***Appendix. Parameter Values, Treatment Cost Calculations, and Distributions***

Table A.1 details the input values used in the model and respective sources. Table A.2 shows ranges used in one-way sensitivity analysis and distributions used in probabilistic sensitivity analysis.

Table A.1. Parameters Used in the Model of Increasing Use of Anti-TNF Therapy for Crohn’s Disease

| Parameter Description | Value | Source |
| --- | --- | --- |
| **Population Parameters** | | |
| U.S. adults 18 and older | 253,227,594 | U.S. Census, n.d. [4] |
| Crohn’s disease prevalence | 201 per 100,000 | Kappelman et al., 2007 [1] |
| Crohn’s disease incidence | 8.9 per 100,000 | Average calculated from Loftus et al., 2004 [5] |
| Crohn’s patients with moderate-to-severe disease | 60% | Subject matter expert opinion [6] |
| Crohn’s patients aged 65+ | 35% | Lewis et al., 2018; used as estimate of proportion of patients with Medicare as primary payer [2] |
| Patients using CS | 85% | Subject matter expert opinion, consistent with Lewis et al. (2018) [2,6] |
| Patients using anti-TNF therapy | 15% | Subject matter expert opinion, consistent with Lewis et al. (2018) [2,6] |
| **Healthcare** | | |
| ***Payer Costs (2018$)*** | | |
| CS treatment | $408 | Authors’ calculations based on GoodRx (2019) and subject matter expert input [6] |
| Anti-TNF treatment | $27,160 | Institute for Clinical and Economic Review, 2017 [12] |
| Death | $26,060 | Hospital spending for last year of life from French et al., 2017 [11] |
| Hip fracture | $20,390 | Authors’ calculations using Shi, Foley, Lenhart, & Badamgarav, 2009 [13] |
| MACE | $36,980 | Authors’ calculations using O’Sullivan et al., 2011 [14] |
| IBD-related hospitalization | $12,060 | Centers for Disease Control and Prevention, 2019 [17] |
| Office visit | $410 | Authors’ Analysis of MEPS 2010–2015 data [16] |
| Adult patients <65 with Medicaid as primary payer | 12.5% | Medicaid and CHIP Access and Payment Commission, 2018 [18] |
| ***Patient Out-of-Pocket Costs (2018$)*** | | |
| CS treatment | $22 | Authors’ analysis of MEPS 2006–2015 data [16] |
| Anti-TNF treatment | $111 | Authors’ calculations, assuming $25 copay per infliximab infusion visit |
| Hip fracture | $1,192 | Authors’ calculations using Song et al., 2011 [19] |
| MACE event | $343 | Authors’ analysis of MEPS 2010–2015 data [16] |
| Travel | $71 | Authors’ calculations using Park et al., 2014, estimate of 68% of Crohn’s anti-TNF users receiving infliximab, assumes $16 travel cost per infliximab infusion visit (Schmier et al., 2017) [24] |
| IBD-related hospitalization | $249 | Authors’ analysis of MEPS 2010–2015 data [16] |
| Office visit | $46 | Authors’ analysis of MEPS 2010-2015 data [16] |
| ***Utilization*** | | |
| Number of annual visits, CS users | 4 | Subject matter expert opinion [6] |
| Number of annual visits, anti-TNF users | 2 | Subject matter expert opinion [6] |
| **Probabilities and Fractions** | | |
| Stopping treatment, CS | 0.48 | Assumed for modeling purposes |
| Stopping treatment, anti-TNF | 0.48 | Subject matter expert opinion [6] |
| Death, CS | 0.0301 | Lewis et al., 2018 [2] |
| Death, anti-TNF | 0.0214 | Lewis et al., 2018 [2] |
| Death, hip fracture | 0.075 | Alzahrani, Gandhi, Davis, & Mahomed, 2010 [7] |
| Death, MACE | 0.090 | Benjamin et al., 2017 [8] |
| Death, IBD-related hospitalization | 0.009 | Sewell & Yee, 2012 [9] |
| Hip fracture, CS | 0.0065 | Lewis et al., 2018 [2] |
| Hip fracture, anti-TNF | 0.0032 | Lewis et al., 2018 [2] |
| MACE, CS | 0.0225 | Lewis et al., 2018 [2] |
| MACE, anti-TNF | 0.0134 | Lewis et al., 2018 [2] |
| IBD-related hospitalization, CS | 0.0210 | Lewis et al., 2018 [2] |
| IBD-related hospitalization, anti-TNF | 0.0213 | Lewis et al., 2018 [2] |
| **Time** | | |
| Days lost to hip fracture | 12.4 | Bonafede, Espindle, & Bower, 2012 [20] |
| Days lost of MACE | 17.3 | Sasser et al., 2005 [30] |
| Days lost to IBD-related hospitalization | 8.7 | Cohen et al., 2000 [21] |
| Hours spent in treatment, CS | 2.0 | Subject matter expert opinion [6] |
| Hours spent in treatment, anti-TNF | 13.2 | Authors’ calculations of Daniel et al., 2018; Yokomizo et al., 2016; Park et al., 2014; and subject matter expert opinion [6] |
| **Productivity Losses** | | |
| Value of patient time, median hourly wage | $29.95 | BLS DOL, 2018a [25] |
| Proportion of patient healthcare time with a family member providing unpaid caregiving | 0.38 | Wolff & Roter, 2011 [33] |
| Value of unpaid caregiving time, median hourly wage of nurse or home health aide | $16.90 | BLS DOL, 2018b [28] |
| Civilian labor force participation rate, December 2018 | 0.63 | BLS DOL, 2018c [29] |

