**Population Characteristics from Truven**

|  |  |  |
| --- | --- | --- |
| **1. Breakdown of overall MASLD patients (no diagnosis code for cirrhosis at MASLD diagnosis)** | | |
| Overall (N= 859970) | Male | Female |
| Age <50 | 187674 (21.8%) | 179391 (20.9%) |
| Age >=50 | 222642 (25.9%) | 270263 (31.4%) |
| **2. Breakdown of patients who were diagnosed with cirrhosis before HCC**  (These patients will be censored.) | | |
| Diagnosed cirrhosis (N = 993) | Male | Female |
| Age <50 | 69 (6.9%) | 41 (4.1%) |
| Age >=50 | 587 (59.1%) | 236 (23.8%) |
| **3. N(%) of patients with undiagnosed cirrhosis** (PLT<140 or FIB-4>=2.67 w/o cirrhosis diagnosis). Denominator is % out of our final MASLD cohort who have PLT/FIB-4 data. | | |
| Out of overall final MASLD cohort | 2,236/40,630 (5.5%)  **From literature: 19%-50% --> ~35%** | |
| Subgroup of male aged >=50 | 663/14738 (4.5%)  **From literature: 40% among patients aged >65 (Walker 2017)** | |
| **4.** **Breakdown of patients who develop HCC (exclude pts who get diagnosed with cirrhosis before HCC)** | | |
| HCC (N=804) | Male | Female |
| Age <50 | 67 (8.3%) | 69 (8.6%) |
| Age >=50 | 442 (55.0%) | 226 (28.1%) |
| **5.** **Breakdown of HCC patients who die (exclude pts who get diagnosed with cirrhosis before HCC)** -- Hold off on weighing transition rate from HCC to death by sex and age. See comment. | | |
| Death (N=) | Male | Female |
| Age <50 | N (%) | N (%) |
| Age >=50 | N (%) | N (%) |

**Age distribution from Truven**

|  |  |
| --- | --- |
| **Age at MASLD diagnosis** | **N(%)=859970** |
| 18-30 | 51377 (5.97%) |
| 31-40 | 125093 (14.55%) |
| 41-50 | 217122 (25.25%) |
| 51-60 | 288411 (33.54%) |
| 61-70 | 133141 (15.48%) |
| 71-80 | 33801 (3.93%) |
| 81-90 | 9753 (1.13%) |
| 91-100 | 1258 (0.15%) |
| 101-110 | 14 (0.002%) |
| >110 (if any) | - |

**Annual incidence in MASLD patients:**

|  |  |  |
| --- | --- | --- |
|  | **Annual Incidence %** | **Reference from literature** |
| No cirrhosis to cirrhosis | 10.85 per 1000 person-years =1.08% | Le 2024 |
| No cirrhosis to HCC (any stage) | 1.1 per 1000 person-years =0.11% | Behari 2023 |
| Compensated cirrhosis to HCC (we use this to account for undiagnosed cirrhosis cases) | 2.6% | Ascha 2010 |

**HCC stage upon diagnosis:**

|  |  |  |
| --- | --- | --- |
|  | **% Value** | **Reference from literature** |
| **Without HCC screening** | | |
| % Early stage | 45.7% | Daher 2024 |
| % Intermediate stage | 23.0% |
| % Late stage | 31.3% |
| **With HCC screening** | | |
| % Early stage | 70.7% | Daher 2024 |
| % Intermediate stage | 15.6% |
| % Late stage | 13.7% |

(\*We assume that the age and sex distribution will be uniform across the above HCC stages upon diagnosis)

**Breakdown of HCC treatment received by HCC stage**

These values are taken from SEER-Medicare, 2010-2015 data (by HCC diagnosis date). I limited the data to these 5 years to account for the introduction of sorafenib after 2007 and also HCC staging after 2015 looks odd due to coding changes. In here, radiotherapy group is updated with additional codes taken from the SEER Medicare resource page ([link](https://healthcaredelivery.cancer.gov/seermedicare/considerations/procedure_codes.html)). (I used HCC diagnosis date instead of treatment administration date because patients who didn’t receive treatment don’t have treatment date).

1. Out of patients without cirrhosis (we will use this one first)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| HCC Stage | | Early | Intermediate | Late |
| N |  | 450 | 376 | 372 |
| First Treatment Type | Ablation | 18 (4.0) | 12 (3.2) | 1 (0.3) |
|  | Radiotherapy | 2 (0.4) | 0 (0.0) | 5 (1.3) |
|  | Resection | 72 (16.0) | 36 (9.6) | 5 (1.3) |
|  | Systemic | 50 (11.1) | 68 (18.1) | 94 (25.3) |
|  | TACE | 65 (14.4) | 59 (15.7) | 40 (10.8) |
|  | Transplant | 5 (1.1) | 5 (1.3) | 0 (0.0) |
|  | No treatment | 238 (52.9) | 196 (52.1) | 227 (61.0) |

1. Compensated cirrhosis (use if we want to adjust for % of undiagnosed patients)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| HCC Stage | | Early | Intermediate | Late |
| N |  | 668 | 549 | 269 |
| First Treatment Type | Ablation | 79 (11.8) | 43 (7.8) | 4 (1.5) |
|  | Radiotherapy | 1 (0.1) | 0 (0.0) | 1 (0.4) |
|  | Resection | 88 (13.2) | 40 (7.3) | 7 (2.6) |
|  | Systemic | 41 (6.1) | 77 (14.0) | 76 (28.3) |
|  | TACE | 217 (32.5) | 201 (36.6) | 34 (12.6) |
|  | Transplant | 59 (8.8) | 25 (4.6) | 1 (0.4) |
|  | No treatment | 183 (27.4) | 163 (29.7) | 146 (54.3) |

