

Manuscript Results

Base case

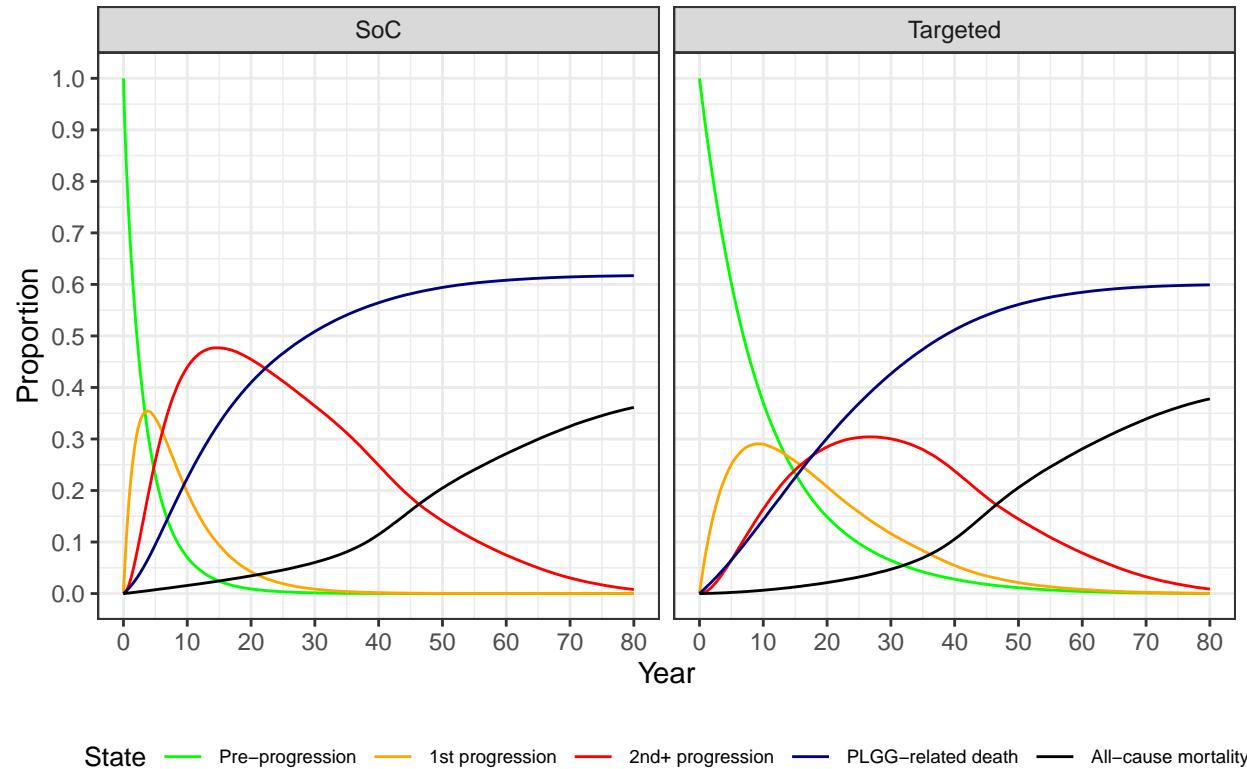
Scenario #1a

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

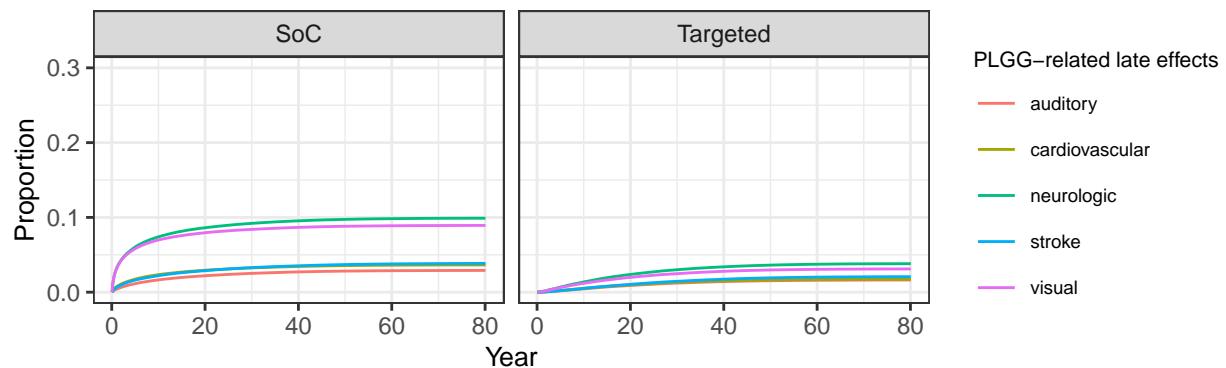
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	15.6 (11.99;19.4)	12.76 (8.92;16.08)	2.84 (0.95;6.51)
Total Cost	\$2,975,092 (\$2,340,408;\$3,588,480)	\$389,911 (\$360,422;\$415,954)	\$2,585,181 (\$1,957,041;\$3,203,631)
Non-Targeted PLGG related costs	\$176,369 (\$114,324;\$227,184)	\$255,203 (\$201,070;\$310,562)	\$-78,834 (\$-117,476;\$-48,429)
Late effect costs	\$78,352 (\$39,526;\$141,805)	\$100,978 (\$40,220;\$177,609)	\$-22,626 (\$-38,060;\$2,780)
General population costs	\$52,085 (\$28,857;\$75,880)	\$33,730 (\$15,256;\$54,700)	\$18,355 (\$9,256;\$36,715)
Targeted costs	\$2,668,286 (\$2,020,708;\$3,291,327)	\$0 (\$0;\$0)	\$2,668,286 (\$2,020,708;\$3,291,327)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

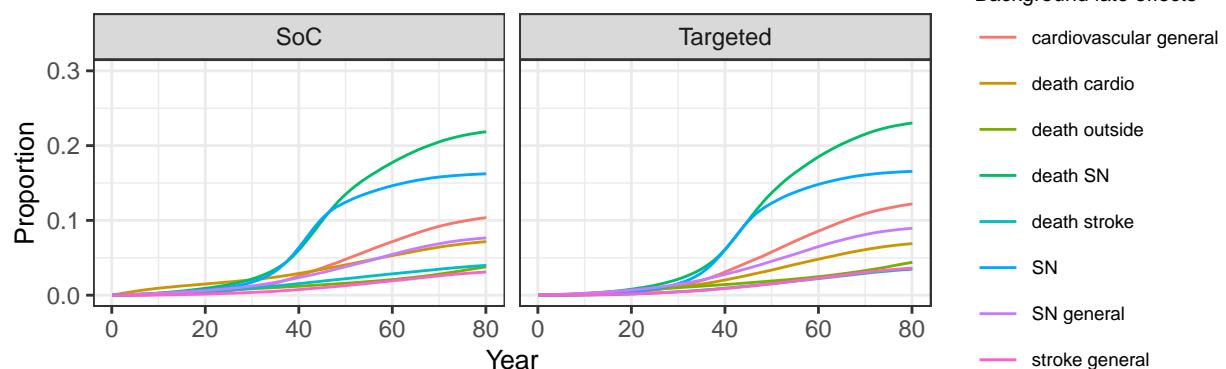
Trace Plot of PLGG States Across Cycles



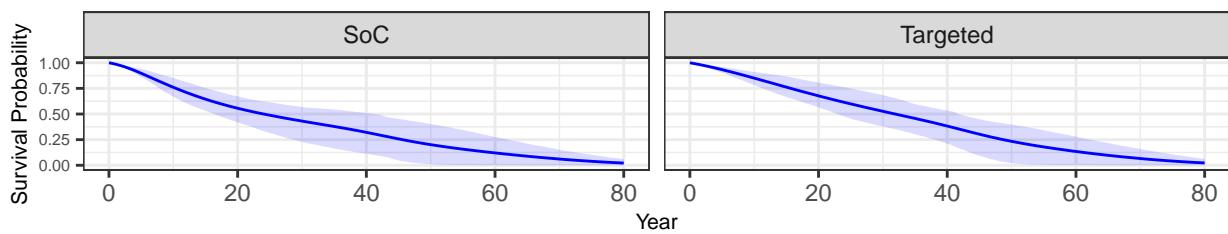
Cumulative Incidence of PLGG-related Late Effects Across Cycles



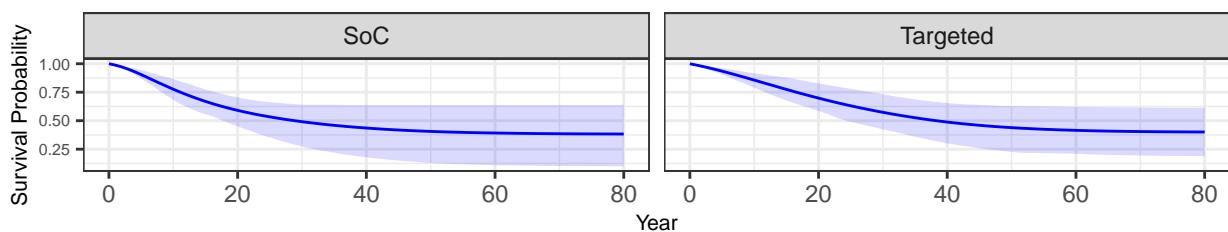
Cumulative Incidence of Background Late Effects Across Cycles



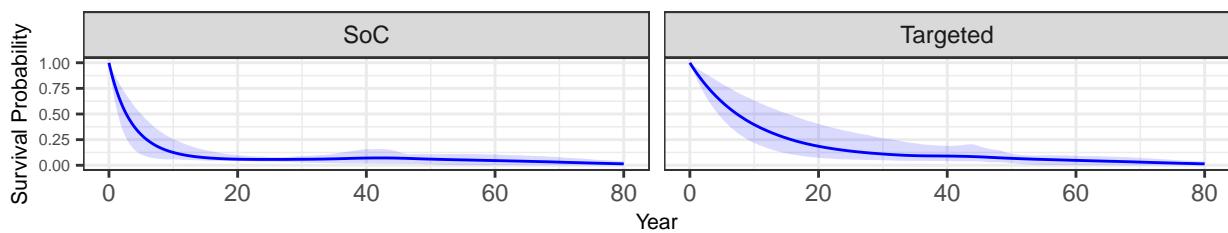
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



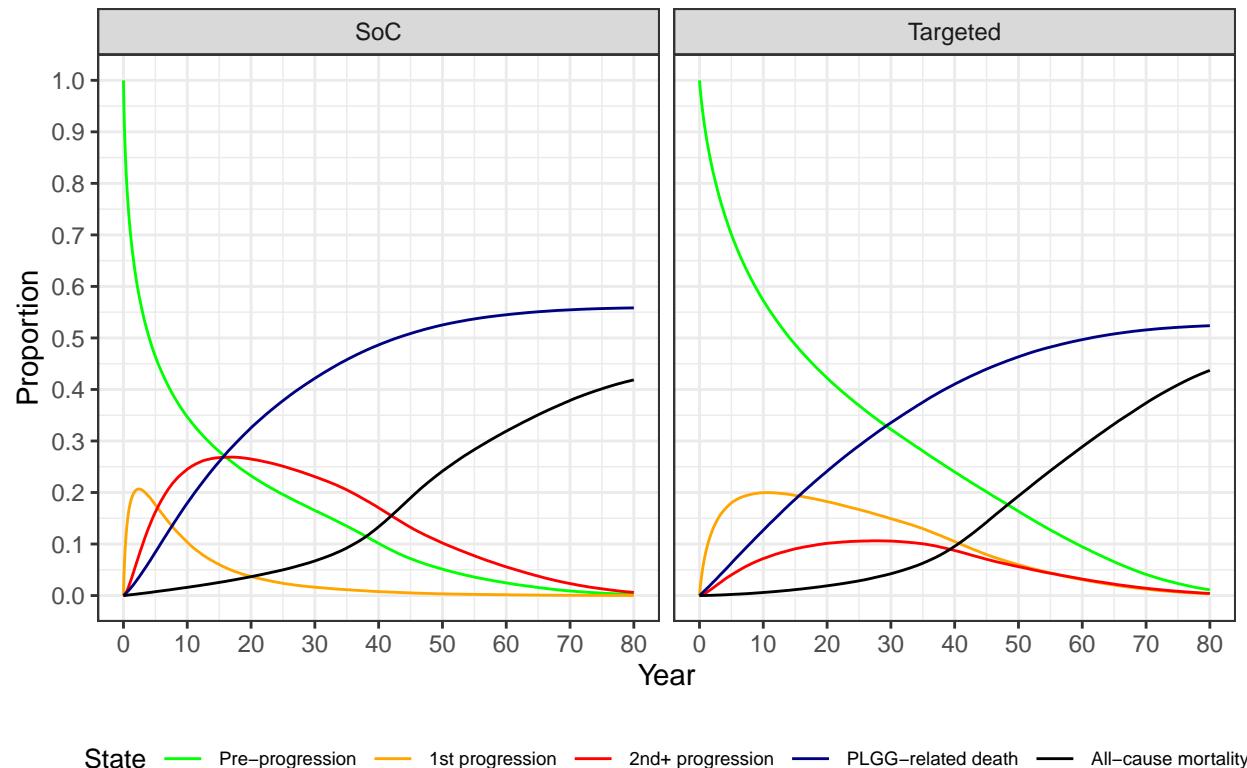
Progression-Free Survival with 95% CI



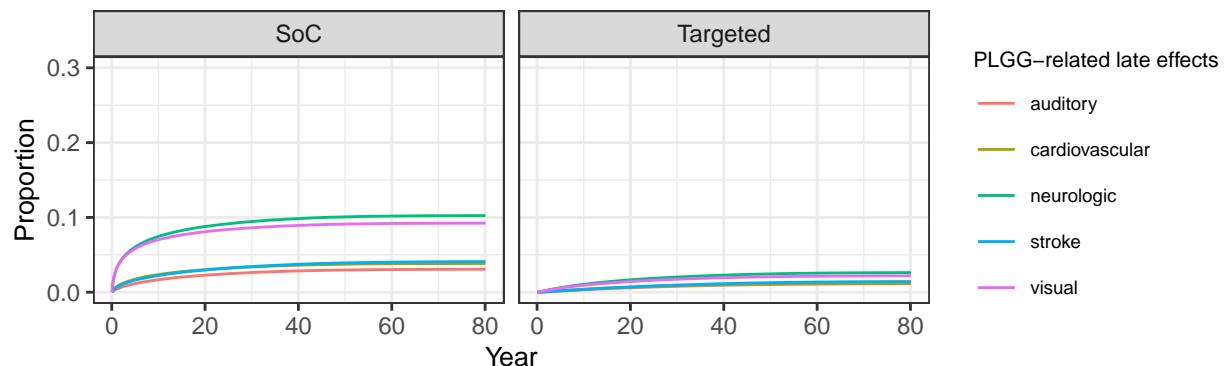
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	18.19 (14.87;21.42)	14.07 (11.27;16.86)	4.11 (1.25;8.3)
Total Cost	\$3,386,662 (\$2,817,571;\$3,939,055)	\$371,619 (\$354,092;\$392,255)	\$3,015,044 (\$2,447,866;\$3,552,931)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$218,112 (\$161,312;\$259,601)	\$-73,193 (\$-130,140;\$-32,368)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$115,226 (\$75,174;\$185,091)	\$-35,176 (\$-63,913;\$-8,058)
General population costs	\$69,909 (\$46,483;\$93,955)	\$38,281 (\$20,916;\$59,355)	\$31,628 (\$14,147;\$56,008)
Targeted costs	\$3,091,785 (\$2,519,167;\$3,651,217)	\$0 (\$0;\$0)	\$3,091,785 (\$2,519,167;\$3,651,217)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

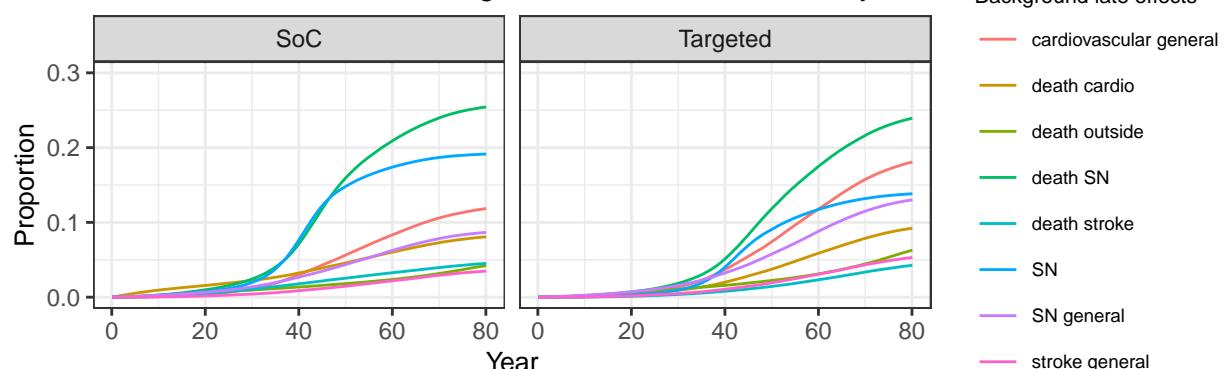
Trace Plot of PLGG States Across Cycles



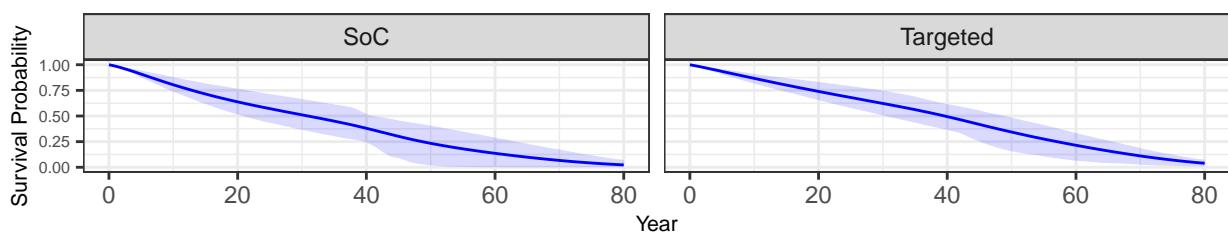
Cumulative Incidence of PLGG-related Late Effects Across Cycles



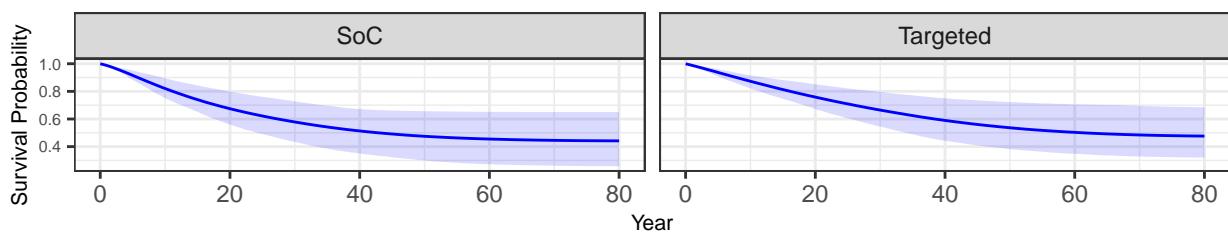
Cumulative Incidence of Background Late Effects Across Cycles



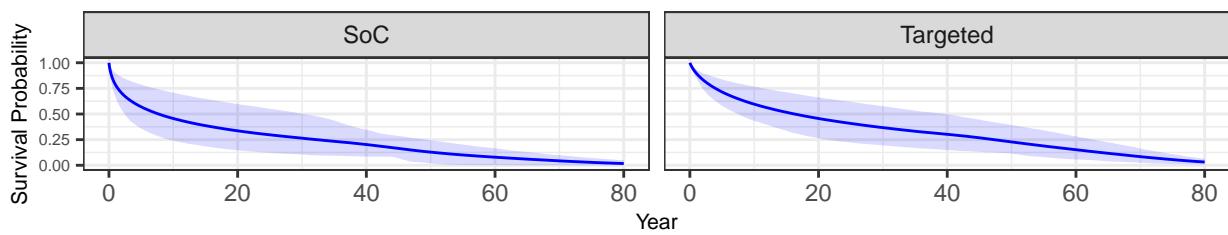
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



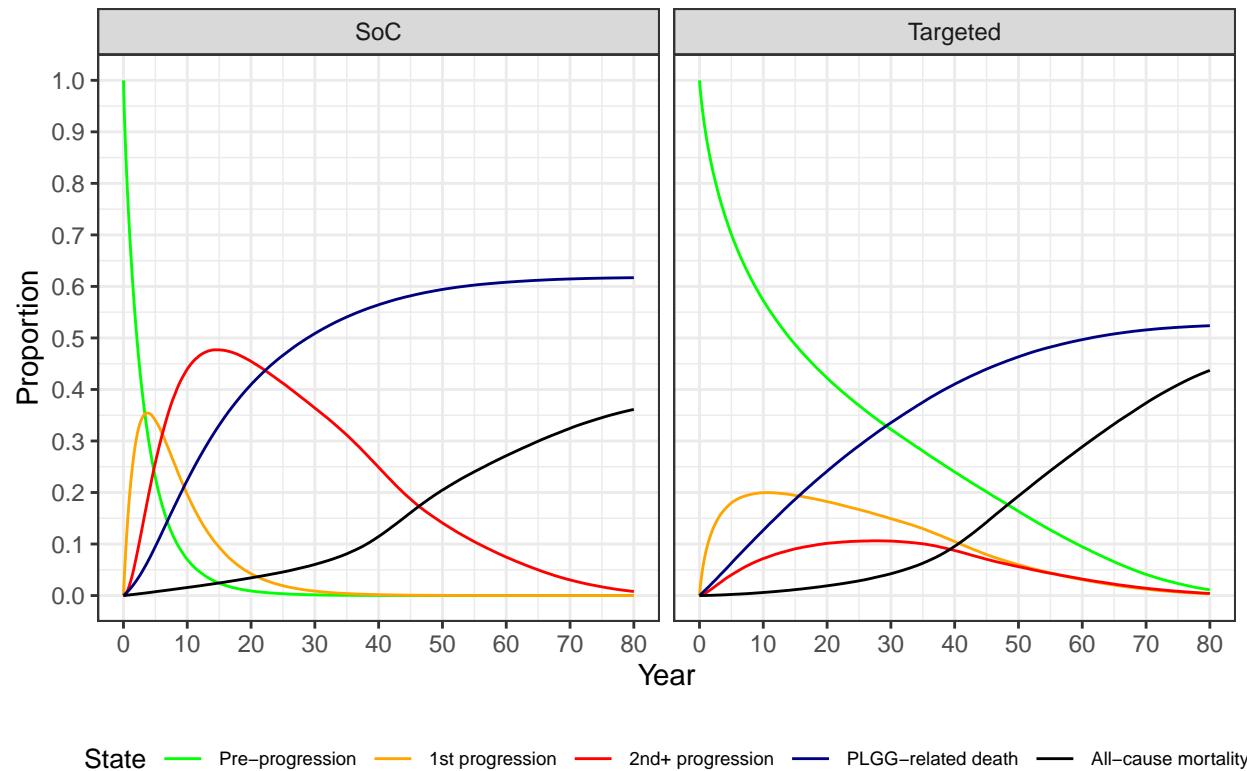
Progression-Free Survival with 95% CI



Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

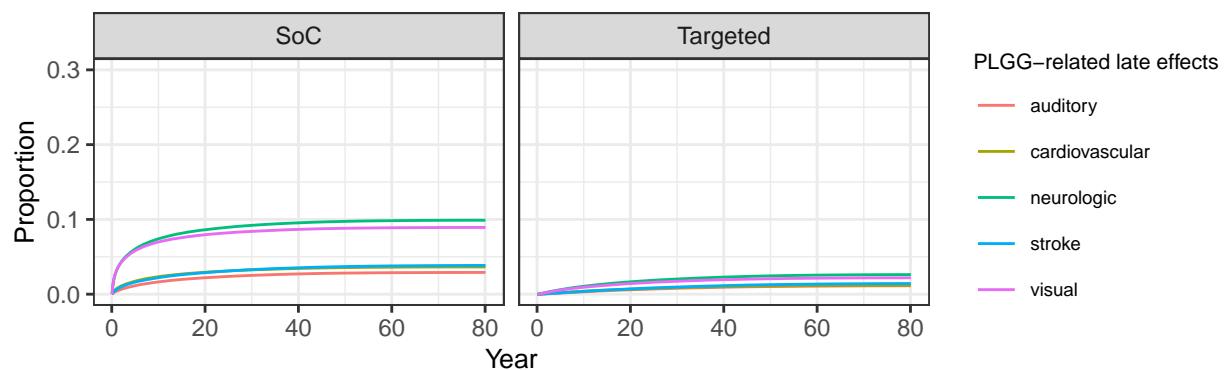
Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	18.19 (14.87;21.42)	12.76 (8.92;16.08)	5.43 (2.05;10.99)
Total Cost	\$3,386,662 (\$2,817,571;\$3,939,055)	\$389,911 (\$360,422;\$415,954)	\$2,996,752 (\$2,433,682;\$3,552,209)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$255,203 (\$201,070;\$310,562)	\$-110,284 (\$-179,940;\$-56,144)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$100,978 (\$40,220;\$177,609)	\$-20,928 (\$-62,263;\$24,303)
General population costs	\$69,909 (\$46,483;\$93,955)	\$33,730 (\$15,256;\$54,700)	\$36,179 (\$19,416;\$62,749)
Targeted costs	\$3,091,785 (\$2,519,167;\$3,651,217)	\$0 (\$0;\$0)	\$3,091,785 (\$2,519,167;\$3,651,217)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

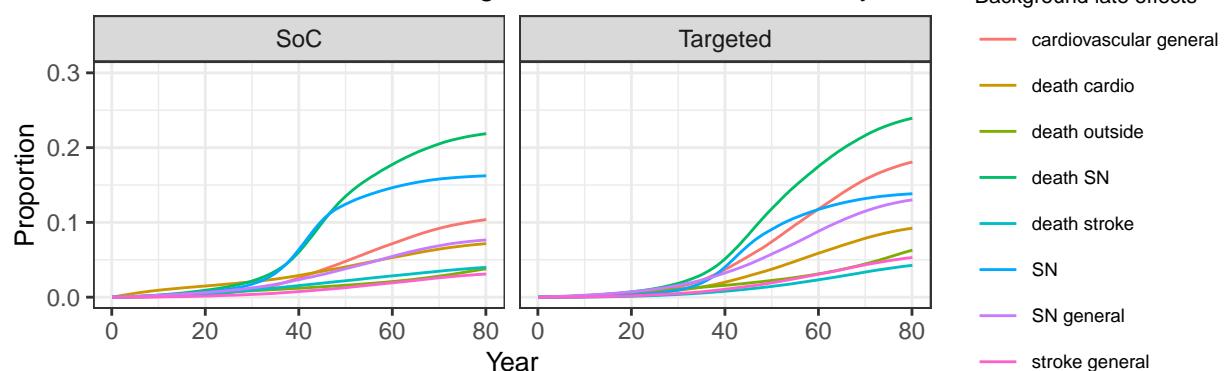


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

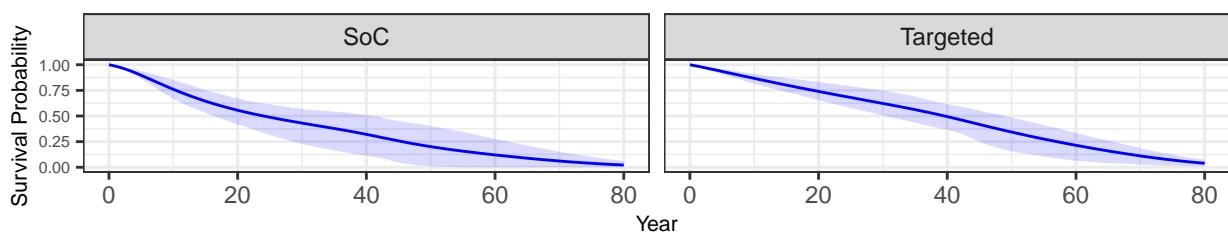
Cumulative Incidence of PLGG-related Late Effects Across Cycles



