**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 | Truven: 2,236/40,630 (5.5%) à this is very low, possibly because we limit to patients who have lab data recorded.  ([Singal 2012](https://pubmed.ncbi.nlm.nih.gov/22846843/) (19%), [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/) (24.6%), [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/) (23.7%)) **🡪 average** 22.4% (16.8%-28.0%)  *Range is +/-25%*  [Didn’t include Guss 2018](https://pubmed.ncbi.nlm.nih.gov/30344803/) (reported 36 out of 45 HCC pts without cirrhosis dx had features of cirrhosis, but this was probs skewed since it is a HCC population without including HBV pts) | |
| Subgroup by older age | Truven: 663/14738 (4.5%)  From literature: undx rate of 40.3% among patients aged >65, 17.9% among those <65  (Calculated from [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/))  **40.3% (30.2%-50.4%)**  *Range is +/-25%* | |
| Subgroup by sex | From literature: 33.3% in men vs. 15.0% in women  (Calculated from [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/))  **33.3% (25.0%-41.6%)**  *Range is +/-25%* | |
| Subgroup by diabetes status | Assume same undx rate as overall cohort? | |
| **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%) |

**Age distribution from Truven – use to adjust death rate**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age at MASLD diagnosis | N(%) | Male diabetic | Male non-diabetic | Female diabetic | Female non-diabetic |
| 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%) |  |  |  |  |