Note: Negative risk difference means CS is associated with lower risk than anti-TNF.

We calculated average annual payer costs for infliximab as follows:

Number of infusions per year × [(average adult weight [kg] × dose [mg/kg/infusion] × average cost per mg + facility fees [$/infusion]].

The average adult weight was assumed to be 70 kg, and the average cost of infliximab per 100 mg was $844 [12]. Administration costs paid by the payer were approximately $1,500 per year [34]. We allowed this cost to have an upper bound of $28,300 in one-way sensitivity analyses [23,34]. We calculated annual adalimumab costs assuming an average per-dose payer cost of $1,581 [12]. We assumed that a patient would self-administer one dose of adalimumab every two weeks, resulting in a total annual payer cost of $41,100 per patient. We weighted annual infliximab and adalimumab costs to obtain an estimated payer cost for anti-TNF of $27,160 per patient per year, although the true costs for anti-TNF therapy may be lower if some payers have negotiated lower prices with manufacturers. The estimated out-of-pocket cost to patients was $110 per year, with an upper bound of $263 used in one-way sensitivity analyses.

For CS users, we assumed that prednisone was prescribed 75% of the time, an assumption guided by a clinical expert’s input. We assumed an annual cost to payers of $10 per patient for prednisone; budesonide was assumed for the remaining CS users, with an annual estimated cost to payers of $1,600 per patient (see table A.1 for details). The upper limit assumes payer costs for budesonide as high as $3,000 per year, consistent with the upper end of the GoodRX price range [15]. Sensitivity analysis used an upper limit of $510 for CS out-of-pocket spending.

Authors’ calculations for the healthcare costs of death inflated the hospital costs in the last calendar year of life for the United States, as reported in a supplement ($24,513 in 2014 dollars; [11]), to 2018 dollars using the Personal Consumption Expenditures for Health (PCE-H) index (<https://fred.stlouisfed.org/series/DHLTRG3A086NBEA>). To calculate the average costs of a hip fracture, we generated a weighted average using costs for people 50 to 64 years and costs for those 65 years and older [13]. For cardiovascular event costs, we calculated a weighted average of costs of myocardial infarction (fatal and nonfatal), ischemic stroke (fatal and nonfatal), hemorrhagic stroke (fatal and nonfatal), percutaneous transluminal coronary angioplasty, and coronary artery bypass graft (CABG) [14]. We used the 2014 estimated cost of IBD hospitalization [19] and inflated all costs to 2018 dollars using the PCE-H.