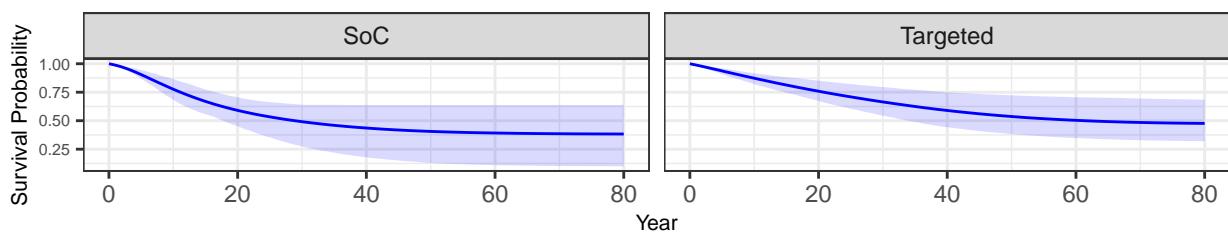
Cumulative Incidence of Background Late Effects Across Cycles



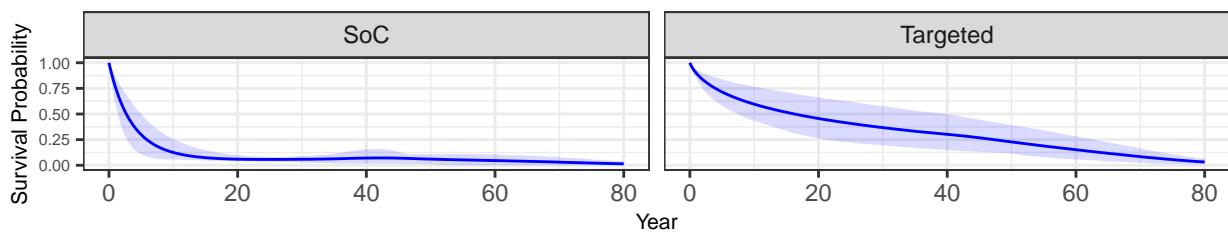
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



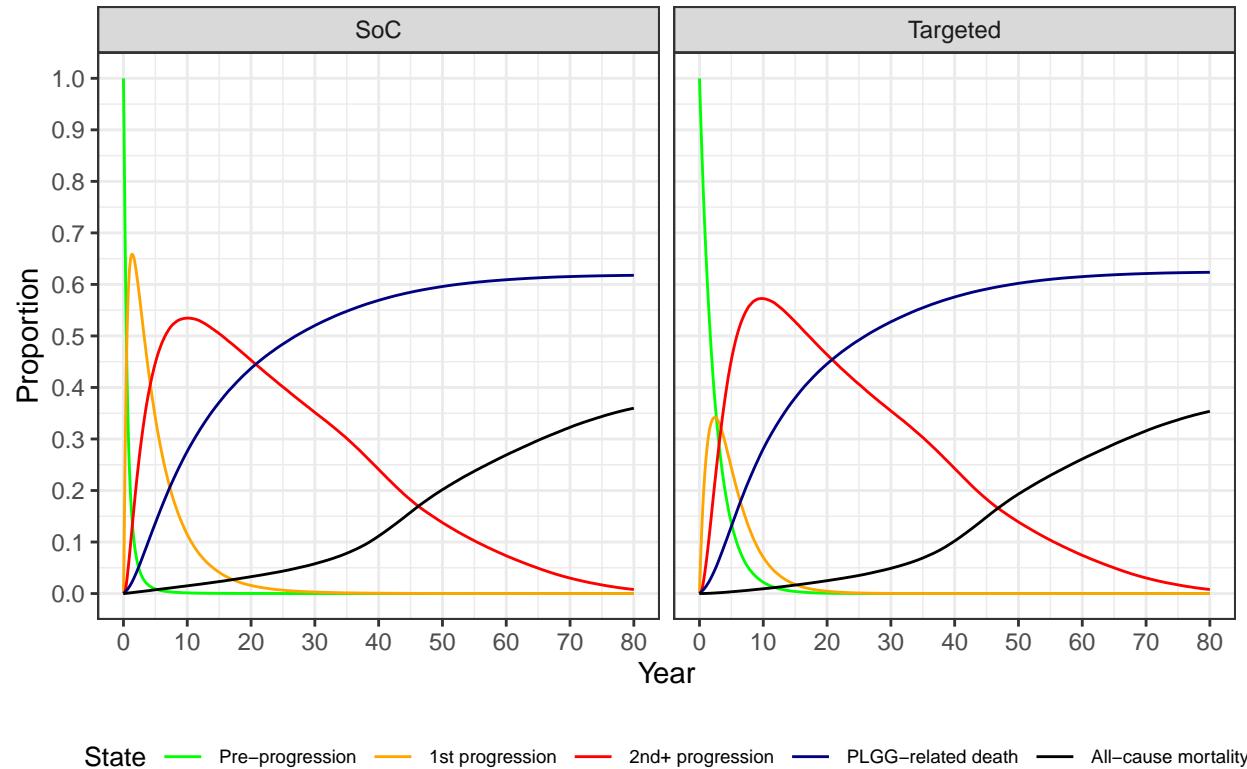
Progression-Free Survival with 95% CI



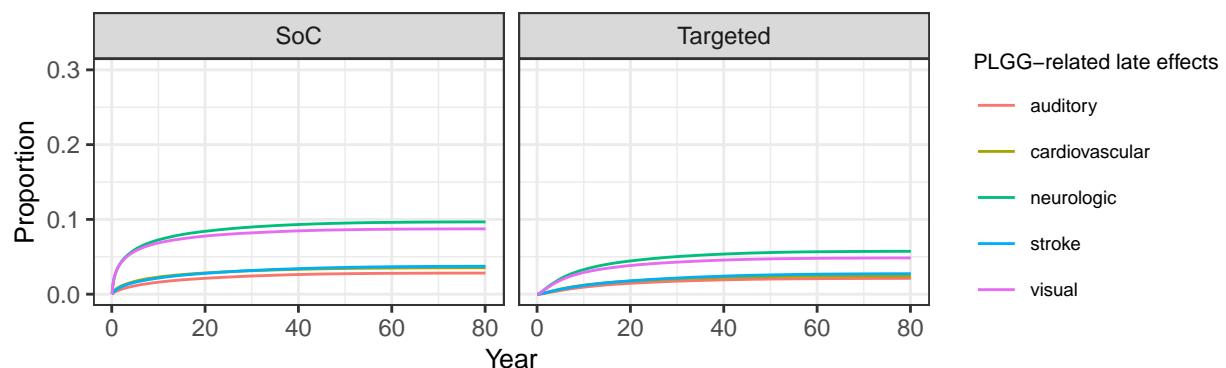
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	12.96 (8.12;17.24)	12.36 (7.65;16.39)	0.6 (-0.21;1.23)
Total Cost	\$2,627,997 (\$1,709,635;\$3,462,310)	\$395,495 (\$365,854;\$423,395)	\$2,232,502 (\$1,346,918;\$3,034,954)
Non-Targeted PLGG related costs	\$231,834 (\$169,279;\$287,311)	\$262,516 (\$200,713;\$317,931)	\$-30,682 (\$-42,976;\$-18,726)
Late effect costs	\$83,369 (\$23,798;\$169,727)	\$99,863 (\$34,492;\$182,812)	\$-16,495 (\$-23,406;\$-10,004)
General population costs	\$38,974 (\$17,304;\$64,281)	\$33,116 (\$13,362;\$56,145)	\$5,858 (\$2,487;\$9,020)
Targeted costs	\$2,273,821 (\$1,382,654;\$3,070,628)	\$0 (\$0;\$0)	\$2,273,821 (\$1,382,654;\$3,070,628)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

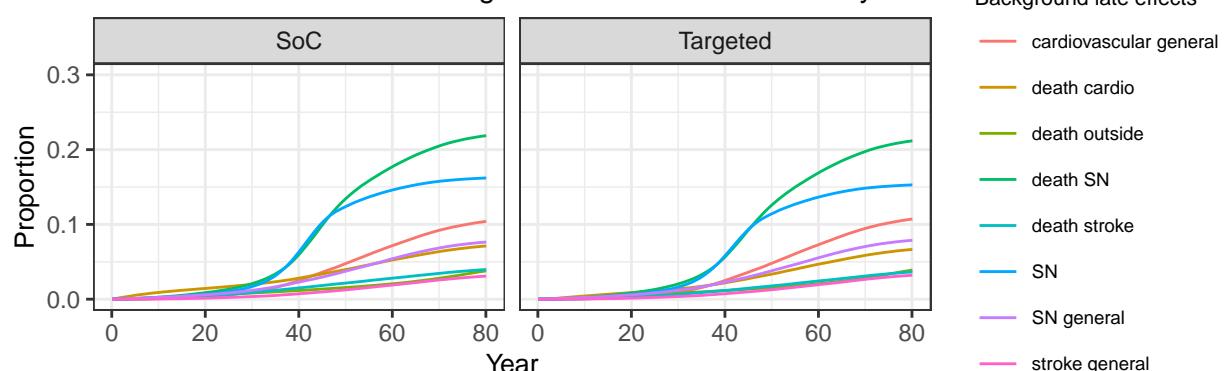
Trace Plot of PLGG States Across Cycles



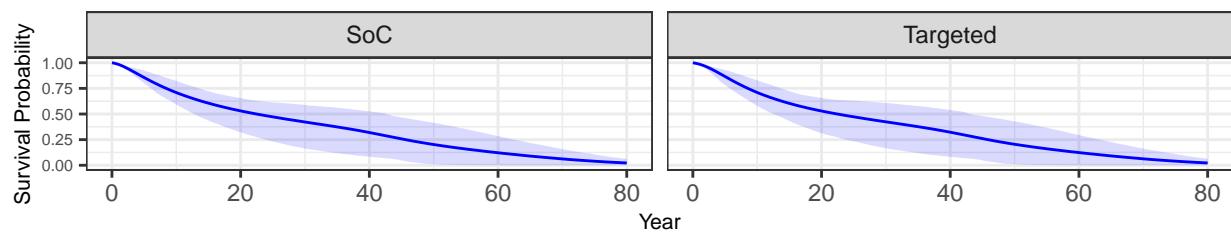
Cumulative Incidence of PLGG-related Late Effects Across Cycles



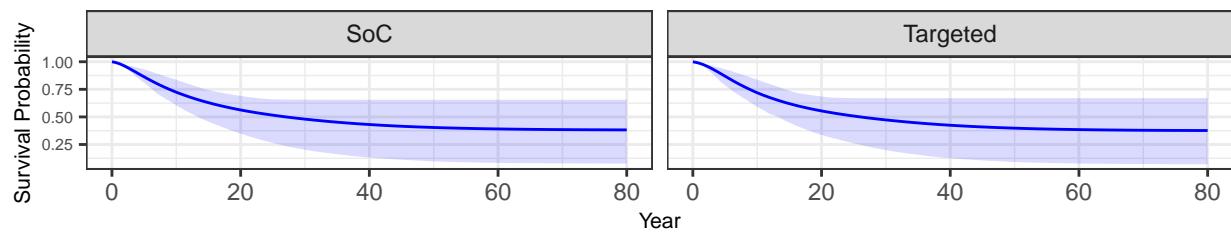
Cumulative Incidence of Background Late Effects Across Cycles



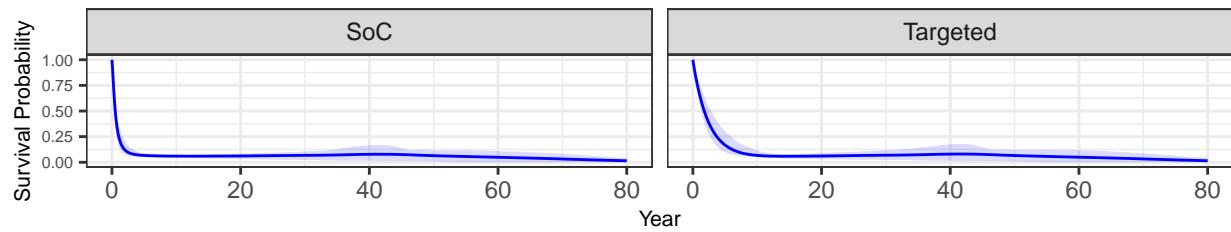
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



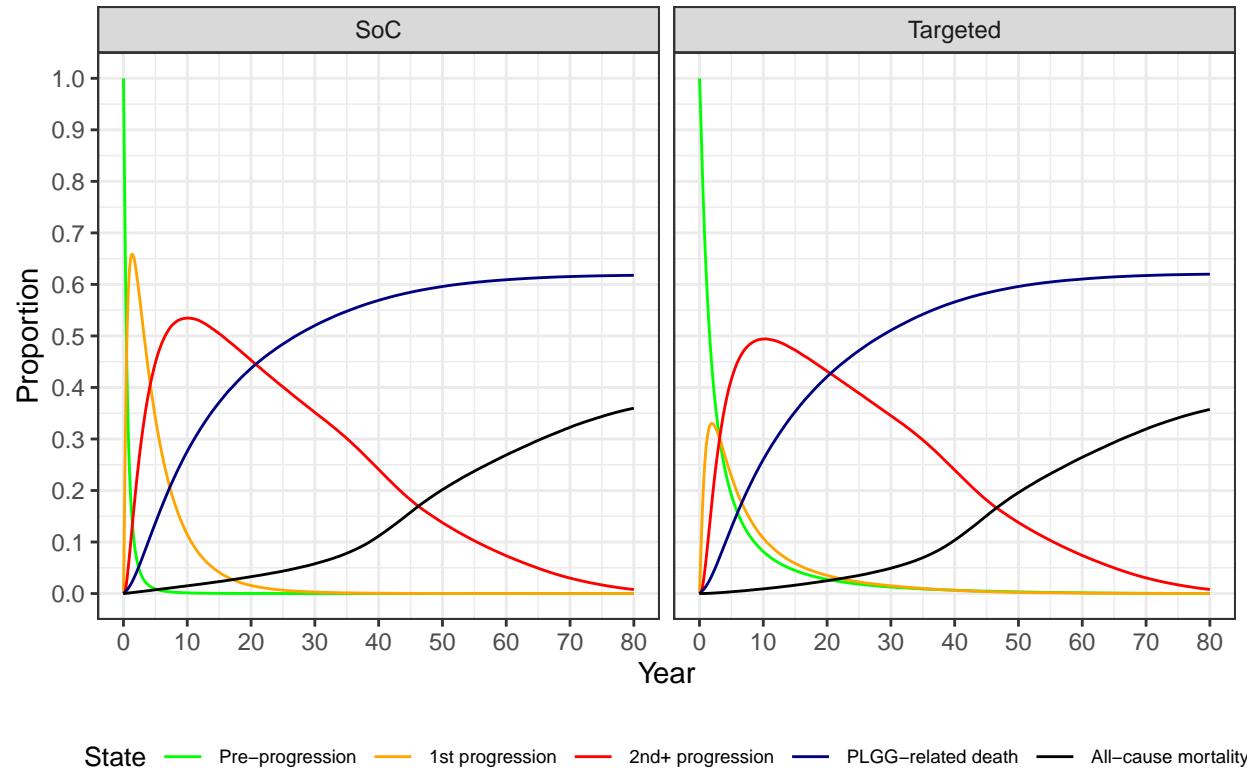
Progression–Free Survival with 95% CI



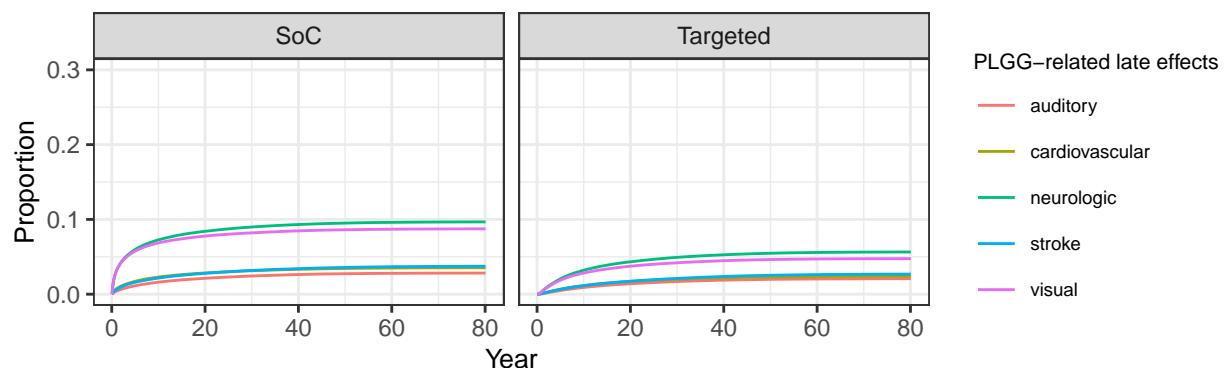
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	13.32 (9.59;17.27)	12.36 (7.65;16.39)	0.96 (0.16;1.79)
Total Cost	\$2,680,570 (\$1,959,348;\$3,435,311)	\$395,495 (\$365,854;\$423,395)	\$2,285,075 (\$1,575,697;\$3,028,835)
Non-Targeted PLGG related costs	\$224,818 (\$163,015;\$278,995)	\$262,516 (\$200,713;\$317,931)	\$-37,698 (\$-50,858;\$-24,969)
Late effect costs	\$83,572 (\$34,209;\$167,168)	\$99,863 (\$34,492;\$182,812)	\$-16,291 (\$-25,665;\$-7,532)
General population costs	\$40,529 (\$20,474;\$65,164)	\$33,116 (\$13,362;\$56,145)	\$7,413 (\$4,170;\$11,552)
Targeted costs	\$2,331,651 (\$1,623,258;\$3,074,867)	\$0 (\$0;\$0)	\$2,331,651 (\$1,623,258;\$3,074,867)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

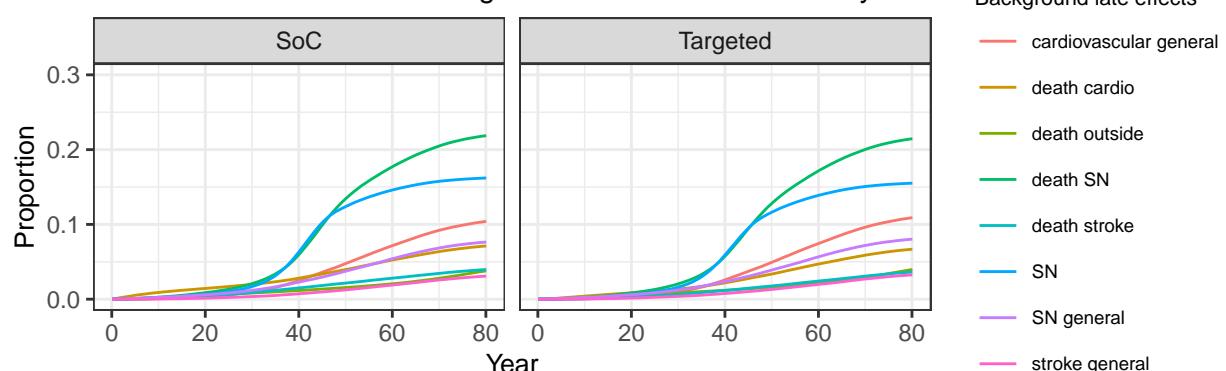
Trace Plot of PLGG States Across Cycles



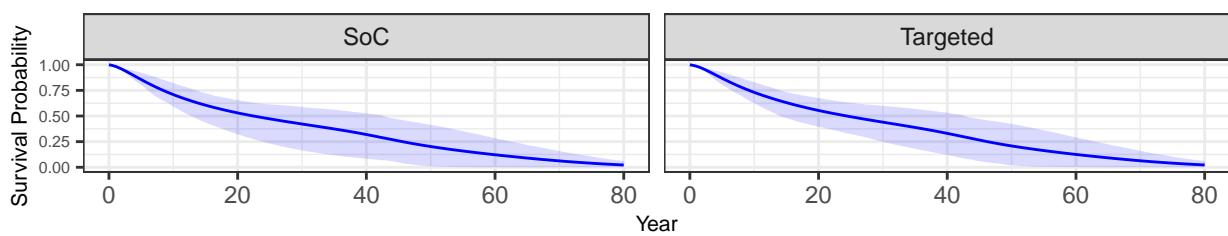
Cumulative Incidence of PLGG-related Late Effects Across Cycles



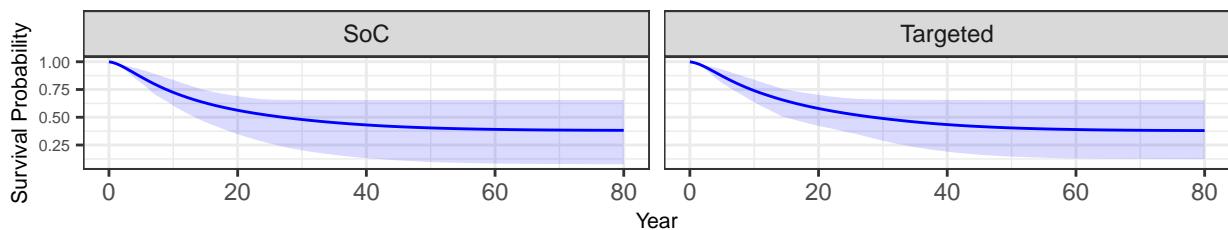
Cumulative Incidence of Background Late Effects Across Cycles



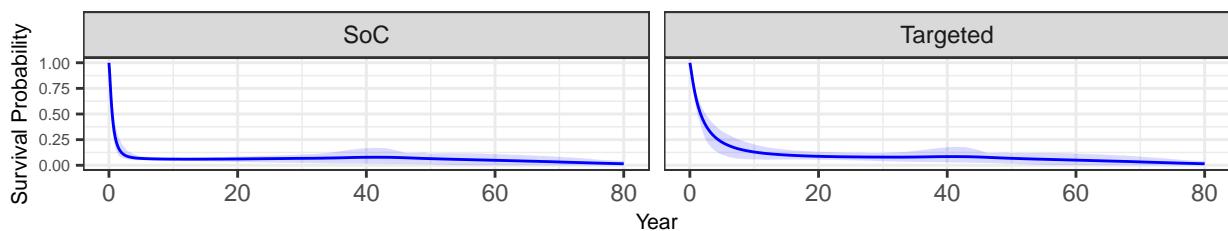
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



Progression–Free Survival with 95% CI



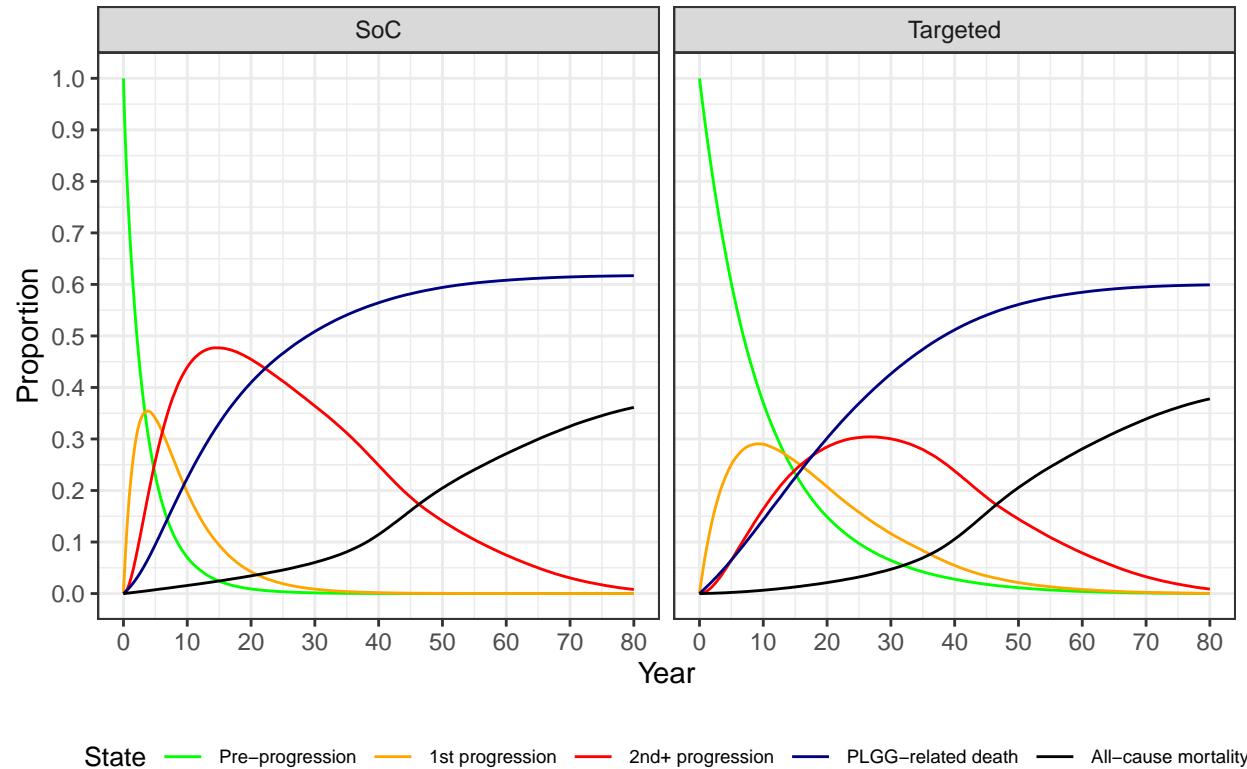
Scenario #1c

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **50% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

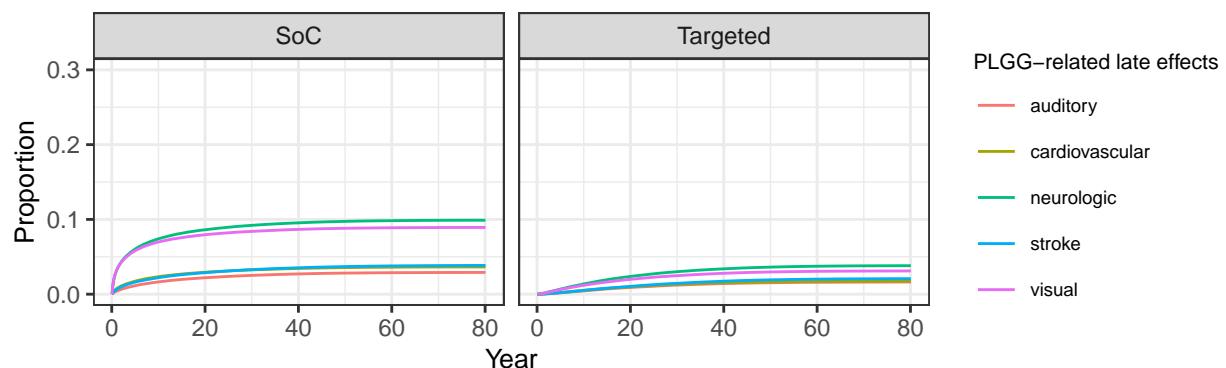
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	15.6 (11.99;19.4)	12.76 (8.92;16.08)	2.84 (0.95;6.51)
Total Cost	\$1,640,949 (\$1,328,025;\$1,942,816)	\$389,911 (\$360,422;\$415,954)	\$1,251,038 (\$938,568;\$1,554,530)
Non-Targeted PLGG related costs	\$176,369 (\$114,324;\$227,184)	\$255,203 (\$201,070;\$310,562)	\$-78,834 (\$-117,476;\$-48,429)
Late effect costs	\$78,352 (\$39,526;\$141,805)	\$100,978 (\$40,220;\$177,609)	\$-22,626 (\$-38,060;\$2,780)
General population costs	\$52,085 (\$28,857;\$75,880)	\$33,730 (\$15,256;\$54,700)	\$18,355 (\$9,256;\$36,715)
Targeted costs	\$1,334,143 (\$1,010,354;\$1,645,664)	\$0 (\$0;\$0)	\$1,334,143 (\$1,010,354;\$1,645,664)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