**Annual incidence in MASLD patients:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Original data from reference** | **Calculated Annual Incidence %** | **Reference** |
| MASLD without cirrhosis to cirrhosis (censored) | a. 10.85 (6.65–15.06) per 1000 person-years  b. 124.35 (119.28–129.59) per 100,000 PYs  c. 10 year incidence of 3.70% (3.66-3.74) (🡪 0.376% per year) | 0.528% (0.119%-1.51%) | a. [Le 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC11016479/) (meta analysis)  b. [Lee 2024](https://www.sciencedirect.com/science/article/pii/S1542356524001988) (Taiwan)  c. [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) (VA) |
| MASLD to no MASLD (use in potential sensitivity analysis) | 2.4 per 100 person-years | 2.4% | [Le 2023](https://pdf.sciencedirectassets.com/273402/1-s2.0-S1542356522X00190/1-s2.0-S1542356522007339/main.pdf?X-Amz-Security-Token=IQoJb3JpZ2luX2VjEBMaCXVzLWVhc3QtMSJGMEQCIFWzDDbciGcyZC%2BjoXA%2Be6wAkBIqyNwhdzapycJMIDFHAiBCQtUsqckBy9ZM3vvkTcyoPicRqcxKWzklvl28iDrqSiq8BQis%2F%2F%2F%2F%2F%2F%2F%2F%2F%2F8BEAUaDDA1OTAwMzU0Njg2NSIMX1bogxcZPh3zHeQWKpAFKk%2F3lL8wopJvxFcJEfHPQ0EQFk3kwwHAu17vI2GS8vmpsY4qaPhwJl%2FrAgkrDpveQXvjGI7XZwoyg4lYZN7RnIuuxBZofDokaXXzGPbIbIrWinUeYaUAzk0JHoC%2F49yU0WC3%2BGAp9CIYND9Lpb0EblBNv25KN8ryWWw7%2B9GUcNHcItZMGwIaU%2BKo%2B6V30kFp%2FWk4GOboHZ%2FCpeqKKdxyElYMYCT6%2BOVUqh7txW%2FgBD%2FbhGEs3JbwGBOJtH4djnVtn%2B%2Fo3iJ1PoW7pOVFnbpRjWk5ScIpLYYfJZBtTbPZqdiiOV2ZN4RiTBnqCKK%2F5eRzVblq9fky0wcQH9%2BHAdjR4r171bz3t784wb64G%2BHgtgs51PTM2IwixTwBKiU58d4ULrRSDdES6u2lnhHAs2MYzFILNf9yDM5GtDJcbB3ANUhFLhwuIAC8Sns0rzEjzHOO1oyWTPb8Ga8f%2FVfjBFU1rMJSnFR88xQ3LfTht1EeB1sG0fYFYRg3LGlVqIdwyJpH%2FZ9ZLpDfswBJhPdK%2FWq%2BuFv0%2FeKI1F5xqWLxTZXaHl%2Bqfvv9SUdiJyuuXk1MZkiURkGEbJTbJlcvl09qAdZ99DoapZMBVLXvXhj4pEXg2PUl0E1CzyXNl%2FQ%2BfPH9rI4M3Sw3jLjGd8WtEjaoYvBoOYH8k0Yt0xaOhWfNurdVmjoFT3AmeAEx9GdKNlUx2cI1%2BSIRQ%2FGNsrBc14aocoyINSFBdJy%2BhGaFTXsZ6plmd9g2dyqbipAQwlXVxYeb6MufrnT3Q8IThWg8i7LwTCf7K3mmZw6Lf81DHFhkSXwM%2FMgeVk0g2YCqym52gUNSC%2B0XW%2FSLq8v2u6MvEcmwdK0L54BGsOlmzVb35DZeqcLEEcQww%2Ff9uQY6sgFKUlSZET8l4s8wtxCdEIZrD6ao%2BXf%2B%2BKvt7UUOEYqUadvc3lx0w3qxc4yMDE79TJwcVrBAYVLsq7X050%2B2TMLwPG%2BiEJ%2FGGadBXSicUNcRCAXSZocxC84d8VSKX5oPWmxrHe%2B4ix4dIYXn7ZxyphBbDjHlnRlxgc90ftaMIHnk3zUUwTZfz4OdlRmxjSO8m47XmiGHLRJD1jeIsmjvJXHmy8pV89kKICmVu%2BNE9eM3kqBF&X-Amz-Algorithm=AWS4-HMAC-SHA256&X-Amz-Date=20241121T192832Z&X-Amz-SignedHeaders=host&X-Amz-Expires=300&X-Amz-Credential=ASIAQ3PHCVTY4KCZXJJW%2F20241121%2Fus-east-1%2Fs3%2Faws4_request&X-Amz-Signature=cdac41576781d7d525ff79583122b9938aa8aae4152eb0ae8f033b29b7b0e913&hash=c3e919ee7ce1a6f80b737740a0096133d09bca2998ddf9bedefd900ca18f4bf9&host=68042c943591013ac2b2430a89b270f6af2c76d8dfd086a07176afe7c76c2c61&pii=S1542356522007339&tid=spdf-454f55a2-60fb-48a8-a76a-75ebb1bdfce6&sid=56a7afa01d4eb148b1492f4978f7d95edc68gxrqa&type=client&tsoh=d3d) |
| No cirrhosis to HCC (any stage) | a. 0.7 (0.5–1.0) per 1000 person-years (for those FIB4<1.30)  ~~b. 0.44 (0.29‐0.66) per 1000 PYs for NAFLD (and 5.29 (0.75‐37.56) for NASH)~~  c. 0.043%  ~~d. 0.04 (0.03-0.05) per 1000 PYs, for pts w/o evidence of high FIB-4~~  e. ~~0.03 (0.01–0.07)per 100 PYs~~  ~~f. 10 year incidence of 0.69% (0.67-0.70) (🡪 0.069% per year)~~  g. 0.04 per 1000 PYs (95% CI 0.04–0.06) | 0.039% (0.004-0.1) | a. [Behari 2023](https://pubmed.ncbi.nlm.nih.gov/37395730/#:~:text=The%20annual%20incidence%20of%20HCC%20in%20patients%20with,and%200.7%20per%201000%20person-years%20with%20FIB-4%20%3C1.30.)  b. [~~Younossi 2016~~](https://journals.lww.com/hep/fulltext/2016/07000/global_epidemiology_of_nonalcoholic_fatty_liver.14.aspx)  c. [Kawamura 2012](https://journals.lww.com/ajg/abstract/2012/02000/large_scale_long_term_follow_up_study_of_japanese.19.aspx)  ~~d.~~ [~~Kanwal 2018~~](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20)  ~~e.~~ [~~Orci 2022~~](https://www.cghjournal.org/article/S1542-3565(21)00505-X/fulltext)  ~~f.~~ [~~Yeoh 2024~~](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx)  g. [Huang 2024](https://pubmed.ncbi.nlm.nih.gov/38079023/) |
| Cirrhosis to HCC\* | a. 2.6%  b. 3.78 (2.47–5.78) per 100 PYs (4.62 if patient was screened regularly)  c. 22.5 (20.8–24.3) per 1000 PYs  d. 10.6 (9.46-11.91) per 1000 PYs | 2.42% (0.946%-5.78%) | a. [Ascha 2010](https://pubmed.ncbi.nlm.nih.gov/20209604/)  b. [Orci 2022](https://www.cghjournal.org/article/S1542-3565(21)00505-X/fulltext)  c. [Behari 2023](https://pubmed.ncbi.nlm.nih.gov/37395730/#:~:text=The%20annual%20incidence%20of%20HCC%20in%20patients%20with,and%200.7%20per%201000%20person-years%20with%20FIB-4%20%3C1.30.)  d. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |

**\*** We use this to account for undiagnosed cirrhosis cases in HCC incidence rate.

**HCC stage upon diagnosis:**

|  |  |  |
| --- | --- | --- |
|  | **% Value** | **Reference from literature** |
| **Without HCC screening** | | |
| % Early stage | 45.7% | [Daher 2024](https://pubmed.ncbi.nlm.nih.gov/38683607/) |
| % Intermediate stage | 23.0% |
| % Late stage | 31.3% |
| **With HCC screening** | | |
| % Early stage | 70.7% | [Daher 2024](https://pubmed.ncbi.nlm.nih.gov/38683607/) |
| % Intermediate stage | 15.6% |
| % Late stage | 13.7% |

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

We use this data to calculate different survival rates by HCC stage, depending on what treatment patients receive. These values are derived from SEER-Medicare, 2011-2015 data by HCC diagnosis date. I limited the data to these 5 years to account for the introduction of sorafenib after 2007 (the systemic chemotherapy receipt % stabilized around 2010).

