories (ie, all diabetes-related claims were coded as “diabetes”). Specific codes used to create groups are available in Appendix 2.

All analyses were conducted in RStudio (2022.07.1), with the readr, tidyverse, and data.table packages.

Results

Overall, there were 6358 MASLD patients in the cohort (Table 2). Half of the cohort (50.7%, n = 3221) were female, most (70.2%, n = 4455) were over 45 years of age, and most (93.1%, n = 5921) lived in an urban location. Of the cohort, 90.0% (n = 5724) were classified as having F0/F1

Table 1. ICD-9 and ICD-10 Codes Used for Liver-Specific Costs

Encounter	ICD-9 code	ICD-10 code
Specialist visit	In-person consult: 03.08AZ Teleconsult: 03.08CV Minor consult: 03.07BZ, 0.307AZ	N/a
Fibroscan HCC screening with ultrasound	Other diagnostic procedures on liver: 50.19	Abnormal findings on diagnostic imaging of liver and biliary tract: R93.2
Esophageal varices	Esophageal varices with bleeding: 456.0 Esophageal varices without mention of bleeding: 456.1	Esophageal varices with bleeding: I85.01, I983 Esophageal varices without mention of bleeding: I85.00, I859, I982 Secondary esophageal varices with bleeding: I85.11 Secondary esophageal varices without bleeding: I85.10
Decompensation event	Esophageal varices without mention of bleeding: 456.21 Hepatorenal syndrome: 572.4 Portal hypertension: 572.3	Other and unspecified encephalopathy: G934 Hepatic failure, unspecified: K729 Gastric varices: I864 Hepatorenal syndrome: K767 Portal hypertension: K766
HCC development	Liver, primary: 155.0 (includes carcinoma, hepatocellular) Abnormal liver scan: 794.8 Liver scan and radioisotope function study: 92.02	Liver cell carcinoma (hepatocellular carcinoma): C22.0
Ascites	Ascites: 789.5 Malignant ascites: 789.51	Ascites: R18 Other ascites: R18.8
Hepatic encephalopathy	Hepatic encephalopathy: 572.2 (hepatic coma, includes hepatic encephalopathy)	Hepatic encephalopathy: K76.82 Hepatic failure, unspecified with coma (includes hepatic encephalopathy): K72.91, K72.90
Jaundice	Jaundice, unspecified, not of newborn: 782.4	Unspecified jaundice: r17
Spontaneous bacterial peritonitis	Spontaneous bacterial peritonitis: 567.23	Spontaneous bacterial peritonitis: K65.2
Neoplasm of liver	Malignant neoplasm of liver and intrahepatic bile ducts: 155 Other disorders of liver: 573	Benign neoplasm of liver: D13.4 Malignant neoplasm of liver, primary, unspecified as to type: C22.8 Malignant neoplasm of liver, not specified as primary or secondary: C22.9
Liver resection	Partial hepatectomy, includes wedge resection of liver: 50.22	Resection of liver, percutaneous endoscopic approach: 0FT04ZZ Resection of liver, open approach: 0FT00ZZ
Radiofrequency ablation	Open ablation of liver lesion or tissue: 50.23	Destruction of liver, open approach: 0F500ZZ
Microwave ablation	Percutaneous ablation of liver lesion or tissue: 50.24 Laparoscopic ablation of liver lesion or tissue: 50.25 Other and unspecified ablation of liver lesion or tissue: 50.26	Destruction of liver, percutaneous approach: 0F503ZZ Destruction of liver, percutaneous endoscopic approach: 0F504ZZ
Trans arterial chemoembolization (TACE)	Injection or infusion of cancer chemotherapeutic substance: 99.25	Introduction of other antineoplastic into peripheral vein, percutaneous approach: 3E03305 Introduction of other antineoplastic into central vein, percutaneous approach: 3E04305