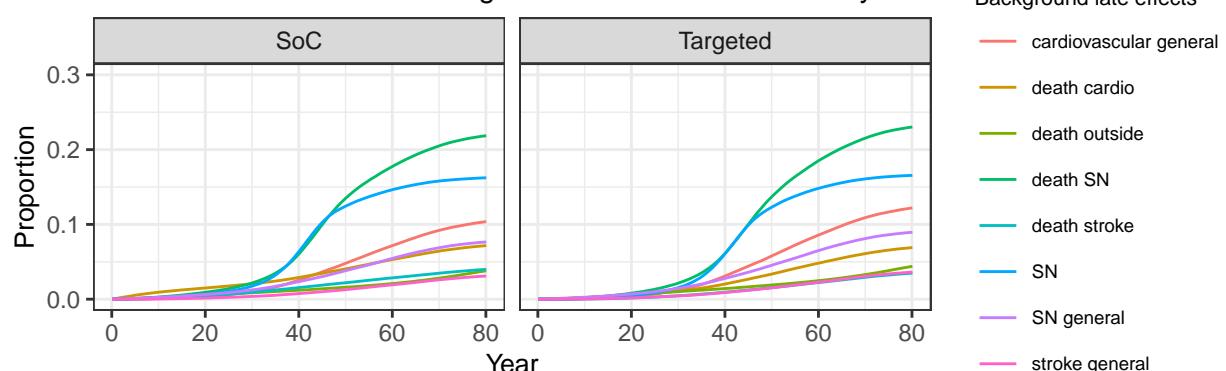
Trace Plot of PLGG States Across Cycles



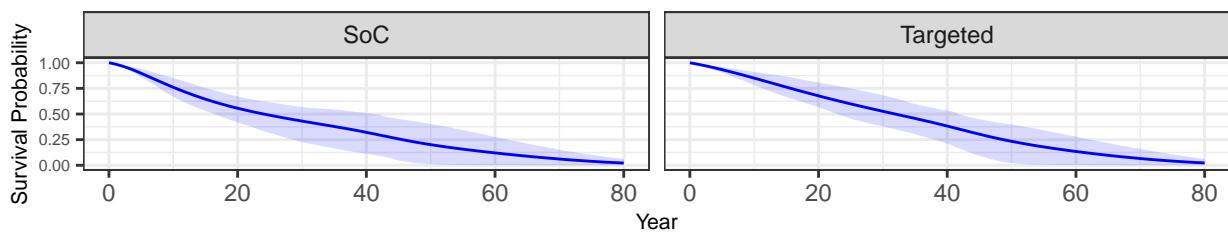
Cumulative Incidence of PLGG-related Late Effects Across Cycles



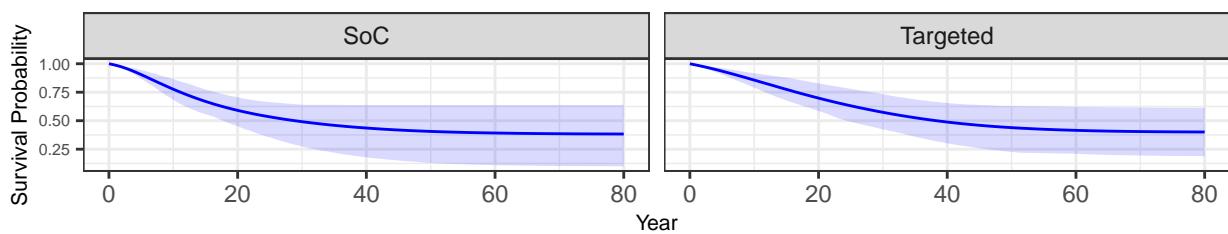
Cumulative Incidence of Background Late Effects Across Cycles



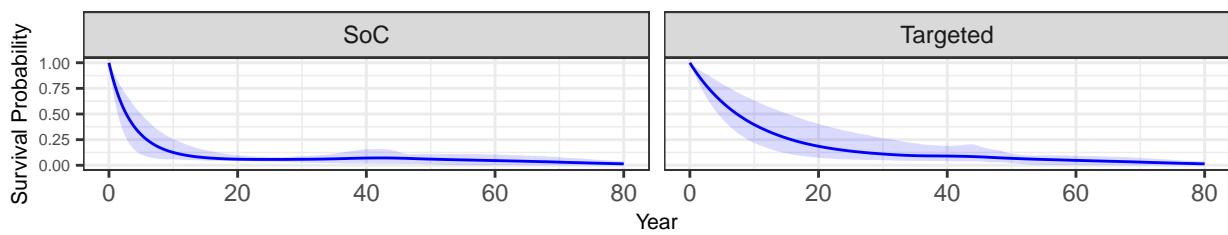
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



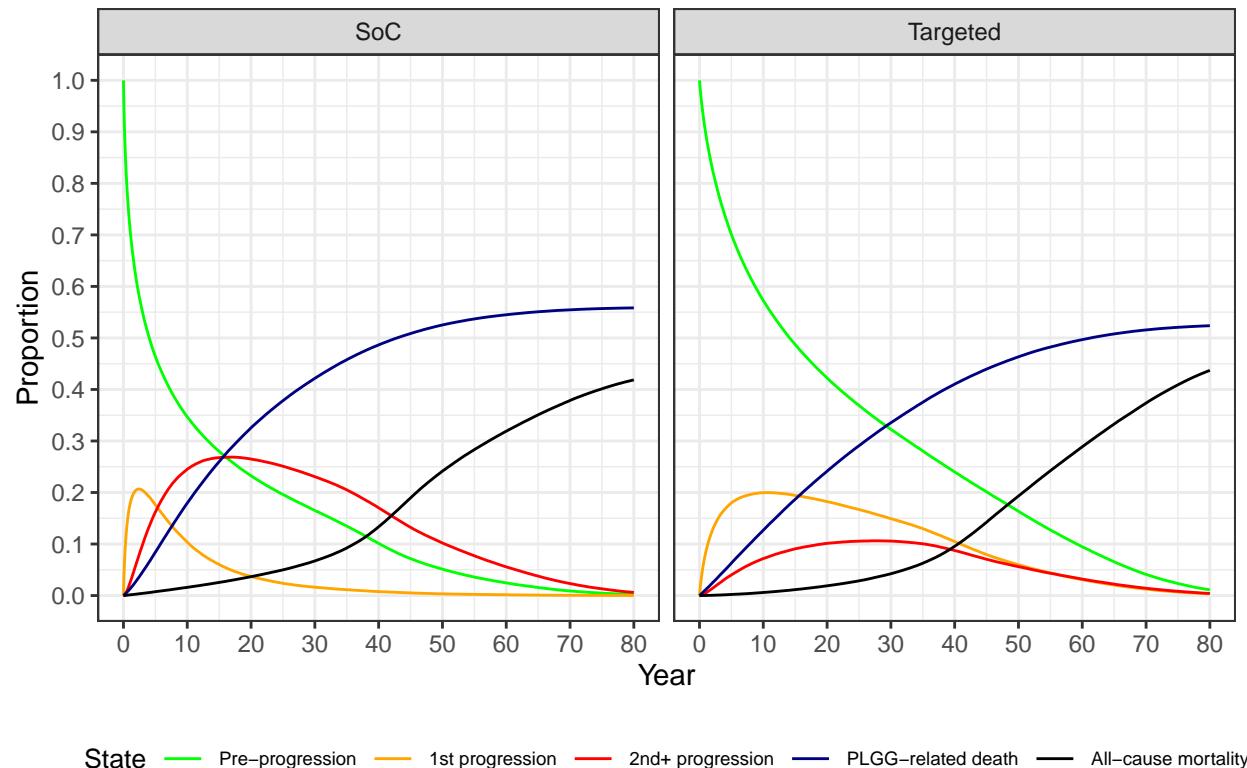
Progression-Free Survival with 95% CI



Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

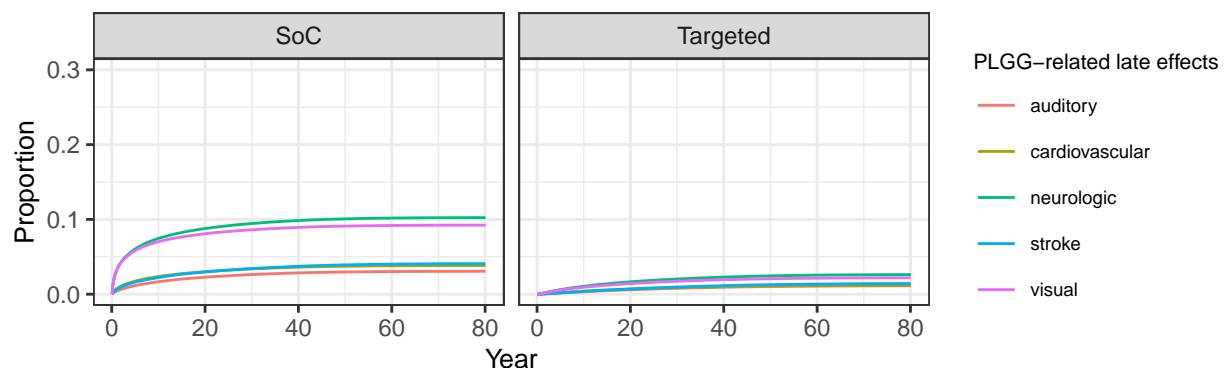
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QALY	18.19 (14.87;21.42)	14.07 (11.27;16.86)	4.11 (1.25;8.3)
Total Cost	\$1,840,770 (\$1,557,662;\$2,113,447)	\$371,619 (\$354,092;\$392,255)	\$1,469,152 (\$1,187,957;\$1,727,323)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$218,112 (\$161,312;\$259,601)	\$-73,193 (\$-130,140;\$-32,368)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$115,226 (\$75,174;\$185,091)	\$-35,176 (\$-63,913;\$-8,058)
General population costs	\$69,909 (\$46,483;\$93,955)	\$38,281 (\$20,916;\$59,355)	\$31,628 (\$14,147;\$56,008)
Targeted costs	\$1,545,892 (\$1,259,584;\$1,825,608)	\$0 (\$0;\$0)	\$1,545,892 (\$1,259,584;\$1,825,608)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

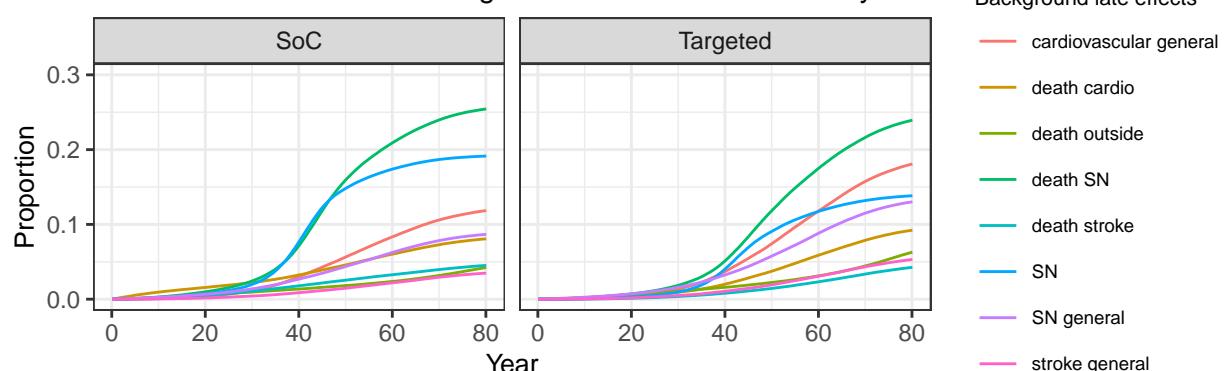


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

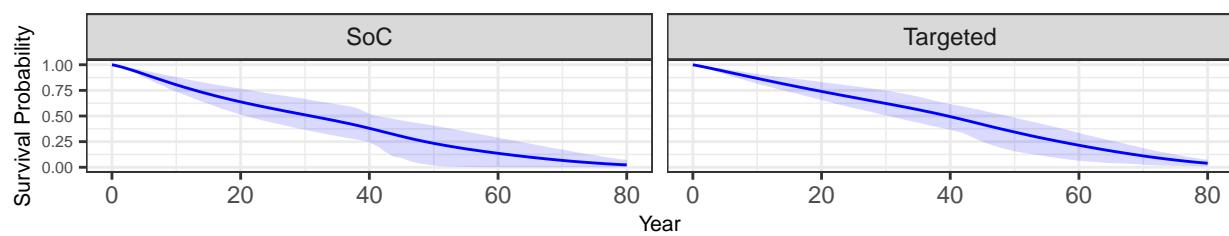
Cumulative Incidence of PLGG-related Late Effects Across Cycles



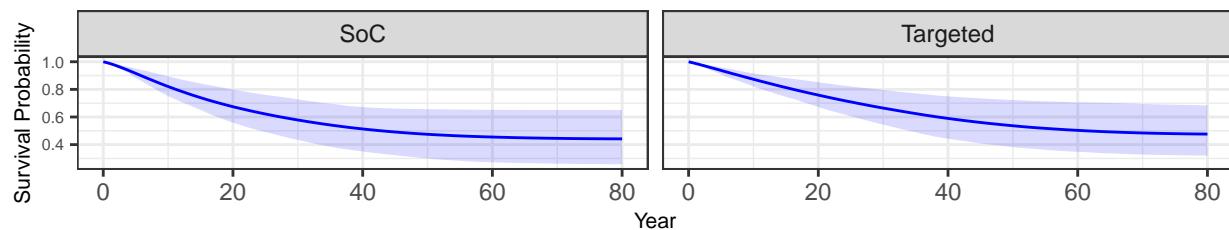
Cumulative Incidence of Background Late Effects Across Cycles



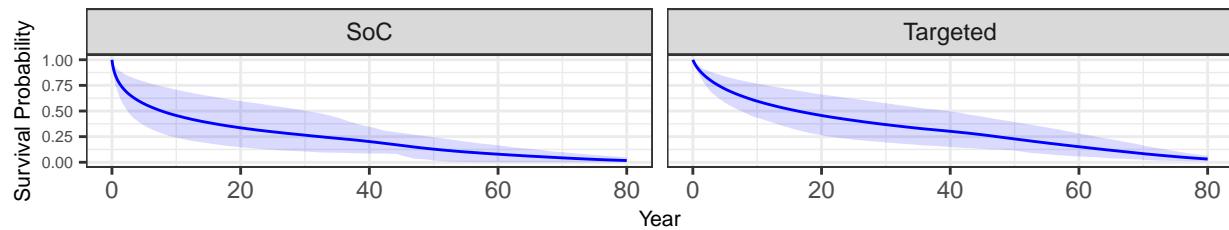
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



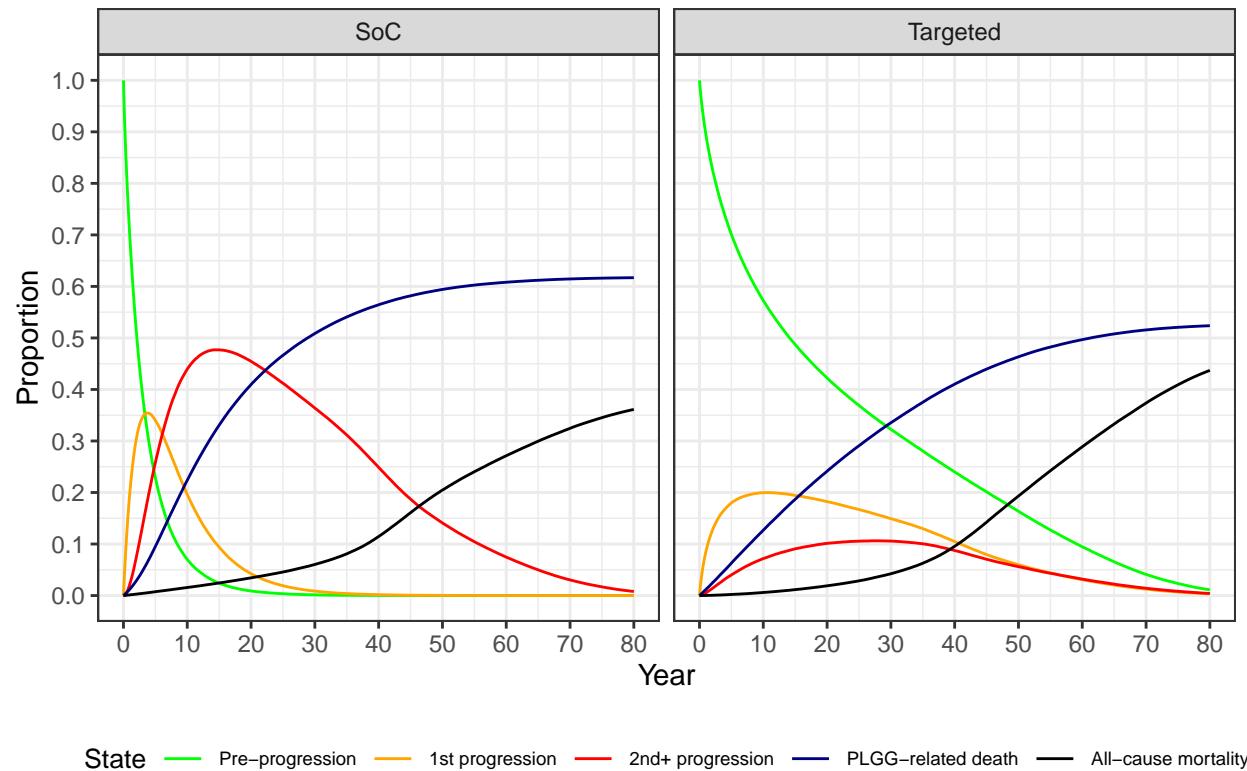
Progression-Free Survival with 95% CI



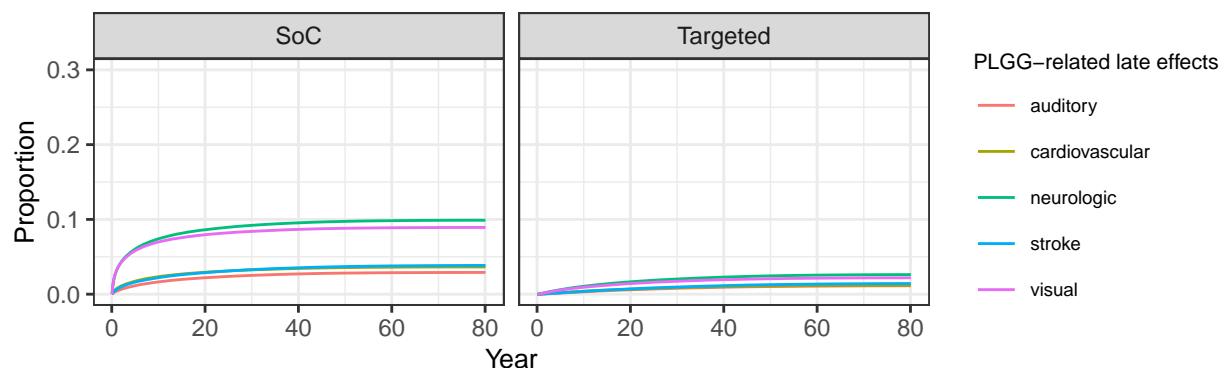
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	18.19 (14.87;21.42)	12.76 (8.92;16.08)	5.43 (2.05;10.99)
Total Cost	\$1,840,770 (\$1,557,662;\$2,113,447)	\$389,911 (\$360,422;\$415,954)	\$1,450,859 (\$1,172,391;\$1,726,600)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$255,203 (\$201,070;\$310,562)	\$-110,284 (\$-179,940;\$-56,144)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$100,978 (\$40,220;\$177,609)	\$-20,928 (\$-62,263;\$24,303)
General population costs	\$69,909 (\$46,483;\$93,955)	\$33,730 (\$15,256;\$54,700)	\$36,179 (\$19,416;\$62,749)
Targeted costs	\$1,545,892 (\$1,259,584;\$1,825,608)	\$0 (\$0;\$0)	\$1,545,892 (\$1,259,584;\$1,825,608)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

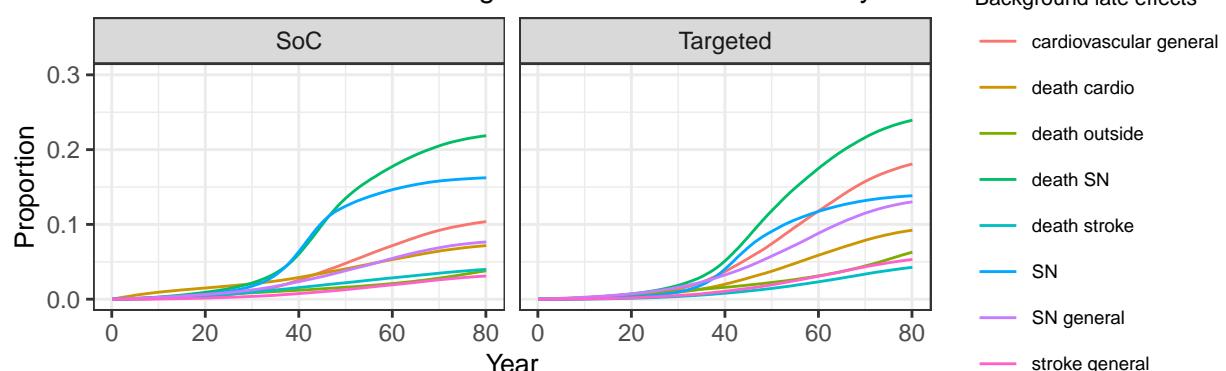
Trace Plot of PLGG States Across Cycles



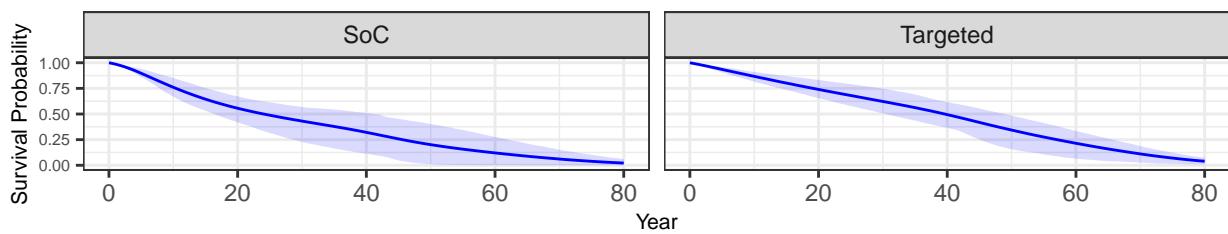
Cumulative Incidence of PLGG-related Late Effects Across Cycles



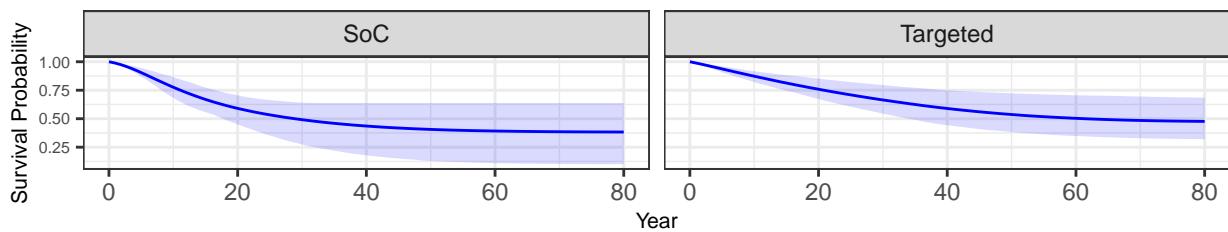
Cumulative Incidence of Background Late Effects Across Cycles



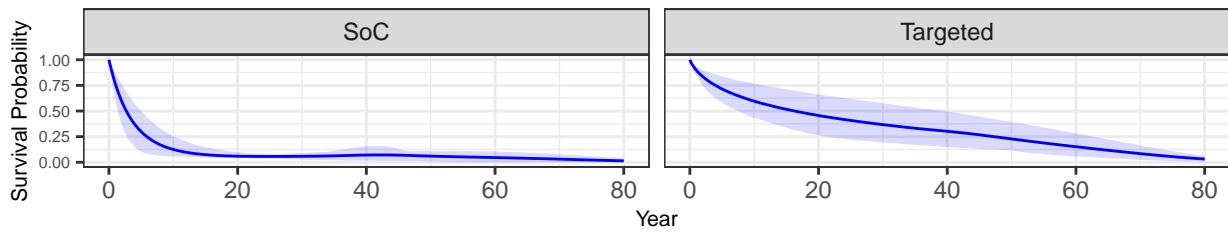
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



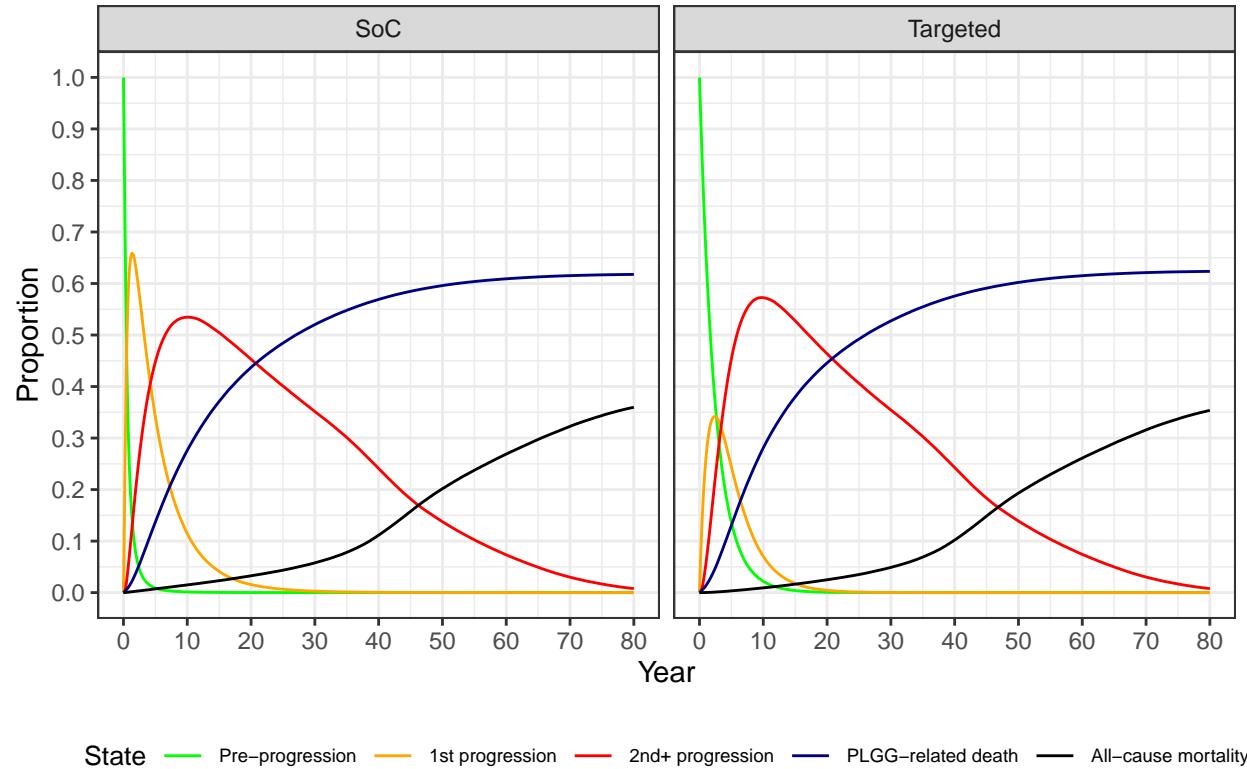
Progression-Free Survival with 95% CI



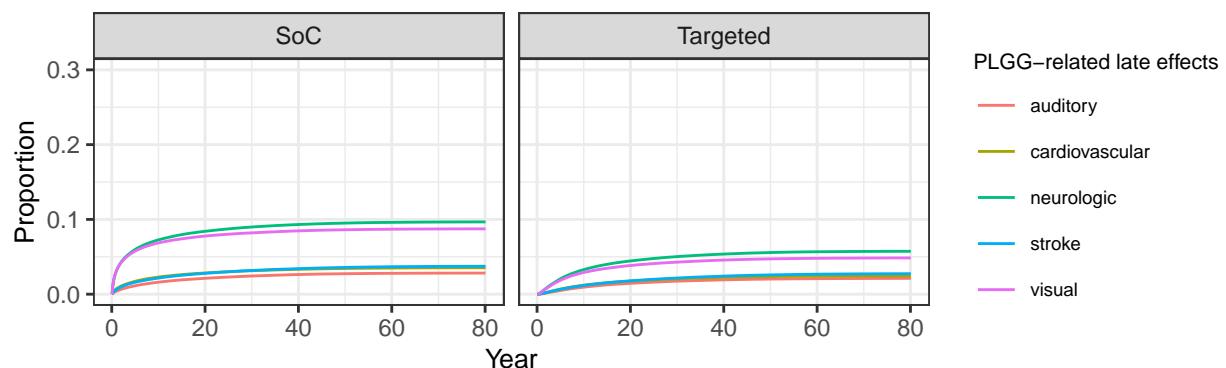
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	12.96 (8.12;17.24)	12.36 (7.65;16.39)	0.6 (-0.21;1.23)
Total Cost	\$1,491,087 (\$1,018,308;\$1,910,528)	\$395,495 (\$365,854;\$423,395)	\$1,095,592 (\$655,591;\$1,499,640)
Non-Targeted PLGG related costs	\$231,834 (\$169,279;\$287,311)	\$262,516 (\$200,713;\$317,931)	\$-30,682 (\$-42,976;\$-18,726)
Late effect costs	\$83,369 (\$23,798;\$169,727)	\$99,863 (\$34,492;\$182,812)	\$-16,495 (\$-23,406;\$-10,004)
General population costs	\$38,974 (\$17,304;\$64,281)	\$33,116 (\$13,362;\$56,145)	\$5,858 (\$2,487;\$9,020)
Targeted costs	\$1,136,911 (\$691,327;\$1,535,314)	\$0 (\$0;\$0)	\$1,136,911 (\$691,327;\$1,535,314)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