1. Out of MASLD patients without cirrhosis (we will use this one first. Update 3/5/25: we will further weigh by data for cirrhotic patients)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| First Treatment Type | Early (TNM stage1)  (N=450, 212 treated)   * 47.1% treated | | Intermediate (TNM sage 2/3A)  (N=376, 180 treated)   * 47.9% treated | | Late (TNM stage 3B/3C/4)  (N=372, 140 treated)   * 37.6% treated | |
| Ablation | 18 (4.0) | 8.5% | 12 (3.2) | 6.6% | 1 (0.3) | 0.7% |
| Radiotherapy | 2 (0.4) | 0.9% | 0 (0.0) | 0% | 5 (1.3) | 3.6% |
| Resection | 72 (16.0) | 34.0% | 36 (9.6) | 20% | 5 (1.3)\* | 0% |
| Systemic | 50 (11.1) | 23.6% | 68 (18.1) | 37.8% | 94 (25.3) | 67.1% |
| TACE | 65 (14.4) | 30.7% | 59 (15.7) | 32.8% | 40 (10.8) | 28.6% |
| Transplant | 5 (1.1) | 2.3% | 5 (1.3) | 2.8% | 0 (0.0) | 0% |
| No treatment | 238 (52.9) | | 196 (52.1) | | 227 (61.0) 🡪232 (62.4%) | |

\*Will add this to the untreated group because it is unlikely that late stage HCC would be treated with resection and transplant. Also, we can't find data on survival after resection/transplant in late HCC patients.

Percent out of those treated are highlighted in blue (these percentages exclude the untreated patients)

1. MASLD with Compensated cirrhosis (Use if we want to adjust for % of undiagnosed cirrhosis patients. **~~Not using this for the initial model~~**~~, because the data for the “non-cirrhotic” group above could actually include undiagnosed patients as well, looking at the high % of untreated patients.)~~

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| First Treatment Type | Early  (N=668, 485 treated🡪 72.6% treated) | | Intermediate  (N=549, 386 treated 🡪 70.3% treated) | | Late  (N=269, 115 treated, 42.8% treated) | |
| Ablation | 79 (11.8) | 16.3% | 43 (7.8) | 11.1% | 4 (1.5) | 3.5 |
| Radiotherapy | 1 (0.1) | 0.2% | 0 (0.0) | 0% | 1 (0.4) | 0.9 |
| Resection | 88 (13.2) | 18.1% | 40 (7.3) | 10.4% | 7 (2.6) | 0% |
| Systemic | 41 (6.1) | 8.5% | 77 (14.0) | 19.9% | 76 (28.3) | 66.1 |
| TACE | 217 (32.5) | 44.7% | 201 (36.6) | 52.1% | 34 (12.6) | 29.5 |
| Transplant | 59 (8.8) | 12.2% | 25 (4.6) | 6.5% | 1 (0.4) | 0% |
| No treatment | 183 (27.4) | | 163 (29.7) | | 146 (54.3)🡪154(57.2%) | |

Percent out of those treated are highlighted in blue (these percentages exclude the untreated patients)

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

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Original data from reference** | **Calculated Annual death rate** | **Reference** |
| No cirrhosis (MASLD)  *Limit to liver related death only bc MASLD 🡪 death rate is adjusted by age specific death rate as well. We want this death rate to be the combined probability of death due to age AND MASLD* | a. 0.3-7.92 per 1000 PYs liver-related for F0-F3  F0: 38.1%\*0.30  F1: 28.9%\*0.64  F2: 13.6%\*4.28  F3: 12.0%\*7.92  🡪 weighed avg =1.83 per 1000 PYs  b. 0.77 (0.33‐1.77) per 1000 PYs liver-related for NAFLD (11.77 (7.1‐19.53) for NASH)  c. 1.75(0.58–2.91) per 1000 PYs for liver related all NAFLD | 0.145% (0.03%-0.291%) | a. [Dulai 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC5397356/)  b. [Younossi 2016](https://journals.lww.com/hep/fulltext/2016/07000/global_epidemiology_of_nonalcoholic_fatty_liver.14.aspx)  c. [Younossi 2023](https://pmc.ncbi.nlm.nih.gov/articles/PMC10026948/#sec12) |
| Compensated cirrhosis\* | a. 0.3% (0.0–0.5) 1y all-cause mortality  b. 1.7% 1y liver related mortality | 1% (0.01%-2%) | a. [Cheng 2023](https://pubmed.ncbi.nlm.nih.gov/35513235/)  b. [Wang 2023](https://pubmed.ncbi.nlm.nih.gov/37378630/) (figure 4) |
| Early stage HCC |  |  |  |
| Transplant | 60%-70% 5-year OS rate | 8.25% | [American cancer society data](https://www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/survival-rates.html) |
| Resection | 88.9% 1-year OS rate | 11.1% | [Thornton 2022](https://pubmed.ncbi.nlm.nih.gov/35234371/) |
| TACE | 93.3% 1-year OS rate | 6.7% | [Kim 2017](https://pubmed.ncbi.nlm.nih.gov/28263954/) |
| Ablation | 43.2% 5-year OS rate | 15.5% | [Zhang 2021](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784529) |
| Systemic chemotherapy |  | 61.9% | SEER-Medicare, calculated from MASLD patient data |
| Radiotherapy | 70.4% 3-year OS rates | 11.0% | [Hara 2019](https://pubmed.ncbi.nlm.nih.gov/30805950/) |
| Untreated | 64% 1-year OS rate | 35.7% | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Intermediate stage HCC |  |  |  |
| Transplant | 88% 1-year OS rate | 12% | [Kamo 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC5985555/) |
| Resection | 92% 1-year OS rate | 8% | [Zhong 2015](https://www.nature.com/articles/nrclinonc.2014.122-c3) |
| TACE | 70% 1-year OS rate | 30% | [Prince 2020](https://pubmed.ncbi.nlm.nih.gov/33224278/) |
| Ablation | 93.0% 1-year OS rate | 7% | [Tanaka 2023](https://www.nature.com/articles/s41598-023-43516-w) |
| Systemic chemotherapy |  | 69.6% | SEER-Medicare,  calculated from MASLD patient data |
| Radiotherapy | 63% 2-year OS rate | 20.6% | [Prince 2020](https://pubmed.ncbi.nlm.nih.gov/33224278/) |
| Untreated |  | 63.2% | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Late stage HCC |  |  |  |
| TACE | 33.3% 1-year OS rate | 66.7% | [Kong 2018](https://pubmed.ncbi.nlm.nih.gov/30113483/) |
| Ablation | 73.1% 1-year OS rate | 26.9% | [Dai 2014](https://pubmed.ncbi.nlm.nih.gov/25284590/) |
| Systemic chemotherapy |  | 86.2% | SEER-Medicare, calculated from MASLD patient data |
| Radiotherapy | 31.3% 1-year OS rate | 68.7% | [Lin 2019](https://pubmed.ncbi.nlm.nih.gov/30656831/) |
| Untreated |  | 87.2% | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |

\* We use this to account for undiagnosed cirrhosis cases in the death rate.

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Probability** | **Original value from reference** | **Value** | **Reference** |
| Sensitivity of US/AFP |  | 0.851 = 85.1% | [Singal 2022](https://pubmed.ncbi.nlm.nih.gov/35945907/) |
| Specificity of US/AFP |  | 0.839 = 83.9% | [Singal 2022](https://pubmed.ncbi.nlm.nih.gov/35945907/) |
| False positive HCC | specificity 85% (95% CI 73% to 93%) | 15% (7%-27%) | [Colli 2021](https://pmc.ncbi.nlm.nih.gov/articles/PMC8078581/) (15% false positive rate, meta analysis) |
| Screening adherence | a. 8.78%  b. 42% (27-57%)  c. 60% | 25.4% (8.8%-57%)  60% (45-75%) | a. [Yeo 2021](https://www.sciencedirect.com/science/article/pii/S016882782100307X)  b. [Zhao 2017](https://onlinelibrary.wiley.com/doi/full/10.1111/liv.13555)  c. [Singal 2024](https://karger.com/lic/article/13/6/643/909485/Cost-Effectiveness-of-a-Biomarker-Based-Screening) |

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Health State** | **Original value from reference** | **Base-case value with range** | **Reference** |
| MASLD without cirrhosis | 0.660±0.107 | 0.880 (0.773-0.987) | Derived from [Sayiner 2016](https://pmc.ncbi.nlm.nih.gov/articles/PMC5013331/)\*  [Kowada 2024](https://bmjopen.bmj.com/content/14/11/e080549.abstract)  ([Ock 2017](https://pmc.ncbi.nlm.nih.gov/articles/PMC5584479/) ; [Zhang 2015](https://link.springer.com/article/10.1007/s00330-015-3731-2#ref-CR41) reports similar value of 0.85) |
| Compensated cirrhosis |  | 0.78 (0.71-0.89) | [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11) |
| False positive HCC |  | Same as utility of MASLD (see note) |  |
| Early stage HCC |  | 0.72 (0.62–0.82) | [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11) |
| Intermediate stage HCC |  | 0.69 (0.62-0.78) | [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11) |
| Late stage HCC | 0.65 (0.52–0.78)  0.40 (0.2-0.6) | 0.53 (0.2-0.78) | a. [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11)  b. [Bremner 2007](https://pmc.ncbi.nlm.nih.gov/articles/PMC2657973/) |

\* Derived by subtracting the incremental decrease in health utility between the general population (0.78) and non-cirrhotic MASLD (0.66) according to the reference (uses SF-6D health utility) from 1.

Note: We assume the utility of false positive HCC node to be the same as MASLD. We assume that the disutility associated with false positive HCC is almost negligible because patients only spend a fraction of one cycle in this state. We assume that patients who are falsely diagnosed with HCC from ultrasound will receive average of 2.5 CT/MRI (Parikh 2020) to confirm the diagnosis, and will not spend a significant amount of time in a false positive state. Thus, patients in the false positive HCC node will just accrue a cost for the 2.5 CT/MRI but will not be penalized with any disutility.