Ranges used for one-way sensitivity analysis and distributions used for probabilistic sensitivity analysis appear in table A-2.

Table A.2. Distributions Used for Probabilistic Sensitivity Analysis of Impact of Expanding Anti-TNF Therapy for Crohn’s Disease

| **Study Population Parameters** | **Default** | **< Range >** | | **SE** | **Alpha** | | **Beta** | **Distribution** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Incidence and Prevalence of Moderate-to-severe Crohn’s Disease** | | | | | | | | |
| Prevalence | 0.002010 | 0.001500 | 0.013000 | 0.000205 | 96 | 47588 | | Beta |
| Incidence | 0.000089 | 0.000071 | 0.000106 | 0.000009 | 96 | 1085005 | | Beta |
| Proportion of patients with moderate-to-severe disease | 0.600 | 0.480000 | 0.720000 | 0.061 | 38 | 25 | | Beta |
| **Current Treatment Practice** | | | | | | | | |
| Patients using CS to treat Crohn's | Equals 1 – proportion using anti-TNF; not varied in PSA | | | | | | | |
| Patients using anti-TNF therapy to treat Crohn's | 0.150 | 0.120 | 0.180 | 0.015 | 81 | 462 | | Beta |
| **Treatment-Related Parameters** | | | | | | | | |
| Stop anti-TNF treatment each year | 0.480 | 0.384 | 0.576 | 0.049 | 49 | 54 | | Beta |
| Stop CS treatment each year | Equals P (stopping anti-TNF); not varied in PSA | | | | | | | |
| **Lewis et al., 2018** | | | | | | | | |
| ***CS Treatment for Crohn's Disease*** | | | | | | | | |
| Death | 0.0301 | 0.024 | 0.036 | 0.003 | 93 | 3001 | | Beta |
| Hip fracture | 0.0065 | 0.005 | 0.008 | 0.001 | 95 | 14583 | | Beta |
| MACE | 0.0225 | 0.018 | 0.027 | 0.002 | 94 | 4078 | | Beta |
| IBD-related hospitalization | 0.0210 | 0.017 | 0.025 | 0.002 | 94 | 4382 | | Beta |
| ***Anti-TNF Treatment for Crohn's Disease*** | | | | | | | | |
| Death | 0.0214 | 0.017 | 0.026 | 0.002 | 94 | 4297 | | Beta |
| Hip fracture | 0.0032 | 0.003 | 0.004 | 0.000 | 96 | 29820 | | Beta |
| MACE | 0.0134 | 0.011 | 0.016 | 0.001 | 95 | 6975 | | Beta |
| IBD-related hospitalization | 0.0213 | 0.017 | 0.026 | 0.002 | 94 | 4318 | | Beta |
| **Direct Medical Costs** | | | | | | | | |
| ***Medical Treatment Costs*** | | | | | | | | |
| CS treatment cost, per patient per year | $408 | $326 | $1,000 | $42 | 96 | 4 | | Gamma |
| Anti-TNF treatment cost, per patient per year | $27,161 | $16,000 | $32,500 | $2,772 | 96 | 283 | | Gamma |
| ***Health-Outcomes-Related Costs, Payer Spending*** | | | | | | | | |
| Death, per event | $26,055 | $20,844 | $31,266 | $2,659 | 96 | 271 | | Gamma |
| Hip fracture, per event | $20,390 | $16,312 | $24,468 | $2,081 | 96 | 212 | | Gamma |
| MACE, per event | $36,981 | $29,584 | $44,377 | $3,774 | 96 | 385 | | Gamma |
| IBD-related hospitalization, per event | $12,059 | $9,647 | $14,470 | $1,230 | 96 | 126 | | Gamma |
| Office visit | $410 | $328 | $493 | $42 | 96 | 4 | | Gamma |
| ***Payer Assumptions*** | | | | | | | | |