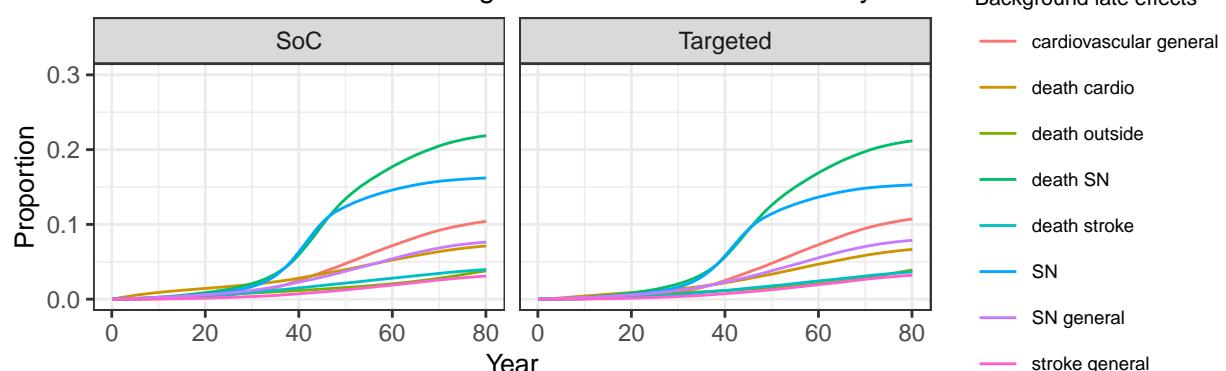
Trace Plot of PLGG States Across Cycles



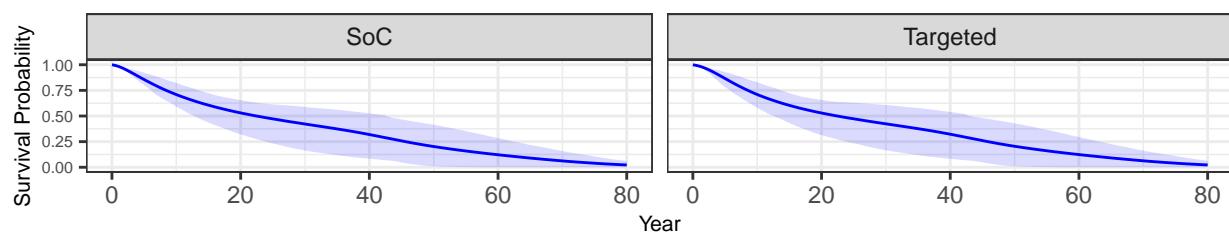
Cumulative Incidence of PLGG-related Late Effects Across Cycles



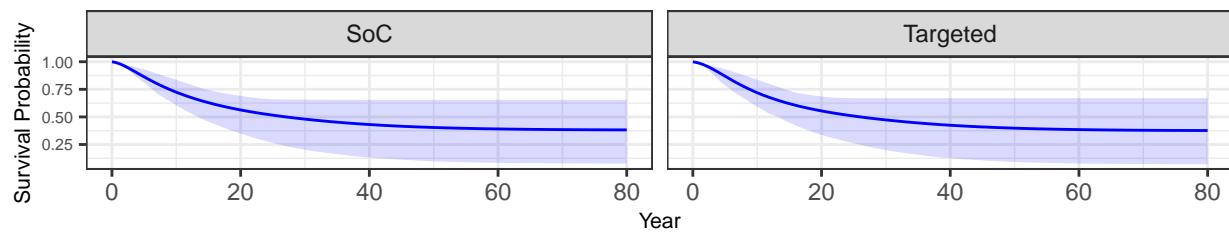
Cumulative Incidence of Background Late Effects Across Cycles



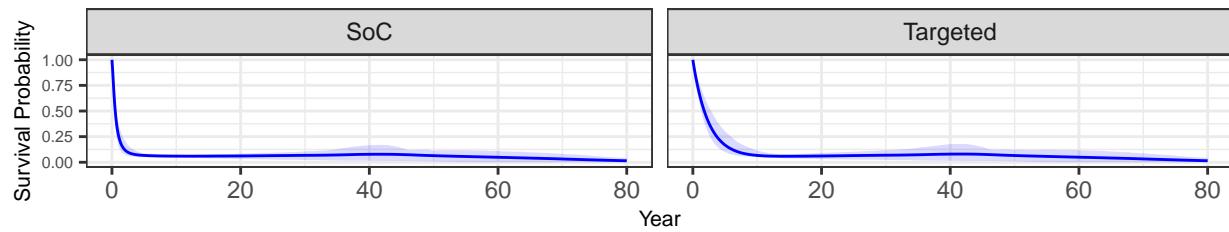
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



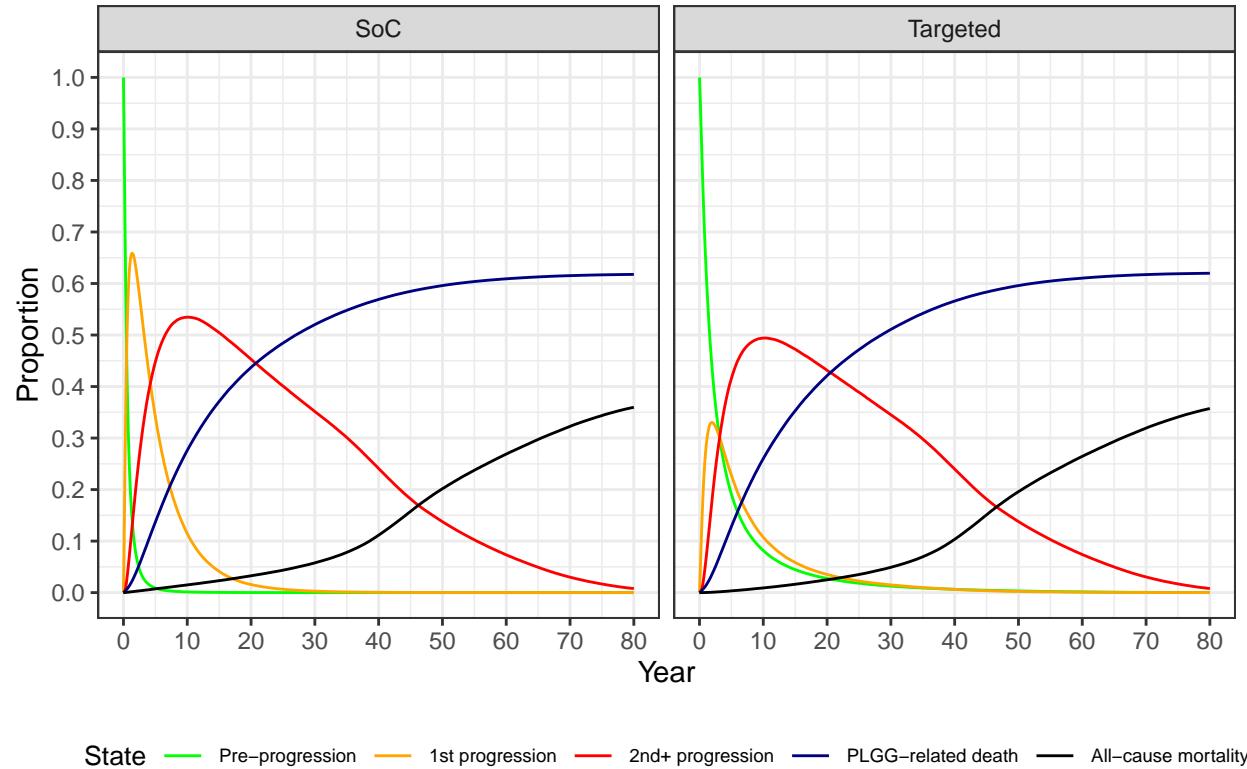
Progression-Free Survival with 95% CI



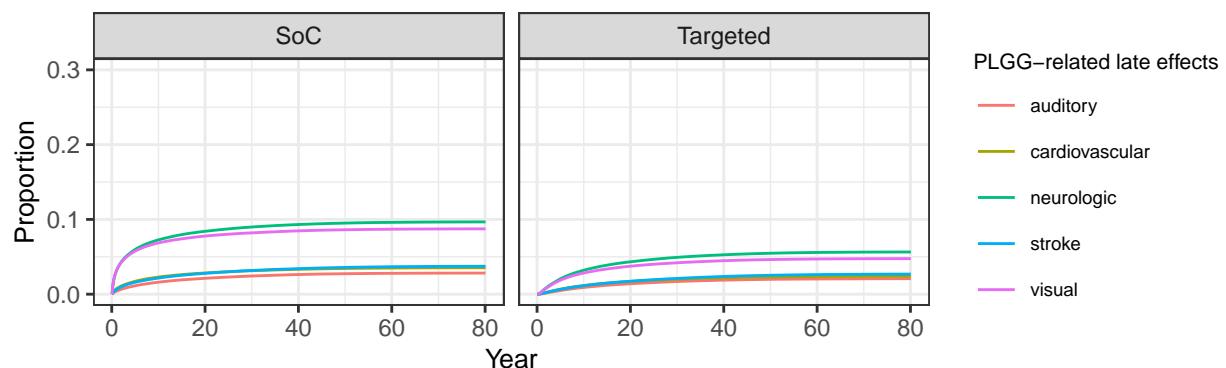
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	13.32 (9.59;17.27)	12.36 (7.65;16.39)	0.96 (0.16;1.79)
Total Cost	\$1,514,744 (\$1,146,494;\$1,912,898)	\$395,495 (\$365,854;\$423,395)	\$1,119,249 (\$764,045;\$1,491,402)
Non-Targeted PLGG related costs	\$224,818 (\$163,015;\$278,995)	\$262,516 (\$200,713;\$317,931)	\$-37,698 (\$-50,858;\$-24,969)
Late effect costs	\$83,572 (\$34,209;\$167,168)	\$99,863 (\$34,492;\$182,812)	\$-16,291 (\$-25,665;\$-7,532)
General population costs	\$40,529 (\$20,474;\$65,164)	\$33,116 (\$13,362;\$56,145)	\$7,413 (\$4,170;\$11,552)
Targeted costs	\$1,165,826 (\$811,629;\$1,537,434)	\$0 (\$0;\$0)	\$1,165,826 (\$811,629;\$1,537,434)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

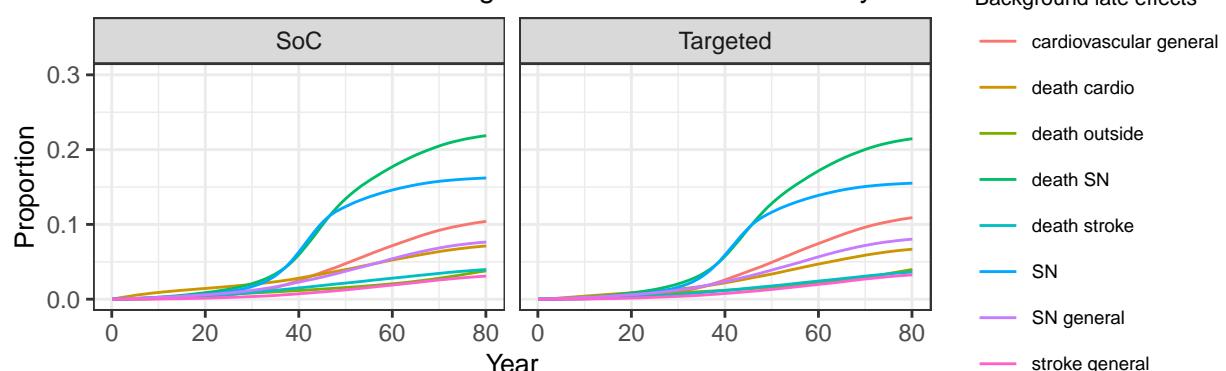
Trace Plot of PLGG States Across Cycles



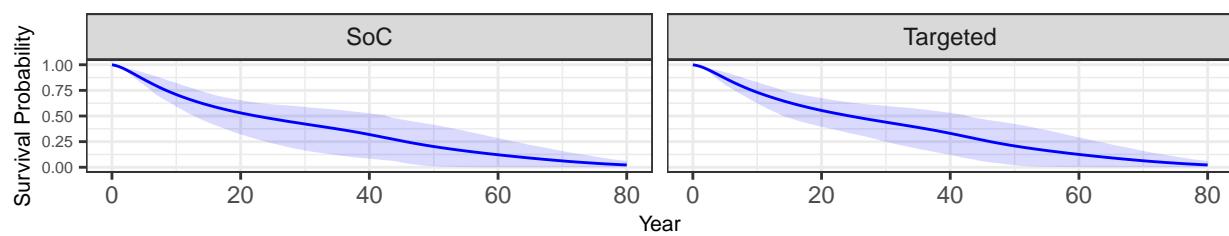
Cumulative Incidence of PLGG-related Late Effects Across Cycles



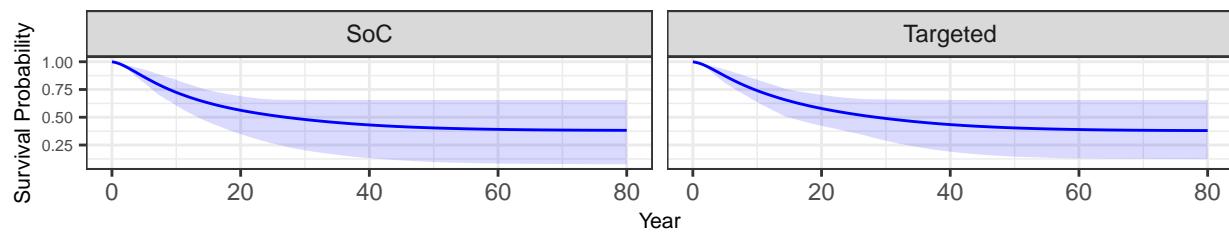
Cumulative Incidence of Background Late Effects Across Cycles



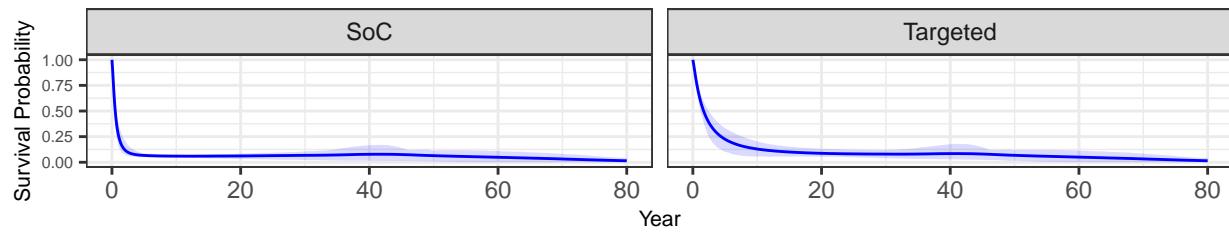
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



Progression-Free Survival with 95% CI



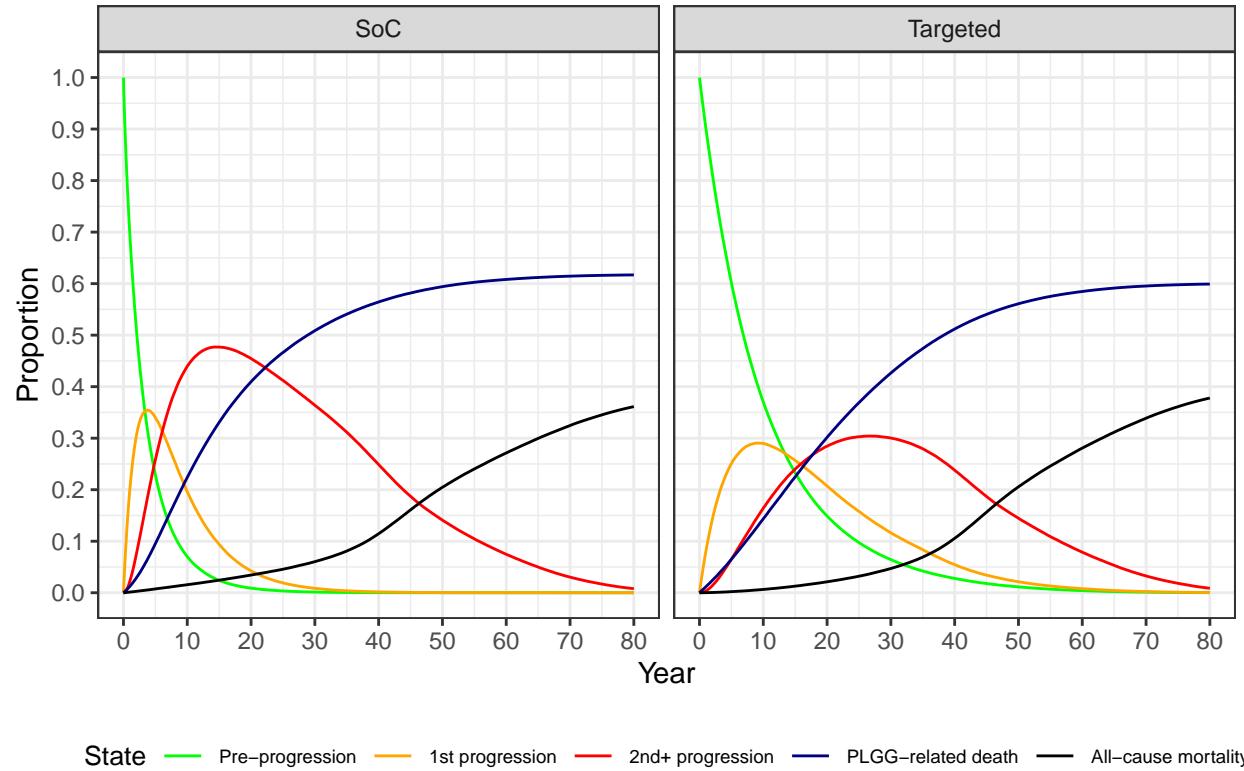
Scenario #1d

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **75% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

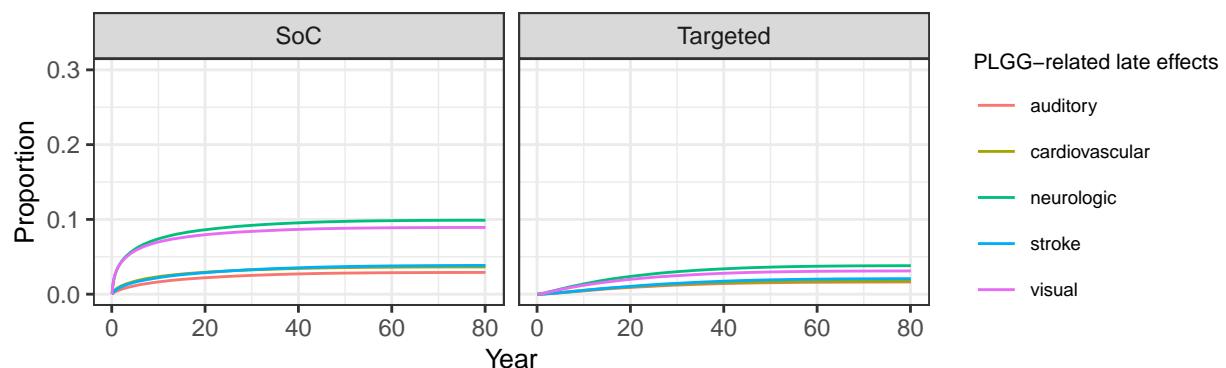
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	15.6 (11.99;19.4)	12.76 (8.92;16.08)	2.84 (0.95;6.51)
Total Cost	\$973,877 (\$818,681;\$1,119,984)	\$389,911 (\$360,422;\$415,954)	\$583,967 (\$428,716;\$724,001)
Non-Targeted PLGG related costs	\$176,369 (\$114,324;\$227,184)	\$255,203 (\$201,070;\$310,562)	\$-78,834 (\$-117,476;\$-48,429)
Late effect costs	\$78,352 (\$39,526;\$141,805)	\$100,978 (\$40,220;\$177,609)	\$-22,626 (\$-38,060;\$2,780)
General population costs	\$52,085 (\$28,857;\$75,880)	\$33,730 (\$15,256;\$54,700)	\$18,355 (\$9,256;\$36,715)
Targeted costs	\$667,071 (\$505,177;\$822,832)	\$0 (\$0;\$0)	\$667,071 (\$505,177;\$822,832)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

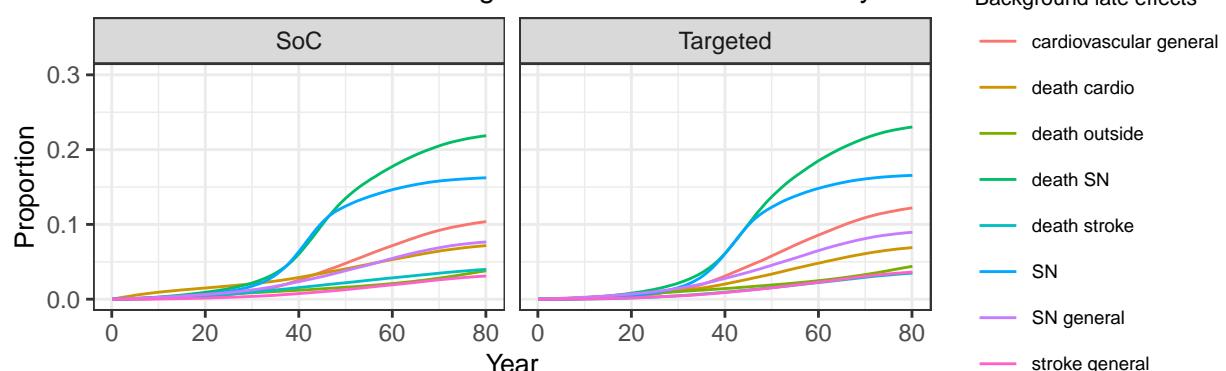
Trace Plot of PLGG States Across Cycles



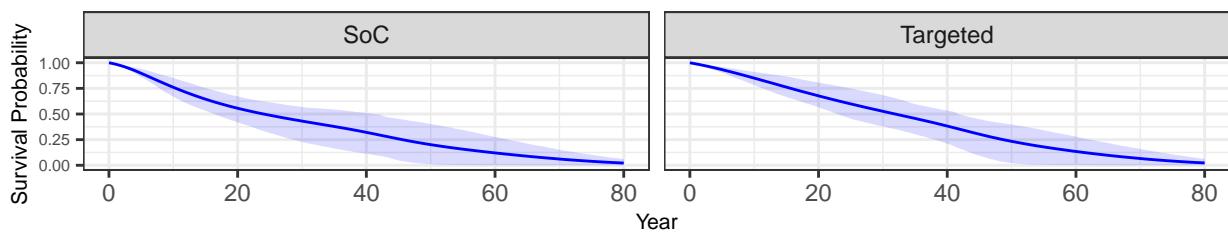
Cumulative Incidence of PLGG-related Late Effects Across Cycles



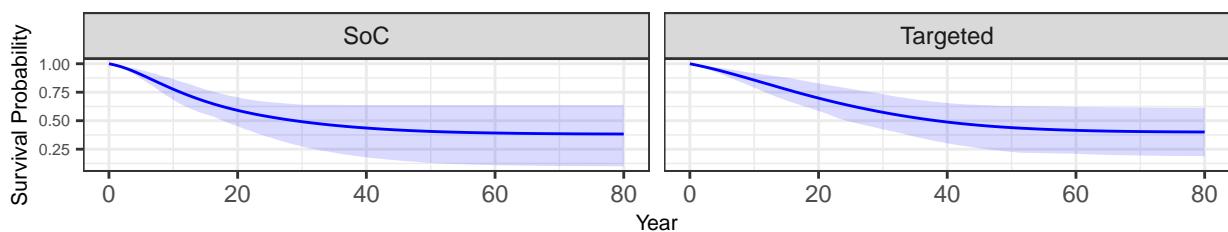
Cumulative Incidence of Background Late Effects Across Cycles



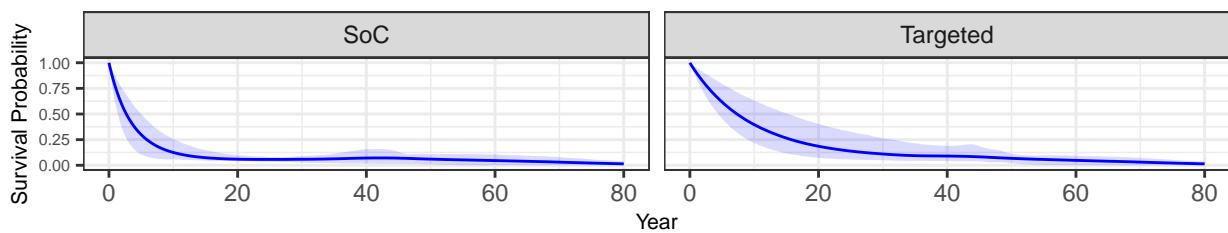
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



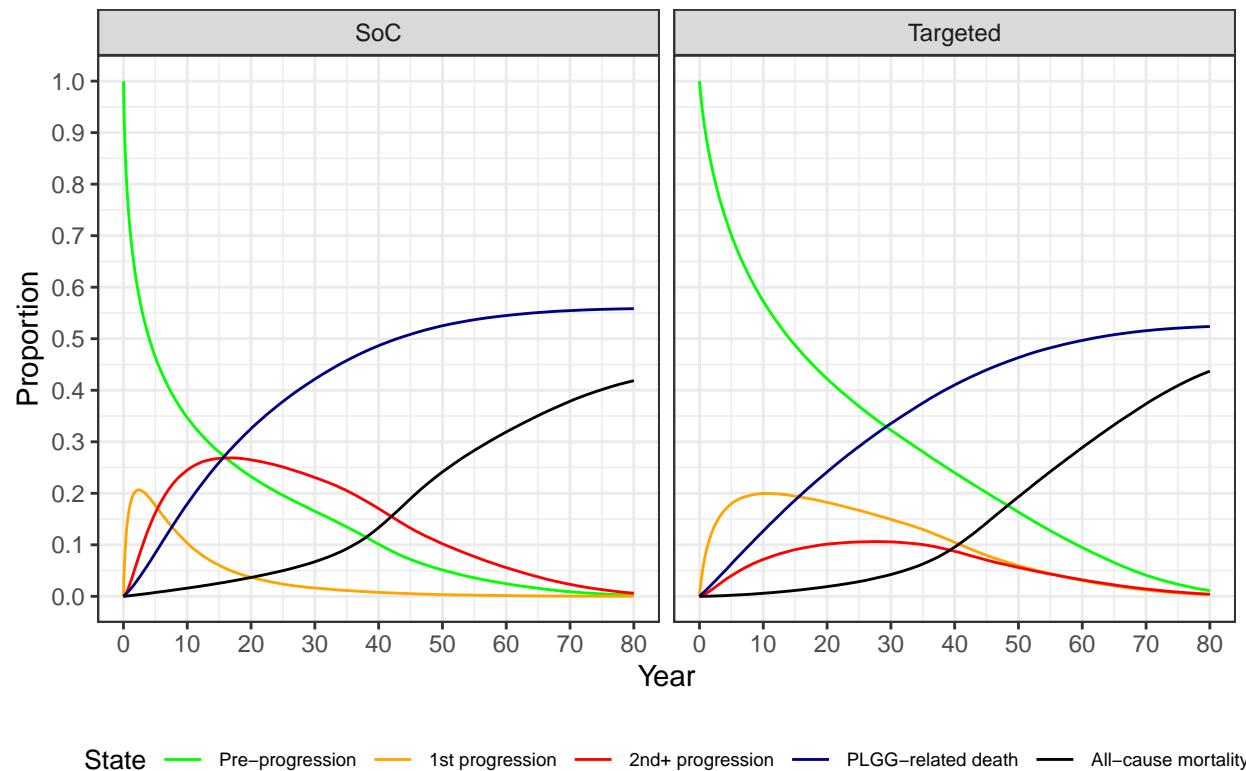
Progression-Free Survival with 95% CI



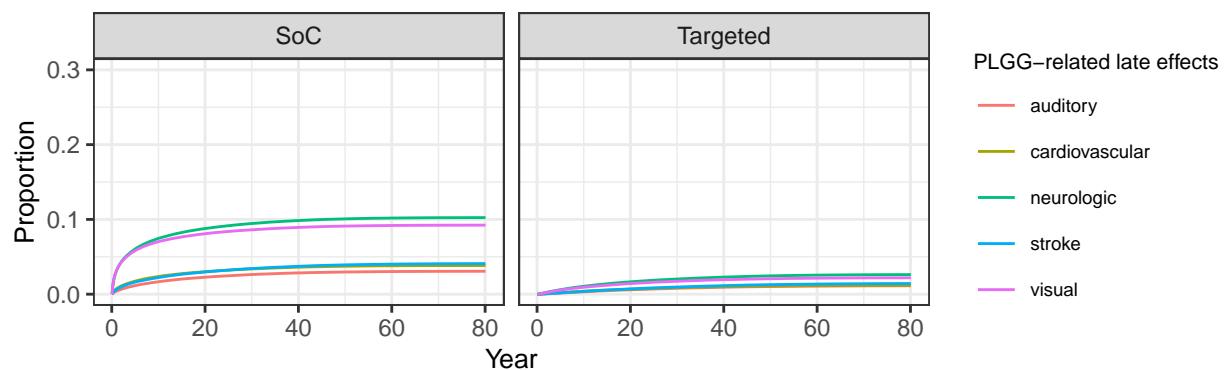
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	18.19 (14.87;21.42)	14.07 (11.27;16.86)	4.11 (1.25;8.3)
Total Cost	\$1,067,824 (\$928,667;\$1,200,642)	\$371,619 (\$354,092;\$392,255)	\$696,205 (\$558,003;\$814,519)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$218,112 (\$161,312;\$259,601)	\$-73,193 (\$-130,140;\$-32,368)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$115,226 (\$75,174;\$185,091)	\$-35,176 (\$-63,913;\$-8,058)
General population costs	\$69,909 (\$46,483;\$93,955)	\$38,281 (\$20,916;\$59,355)	\$31,628 (\$14,147;\$56,008)
Targeted costs	\$772,946 (\$629,792;\$912,804)	\$0 (\$0;\$0)	\$772,946 (\$629,792;\$912,804)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