**Annual rate of death in MASLD patients:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Original data** | **Calculated Annual death rate** | **Reference from literature** |
| No cirrhosis (MASLD) | 0.1% 1y all-cause mortality | 0.1% | Cheng 2023 |
| Compensated cirrhosis (we use this to account for undiagnosed cirrhosis cases) | 9.6% 1y all-cause mortality | 9.6% | Wang 2023  (derived by adding % mortality due to all causes in figure 4 – compensated) |
| Early stage HCC |  |  |  |
| After Transplant | 60%-70% 5-year OS rate= ~35% 5-year death rate | 8.25% | American cancer society data |
| After resection | 88.9% 1-year OS rate | 11.1% | Thornton 2022 |
| After TACE | 93.3% 1-year OS rate | 6.7% | Kim 2017 |
| After ablation | 43.2% 5-year OS rate= 56.8% 5-year death rate | 15.5% | Zhang 2021 |
| After systemic chemotherapy |  | 61.9% | SEER-Medicare |
| After radiotherapy | 70.4% 3-year OS rates= 29.6% 3-year death rate | 11.0% | Hara 2019 |
| Untreated | 64% 1-year OS rate | 35.7% | Khalaf 2017 |
| Intermediate stage HCC |  |  |  |
| After Transplant | 88% 1-year OS rate | 12% | Kamo 2018 |
| After resection | 92% 1-year OS rate | 8% | Zhong 2015 |
| After TACE | 70% 1-year OS rate | 30% | Prince 2020 |
| After ablation | 93.0% 1-year OS rate | 7% | Tanaka 2023 |
| After systemic chemotherapy | 89.4% 1-year OS =10.6% (Nakamura 2023) | 69.6% | SEER-Medicare |
| After radiotherapy | 63% 2-year OS rate =37% 2-year death rate | 20.6% | Prince 2020 |
| Untreated |  | 63.2% | Khalaf 2017 |
| Late stage HCC |  |  |  |
| After TACE | 33.3% 1-year OS rate | 66.7% | Kong 2018 |
| After ablation | 73.1% 1-year OS rate | 26.9% | Dai 2014 |
| After systemic chemotherapy | 71.4% 1-year OS = 28.6% (Nakamura 2023) | 86.2% | SEER-Medicare |
| After radiotherapy | 31.3% 1-year OS rate | 68.7% | Lin 2019 |
| Untreated |  | 87.2% | Khalaf 2017 |

This paper says age was associated with 10% increase in mortality per 1 year increase in age: [Characterization of hepatocellular carcinoma (HCC) in non-alcoholic fatty liver disease (NAFLD) patients without cirrhosis | Hepatology International](https://link.springer.com/article/10.1007/s12072-015-9679-0)

**Sensitivity/Specificity of HCC screening from literature**

|  |  |  |
| --- | --- | --- |
| **Probability** | **Value** | **Reference from literature** |
| Sensitivity of US/AFP | 0.851 = 85.1% | Singal 2022 |
| Specificity of US/AFP | 0.839 = 83.9% | Singal 2022 |

**Quality of life by health state from literature**

|  |  |  |
| --- | --- | --- |
| **Health State** | **Utility** | **Reference from literature** |
| MASLD without cirrhosis | 0.88 | Sayiner 2016 |
| False positive HCC | 0.77 | Singal 2024 |
| Early stage HCC | 0.72 | Singal 2024 |
| Intermediate stage HCC | 0.69 | Singal 2024 |
| Late stage HCC | 0.65 | Singal 2024 |

**Costs from literature**

|  |  |  |
| --- | --- | --- |
| **Cost** | **Value** | **Reference from literature** |
| US+AFP screening | $179\*2 (multiply by 2 because biannual) = $358 | Medicare fee  schedule |
| Repeat CT/MRI for false positive HCC | $554 | Medicare fee  schedule |
| Medical care of patients with non-cirrhotic MASLD | $3537 (2019 USD) =$4362 (2024 USD) | Younossi 2023 |
| Liver transplant | $62,432 | Medicare fee  schedule |
| Early stage HCC | $62,340 (2024 USD) | Tapper 2016 |
| Intermediate stage HCC | $116,996 (2024 USD) | Tapper 2016 |
| Late stage HCC | $105,591 (2024 USD) | Tapper 2016 |
| Resection | $25,614 (2016 USD)=$33,650 (2024 USD) | Charalel 2024 |
| TACE | $51,696 (2017? USD) = $66497 (2024 USD) | Nugent 2018 |
| Ablation | $6,689 (2016 USD)=$8787 (2024 USD) | Charalel 2024 |
| Systemic chemotherapy in early stage HCC | $10,469 (2024 USD) | Shankaran 2021 |
| Systemic chemotherapy in intermediate stage HCC | $10,209 (2024 USD) | Shankaran 2021 |
| Systemic chemotherapy in late stage HCC | $24,953 (2024 USD) | Shankaran 2021 |
| Radiotherapy | $15,148 (2023 USD) | deBettencourt 2024 |