**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% (19%-50.0%) | 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/)  d. [Guss 2018](https://pubmed.ncbi.nlm.nih.gov/30344803/) a |
| Screening adherence rate | 60% (10-100%) | [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% (0.124%-1.09%) | 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 | 0.051% (0.008%-0.529%) | 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) |
| (Undiagnosed) cirrhosis with MASLD to HCCb | 2.45% (1.06%-4.62%) | 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 | 0.450% (0.03%-1.18%) | 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 | 0.5% (0.3%-0.7%) | 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% (37.1%-57.1%)c | Derived from SEER-Medicare database |
| Treated early stage HCC to death | ()c | Derived by weighed survival across various treatment types, see Supplemental Methods |
| Untreated early-stage HCC to death | 35.7% (25.7%-45.7%)c | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Intermediate stage HCC to treatment | 47.9% (37.9%-57.9%)c | Derived from SEER-Medicare database |
| Treated intermediate stage HCC to death | ()c | Derived by weighed survival across various treatment types, see Supplemental Methods |
| Untreated intermediate stage HCC to death | 63.2% (53.2%-73.2%)c | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| Late stage HCC to treatment | 37.6% (27.6%-47.6%)c | Derived from SEER-Medicare database |
| Treated late stage HCC to death | ()c | Derived by weighed survival across various treatment types, see Supplemental Methods |
| Untreated late stage HCC to death | 87.2% (77.2%-97.2%)c | [Khalaf 2017](https://pubmed.ncbi.nlm.nih.gov/27521507/) |
| **HCC Stage Upon Diagnosis** |  | [Daher 2024](https://pubmed.ncbi.nlm.nih.gov/38683607/) |
| Control |  |  |
| Early | 45.7% (35%-55%)**d** |  |
| Intermediate | 23.0% |  |
| Late | 31.3% (45%-65%)**d** |  |
| Intervention |  |  |
| Early | 70.7% (60%-80%)**d** |  |
| Intermediate | 15.6% |  |
| Late | 13.7% (20%-40%)**d** |  |

a *Data from reference d (Guss 2018) was included in the range but not included in calculating the average due to its unusually higher value and small sample size.*

*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 chosen from reasonable assumption.*

*d Range was chosen from reasonable assumption for the percent diagnosed with early stage HCC. Accordingly, the range for late stage HCC was set as the minimum and maximum percent possible for the total percent to be between 0 and 100%. The range for the intermediate stage will be adjusted accordingly to fit within 0-100% total.*

**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) | Derived from [Sayiner 2016](https://pmc.ncbi.nlm.nih.gov/articles/PMC5013331/)  [Kowada 2024](https://bmjopen.bmj.com/content/14/11/e080549.abstract) |
| False positive HCC | Same as the weighed HCC utility derived from utilities by HCC stage as 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 | 0.53 (0.4-0.65) | a. [Singal 2024](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S11)  b. [Bremner 2007](https://pmc.ncbi.nlm.nih.gov/articles/PMC2657973/) |

**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 | $358 ($258-458) | [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 chosen from reasonable assumption* |
| CT/MRI to confirm HCC diagnosis | $670 ($470-$870) | [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 chosen from reasonable assumption*  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Repeat CT/MRI for false positive HCC | $1116 ($916-$1316) | [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 chosen from reasonable assumption*  [Parikh 2020](https://pmc.ncbi.nlm.nih.gov/articles/PMC7541544/#S6) |
| Medical care of patients with MASLD (non-cirrhotic or with undiagnosed cirrhosis) | $4362 ($2362-$6362) | [Younossi 2023](https://pubmed.ncbi.nlm.nih.gov/37250870/) |
| Early stage HCC (annual) | $62,340 ($49872 - $74808) | [Karim 2023](https://www.sciencedirect.com/science/article/pii/S1542356522010953#sec3) |
| Intermediate stage HCC (annual) | $115442 ($92354 - $138530) | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |
| Late stage HCC (annual) | $104189 ($83351 - $125027) | [Tapper 2016](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/cncr.29855) |

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

*For the annual transition probabilities, the incremental change between that of the male subgroup and the overall cohort in each referenced literature was added to the base case value (the incremental change was averaged across multiple studies if multiple references are listed).*

|  |  |  |
| --- | --- | --- |
| **Variable** | **Base-Case Value and Range** | **Reference** |
| Proportion with undiagnosed cirrhosis | 33.3% (15%-55%) | [Fujimoto 2008](https://pubmed.ncbi.nlm.nih.gov/18822004/)  *Range chosen from reasonable assumption* |
| **Annual transition probabilities** |  |  |
| Non-cirrhotic MASLD to cirrhosis (censored) | 0.537%(0.133-1.099) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to HCC | 0.053%(0.0097-0.58) | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20)  b. [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| (Undiagnosed) cirrhosis with MASLD to HCC | 2.49% (1.102-4.66) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |

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

*For the annual transition probabilities, the incremental change between that of the older subgroup and the overall cohort in each referenced literature was added to the base case value (the incremental change was averaged across multiple studies if multiple references are listed). In all studies referenced below, the age cutoff of the cohort was 60 or 65.*

|  |  |  |
| --- | --- | --- |
| **Variable** | **Base-Case Value and Range** | **Reference** |
| Proportion with undiagnosed cirrhosis | 40.3% (20%-60%) | [Walker 2016](https://pubmed.ncbi.nlm.nih.gov/26784271/)  *Range chosen from reasonable assumption* |
| **Annual transition probabilities** |  |  |
| Non-cirrhotic MASLD to cirrhosis (censored) | 0.501% (0.097%-1.063%) | [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| Non-cirrhotic MASLD to HCC | 0.060% (0.0167%-0.538%) | a. [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20)  b. [Yeoh 2024](https://journals.lww.com/jcge/fulltext/2024/08000/incidence_of_cirrhosis_and_hepatocellular.13.aspx) |
| (Undiagnosed) cirrhosis with MASLD to HCC | 2.73% (1.34% -4.90%) | [Kanwal 2018](https://pmc.ncbi.nlm.nih.gov/articles/PMC6279617/#S20) |

**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, looking only at HCC patients with MASLD.

|  |  |  |  |
| --- | --- | --- | --- |
| **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% |

The annual probability of deaths (below) were weighed by the distribution of patients receiving each type of treatment to get an aggregate overall probability of death for each HCC stage.

|  |  |  |
| --- | --- | --- |
| **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/) |