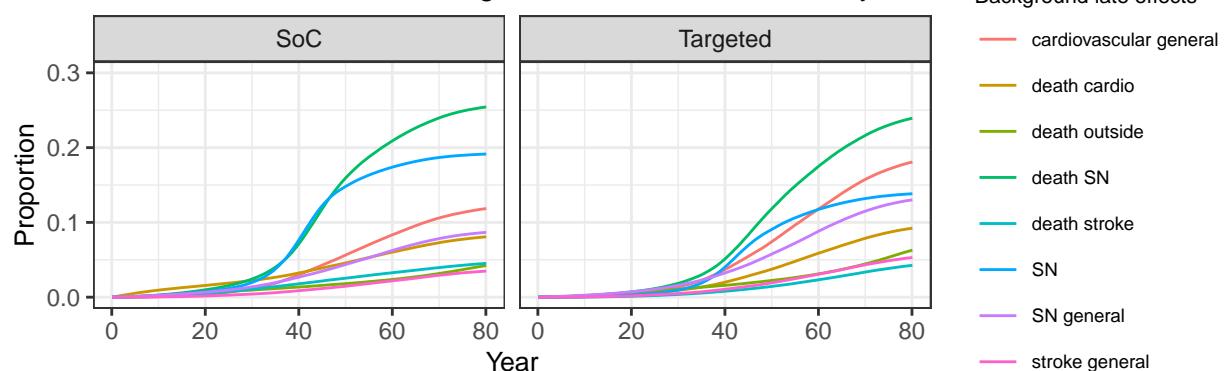
Trace Plot of PLGG States Across Cycles



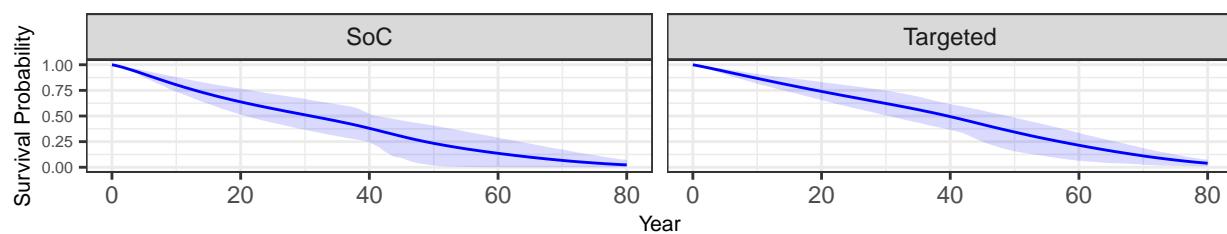
Cumulative Incidence of PLGG-related Late Effects Across Cycles



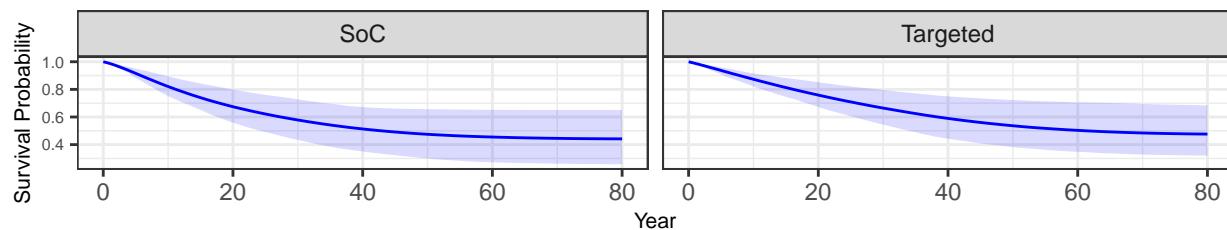
Cumulative Incidence of Background Late Effects Across Cycles



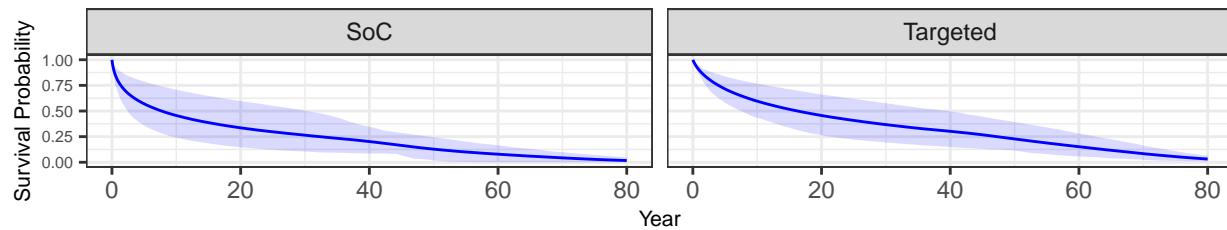
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



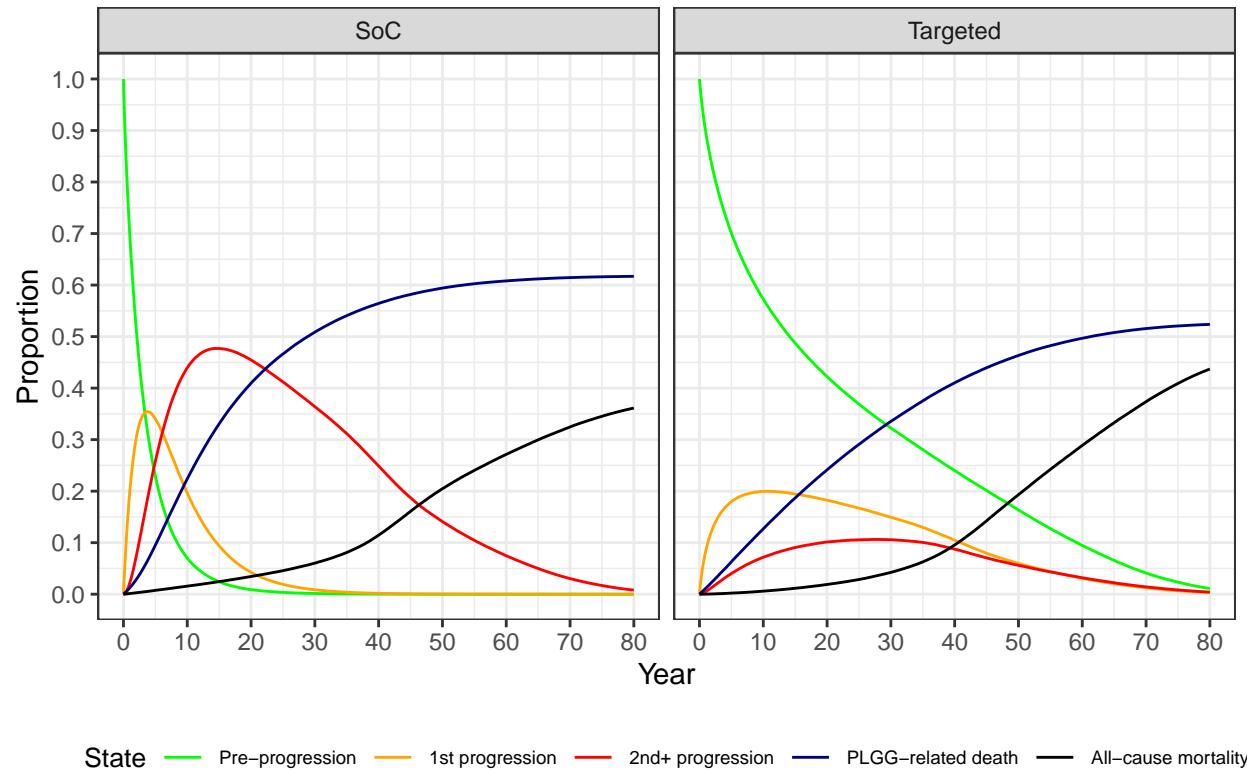
Progression-Free Survival with 95% CI



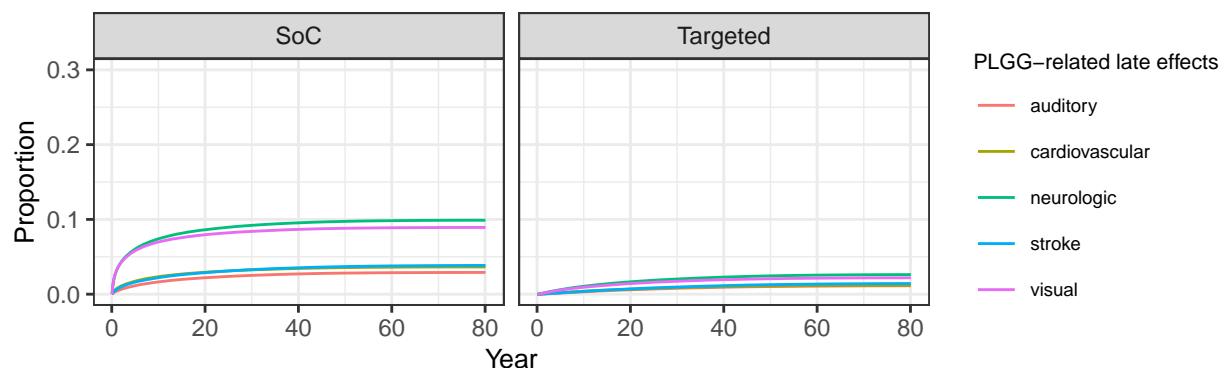
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	18.19 (14.87;21.42)	12.76 (8.92;16.08)	5.43 (2.05;10.99)
Total Cost	\$1,067,824 (\$928,667;\$1,200,642)	\$389,911 (\$360,422;\$415,954)	\$677,913 (\$532,585;\$813,796)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$255,203 (\$201,070;\$310,562)	\$-110,284 (\$-179,940;\$-56,144)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$100,978 (\$40,220;\$177,609)	\$-20,928 (\$-62,263;\$24,303)
General population costs	\$69,909 (\$46,483;\$93,955)	\$33,730 (\$15,256;\$54,700)	\$36,179 (\$19,416;\$62,749)
Targeted costs	\$772,946 (\$629,792;\$912,804)	\$0 (\$0;\$0)	\$772,946 (\$629,792;\$912,804)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

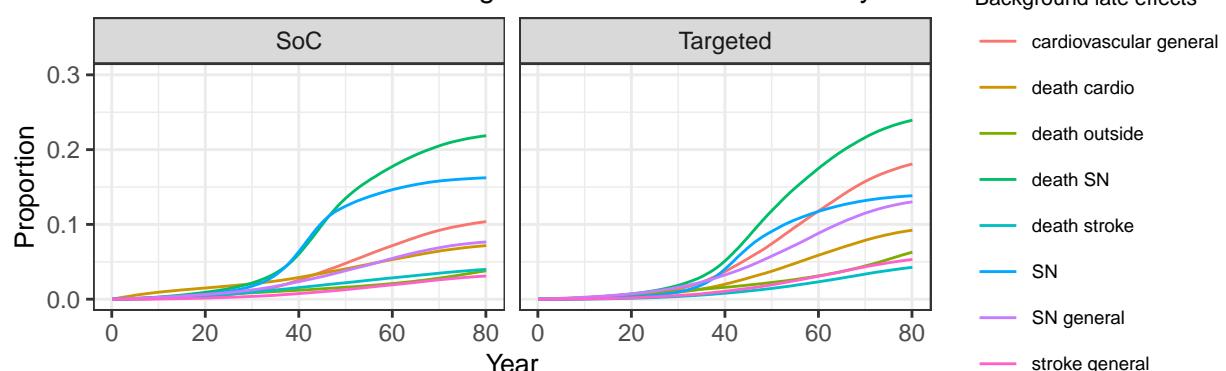
Trace Plot of PLGG States Across Cycles



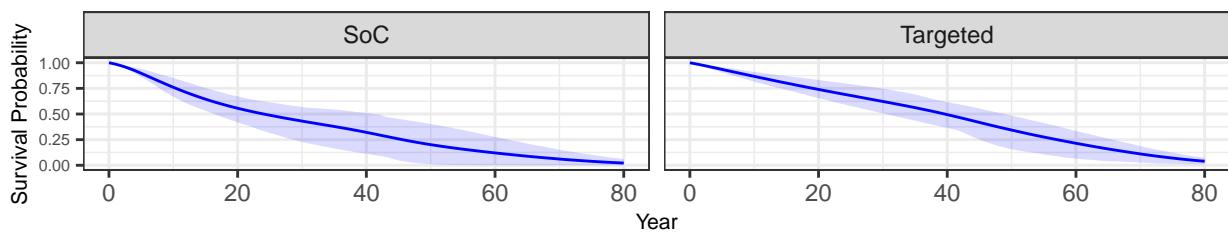
Cumulative Incidence of PLGG-related Late Effects Across Cycles



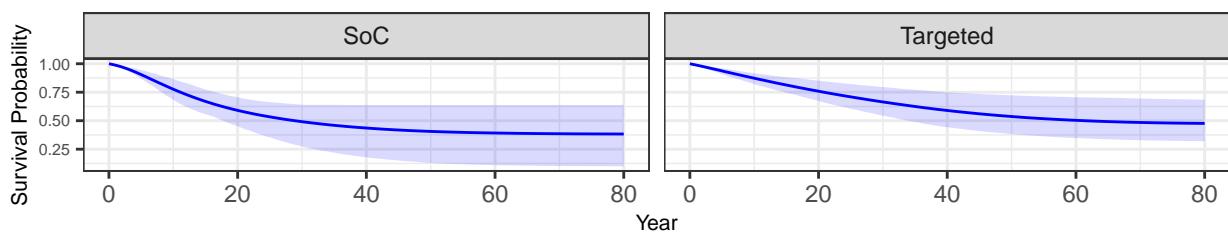
Cumulative Incidence of Background Late Effects Across Cycles



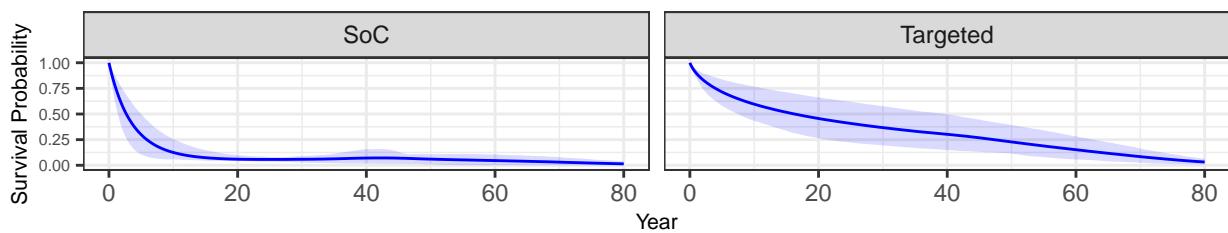
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



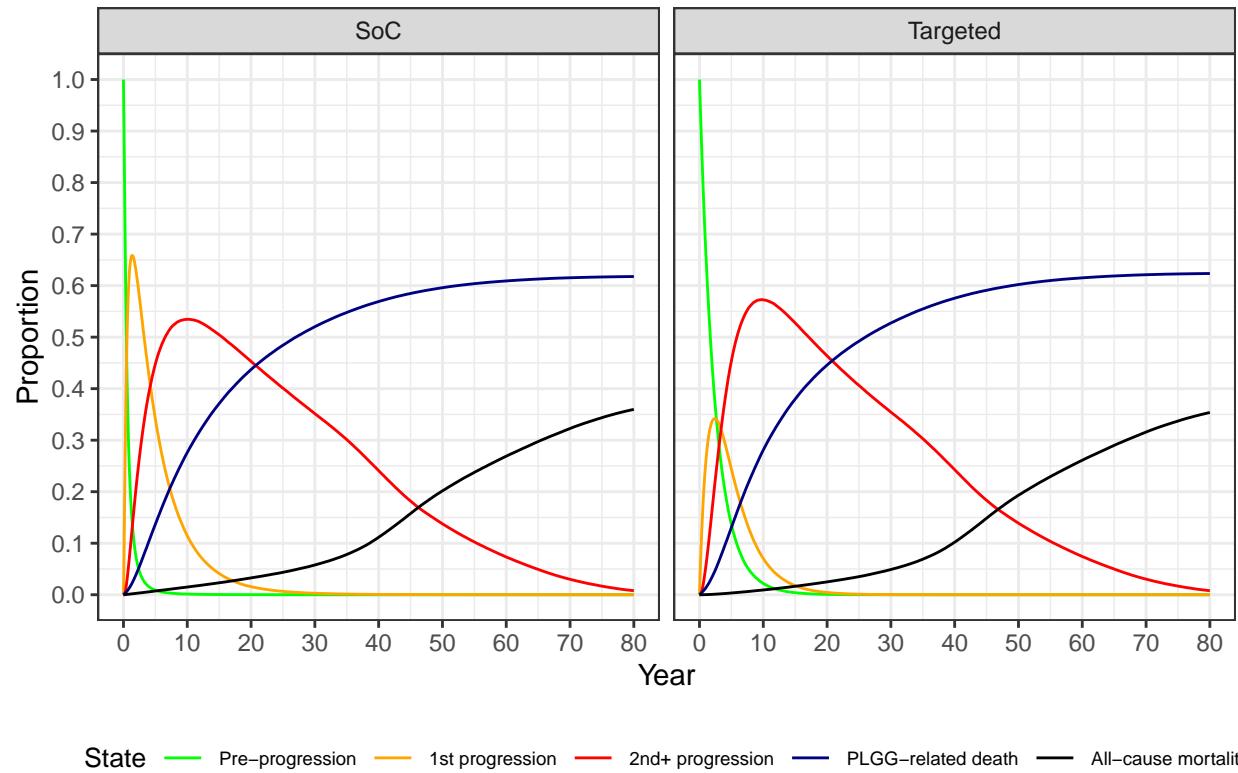
Progression-Free Survival with 95% CI



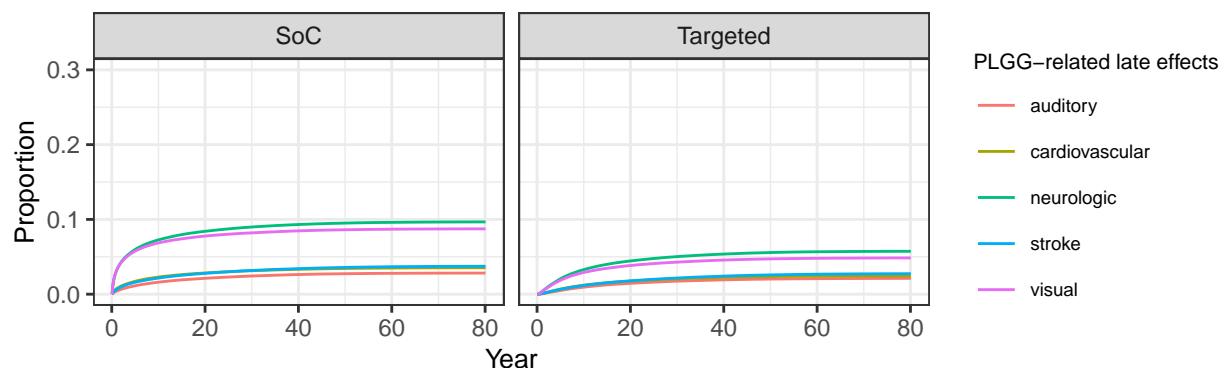
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	12.96 (8.12;17.24)	12.36 (7.65;16.39)	0.6 (-0.21;1.23)
Total Cost	\$922,631 (\$672,006;\$1,129,021)	\$395,495 (\$365,854;\$423,395)	\$527,136 (\$309,928;\$731,983)
Non-Targeted PLGG related costs	\$231,834 (\$169,279;\$287,311)	\$262,516 (\$200,713;\$317,931)	\$-30,682 (\$-42,976;\$-18,726)
Late effect costs	\$83,369 (\$23,798;\$169,727)	\$99,863 (\$34,492;\$182,812)	\$-16,495 (\$-23,406;\$-10,004)
General population costs	\$38,974 (\$17,304;\$64,281)	\$33,116 (\$13,362;\$56,145)	\$5,858 (\$2,487;\$9,020)
Targeted costs	\$568,455 (\$345,664;\$767,657)	\$0 (\$0;\$0)	\$568,455 (\$345,664;\$767,657)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

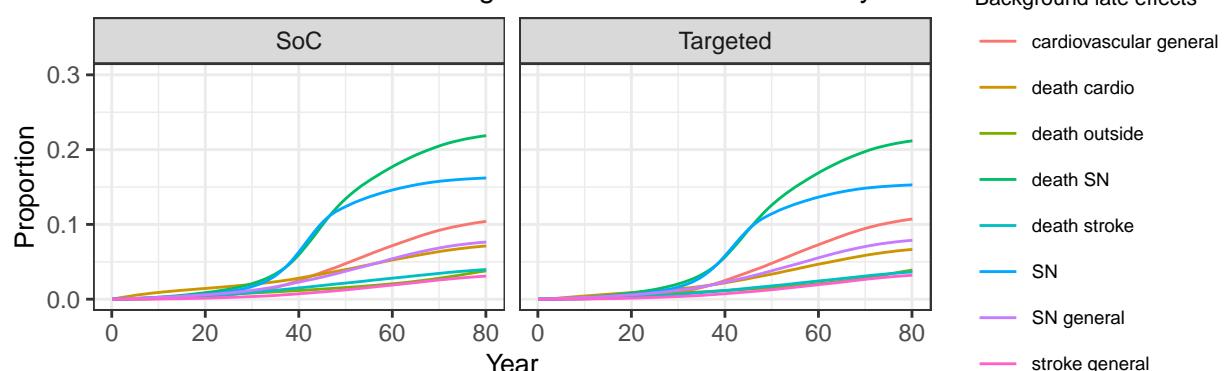
Trace Plot of PLGG States Across Cycles



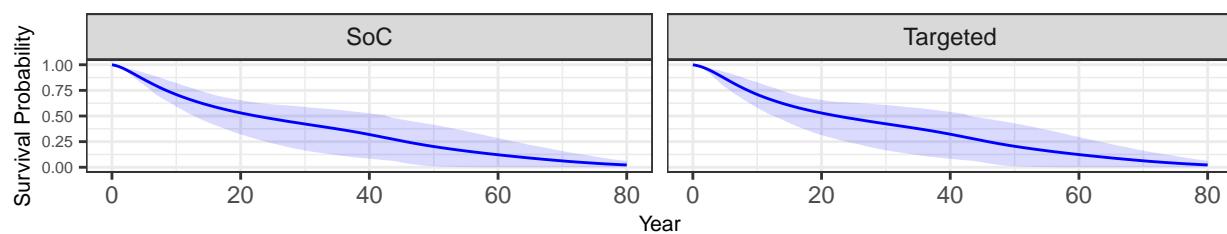
Cumulative Incidence of PLGG-related Late Effects Across Cycles



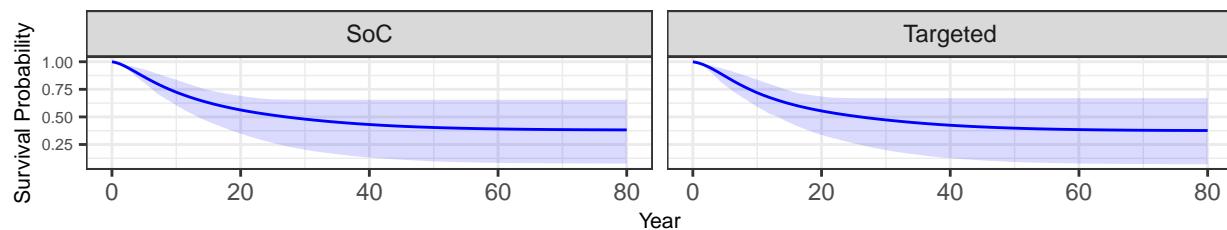
Cumulative Incidence of Background Late Effects Across Cycles