Table 1. Continued

Encounter	ICD-9 code	ICD-10 code
Transplant surgery	Liver transplant: 50.5 Total hepatectomy: 50.4	Transplantation of liver, allogeneic, open approach: 0FY00Z0
Liver transplant	Operations on liver: 50.91 Operations on liver: 50.92 Operations on liver: 50.93 Auxiliary liver transplant: 50.51 Organ or tissue replaced by transplant, liver: V42.7 Other transplant of liver: 50.59	Transplantation of liver, syngeneic, open approach: 0FY00Z1 Transplantation of liver, zooplastic, open approach: 0FY00Z2
Pre and post transplant patient care		Encounter for aftercare following liver transplant: Z48.23
Transplant rejection	Complications of transplanted organ, liver: 996.82	Liver transplant rejection: T86.41 Liver transplant failure: T86.42
Cholangitis	Cholangitis: 576.1	Cholangitis: K83.0 Primary sclerosing cholangitis: K83.01 Other cholangitis: K83.09
Sarcopenia		Sarcopenia: M62.84
Hepatic artery stenosis	Stricture of artery: 447.1	Stricture of artery: I77.1
Hepatic artery dilation		Dilation of hepatic artery, open approach: 04730ZZ Dilation of hepatic artery, percutaneous approach: 04733ZZ
ERCP	Endoscopic retrograde cholangiopancreatography: 51.10	Fluoroscopy of biliary and pancreatic ducts using low osmolar contrast: BF111ZZ
NAFLD	Other chronic nonalcoholic liver disease: 571.8 Cirrhosis of liver without mention of alcohol: 571.5 Unspecified chronic liver disease without mention of alcohol: 571.9	Liver disease, unspecified: K76.9
Liver biopsy	Transjugular liver biopsy: 50.13 Laparoscopic liver biopsy: 50.14 Closed (percutaneous) [needle] biopsy of liver: 50.11 Open biopsy of liver: 50.12	Excision of liver, percutaneous approach, diagnostic: 0FB03ZX Excision of liver, percutaneous endoscopic approach, diagnostic: 0FB04ZX

liver fibrosis, 5.7% (n = 363) were classified as F2 liver fibrosis, 1.9% (n = 120) were classified as F3 liver fibrosis, 2.2% (n = 142) were classified as F4 fibrosis (ie, cirrhosis), 0.09% (n = 6) had decompensated cirrhosis, 0.03% (n = 2) had HCC, and 0.03% (n = 2) had received a liver transplant (Table 2). Given the low numbers of patients with decompensated cirrhosis, HCC, and liver transplants, the analysis was restricted to those with F0/1 to F4 fibrosis.

Liver-specific Costs

Overall, the annual average cost for each fibrosis stage group per patient was $7.02 (95% CI: $6.93-$7.11) for F0/F1, $35.30 (95% CI: $32.15-$38.45) for F2, $60.46 (95% CI: $54.67-$66.26) for F3, and $72.55 (95% CI: $68.66-$76.44) for F4 (Table 3). No patients had liver-specific hospitalizations during this time period (Appendix 2). Most costs identified for patients classified with liver fibrosis stages F0/F1 to F4 were from physician claims (Table 3).

The estimated Canada-wide liver-specific burden was $85,477,678.23 in 2020. Based on the estimated number of people living with MASLD in 2050 (9,766,538), liver-specific costs are expected to increase by $51 million by $2050 to $136,133,509.01 (Figure 1). The biggest change is expected in those with F3 and F4 liver fibrosis, with total health-care costs increasing by $17.2 million and $16.3 million, respectively.

Table 2. Patient Characteristics

Characteristics	Number (n = 6358)	Percent (%)
Health state		
F0/F1	5724	90.0%
F2	363	5.7%
F3	120	1.9%
F4	142	2.2%
Decompensated cirrhosis	6	0.09%
Hepatocellular carcinoma	2	0.03%
Liver transplant	2	0.03%
Sex		
Female	3221	50.7%
Male	3116	49.0%
Age		
Under 18	13	0.2%
18–25	123	1.9%
25–35	618	9.7%
35–45	1149	18.1%
45–55	1576	24.8%
55–65	1733	27.3%
65–75	972	15.3%
75+	174	2.8%
Place of residence		
Rural	437	6.9%
Urban	5921	93.1%

