**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%* | |
| **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(%) |
| 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. 1.1 (0.9–1.1) per 1000 person-years  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. 0.08 (0.03-0.47) per 1000 PYs  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) | 0.051% (0.003-0.11) | 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) |
| 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 patients without cirrhosis (we will use this one first)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| 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. 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/) |
| 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) uses similar value |
| False positive HCC |  | Same as the weighed HCC utility derived from value below |  |
| 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.

**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 | $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 | $86481 (39398- 154373) 2013 USD  Scaled for 2.8% transplant rate (paper provides separate e values for transplanted vs not) | $117,930 ($53,725- $210,510) | [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.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Original data from reference** | **Value (old)** | **Standardized 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%) | 0.039% (0.005-0.072) | 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%)** | 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%) | 0.014% (0.0001-0.109) | 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 | 1.11% (0.983-1.24) | 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%)** | [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 | 0.162% (0.020-0.585) | 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% (0.380%-0.389%) | 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%)** | [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% (0.227%-0.254%) | 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**

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Original data from reference** | **Value** | **Standardized 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%** | 0.0255% (0.002-0.062) | 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%** | 0.046% (0.014-0.076) | 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)~~** | 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 | 0.974% (0.846-1.12%) | 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 | 1.34% (1.08%-1.65%) | 1.063%🡪1.343% = +0.280%  +0.280+2.45 (1.06%-4.62%)= **2.73% (1.34 -4.90)** | [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)** | 0.301% (0.131%-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)** | 0.349% (0.397%-0.354%) | 0.376%-> 0.349%=  -0.027%  -0.027%+0.528% (0.124%-1.09%)= **0.501% (0.097-1.063)** | [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) |