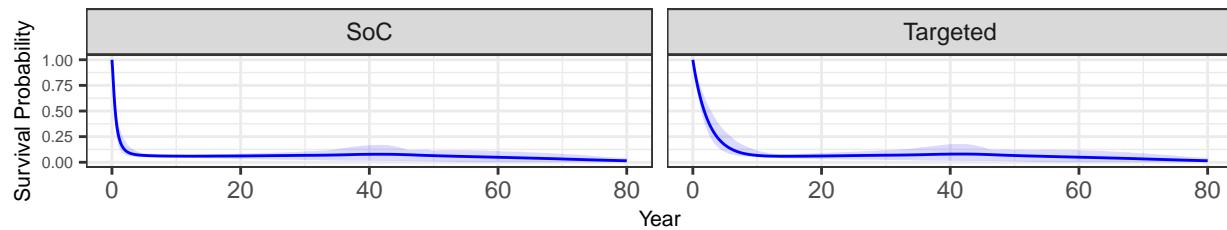
Overall Survival with 95% CI



PLGG-death–related Survival with 95% CI



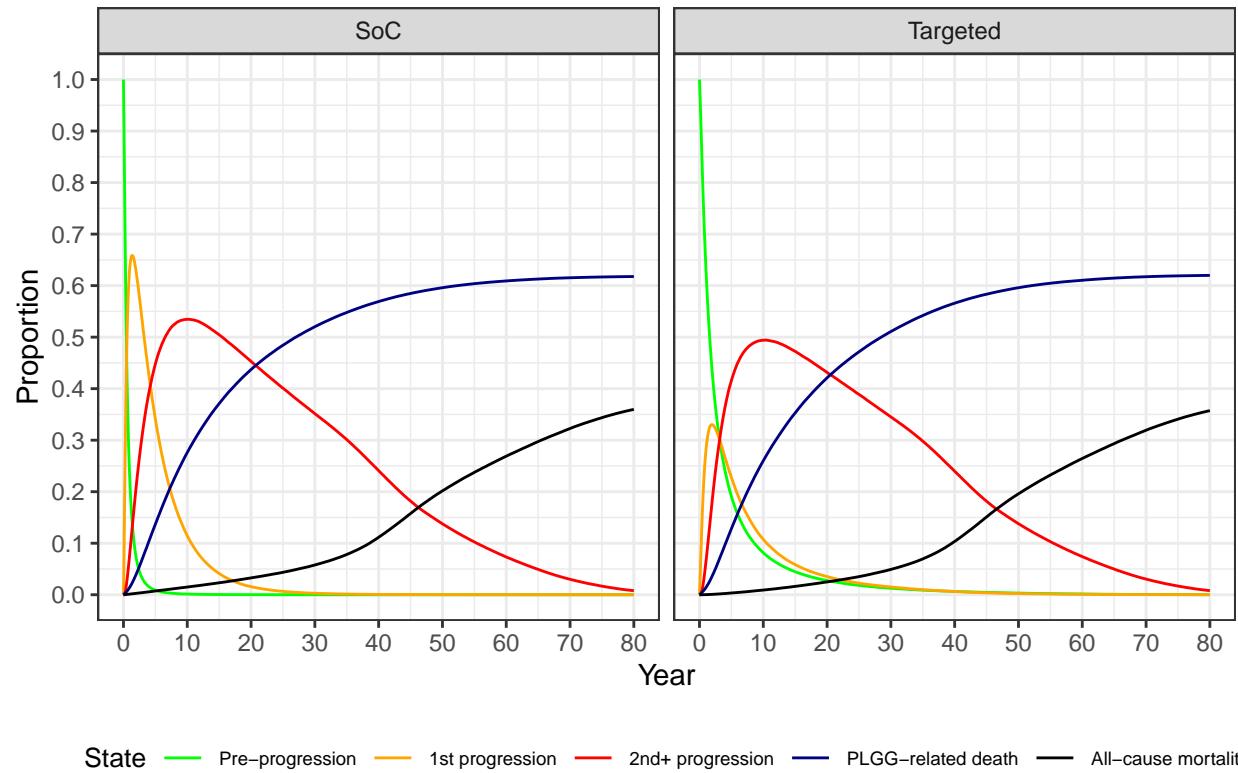
Progression-Free Survival with 95% CI



Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

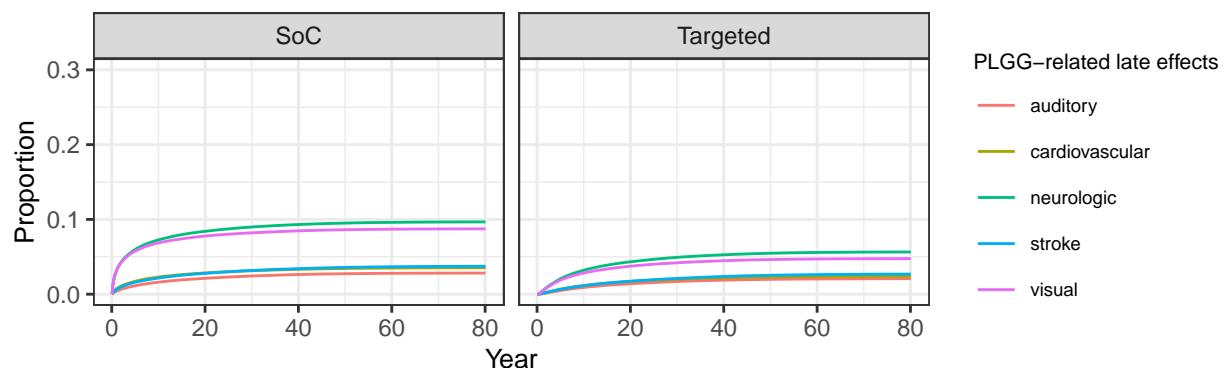
Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	13.32 (9.59;17.27)	12.36 (7.65;16.39)	0.96 (0.16;1.79)
Total Cost	\$931,831 (\$732,521;\$1,126,724)	\$395,495 (\$365,854;\$423,395)	\$536,336 (\$358,220;\$723,332)
Non-Targeted PLGG related costs	\$224,818 (\$163,015;\$278,995)	\$262,516 (\$200,713;\$317,931)	\$-37,698 (\$-50,858;\$-24,969)
Late effect costs	\$83,572 (\$34,209;\$167,168)	\$99,863 (\$34,492;\$182,812)	\$-16,291 (\$-25,665;\$-7,532)
General population costs	\$40,529 (\$20,474;\$65,164)	\$33,116 (\$13,362;\$56,145)	\$7,413 (\$4,170;\$11,552)
Targeted costs	\$582,913 (\$405,815;\$768,717)	\$0 (\$0;\$0)	\$582,913 (\$405,815;\$768,717)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

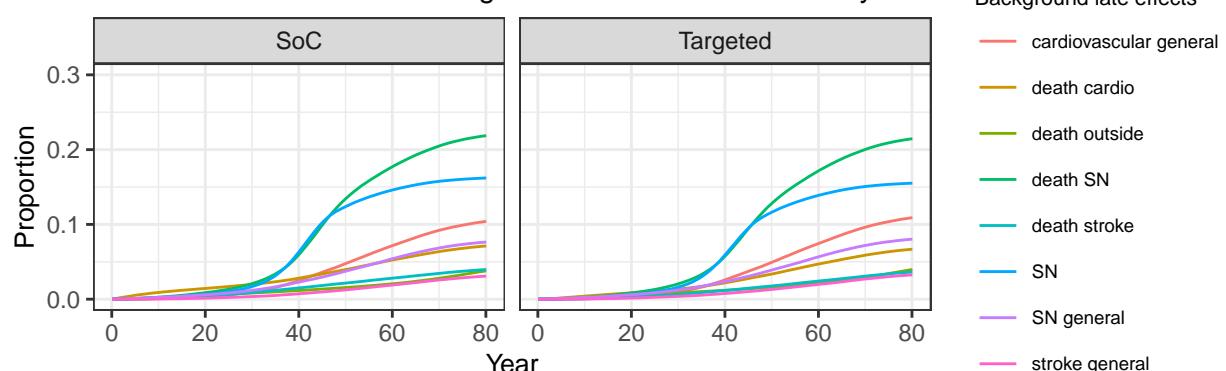


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

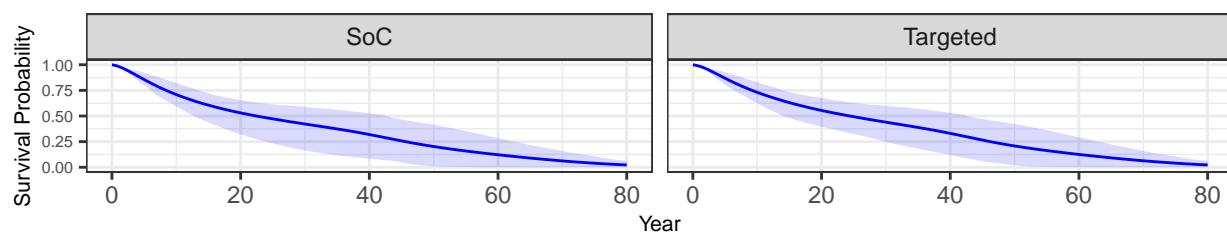
Cumulative Incidence of PLGG-related Late Effects Across Cycles



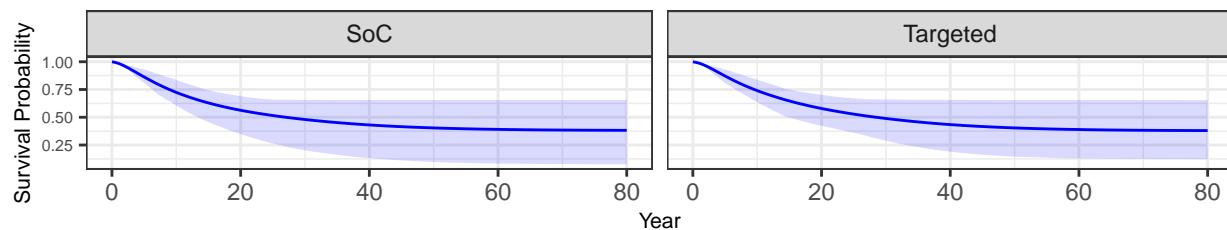
Cumulative Incidence of Background Late Effects Across Cycles



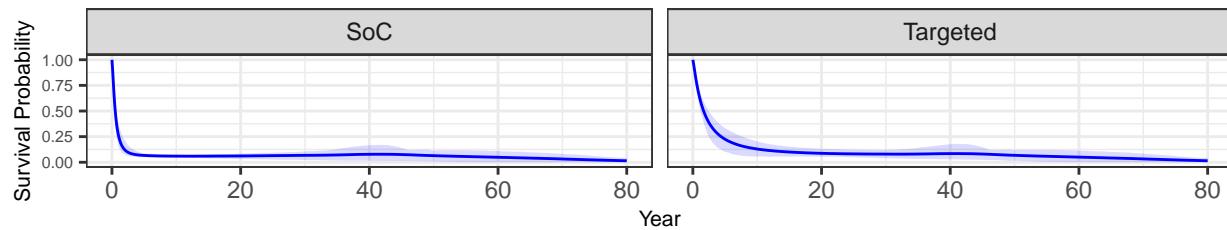
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



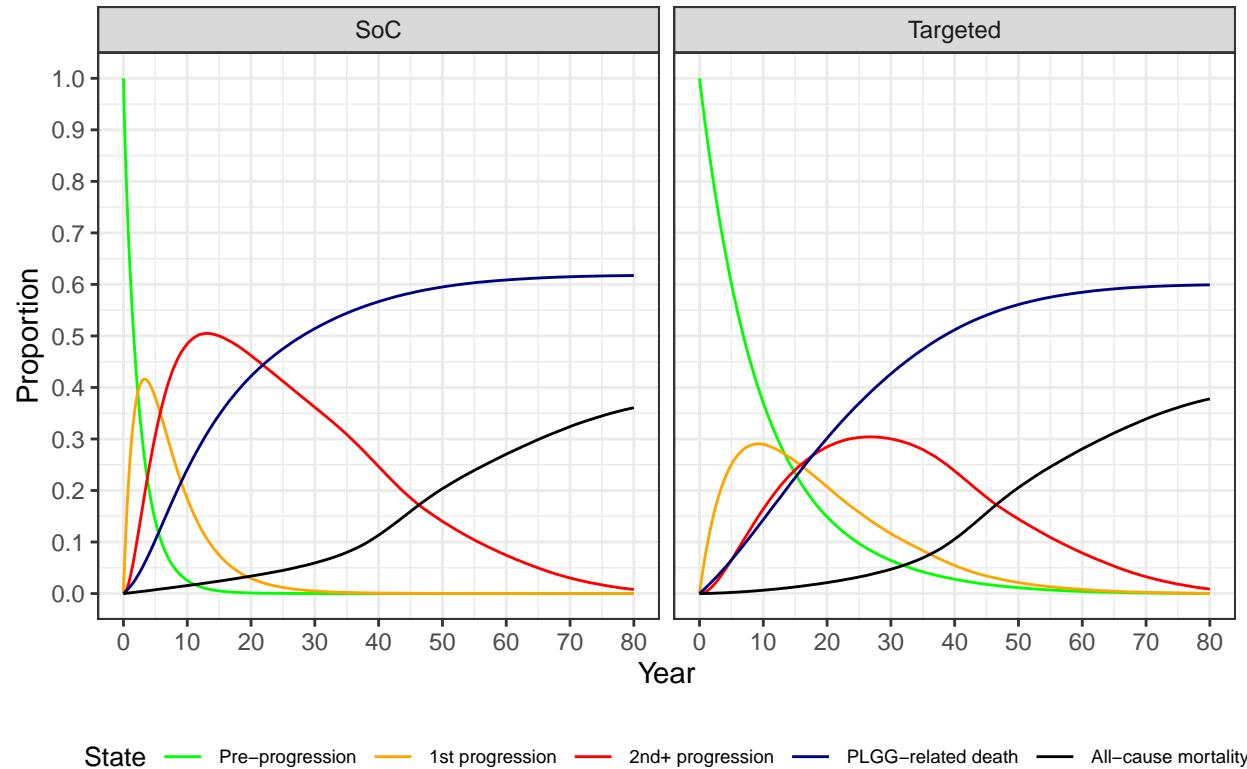
Scenario #1e

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 1.5
- **Data source for controls: n=34 SickKids controls**
- **Data source for exposed: Investigator assessment - Bouffet et al., NEJM 2023.**
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

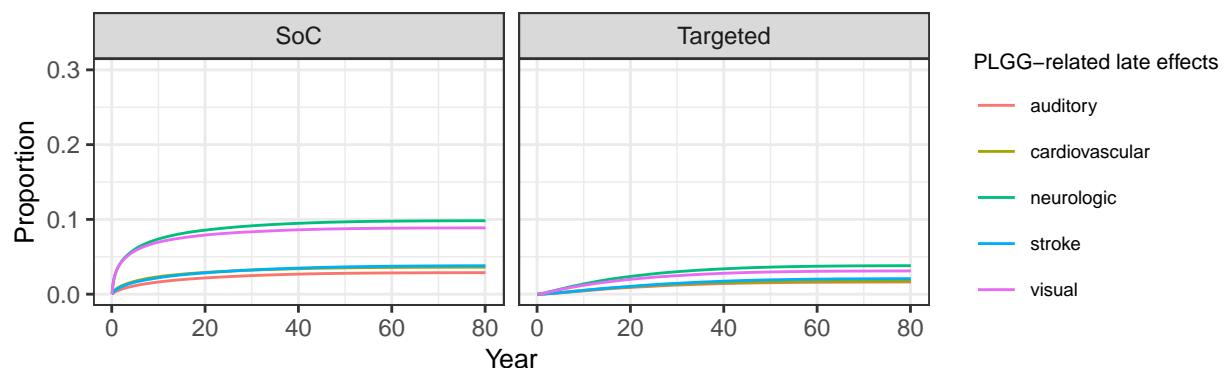
Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.17 (18.71;37.96)	4.54 (0.07;13.37)
QALY	15.6 (11.99;19.4)	12.61 (8.3;16.24)	2.98 (0.91;7.13)
Total Cost	\$2,975,092 (\$2,340,408;\$3,588,480)	\$394,517 (\$368,238;\$419,239)	\$2,580,574 (\$1,954,625;\$3,199,583)
Non-Targeted PLGG related costs	\$176,369 (\$114,324;\$227,184)	\$260,478 (\$202,621;\$318,205)	\$-84,110 (\$-128,106;\$-55,049)
Late effect costs	\$78,352 (\$39,526;\$141,805)	\$100,564 (\$36,947;\$180,699)	\$-22,212 (\$-41,746;\$5,551)
General population costs	\$52,085 (\$28,857;\$75,880)	\$33,475 (\$14,717;\$54,983)	\$18,611 (\$9,163;\$39,329)
Targeted costs	\$2,668,286 (\$2,020,708;\$3,291,327)	\$0 (\$0;\$0)	\$2,668,286 (\$2,020,708;\$3,291,327)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

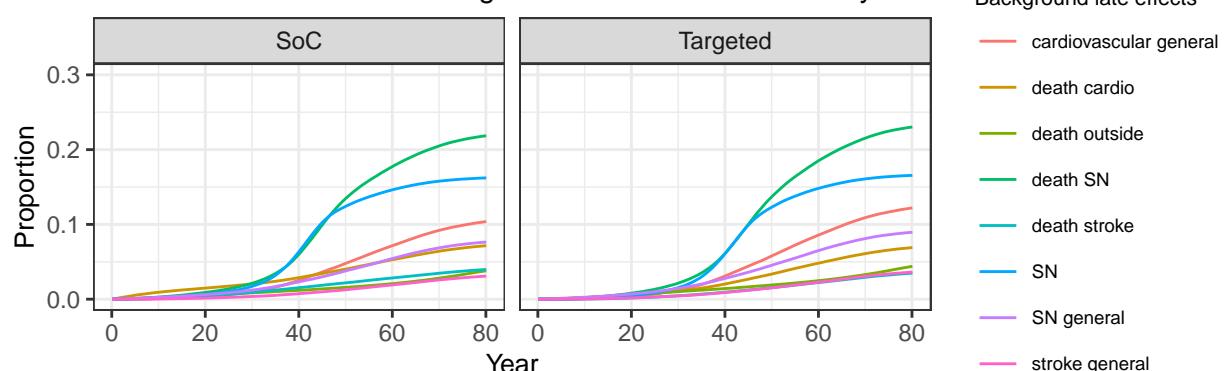
Trace Plot of PLGG States Across Cycles



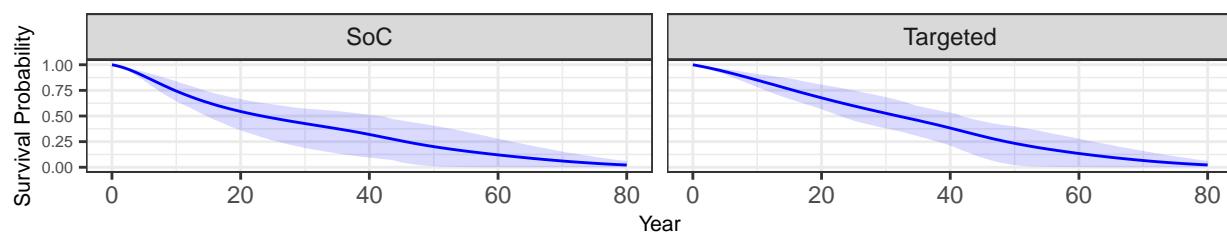
Cumulative Incidence of PLGG-related Late Effects Across Cycles



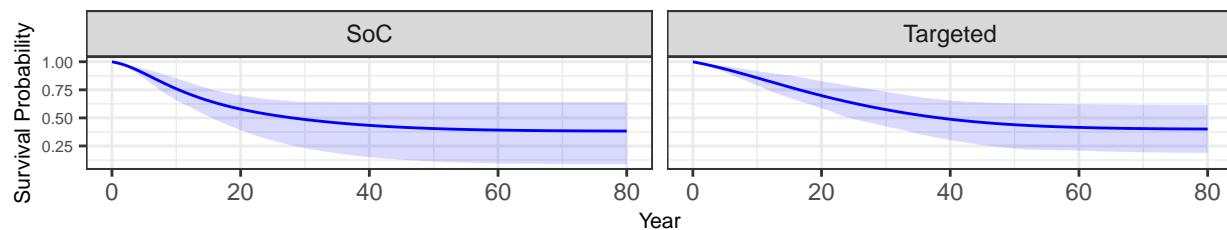
Cumulative Incidence of Background Late Effects Across Cycles



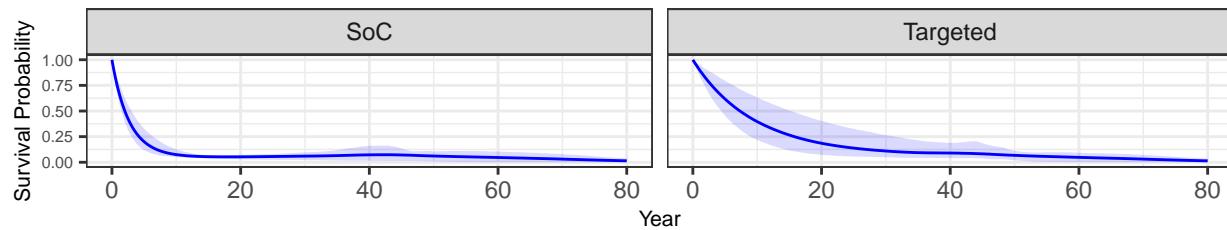
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



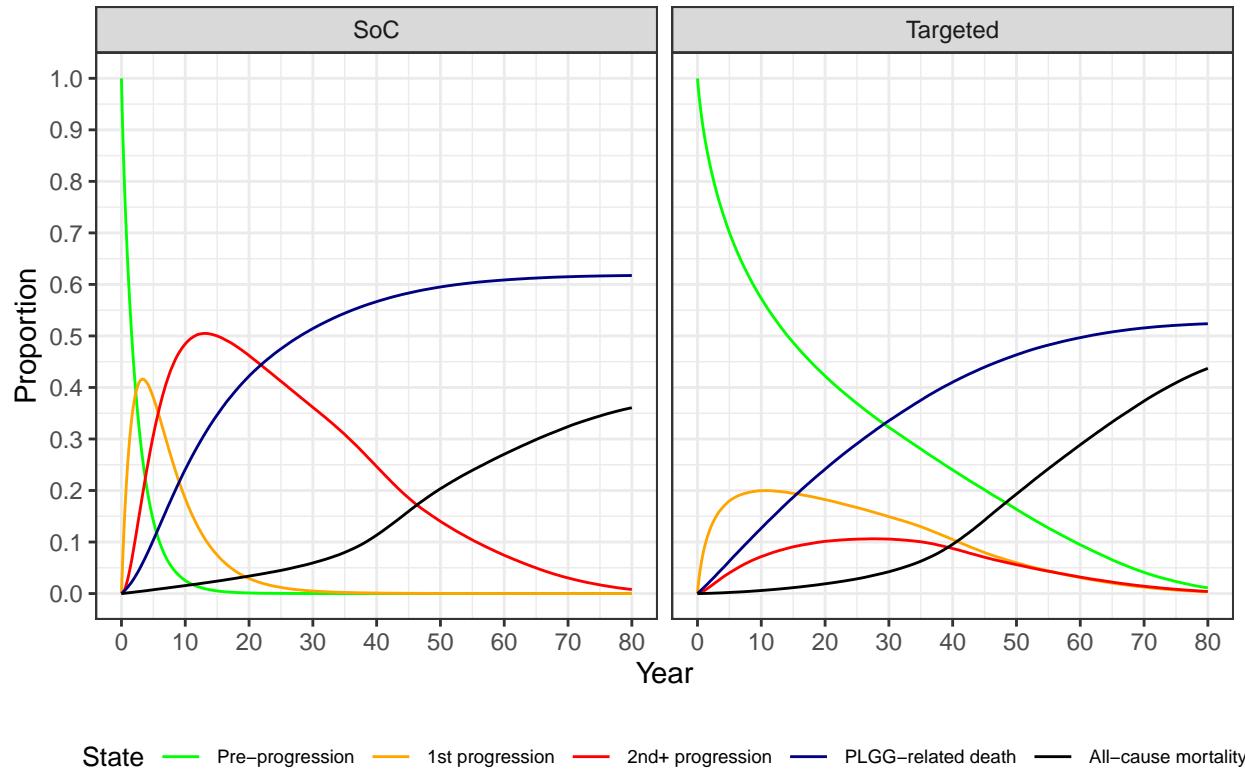
Progression–Free Survival with 95% CI



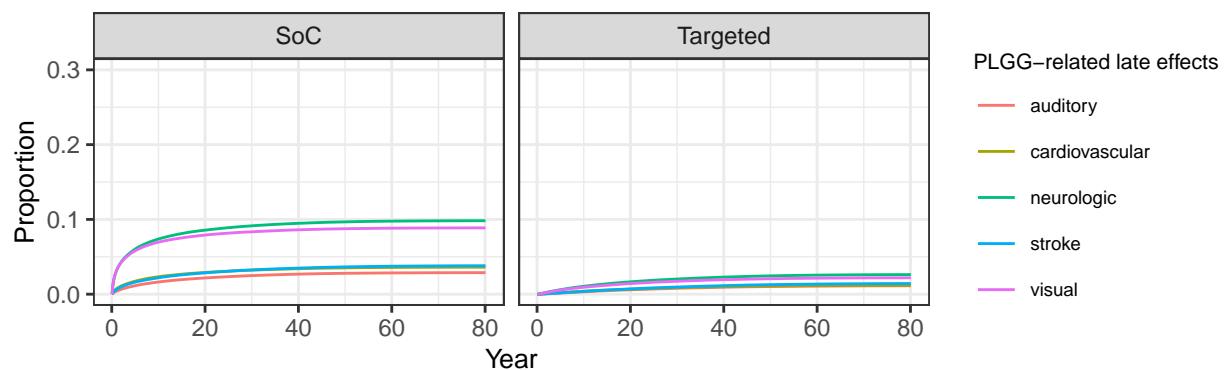
Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.17 (18.71;37.96)	9.85 (1.25;22.84)
QALY	18.19 (14.87;21.42)	12.61 (8.3;16.24)	5.57 (2.01;11.48)
Total Cost	\$3,386,662 (\$2,817,571;\$3,939,055)	\$394,517 (\$368,238;\$419,239)	\$2,992,145 (\$2,425,426;\$3,537,320)
Non-Targeted PLGG related costs	\$144,919 (\$105,692;\$186,333)	\$260,478 (\$202,621;\$318,205)	\$-115,560 (\$-184,344;\$-61,696)
Late effect costs	\$80,050 (\$51,100;\$120,690)	\$100,564 (\$36,947;\$180,699)	\$-20,514 (\$-66,141;\$24,596)
General population costs	\$69,909 (\$46,483;\$93,955)	\$33,475 (\$14,717;\$54,983)	\$36,434 (\$19,026;\$64,304)
Targeted costs	\$3,091,785 (\$2,519,167;\$3,651,217)	\$0 (\$0;\$0)	\$3,091,785 (\$2,519,167;\$3,651,217)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