Overall Health-care Costs

Overall, the average annual health-care cost per patient was $397.90 (95% CI: $395.45–$400.35) for liver fibrosis stage F0/F1, $781.53 (95% CI: $722.60–$840.46) for F2, $2881.84 (95% CI: $2556.33–$3207.35) for F3, and $1598.82 (95% CI: $1498.50–$1699.15) for F4 (Table 3). For all patients, most health-care encounters were physician encounters (Appendix 2). For patients classified with liver fibrosis stages F0/F1 and F2, about half the costs were due to physician claims ($194.82, 49.0% for F0/F$1 and $372.65, 47.7% for F2). For those classified with liver fibrosis stage F3, most costs were due to ambulatory care ($1751.32, 60.8%). For patients with liver fibrosis stage F4, the total cost was fairly even between hospitalization, ambulatory, and physician costs (Table 3).

The estimated Canada-wide total health-care cost associated with MASLD patients was $3.76 billion in 2020. Moreover, total health-care costs are expected to increase by almost $2 billion by 2050, to $5.81 billion (Figure 2). The biggest change is expected in those with F3 liver fibrosis, with total health-care costs increasing by $820 million.

Common Reasons for Seeing Physicians

In our overall cohort, 11.5% of patients had a liver-related health-care claim. The most commonly coded reasons for MASLD patients visiting physicians were diabetes (65.2%), hypertension (19.6%), mental illnesses (18.6%), obesity (7.9%), renal failure (4.3%), and high cholesterol (2.0%) (Figure 3). This distribution was largely similar across all liver fibrosis stages, although the number of liver-related health-care claims were higher in liver fibrosis patient cohorts for F2 fibrosis (16.5%), F3 fibrosis (16.1%), and F4 fibrosis (29.9%) (Figure 3). Additionally, health-care claims for renal failure were more prevalent in those classified as having F3 liver fibrosis (25.6%).

Discussion

Based on our cohort from Calgary, Alberta, Canada, the Canada-wide health-care–associated economic burden of people with MASLD and liver fibrosis stages F0/1 to F4 was

Table 3. Liver-Specific and Total Health-care Costs

Liver-specific costs

Fibrosis stage	Annual average hospitalization cost per person (95% CI)	Annual average ambulatory care cost per person (95% CI)	Annual average physician claim cost per person (95% CI)	Annual average cost per person (95% CI)
F0/F1	–	$1.50 ($1.49, $1.51)	$5.52 ($5.44, $5.60)	$7.02 ($6.93, $7.11)
F2	–	$7.02 ($6.42, $7.62)	$28.28 ($25.86, $30.70)	$35.3 ($32.15, $38.45)
F3	–	$23.71 ($20.86, $26.57)	$36.75 ($31.55, $41.95)	$60.46 ($54.67, $66.26)
F4	–	$30.77 ($27.12, $34.42)	$41.78 ($41.54, $42.02)	$72.55 ($68.66, $76.44)

Total health-care costs

Fibrosis stage	Annual average hospitalization cost per person (95% CI)	Annual average ambulatory care cost per person (95% CI)	Annual average physician claim cost per person (95% CI)	Annual average cost per person (95% CI)
F0/F1	$78.66 ($77.77, $79.55)	$124.41 ($123.60, $125.22)	$194.82 ($194.08, $195.56)	$397.9 ($395.45, $400.35)
F2	$145.45 ($142.07, $148.83)	$263.43 ($243.41, $283.45)	$372.65 ($346.10, $399.20)	$781.53 ($722.60, $840.46)
F3	$325.01 ($316.67, $333.35)	$1751.32 ($1469.68, $2032.96)	$805.51 ($768.83, $842.19)	$2881.84 ($2556.33, $3207.35)
F4	$433.26 ($371.08, $495.44)	$539.43 ($489.22, $589.64)	$626.12 ($604.56, $647.68)	$1598.82 ($1498.50, $1699.15)

