**Table 1A**: Model input parameters for base case analysis. The base case value is derived by averaging the values reported in the references unless specified otherwise.

|  |  |  |
| --- | --- | --- |
| **Variable** | **Base-Case Value and Range** | **Reference** |
| Proportion with undiagnosed cirrhosis | 22.4% (16.8%-28.0%)a | a. [Singal 2012](https://pubmed.ncbi.nlm.nih.gov/22846843/)  b. [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/)  c. [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/) |
| Screening adherence rate | 60% (45%-75%)a | [Singal 2024](https://karger.com/lic/article/13/6/643/909485/Cost-Effectiveness-of-a-Biomarker-Based-Screening) |
| **Annual transition probabilities** |  |  |
| Non-cirrhotic MASLD to cirrhosis (censored) | 0.528% (0.119%-1.51%) | a. [Le 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC11016479/)  b. [Lee 2024](https://www.sciencedirect.com/science/article/pii/S1542356524001988)  c. [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to HCCb | 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.)  c. [Kawamura 2012](https://journals.lww.com/ajg/abstract/2012/02000/large_scale_long_term_follow_up_study_of_japanese.19.aspx)  d. [Huang 2024](https://pubmed.ncbi.nlm.nih.gov/38079023/) |
| (Undiagnosed) cirrhosis with MASLD to HCCb | 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) |
| MASLD (non-cirrhotic or with undiagnosed cirrhosis) to false positive HCC | 15% (7%-27%) | [Colli 2021](https://pmc.ncbi.nlm.nih.gov/articles/PMC8078581/) |
| Non-cirrhotic MASLD to death | 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) |
| (Undiagnosed) cirrhosis with MASLD to death | 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 to treatment | 47.1% (35.3%-58.9%) a | Derived from SEER-Medicare database |
| Treated early-stage HCC to death | 22.1% (16.6%-27.6%)a | Derived by weighed survival across various treatment types. See Supplemental Methods. |
| Untreated early-stage HCC to death | 35.7% (26.8%-44.6%)a | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Intermediate-stage HCC to treatment | 47.9% (35.9%-59.9%)a | Derived from SEER-Medicare database |
| Treated intermediate-stage HCC to death | 38.6% (29.0%-48.3%)a | Derived by weighed survival across various treatment types, see Supplemental Methods |
| Untreated intermediate-stage HCC to death | 63.2% (47.4%-79.0%)a | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Late-stage HCC to treatment | 37.6% (28.2%-47.0%)a | Derived from SEER-Medicare database |
| Treated late-stage HCC to death | 79.6% (59.7%-99.5%)a | Derived by weighed survival across various treatment types, see Supplemental Methods |
| Untreated late-stage HCC to death | 87.2% (65.4%-100%)a | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| **HCC Stage Upon Diagnosis** |  |  |
| Control |  | [Daher 2024](https://pubmed.ncbi.nlm.nih.gov/38683607/) |
| Early | 45.7% (34.3%-57.1%)c |
| Intermediate | 23.0% |
| Late | 31.3% (23.5%-39.1%)c |
| Interventiond |  |
| Early | 70.7% (53.0%-88.4%)c |
| Intermediate | 15.6% |
| Late | 13.7% (10.3%-17.1%)c |

*a Range is +/-25% of the base case value.*

*b The overall transition rate from MASLD to HCC used in the model is the combination of HCC incidence in patients with MASLD without cirrhosis or with undiagnosed cirrhosis, weighed using the percentage of undiagnosed cirrhosis.*

*c Range was set to be +/- 25% of the base case value for the percent diagnosed with early and late stage HCC. The values for the intermediate stage will be adjusted accordingly such that the total percentages add to 100% across the three stages. The early and late stage values must also not exceed 100% when these values are being tested.*

*d**The distributions of early, intermediate, and late stage HCC in the intervention arm listed here is further weighed by the treatment adherence rate.*

**Table 1B**: Utilities for base case analysis. The base case value is derived by averaging the values reported in the references unless specified otherwise.

|  |  |  |
| --- | --- | --- |
| **Health State** | **Base-Case Value and Range** | **Reference** |
| MASLD without cirrhosis | 0.880 (0.773-0.987) | a. [Sayiner 2016](https://pmc.ncbi.nlm.nih.gov/articles/PMC5013331/)  b. [Kowada 2024](https://bmjopen.bmj.com/content/14/11/e080549.abstract) |
| Compensated cirrhosisa | 0.78 (0.71-0.89) | [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11) |
| 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 | 0.53 (0.20-0.78) | a. [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11)  b. [Bremner 2007](https://pmc.ncbi.nlm.nih.gov/articles/PMC2657973/) |
| False positive HCC | Same as the weighed HCC utility derived from utilities by HCC stage as above. |  |