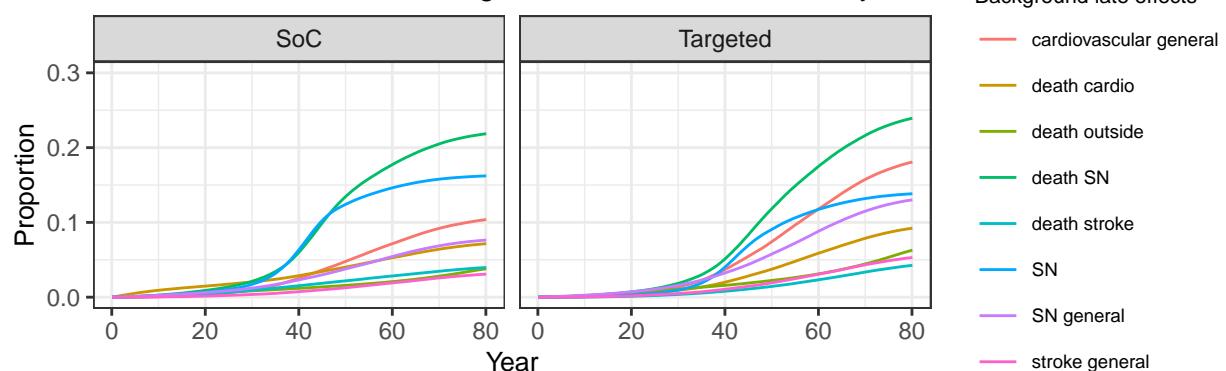
Trace Plot of PLGG States Across Cycles

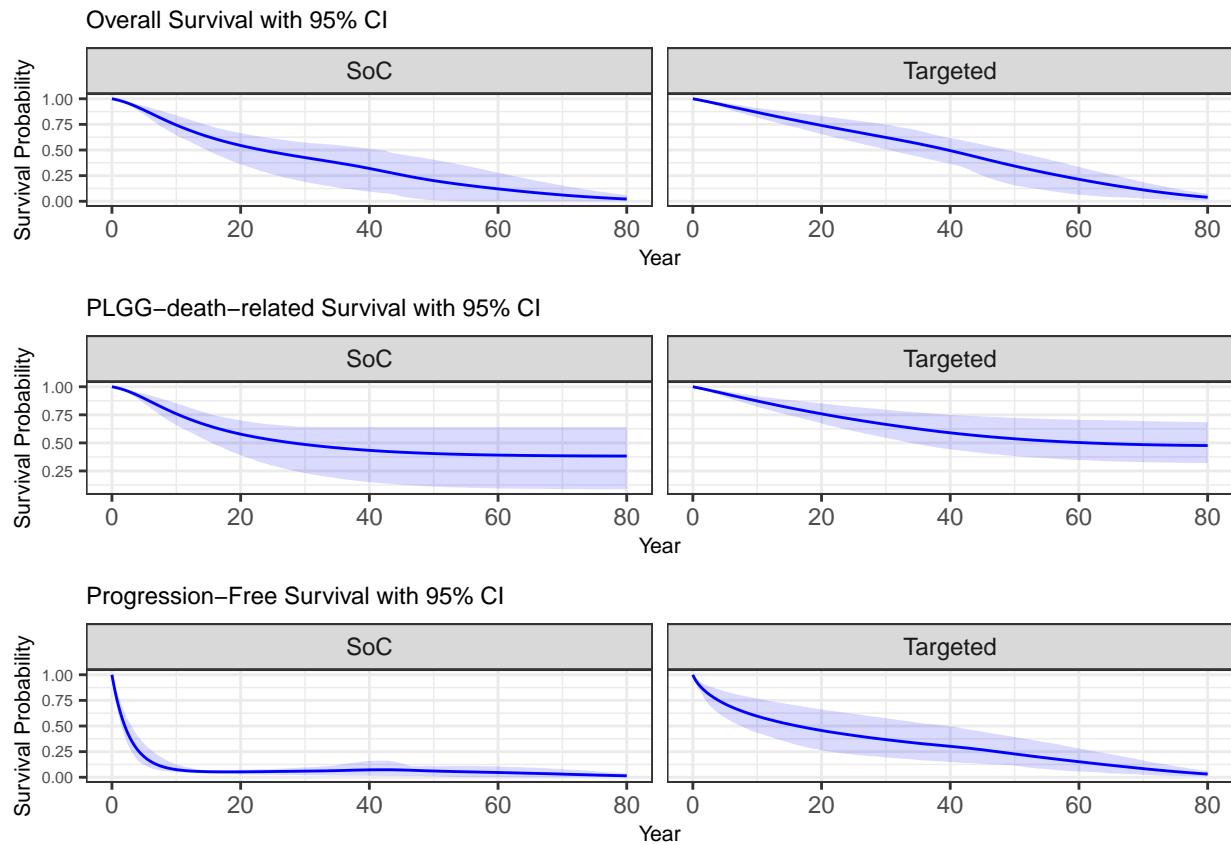


Cumulative Incidence of PLGG-related Late Effects Across Cycles



Cumulative Incidence of Background Late Effects Across Cycles





0% discount rate

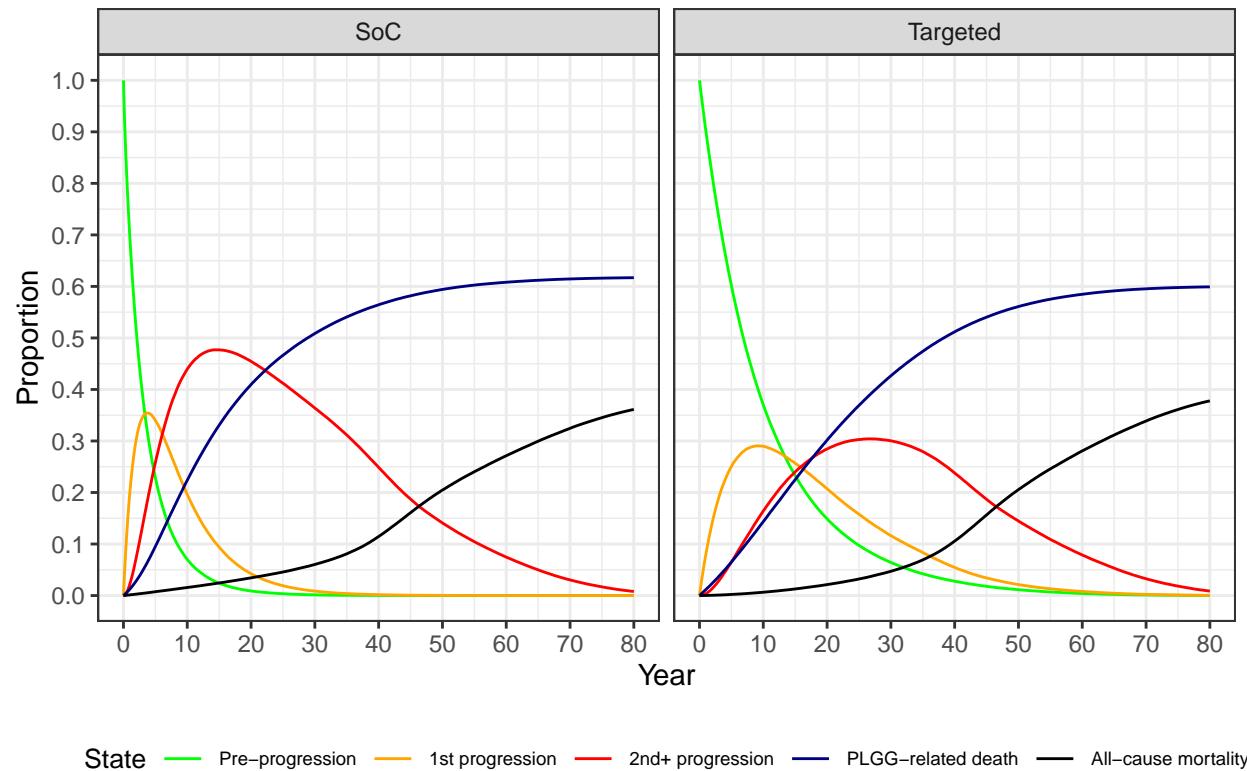
Scenario #1a

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 0
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

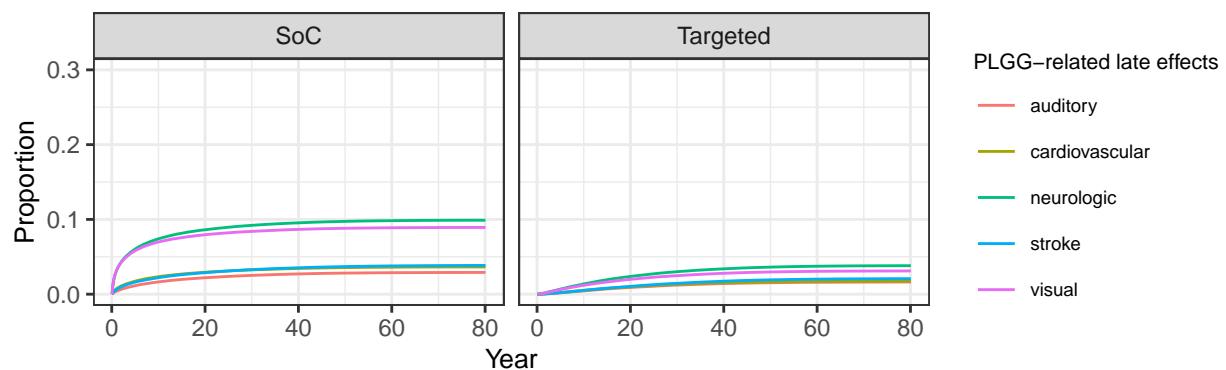
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	26.77 (20.58;33.3)	21.9 (15.31;27.6)	4.87 (1.63;11.18)
Total Cost	\$5,106,341 (\$4,016,915;\$6,159,355)	\$669,031 (\$618,470;\$713,864)	\$4,437,310 (\$3,359,156;\$5,499,069)
Non-Targeted PLGG related costs	\$302,455 (\$195,734;\$389,915)	\$437,804 (\$344,779;\$532,700)	\$-135,349 (\$-201,858;\$-83,310)
Late effect costs	\$134,485 (\$67,848;\$243,360)	\$173,329 (\$69,038;\$304,887)	\$-38,844 (\$-65,377;\$4,732)
General population costs	\$89,405 (\$49,536;\$130,247)	\$57,898 (\$26,185;\$93,891)	\$31,507 (\$15,887;\$63,026)
Targeted costs	\$4,579,996 (\$3,468,505;\$5,649,507)	\$0 (\$0;\$0)	\$4,579,996 (\$3,468,505;\$5,649,507)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

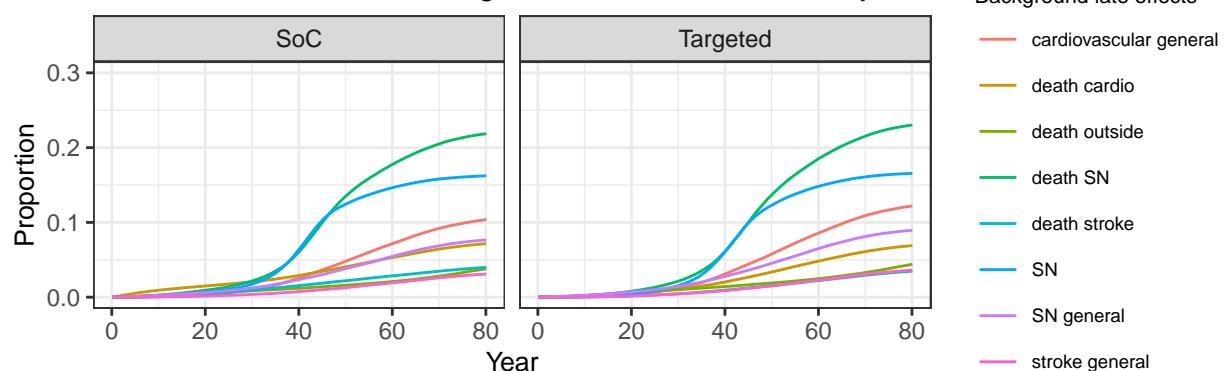
Trace Plot of PLGG States Across Cycles



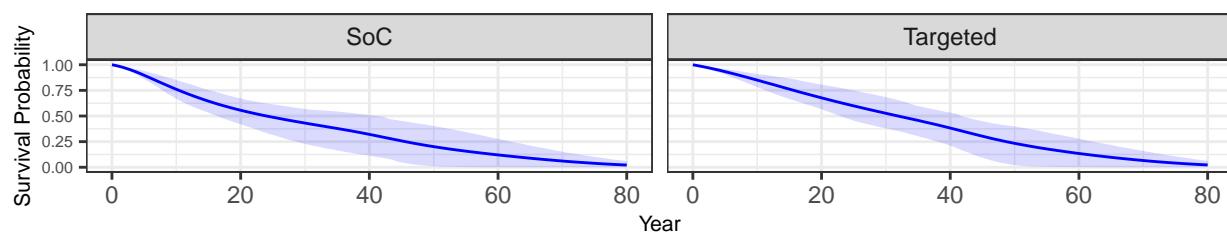
Cumulative Incidence of PLGG-related Late Effects Across Cycles



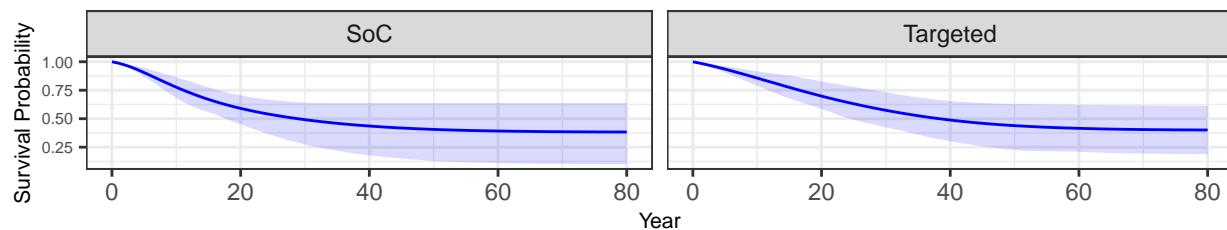
Cumulative Incidence of Background Late Effects Across Cycles



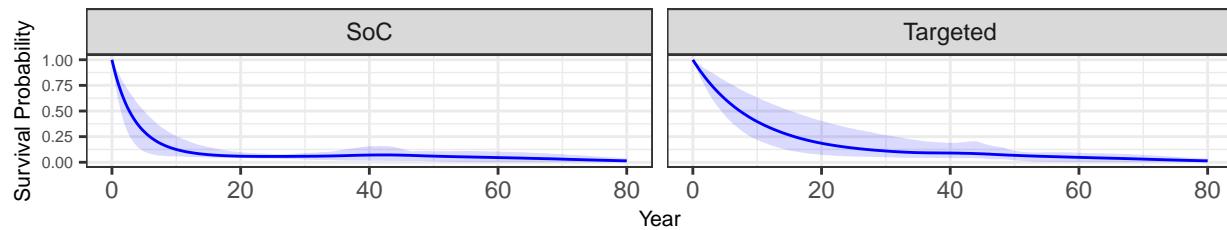
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



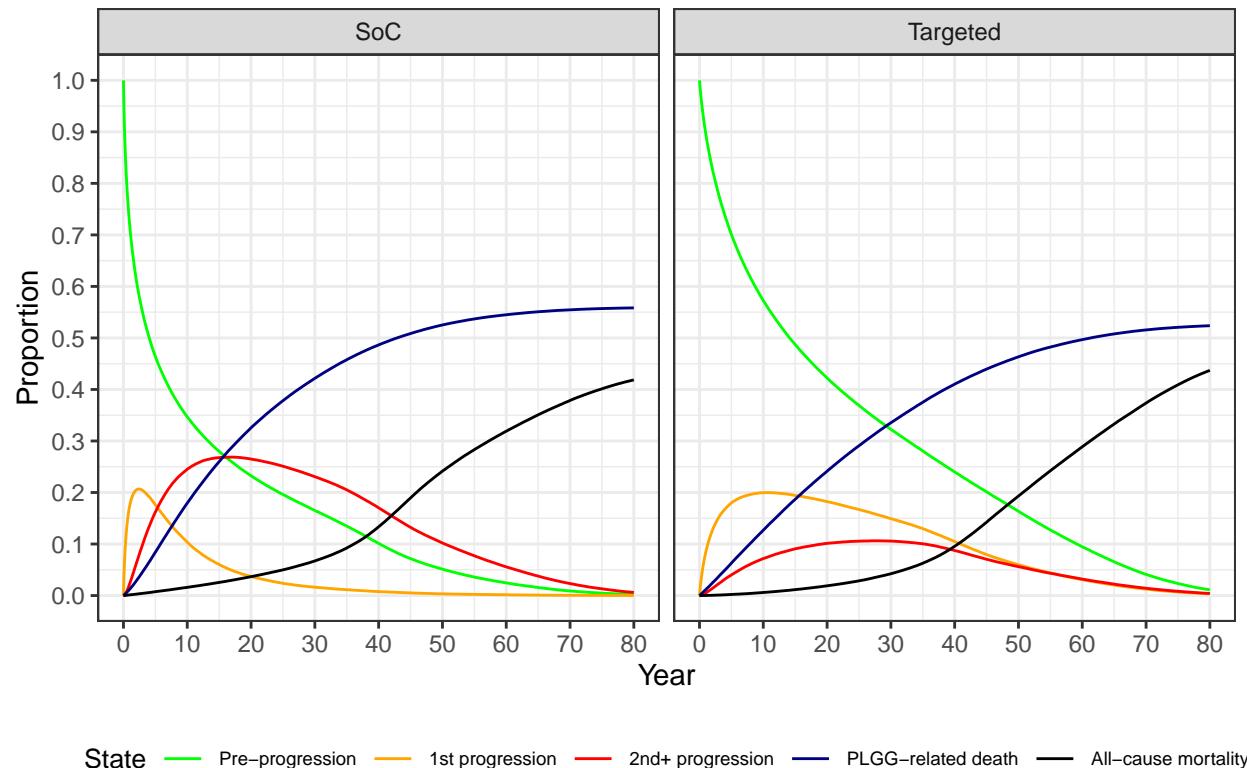
Progression-Free Survival with 95% CI



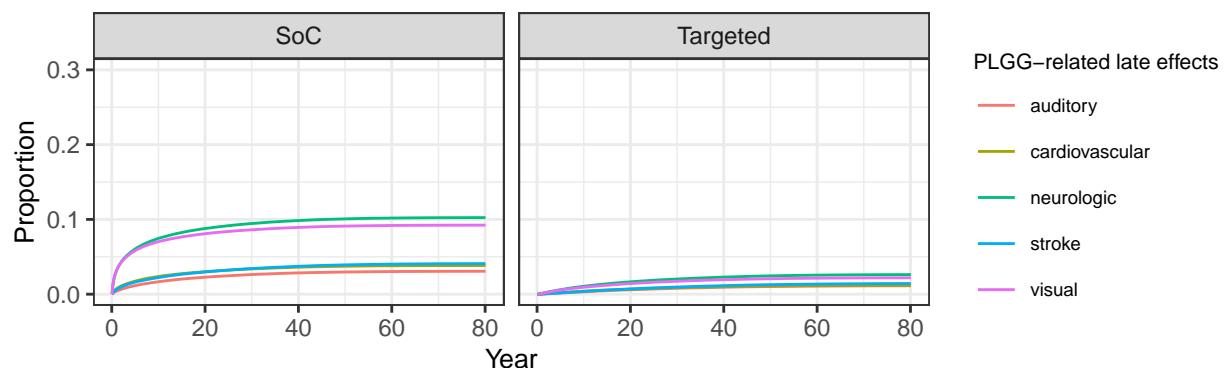
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	31.22 (25.52;36.76)	24.16 (19.35;28.94)	7.06 (2.14;14.24)
Total Cost	\$5,812,759 (\$4,835,804;\$6,761,060)	\$637,609 (\$607,693;\$673,120)	\$5,175,150 (\$4,201,454;\$6,098,632)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$374,113 (\$276,566;\$445,286)	\$-125,666 (\$-223,245;\$-55,768)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$197,787 (\$128,966;\$317,691)	\$-60,384 (\$-109,682;\$-13,918)
General population costs	\$119,998 (\$79,788;\$161,275)	\$65,708 (\$35,900;\$101,890)	\$54,290 (\$24,285;\$96,138)
Targeted costs	\$5,306,910 (\$4,323,989;\$6,267,205)	\$0 (\$0;\$0)	\$5,306,910 (\$4,323,989;\$6,267,205)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

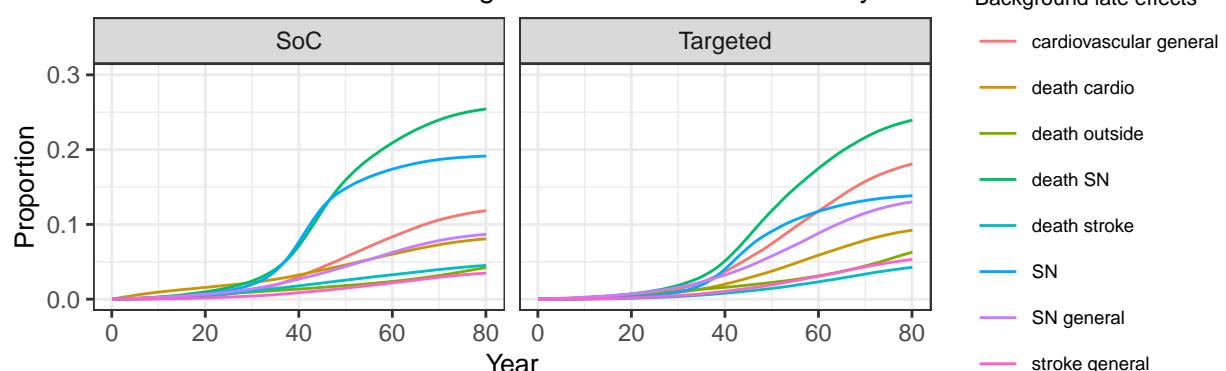
Trace Plot of PLGG States Across Cycles



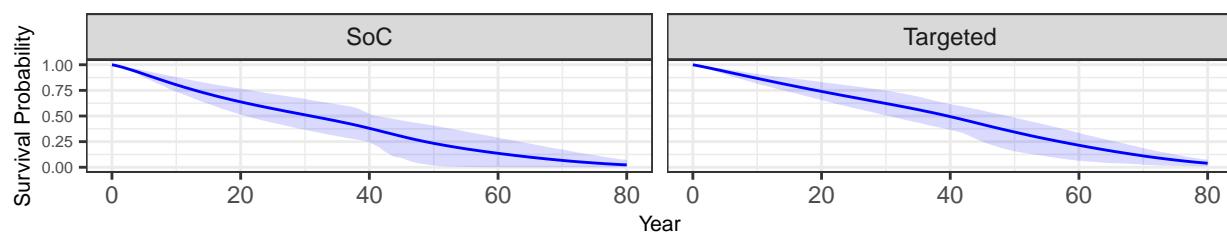
Cumulative Incidence of PLGG-related Late Effects Across Cycles



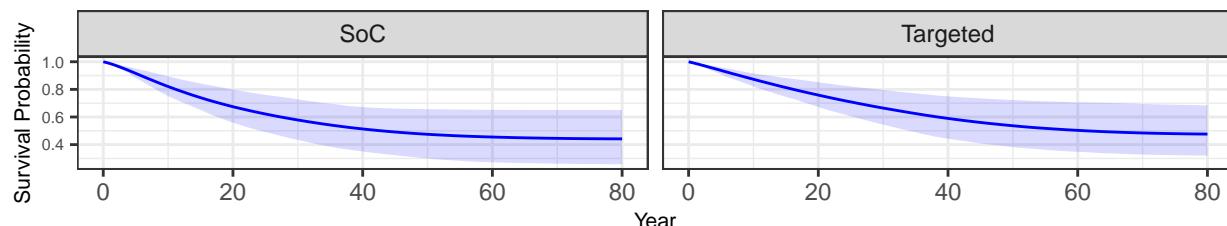
Cumulative Incidence of Background Late Effects Across Cycles



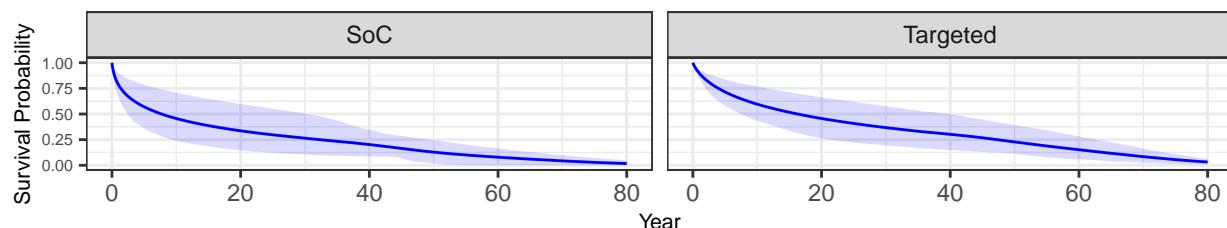
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



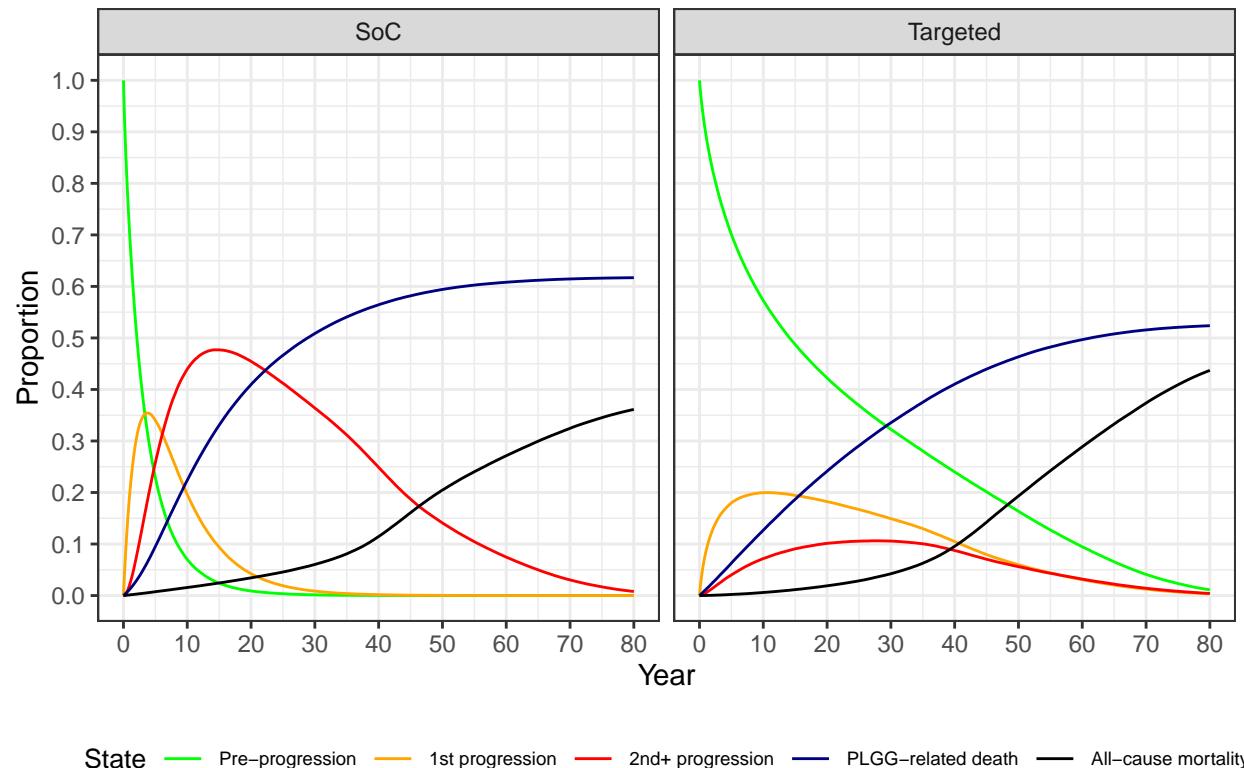
Progression-Free Survival with 95% CI



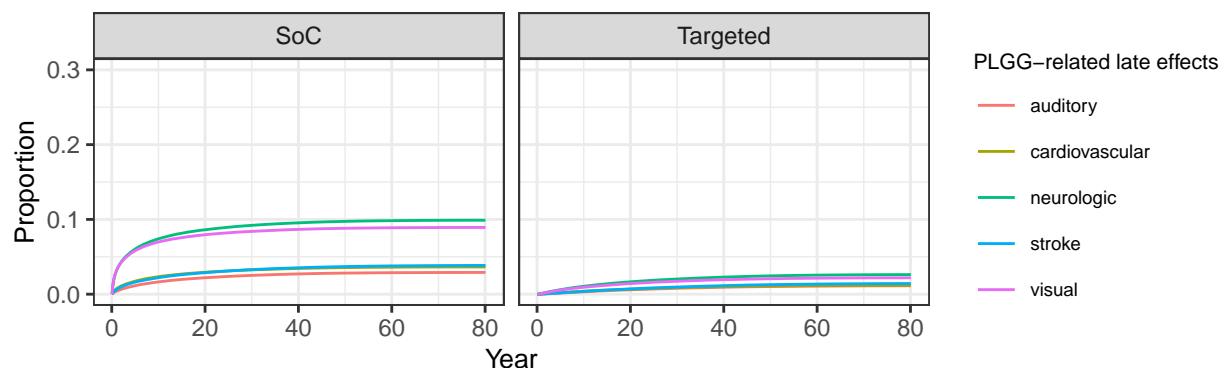
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	31.22 (25.52;36.76)	21.9 (15.31;27.6)	9.32 (3.51;18.86)
Total Cost	\$5,812,759 (\$4,835,804;\$6,761,060)	\$669,031 (\$618,470;\$713,864)	\$5,143,728 (\$4,177,189;\$6,097,283)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$437,804 (\$344,779;\$532,700)	\$-189,357 (\$-308,775;\$-96,462)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$173,329 (\$69,038;\$304,887)	\$-35,925 (\$-106,871;\$41,692)
General population costs	\$119,998 (\$79,788;\$161,275)	\$57,898 (\$26,185;\$93,891)	\$62,100 (\$33,325;\$107,702)
Targeted costs	\$5,306,910 (\$4,323,989;\$6,267,205)	\$0 (\$0;\$0)	\$5,306,910 (\$4,323,989;\$6,267,205)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

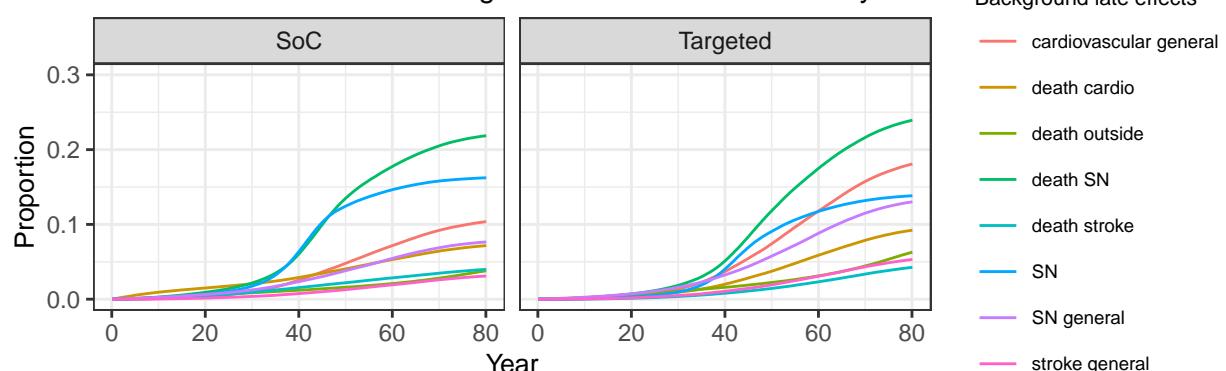
Trace Plot of PLGG States Across Cycles



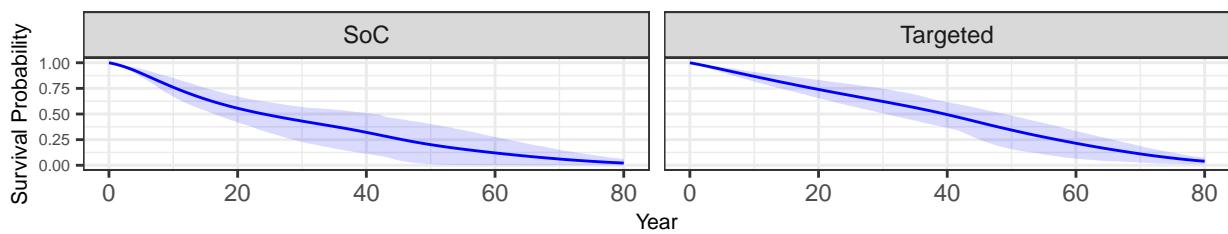
Cumulative Incidence of PLGG-related Late Effects Across Cycles