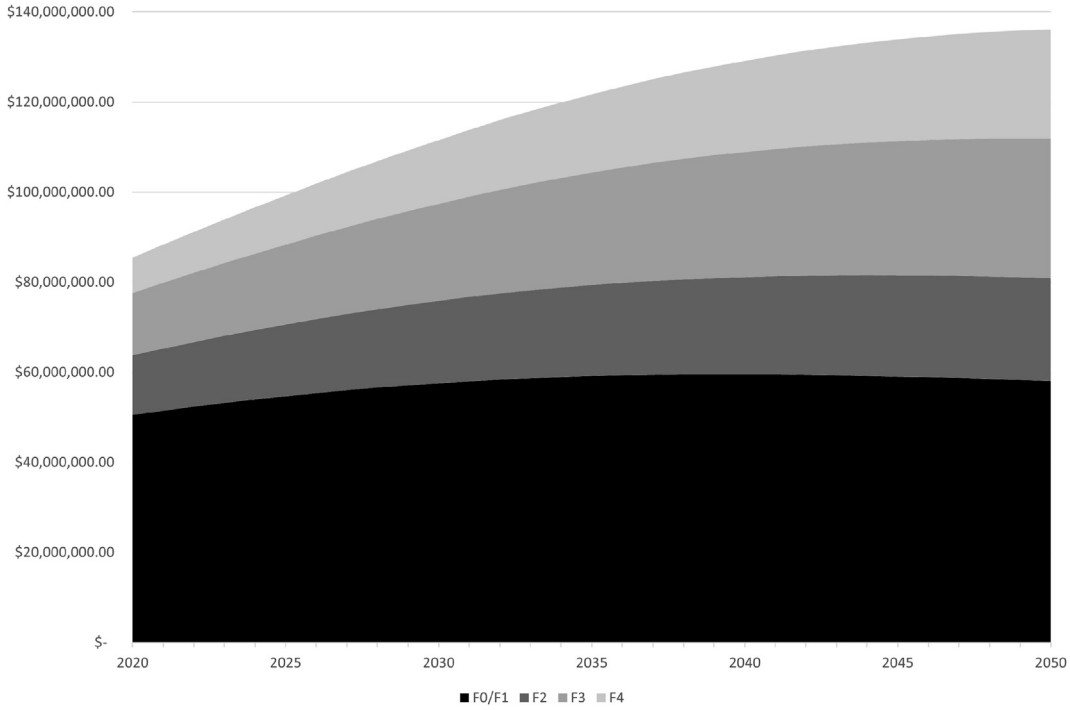

Figure 1. Projected annual health-care expenditures, liver-specific costs.

estimated to be a staggering $3.76 billion in 2020, growing to $5.81 billion in 2050 without considering inflation or changes in health-care costs. Furthermore, total liver-specific health-care costs for our cohort were $85.5 million in 2020, about 2% of the total health-care costs of people with MASLD. The vast majority of health-care costs were not due to liver-related complications from MASLD, but rather from the high costs associated with treating MASLD-associated comorbidities, including diabetes, hypertension, mental illness, and obesity.

These health-care cost estimates underscore the need for a holistic MASLD disease management framework that focuses on both prevention and care models, as well as on establishing collaborative care approaches aimed at addressing common MASLD-associated comorbidities. Currently, few countries have a written strategy for addressing MASLD, and MASLD is largely absent from global health policies.[7] Optimally, a health-care policy generated to address MASLD should focus on both prevention and treatment. MASLD is typically managed through lifestyle