| Proportion of patients with Medicare as primary payer | 0.35 | | | | Not varied in PSA | | | |
| Proportion of patients with Medicaid as primary payer | 0.08 | | | | Not varied in PSA | | | |
| ***Proportion of Health Outcomes Resulting in Death*** | | | | | | | | |
| Hip fracture, proportion dying within 30 days | 0.075 | 0.060 | 0.090 | 0.008 | 89 | 1095 | | Beta |
| MACE, proportion resulting in death | 0.090 | 0.072 | 0.108 | 0.009 | 87 | 886 | | Beta |
| IBD-related hospitalization, proportion resulting in death | 0.009 | 0.007 | 0.011 | 0.001 | 95 | 10479 | | Beta |
| ***Health-Outcomes-Related Costs, Out-of-Pocket Spending*** | | | | | | | | |
| Death, per event | $0 | $0.01 | $0.01 | $0.00 | 96 | 0 | | Gamma |
| Hip fracture, per event | $1,192 | $954 | $1,431 | $122 | 96 | 12 | | Gamma |
| MACE, per event | $343 | $274 | $412 | $35 | 96 | 4 | | Gamma |
| IBD-related hospitalization, per event | $249 | $200 | $299 | $25 | 96 | 3 | | Gamma |
| Office visit | $46 | $37 | $55 | $5 | 96 | 0 | | Gamma |
| ***Treatment Out-of-Pocket Costs*** | | | | | | | | |
| CS treatment, per patient per year | $22 | $18 | $510 | $2 | 96.0 | 0.2 | | Gamma |
| Anti-TNF treatment, per patient per year | $111 | $89 | $263 | $11 | 96.0 | 1.2 | | Gamma |
| CS visits, per patient per year | 4 | 3.00 | 6.00 | 0.408163 | - | - | | Normal |
| Anti-TNF visits, per patient per year | 2 | 1.00 | 4.00 | 0.204082 | - | - | | Normal |
| Travel per office visit | $15.67 | $12.54 | $18.80 | $1.60 | 96.0 | 0.2 | | Gamma |
| **Indirect Costs** | | | | | | | | |
| ***Time Lost to Adverse Events (Days)*** | | | | | | | | |
| Hip fracture, per event | 12.4 | 9.92 | 14.88 | 1.265 | - | - | | Normal |
| MACE, per event | 17.3 | 13.84 | 20.76 | 1.765 | - | - | | Normal |
| IBD-related hospitalization, per event | 8.7 | 6.96 | 10.44 | 0.888 | - | - | | Normal |
| ***Lost Patient Time (Hours)*** | | | | | | | | |
| Patient hours spent in treatment/monitoring per year, CS | 2.00 | 1.00 | 4.00 | 0.204082 | - | - | | Normal |
| Patient hours spent in treatment/monitoring per year, anti-TNF | 13.2 | 10.00 | 16.00 | 1.346890 | - | - | | Normal |
| ***Value of Lost Time*** | | | | | | | | |
| Hourly wage rate plus fringe | $29.95 | $23.96 | $35.94 | 3.056 | 96.0 | 0.3 | | Gamma |
| Caregiver hourly wage rate plus fringe | $16.90 | $13.52 | $20.28 | 1.724 | 96.0 | 0.2 | | Gamma |
| ***Additional Productivity Loss Parameters*** | | | | | | | | |
| Productivity loss multiplier for employer | 1.00 | 0.80 | 1.20 | 0.102 | - | - | | Lognormal |
| Proportion of visits with family accompanying patient | 0.38 | 0.301 | 0.451 | 0.038 | 60 | 99 | | Beta |
| Hours lost per missed day because of illness, recovery | 16.00 | | | | Not varied in PSA | | | |
| Hours missed from work per day | 8.00 | | | | Not varied in PSA | | | |
| Labor force participation rate among adults 16 or older | 0.63 | 0.50 | 0.76 | 0.064 | 35 | 20 | | Beta |