**Costs from literature (2025 USD; inflation calculator used:** [Inflation Calculator | Find US Dollar's Value From 1913-2025](https://www.usinflationcalculator.com/)**)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cost** | **Original value from reference** | **Base case value with range** | **Reference** |
| US+AFP screening | $179\*2 (multiply by 2 because biannual) = $358 (2024 USD) | $363 ($272-454) | [Medicare fee](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5)  [schedule](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5)  *Range is +/- 25%* |
| CT/MRI to confirm HCC diagnosis | ($349 CT+ $491 MRI)/2 \*1.5 times (from Parikh 2020)  (averaged the cost of CT and MRI and then multiplied by the avg # of imaging done according to Parikh paper) | $630 ($473-$788) | [Medicare fee](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5)  [schedule](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5) (CT: 74170, MRI: 74183)  *Range is +/- 25%*  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Repeat CT/MRI for false positive HCC | ($349 CT+ $491 MRI)/2 \*2.5 times (from Parikh 2020) | $1050 ($788-$1313) | [Medicare fee](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5)  [schedule](https://www.cms.gov/medicare/physician-fee-schedule/search?Y=0&T=4&HT=0&CT=3&H1=0632T&M=5)(CT: 74170, MRI: 74183)  *Range is +/- 25%*  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Medical care of patients with non-cirrhotic MASLD | $3537 (2019 USD) | $4395 ($3296-$5494) | [Younossi 2023](https://pubmed.ncbi.nlm.nih.gov/37250870/)  *Range is +/- 25%* |
| Early stage HCC |  |  |  |
| Treated | $50001 (26777-92637) 2018 USD  Transplant rate in this paper is also 2.3% (makes sense bc also a SEER study) so no further adjustment for LT | $63255 ($33875 - $117193) | [Karim 2023](https://www.sciencedirect.com/science/article/pii/S1542356522010953#sec3) |
| Untreated | $35390 (32681-38161) 2011 USD  Divide by 1.06, the median survival:  $33387 (30831-36001) | $47,151 (43,541-50,843) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) (Table 3) |
| Intermediate stage HCC |  |  |  |
| Treated | 86,675 (38,616-154392) 2013 USD  Scaled for 3.6% transplant rate (paper provides separate e values for transplanted vs not) | $118,194 ($52,659- $210,536) | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |
| Untreated | $38,265 (32,755–44,621) 2011 USD  Divide by 1.04, the median survival:  $36793 (31495-42905) | $51,961 (44,479-60,593) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) (Table 3) |
| Late stage HCC |  |  |  |
| Treated | $77436 (33468-106236) 2013 USD | $105,595 ($45,639- $144,868) | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |
| Untreated | Stage III: 14%: IV: 17%  Weighed average of cumulative cost: $25,640 (22400-29796) 2011 USD  Weighed average of the survival: 0.461 years  Divide by survival time to get yearly cost:  55618 (48590-64633) | $78,547 (68,621-91,278) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) (Table 3) |

**For sensitivity analyses**

**1. By sex**

\*Because we use a different set of studies to gather this data compared to the base case inputs, the male and female HCC incidences were both lower than what we use in the base case. We can’t compare cost-effectiveness of only screening the male patients if the overall HCC incidence isn’t the same as the base case analysis, so we will standardize the data below with respect to the value in the overall cohort according to the base-case inputs. How we do this: For each study, find the increment increase/decrease of the subgroup (by age or sex) incidence compared to incidence in the overall cohort (as reported in the study). Then, average this increment across studies and add to the incidence used in the overall cohort of the base case.