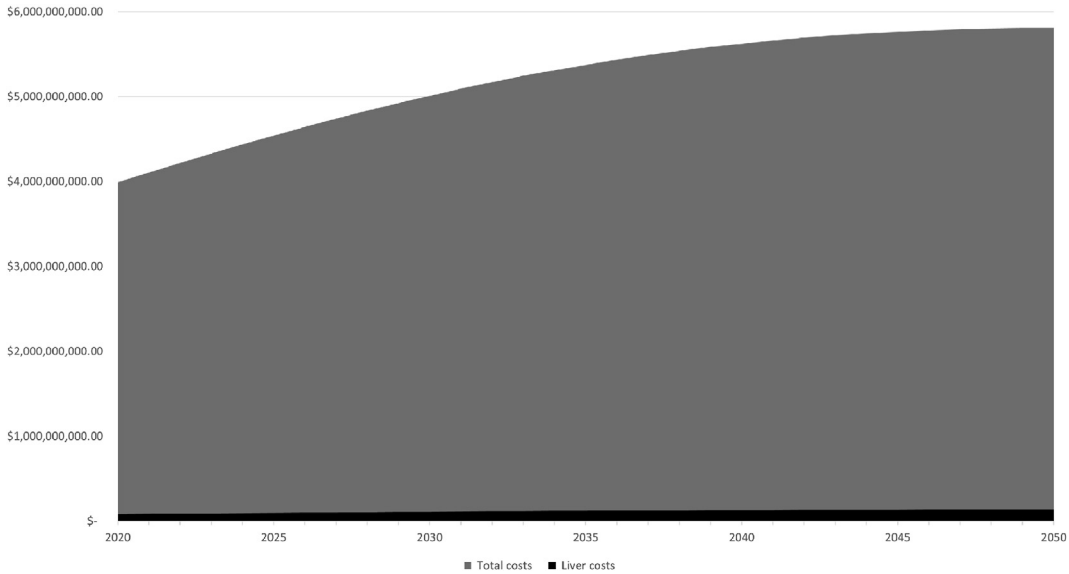

Figure 2. Projected health-care expenditure, total vs liver costs.

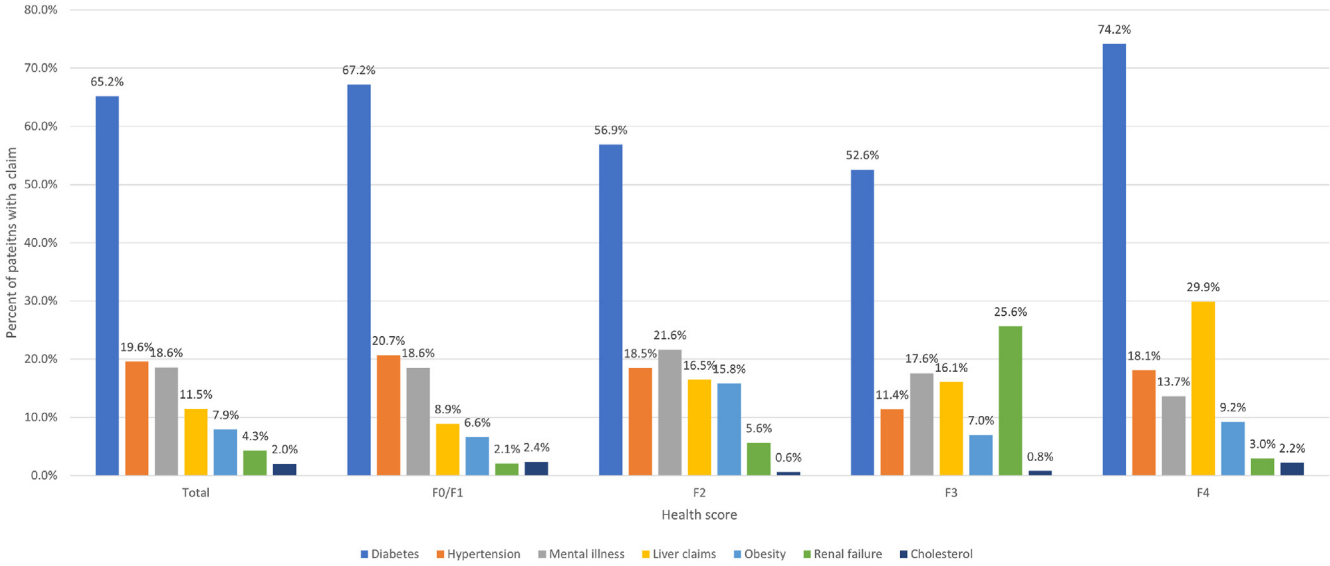

Figure 3. Common comorbidities across health scores.