*a Included in MASLD node utility, weighed by percent of undiagnosed cirrhosis.*

**Table 1C**: Costs for base case analysis. The base case value is derived by averaging the values reported in the references unless specified otherwise.

|  |  |  |
| --- | --- | --- |
| **Cost** | **Base-Case Value and Range** | **Reference** |
| Semiannual US and AFP screening | $363 ($272-$454)a | [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/MRI to confirm HCC diagnosis | $630 ($473-$788)a,b | [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)  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Repeat CT/MRI for false positive HCC | $1050 ($788-$1313)a,c | [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)  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Medical care of patients with MASLD (non-cirrhotic or with undiagnosed cirrhosis) | $4395 ($3296-$5494)a | [Younossi 2023](https://pubmed.ncbi.nlm.nih.gov/37250870/) |
| Early stage HCC (annual costs) |  |  |
| Treated | $63255 ($33875 - $117193) | [Karim 2023](https://www.sciencedirect.com/science/article/pii/S1542356522010953#sec3) |
| Untreated | $47151 ($43541-$50843) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) |
| Intermediate stage HCC (annual costs) |  |  |
| Treated | $117930 ($53725- $210510)d | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |
| Untreated | $51961 (44479-60593) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) |
| Late stage HCC (annual costs) |  |  |
| Treated | $105595 ($45639- $144868) | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |
| Untreated | $78547 ($68621-$91278) | [Shaya 2013](https://link.springer.com/article/10.1007/s40273-013-0109-7#Sec10) |

*a Range is +/-25% of the base case value.*

*b The average cost of a CT or MRI according to the Medicare fee schedule multiplied by 1.5, the average number of CT/MRI completed prior to HCC diagnosis according to Parikh 2020.*

*c The average cost of a CT or MRI according to the Medicare fee schedule multiplied by 2.5, the average number of CT/MRI completed for false positive US for HCC screening according to Parikh 2020.*

*d**The reference for this data provides the cost for treating intermediate stage HCC by liver transplantation status. Thus, we obtained a weighed average of the cost with and without liver transplant, assuming the liver transplant for intermediate stage HCC reported in the SEER-Medicare database of 2.8%.*

**Table X: Model input parameters for subgroup analysis of male patients**

*For the referenced literatures below, the percent change in annual transition probability between the overall cohort (scaled to fit age distribution of our base case cohort) and the older subgroup was calculated and applied to the base case value of our model.*

*The age-adjusted probability of death was also adjusted from the Actuarial Life Table to include only male patients.*

|  |  |  |
| --- | --- | --- |
| **Variable** | **Base-Case Value and Range** | **Reference** |
| Proportion with undiagnosed cirrhosis | 33.3% (25.0%-41.6%)a | [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/) |
| **Annual transition probabilities** |  |  |
| Non-cirrhotic MASLD to cirrhosis (censored) | 0.65% (0.15 %-1.86%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to HCC | 0.056% (0.0043%-0.14%) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |
| (Undiagnosed) cirrhosis with MASLD to HCC | 4.22% (1.65%-10.07 %) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |

*a Range is +/-25% of the base case value.*

**Table X: Model input parameters for subgroup analysis of older patients (around 60-65 and above).**

*For the referenced literatures below, the percent change in annual transition probability between the overall cohort (scaled to fit age distribution of our base case cohort) and the older subgroup was calculated and applied to the base case value of our model. In all studies referenced below, the age cutoff of the cohort was 60 or 65.*

*The age-adjusted probability of death was also adjusted from the Actuarial Life Table to include only patients above the age of 60.*

|  |  |  |
| --- | --- | --- |
| **Variable** | **Base-Case Value and Range** | **Reference** |
| Proportion with undiagnosed cirrhosis | 40.3% (30.2%-50.4%)a | [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/) |
| **Annual transition probabilities** |  |  |
| Non-cirrhotic MASLD to cirrhosis (censored) | 0.485% (0.109%-1.39%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to HCC | 0.15% (0.011%-0.38%) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |
| (Undiagnosed) cirrhosis with MASLD to HCC | 3.17% (1.24%-7.56 %) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |

*a Range is +/-25% of the base case value.*

**Supplementary**

**Calculation of age-dependent rate of death from MASLD (no cirrhosis or HCC)**

The total death rate is the sum of the probability of liver-related death from MASLD (weighed, takes into account undiagnosed cirrhosis) and the probability of death due to older age. We assume that at age 18, there is no additional cause for death due to age, so at age 18, prob of death is just the liver-related prob of death from MASLD. With every increase in age from 18, we add the incremental increase in death probability due to age, from the actuarial life table provided by the Social Security (2021 period life table for the Social Security area population, as used in the 2024 Trustees Report (TR): https://www.ssa.gov/oact/STATS/table4c6.html).

In the base-case and subgroup analysis for older patients, the death probabilities for male and female were averaged. For the subgroup analysis of male patients, only the male death probabilities were used.

For the subgroup analysis of older patients, the starting cohort was set to be 61-100+ years of age, keeping the distribution or age groups within this subgroup as outlined in the table below.

|  |  |  |
| --- | --- | --- |
| **Age at MASLD diagnosis** | **N(%)** | **Reference** |
| 18-30 | 51377 (5.97%) | Truven Health Analytics MarketScan Databases |
| 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%) |

**Deriving the transition probability from treated HCC to death by HCC stage**

Proportion of patients receiving each type of treatment as the first or primary treatment by HCC stage. Data was derived from the SEER-Medicare database, using ICD 9/10-CM codes to identify a cohort of HCC patients with non-cirrhotic MASLD.

The individual probabilities of death for each treatment type (Table B) were weighed by the distribution of patients receiving each type of treatment (Table A) to get a weighed probability of death for each HCC stage. The weighed death probabilities for each HCC stage were further weighed by the HCC stage distribution in the control and intervention arms to obtain a single overall death probability for patients who were treated for HCC across all stages.

Table A.

|  |  |  |  |
| --- | --- | --- | --- |
| **First Treatment Type** | **Early** | **Intermediate** | **Late** |
| Ablation | 8.5% | 6.6% | 0.7% |
| Radiotherapy | 0.9% | 0% | 3.6% |
| Resection | 34.0% | 20% | 0% |
| Systemic | 23.6% | 37.8% | 67.1% |
| TACE | 30.7% | 32.8% | 28.6% |
| Transplant | 2.3% | 2.8% | 0% |

Table B.

|  |  |  |
| --- | --- | --- |
| **First Treatment Type** | **Annual probability of death** | **Reference** |
| Early stage HCC |  |  |
| Transplant | 8.25% | [American cancer society data](https://www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/survival-rates.html) |
| Resection | 11.1% | [Thornton 2022](https://pubmed.ncbi.nlm.nih.gov/35234371/) |
| TACE | 6.7% | [Kim 2017](https://pubmed.ncbi.nlm.nih.gov/28263954/) |
| Ablation | 15.5% | [Zhang 2021](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2784529) |
| Systemic chemotherapy | 61.9% | Derived from SEER-Medicare database |
| Radiotherapy | 11.0% | [Hara 2019](https://pubmed.ncbi.nlm.nih.gov/30805950/) |
| Intermediate stage HCC |  |  |
| Transplant | 12% | [Kamo 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC5985555/) |
| Resection | 8% | [Zhong 2015](https://www.nature.com/articles/nrclinonc.2014.122-c3) |
| TACE | 30% | [Prince 2020](https://pubmed.ncbi.nlm.nih.gov/33224278/) |
| Ablation | 7% | [Tanaka 2023](https://www.nature.com/articles/s41598-023-43516-w) |
| Systemic chemotherapy | 69.6% | Derived from SEER-Medicare database |
| Radiotherapy | 20.6% | [Prince 2020](https://pubmed.ncbi.nlm.nih.gov/33224278/) |
| Late stage HCC |  |  |
| TACE | 66.7% | [Kong 2018](https://pubmed.ncbi.nlm.nih.gov/30113483/) |
| Ablation | 26.9% | [Dai 2014](https://pubmed.ncbi.nlm.nih.gov/25284590/) |
| Systemic chemotherapy | 86.2% | Derived from SEER-Medicare database |
| Radiotherapy | 68.7% | [Lin 2019](https://pubmed.ncbi.nlm.nih.gov/30656831/) |