\*\*We find an adjusted midpoint from which we measure the % increase or decrease from, by weighing the % male and female in the cohort from the reference.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Original data from reference** | **Value (old)\*** | **New value\*\*** | **Reference** |
| Undiagnosis rate of cirrhosis | Male: 33.3%  Women: 15.0% |  |  | [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/) |
| Non-cirrhotic MASLD to HCC |  |  |  |  |
| Male | a. 0.05 (0.04-0.06)/1000 PYs for low FIB-4 (N=258,074; not sex specific);  ~~0.39 (0.32-0.48)/1000 PYs for high FIB-4 (N=34,392; not sex specific)~~  ~~b. 10-year incidence of 0.72% (🡪 0.072%)~~ | Kanwal:  Low fib4: 0.004% -> 0.005%= ~~+0.001%~~ 25% inc  High fib4: 0.039% -> 0.039%= ~~+0.001%~~ 0% inc  *Weighed avg:*  25%(0.882)+0%(0.118)=22.05%  Yeoh: 0.069% -> 0.072%= ~~+0.003%~~  4.35%  ~~Avg increment: +0.0017%~~  Kanwal: N=280,177 (includes pts with cirrhosis but that’s only 0.4% of total cohort.)- 23.4%  Yeoh: N=916,120- 76.6%  Weighed avg across 2 studies:  8.49%  Standardized value: ~~0.0017+0.051(0.008%-0.529%)=~~ **~~0.053%(0.0097-0.58)~~**  0.051(0.008%-0.529%)\*1.0849  =**0.055% (0.009%-0.574%)** | New “overall” in a 50/50 M/F cohort:  0.005%(0.50) + 0.002%(0.50) = 0.0035%  Increment inc for M:  0.005%-0.0035% = +0.0015%  OR 42.9% increase  Base case value: 0.039% (0.003-0.1)  Male subgroup value:  Add increment:  0.041% (0.005%-0.10%)  Add % inc:  0.056% (0.0043%-0.14%) | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 2)  (VA population)  ~~b.~~ [~~Yeoh 2024~~](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) ~~(VA)~~ |
| Female | a. 0.02 (0.00-0.07)/1000 PYs for low FIB-4;  0.20 (0.00-1.09) for high FIB-4  b. 10-year incidence of 0.20% (🡪 0.020%) | Kanwal:  Low fib4: 0.004% -> 0.002%=  -0.002%  High fib4: 0.039% -> 0.02%= -0.019%  Yeoh: 0.069% -> 0.020%=-0.049%  Avg increment:  -0.0233%  Standardized value:  -0.0233+0.051 (0.008%-0.529%)= **0.028% (0-0.506)** |  | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 2)  (VA population)  ~~b.~~ [~~Yeoh 2024~~](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) ~~(VA)~~ |
| Cirrhotic MASLD to HCC |  |  |  |  |
| Male | 11.05 (9.83-12.39)/1000 PYs | 1.063%🡪1.105% = ~~+0.042%~~  3.95% increase  ~~0.042+2.45 (1.06%-4.62%)=~~ **~~2.49% (1.102-4.66)~~**  2.45 (1.06%-4.62%)\*1.0395=**2.55% (1.10%-4.80%)** | New “overall” in a 50/50 M/F cohort:  1.105%(0.50) + 0.162%(0.50) = 0.634%  Increment inc for M:  1.105%-0.634% = +0.471%  OR 74.3% increase  Base case value:  2.42% (0.946%-5.78%)  Male subgroup value:  Add increment:  2.89% (1.42%-6.25%)  Add % inc:  4.22% (1.65%-10.07%) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 1)  (VA mpopulation) |
| Female | 1.62 (0.20-5.85)/1000 PYs | 1.063%🡪0.162% = -0.901  -0.901+2.45 (1.06%-4.62%)= **1.55% (0.159-3.72)** |  | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 1)  (VA population) |
| Non-cirrhotic MASLD to cirrhosis |  |  |  |  |
| Male | 10-year incidence of 3.78% (3.74-3.82)  🡪0.385% | 0.376% -> 0.385%= ~~+0.009~~  2.39% inc    ~~0.009+0.528% (0.124%-1.09%)=~~ **~~0.537%(0.133-1.099~~)**  0.528% (0.124%-1.09%)\*1.0239= **0.541% (0.127%-1.12%)** | New “overall” in a 50/50 M/F cohort:  0.385%(0.50) + 0.241%(0.50) = 0.313%  Increment inc for M:  0.385%-0.313% = +0.072%  OR 23.0% increase  Base case value:  0.528% (0.119%-1.51%)  Male subgroup value:  Add increment:  0.60% (0.191%-1.58%)  Add % inc:  0.65% (0.15 %-1.86%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) (VA) |
| Female | 10-year incidence of 2.38% (2.25-2.51)  🡪 0.241% | 0.376%-> 0.241%=  -0.135%  -0.135%+0.528% (0.124%-1.09%)= **0.393% (0-0.955)** |  | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) (VA) |
| Non-cirrhotic MASLD to death | From actuarial life table  **Make sure to change the death% used in ActuarialTables sheet** |  |  | [Actuarial Life Table](https://www.ssa.gov/oact/STATS/table4c6.html) |

**2. By age < or >= 60~65**

Our base case cohort age distribution:

Yeoh: cutoff is at 60

19% 18-39y/o

57% 40-59 y/o

24% 60+ y/o

Kanwal: cutoff is at 65

85.6% <65

14.4% >=65

**Make sure to change age distribution in sheet. For Actuarial Tables, use probability for M+F**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Original data from reference** | **Old value** | **New Value** | **Reference** |
| Undiagnosis rate of cirrhosis | <65 y/o: 17.9%  >65 y/o: 40.3% |  |  | [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/) |
| Non-cirrhotic MASLD to HCC |  |  |  |  |
| <65 | a. 0.02(0.02-0.03)/1000 PYs for low FIB-4; 🡪 **0.002%**  0.29 (0.20-0.40)/1000 PYs for high FIB-4 🡪 **0.029%**  b. For 18-39 y/o: 10-year incidence of 0.09% (0.06-0.11); 🡪 **0.009%**  for 40-59 y/o: 0.62% (0.59-0.65) 🡪 **0.062%** | Kanwal:  Low fib4: 0.004% -> 0.002%= -0.002%  High fib4: 0.039% -> 0.029%= -0.010%  *Weighed avg:*  Yeoh:  18-39y/o: 0.069% -> 0.009%= -0.060%  40-59y/o: 0.069% -> 0.062%= -0.007%  Avg increment:  -0.01975%  Standardized value: -0.01975+0.051(0.008%-0.529%)= **0.031%(0.0-0.509)** |  | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 2)  (VA population)  ~~b.~~ [~~Yeoh 2024~~](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) ~~(VA)~~ |
| ≥65 | a. 0.14 (0.10-0.18)/1000 PYs for low FIB-4 (N=258,074; not age specific); 🡪 **0.014%**  ~~0.48 (0.37-0.61)/1000 PYs for high FIB-4 (N=34,392; not age specific)🡪~~ **~~0.048%~~**  ~~b. For >60y/o: 10-year incidence of 0.76% (0.74-0.78) 🡪~~ **~~0.076%~~** | Kanwal:  Low fib4: 0.004% -> 0.014%= ~~+0.010%~~  250% inc  High fib4: 0.039% -> 0.048%= ~~+0.009%~~  23.1% inc  *Weighed avg:*  250%(0.882)+23.1%(0.118)=223.2%  Yeoh: 0.069% -> 0.076%=+~~0.007%~~  10.14% inc  ~~Avg increment:+0.00867 %~~  Kanwal: N=  Standardized value:  ~~0.00867 +0.051 (0.008%-0.529%)=~~ **~~0.060% ( 0.0167-0.538)~~** | New “overall”:  0.002%(0.856)+  0.014%(0.144)=  0.0037%  Increment inc for older pts:  0.014%-0.0037% = +0.0103%  OR 277.6% increase  Base case value: 0.039% (0.003-0.1)  Older subgroup value:  Add increment:  0.049% (0.013%-0.110%)  Add % inc:  0.15% (0.011%-0.38%) | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 2)  (VA population)  ~~b.~~ [~~Yeoh 2024~~](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) ~~(VA)~~ |
| Cirrhotic MASLD to HCC |  |  |  |  |
| <65 | 9.74 (8.46-11.17) per 1000 PY | 1.063%🡪0.974 % =  -0.089%  -0.089+2.45 (1.06%-4.62%)= **2.36% (0.971-4.53)** |  | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 1)  (VA mpopulation) |
| ≥65 | 13.43 (10.82-16.49) per 1000 PY | 1.063%🡪1.343% = +0.280%  +0.280+2.45 (1.06%-4.62%)= **2.73% (1.34 -4.90)** | New “overall”:  0.974%(0.856)+  1.343%(0.144)=  1.027%  Increment inc for older pts:  1.343%-1.027 % = +0.316%  OR 30.8% increase  Base case value: 2.42% (0.946%-5.78%)  Older subgroup value:  Add increment:  2.74 % (1.262%-6.096 %)  Add % inc:  3.17% (1.24%-7.56 %) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 1)  (VA population) |
| Non-cirrhotic MASLD to cirrhosis |  |  |  |  |
| <65 | For 18-39 y/o: 10-year incidence of 1.23% (1.13-1.34)🡪 **0.124% (0.131-0.135)**  For 40-59 y/o: 10-year incidence of 4.68% (4.60-4.76)🡪 **0.478% (0.470-0.487)** | For 18-39y/o: 0.376% -> 0.124%=  -0.252  For 40-59y/o: 0.376%-> 0.478%= +0.102  Average increment:  (-0.252+0.102)/2=  -0.075    -0.075%+0.528% (0.124%-1.09%)= **0.453%(0.049-1.015)** |  | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) (VA) |
| ≥65 | For >60 y/o: 10-year incidence of 3.44% (3.39-3.48)🡪 **0.349% (0.397-0.354)** | 0.376%-> 0.349%=  -0.027%  -0.027%+0.528% (0.124%-1.09%)= **0.501% (0.097-1.063)** | New “overall”:  0.124%(0.19)+  0.478%(0.57)+  0.349%(0.24)=  0.380%  Increment dec for older pts:  0.349%-0.380% =  -0.031 %  OR 8.16% decrease  Base case value: 0.528% (0.119%-1.51%)  Older subgroup value:  Subtract increment:  0.497% (0.088%-1.48%)  Add % decrease:  0.485% (0.109%-1.39%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) (VA) |
| Non-cirrhotic MASLD to death | From actuarial life table; assume even distribution across all ages |  |  | [Actuarial Life Table](https://www.ssa.gov/oact/STATS/table4c6.html) |