interventions, focusing on diet, exercise, and maintaining a healthy weight.[19–21] Continuing to promote these interventions will hopefully prevent both MASLD and associated comorbidities, including obesity and diabetes.[22] Interventions that address both MASLD and associated comorbidities are clearly necessary. Importantly, over 90% of the health-care costs for people with MASLD in our cohort were not due to MASLD-associated liver disease, but rather other chronic health conditions linked closely to metabolic dysfunction. Chronic disease costs roughly $68 billion per year in direct health-care costs in Canada, about 58% of overall health-care spending.[23] It has been estimated that reducing the prevalence of chronic diseases by 1% year over year could save $107 billion over 20 years.[24] Therefore, an approach that focuses on preventing and managing chronic diseases overall is needed to reduce the burden of MASLD on the health-care system.

It is important to note that these health-care cost calculations do not include the societal cost of MASLD. Societal costs include premature mortality and disability due to MASLD, losses in productivity, and informal caregiving that is required, and have been estimated to cost nearly $3000 per patient in the US, nearly double that of direct health-care costs.[8] When indirect, non–health care costs are considered, the actual cost of MASLD is likely significantly higher than what is reported here. When indirect costs of comorbidities are also included, the total health-care cost burden of MASLD in Canada is substantial.

There were several limitations to this study. First, the cohort included approximately 6300 patients. In particular, our cohort included a limited number of cases with more advanced liver fibrosis stages, with roughly 10% of patients in our cohort being classified as having F2 liver fibrosis stage or higher, and less than 2% of our cohort having either decompensated cirrhosis, HCC, or a liver transplant. Due to these cohort size limitations, there was significant variation in patient-level costs across years for more advanced liver fibrosis stages. Additionally, our analysis was limited to 3 years of cohort-related data, leading to some uncertainty in projected costs due to unstable trend estimation. In addition, overall health-care cost estimates are based on projected prevalence, rather than actual prevalence of MASLD, leading to potential cost inaccuracies.

Conclusion

These estimates underscore expected rapid growth of the cost of MASLD to the health-care system. There is a need for a MASLD framework that focuses on both prevention and care models. Further, most of the health-care costs for people with MASLD were due to nonliver chronic conditions highlighting the need to focus on collaborative care approach to address common comorbidities.

Supplementary Materials

Material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gastha.2024.05.010.

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Received March 18, 2024. Accepted May 22, 2024.

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Authors' Contributions:
K. Ally Memedovich: assembly, analysis, and interpretation of data, drafting and revision of manuscript; Abdel Aziz Shaheen: funding acquisition, conception and design of study, generation and collection of data, approval of final manuscript; Mark G. Swain: funding acquisition, conception and design of study, approval of final manuscript; Fiona M. Clement: conception and design of study, analysis and interpretation of data, drafting of manuscript, approval of final manuscript.

Conflicts of Interest:
These authors disclose the following: Mark G. Swain: Advisory role: Ipsen, Pfizer, Novo Nordisk, GSK; Speaker: Gilead, Abbott; Clinical trial or research support: Gilead, BMS, CymaBay, Intercept, Genfit, Pfizer, Novartis, Astra Zeneca, GSK, Celgene, Novo Nordisk, Axcella Health Inc, Merck, Galectin Therapeutics, Calliditas Therapeutics, Madrigal, AbbVie, Altimmune, Roche, Kowa, Arbutus, Eiger, Janssen, Ipsen, Allergan, Assembly, Arbutus, Enanta, Galmed, Inventiva, Sagimet. Abdel Aziz Shaheen: Advisory: Novo Nordisk; Research grants: Gilead. The remaining authors disclose no conflicts.

Funding:
Alberta Innovates grant (LiveRx); role of the sponsor: none.

Ethical Statement:
Institutional review board approval was not required for this project as it utilized administrative data.

Data Transparency Statement:
Data, analytic methods, and study materials will be made available on request.

Reporting Guidelines:
Not applicable for this article type.