**3. By diabetes status**

**Use for diabetes prevalence:** [Hepatology](https://journals.lww.com/hep/fulltext/2016/07000/global_epidemiology_of_nonalcoholic_fatty_liver.14.aspx) -- Among NAFLD patients, pooled overall diabetes incidence is: 22.51% (95% CI: 17.92‐27.89) and among NASH, 43.63% (95% CI: 30.28‐57.98) 🡪 we assume our base case has 33% diabetic to find the incremental increase/decrease. This percentage is used to calculate the new input values by diabetes subgroup below:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Original data from reference** | **New Value** | **Reference** |
| Undiagnosis rate of cirrhosis | Same as base case? |  |  |
| Non-cirrhotic MASLD to HCC | 0.08 (0.06-0.11) per 1000 PYs for no evidence of high Fib4  (no diabetes:  0.03 (0.02-0.04)) | New “overall”:  0.008%(0.33)+  0.003%(0.67)=  0.00465%  Increment inc for diabetic pts:  0.008%-0.00465% = +0.00335%  OR 72.0% increase  Base case value: 0.039% (0.003-0.1)  Older subgroup value:  Add increment:  0.042% (0.0064%-0.10%)  Add % inc:  0.067% (0.005%-0.172%) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 2) |
| Cirrhotic MASLD to HCC | 12.36 (10.67-14.24)  (no diabetes:  8.51 (6.96-10.29)) | New “overall”:  1.236%(0.33)+  0.851%(0.67)=  0.978%  Increment inc for older pts:  1.236%-0.978 % = +0.258%  OR 26.4% increase  Base case value: 2.42% (0.946%-5.78%)  Older subgroup value:  Add increment:  2.68 % (1.204%-6.038 %)  Add % inc:  3.06% (1.20%-7.31 %) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) (supp table 1) |
| Non-cirrhotic MASLD to cirrhosis | 10-year incidence: 3.28% (3.23-3.34) **🡪 0.333%**  (no DM: 4.05 (4.00-4.10)🡪 0.413%) | New “overall”:  0.333%(0.33)+  0.413%(0.67)=  0.387%  Increment dec for older pts:  0.333%-0.387% =  -0.054 %  OR 14.0% decrease  Base case value: 0.528% (0.119%-1.51%)  Diabetic subgroup value:  Subtract increment:  0.474% (0.065%-1.46%)  Add % decrease:  0.454% (0.102%-1.299%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to death |  | Multiply the death probability from Actuarial Life Table by the appropriate SMRs below (standardized mortality ratio: ratios between deaths observed in the diabetic cohort, and those expected according to age- and gender-specific regional mortality rates):  SMRs for nonviral and nonalcoholic liver disease in diabetic cohort.  Overall: SMR of 2.86  All ages:  M 2.78 (2.54 – 3.04)  F 3.07 (2.67-3.51)  30-64:  M 4.41 (3.69-5.23)  F 5.51 (3.49-8.26)  65-74:  M 2.82 (2.44-3.24)  F 3.31 (2.49-4.32)  75-89:  M 2.12 (1.81-2.47)  F 2.78 (2.33-3.28) | [Zoppini 2014](https://journals.lww.com/ajg/fulltext/2014/07000/mortality_from_chronic_liver_diseases_in_diabetes.16.aspx)  Italian study  **Provides age and sex stratified data** |

**Literature search notes for combined subgroup data:**

**HCC incidence (cirrhotic and non-cirrhotic):**

**For any combination of risk factors**

[Incidence rates of hepatocellular carcinoma based on risk stratification in steatotic liver disease for precision medicine: A real-world longitudinal nationwide study - PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC11548784/#sec020)

Figure 1 provides HCC incidence for cirrhotic and non cirrhotic pts, by sex, age, DM/no DM

**Cirrhosis incidence**

**MASLD mortality**

**4. Male, older and with diabetes**

Assumptions to get the new overall transition probabilities --- Asked Winnie for Truven data

33% diabetes

19% <40 y/o

24% 40-49 y/o

33% 50-59 y/o

17% 60-69 y/o

7% >=70 y/o

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Original data from reference** | **New Value** | **Reference** |
| Undiagnosis rate of cirrhosis |  | Use underdiagnosis rate of older patients (which is higher than that of male pts) |  |
| Non-cirrhotic MASLD to HCC | 1.36 (0.79-1.92) per 1000 PYs |  | [Lai 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC11548784/#sec020) (Figure 1)  Optum study – may undercode cirrhosis, but authors say that it undergoes “meticulous and rigorous maintenance” to prevent such biases. Also, it is all privately insured patients 🡪 better access to care 🡪 probably lower rate of underdiagnosed cirrhosis. |
| Cirrhotic MASLD to HCC | 19.06 (16.10-22.01) per 1000 PYs |  | [Lai 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC11548784/#sec020) (Figure 1) |
| Non-cirrhotic MASLD to cirrhosis |  | HRs: [Journal of Clinical Gastroenterology](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx)  ORs: [High Prevalence of Advanced Liver Fibrosis Assessed by Transient Elastography Among U.S. Adults With Type 2 Diabetes | Diabetes Care | American Diabetes Association](https://diabetesjournals.org/care/article/44/2/519/35494/High-Prevalence-of-Advanced-Liver-Fibrosis)  Lots of incidence data but no dm stratified: [Flemming 2021](https://journals.lww.com/hep/fulltext/2021/12000/nafld_and_alcohol_associated_liver_disease_will_be.34.aspx)  **No sex or age stratification:** [Fibrosis Progression Rate in Biopsy-proven Nonalcoholic Fatty Liver Disease among People with Diabetes versus People without Diabetes: A Multicenter Study - PMC](https://pmc.ncbi.nlm.nih.gov/articles/PMC10699569/) |  |
| Non-cirrhotic MASLD to death |  | Multiply the death probability from Actuarial Life Table **for older male patients** by the appropriate SMRs below (SMR: ratios between deaths observed in the diabetic cohort, and those expected according to age- and gender-specific regional mortality rates):  SMRs of SMR for nonviral and nonalcoholic liver disease in diabetic cohort.  Overall: SMR of 2.86  All ages:  M 2.78 (2.54 – 3.04)  F 3.07 (2.67-3.51)  30-64:  M 4.41 (3.69-5.23)  F 5.51 (3.49-8.26)  65-74:  M 2.82 (2.44-3.24)  F 3.31 (2.49-4.32)  75-89:  M 2.12 (1.81-2.47)  F 2.78 (2.33-3.28) | [Zoppini 2014](https://journals.lww.com/ajg/fulltext/2014/07000/mortality_from_chronic_liver_diseases_in_diabetes.16.aspx)  Italian study  **Provides age and sex stratified data** |