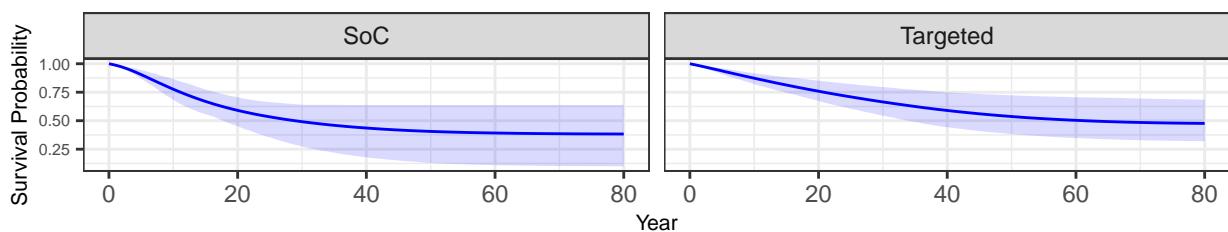
Cumulative Incidence of Background Late Effects Across Cycles



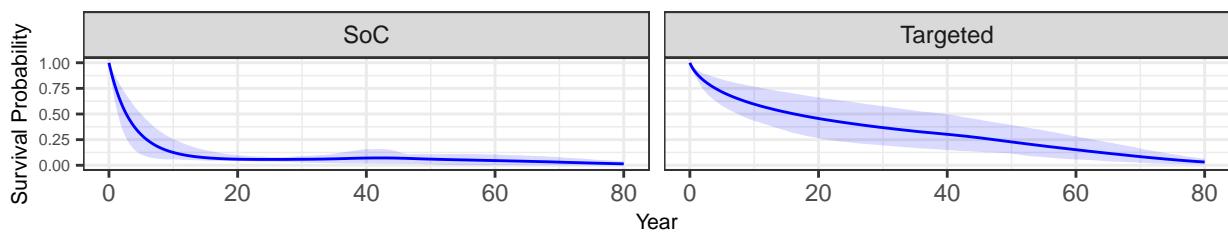
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



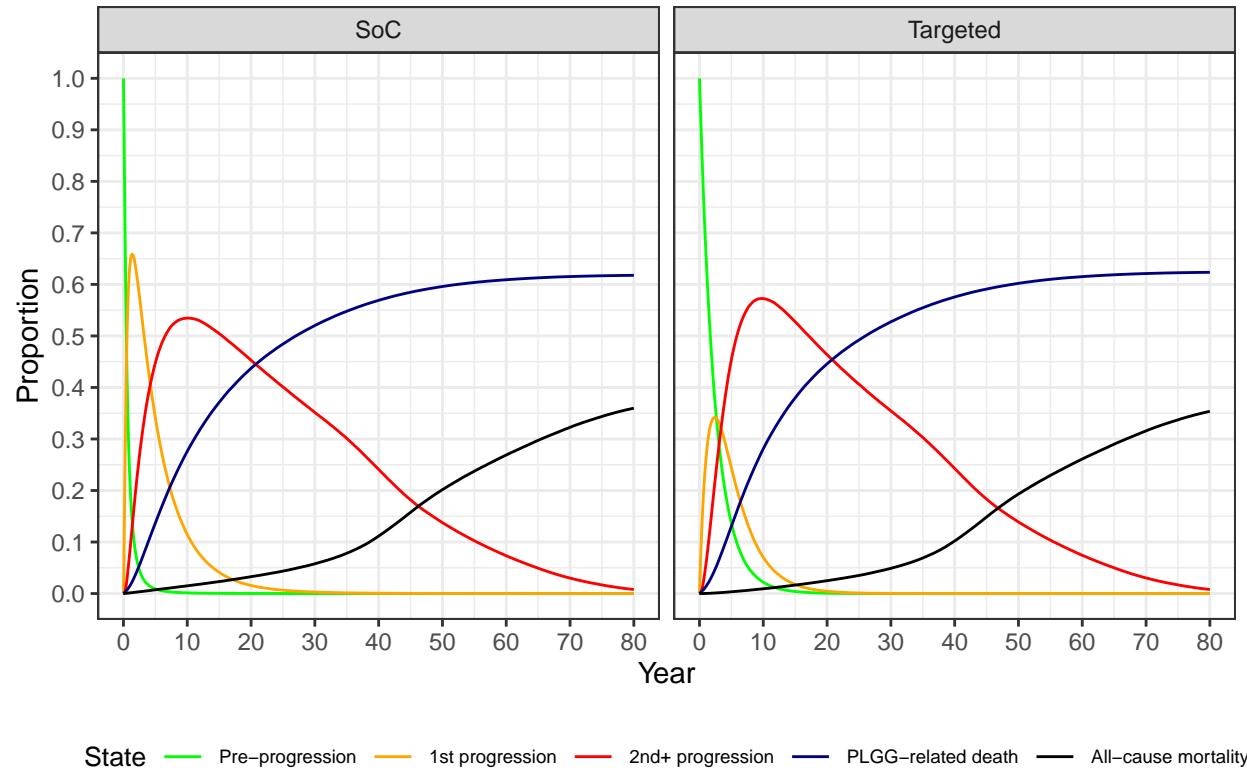
Progression-Free Survival with 95% CI



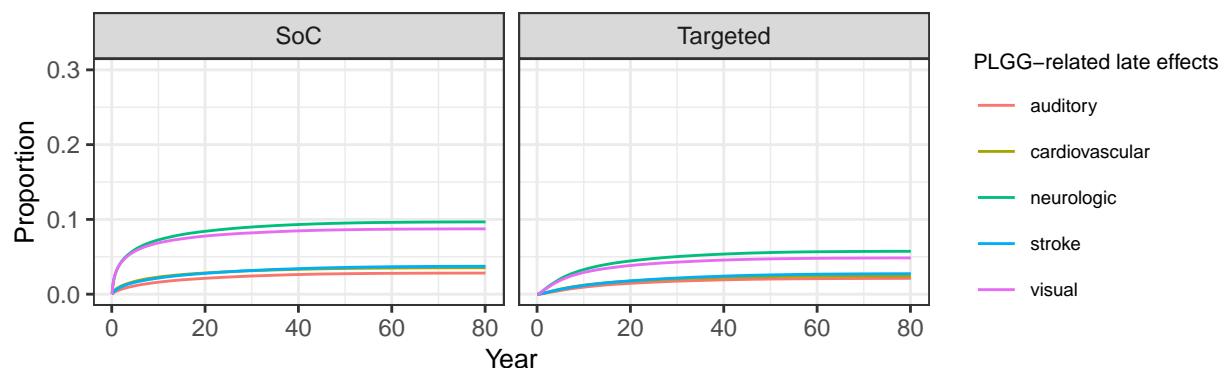
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	22.25 (13.94;29.59)	21.22 (13.13;28.12)	1.03 (-0.36;2.11)
Total Cost	\$4,510,533 (\$2,934,186;\$5,942,613)	\$678,589 (\$627,574;\$726,566)	\$3,831,944 (\$2,312,035;\$5,209,426)
Non-Targeted PLGG related costs	\$397,636 (\$290,330;\$493,089)	\$450,329 (\$344,279;\$545,621)	\$-52,694 (\$-73,926;\$-32,085)
Late effect costs	\$143,101 (\$40,833;\$291,392)	\$171,417 (\$59,221;\$313,821)	\$-28,316 (\$-40,229;\$-17,189)
General population costs	\$66,899 (\$29,702;\$110,339)	\$56,843 (\$22,934;\$96,371)	\$10,056 (\$4,269;\$15,483)
Targeted costs	\$3,902,897 (\$2,373,197;\$5,270,613)	\$0 (\$0;\$0)	\$3,902,897 (\$2,373,197;\$5,270,613)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

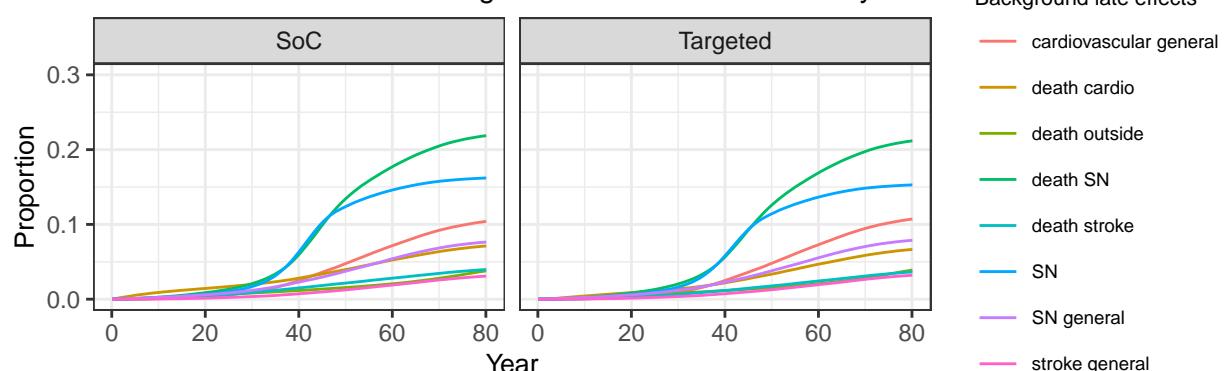
Trace Plot of PLGG States Across Cycles



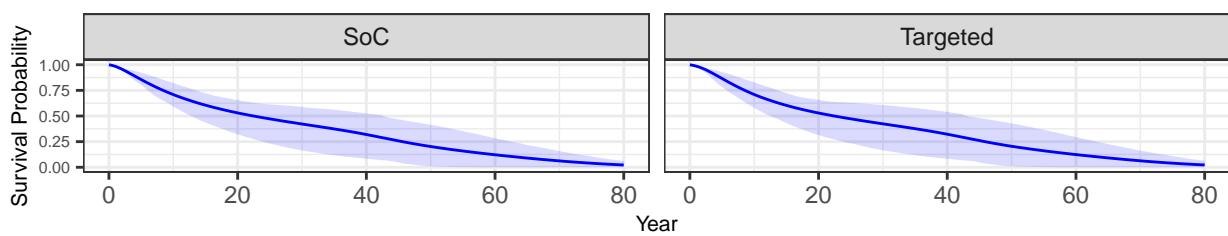
Cumulative Incidence of PLGG-related Late Effects Across Cycles



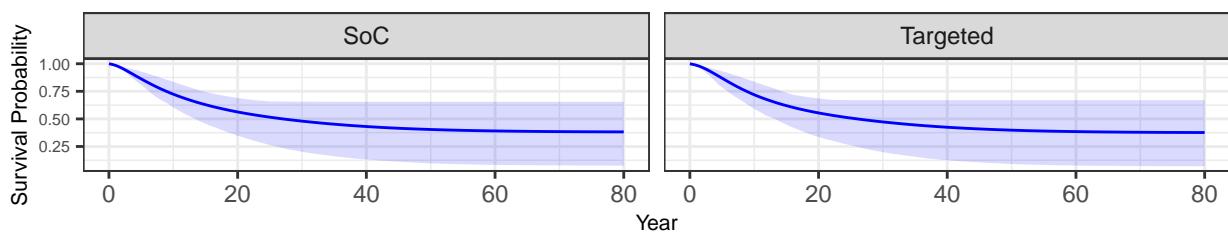
Cumulative Incidence of Background Late Effects Across Cycles



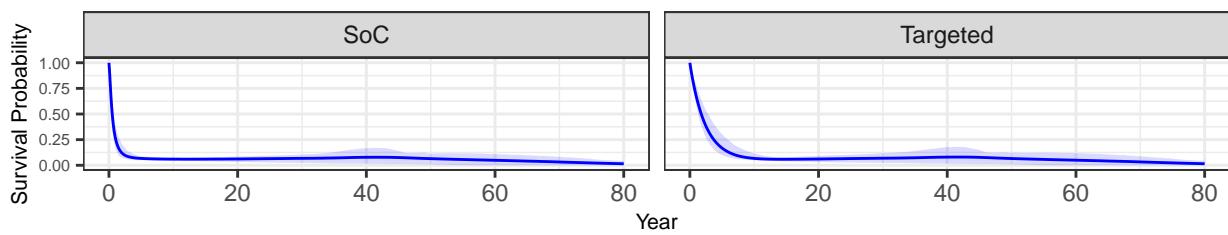
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



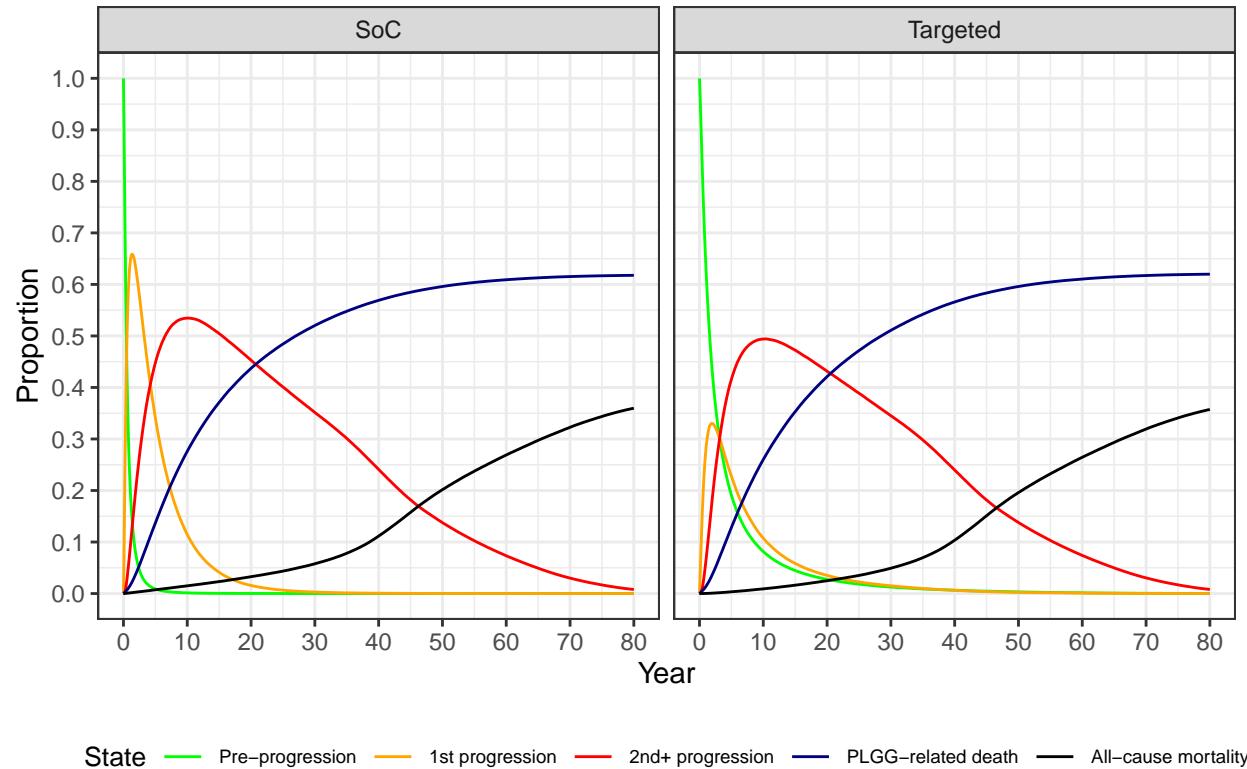
Progression-Free Survival with 95% CI



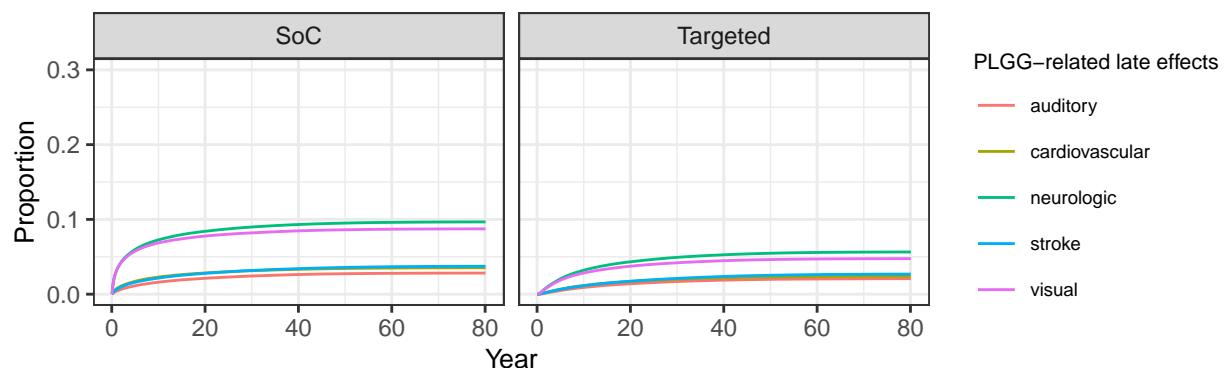
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	22.86 (16.46;29.65)	21.22 (13.13;28.12)	1.64 (0.27;3.07)
Total Cost	\$4,600,785 (\$3,362,679;\$5,896,224)	\$678,589 (\$627,574;\$726,566)	\$3,922,196 (\$2,704,607;\$5,198,823)
Non-Targeted PLGG related costs	\$385,605 (\$279,517;\$478,811)	\$450,329 (\$344,279;\$545,621)	\$-64,724 (\$-87,273;\$-42,861)
Late effect costs	\$143,450 (\$58,686;\$286,967)	\$171,417 (\$59,221;\$313,821)	\$-27,967 (\$-44,034;\$-12,929)
General population costs	\$69,568 (\$35,144;\$111,852)	\$56,843 (\$22,934;\$96,371)	\$12,725 (\$7,158;\$19,831)
Targeted costs	\$4,002,162 (\$2,786,233;\$5,277,880)	\$0 (\$0;\$0)	\$4,002,162 (\$2,786,233;\$5,277,880)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

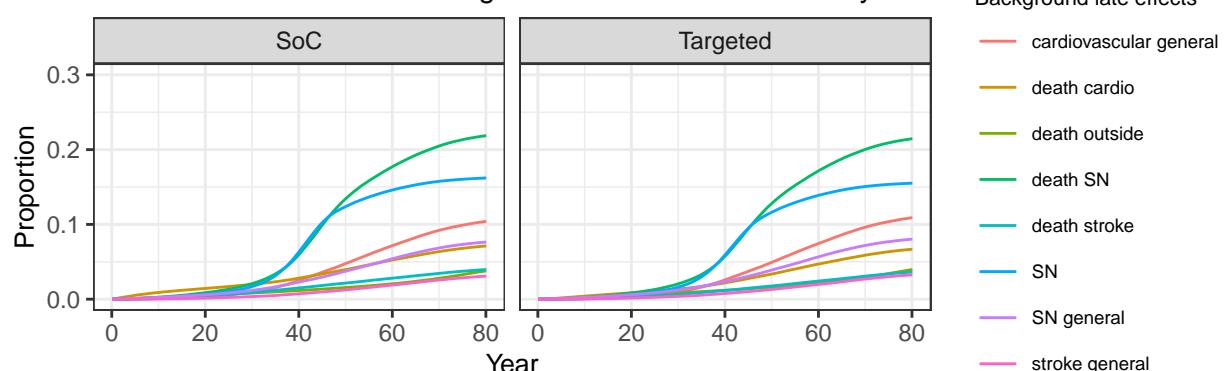
Trace Plot of PLGG States Across Cycles



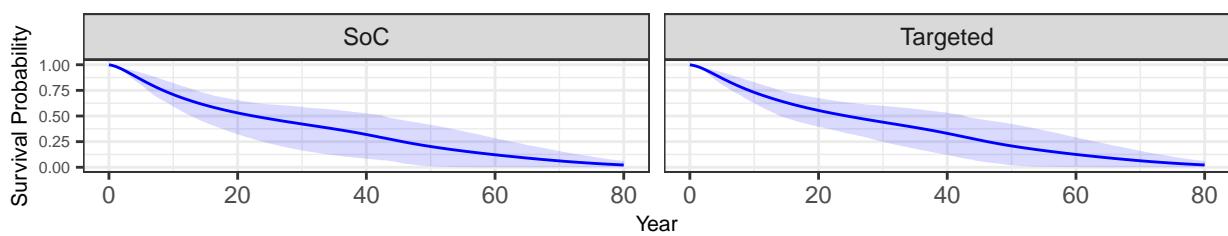
Cumulative Incidence of PLGG-related Late Effects Across Cycles



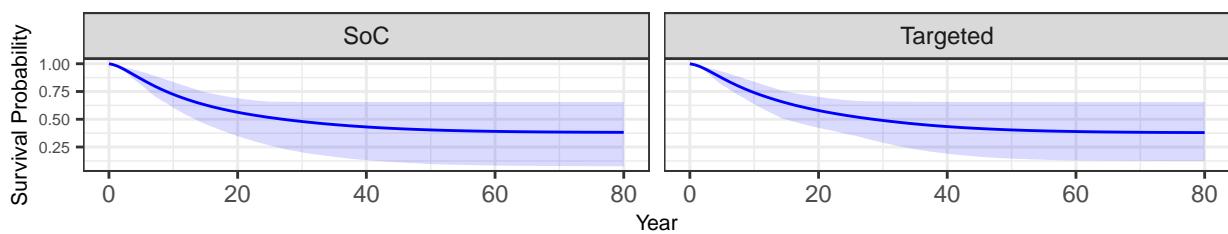
Cumulative Incidence of Background Late Effects Across Cycles



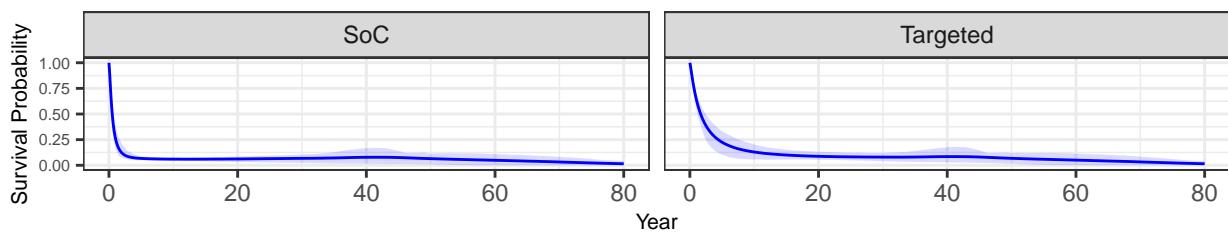
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



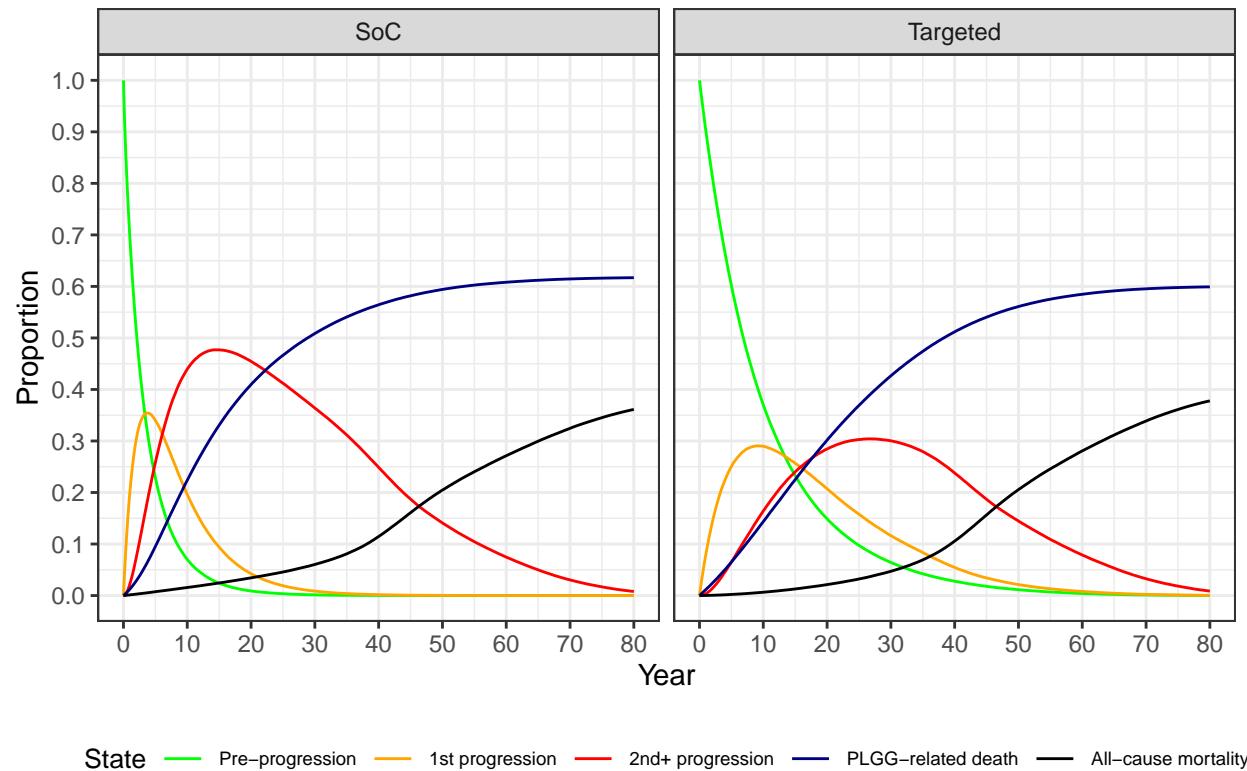
Scenario #1c

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **50% combo price reduction**
- Discount rate: 0
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

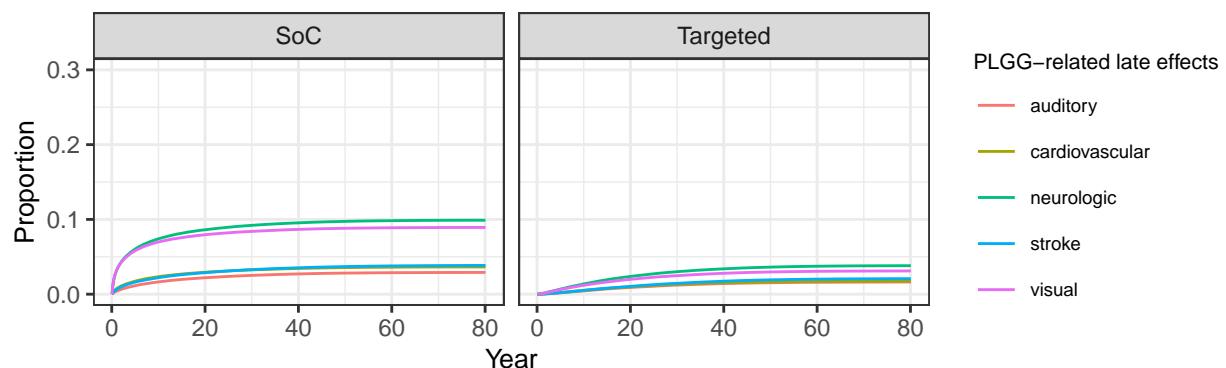
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	26.77 (20.58;33.3)	21.9 (15.31;27.6)	4.87 (1.63;11.18)
Total Cost	\$2,816,343 (\$2,279,227;\$3,334,602)	\$669,031 (\$618,470;\$713,864)	\$2,147,312 (\$1,611,117;\$2,668,122)
Non-Targeted PLGG related costs	\$302,455 (\$195,734;\$389,915)	\$437,804 (\$344,779;\$532,700)	\$-135,349 (\$-201,858;\$-83,310)
Late effect costs	\$134,485 (\$67,848;\$243,360)	\$173,329 (\$69,038;\$304,887)	\$-38,844 (\$-65,377;\$4,732)
General population costs	\$89,405 (\$49,536;\$130,247)	\$57,898 (\$26,185;\$93,891)	\$31,507 (\$15,887;\$63,026)
Targeted costs	\$2,289,998 (\$1,734,252;\$2,824,753)	\$0 (\$0;\$0)	\$2,289,998 (\$1,734,252;\$2,824,753)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

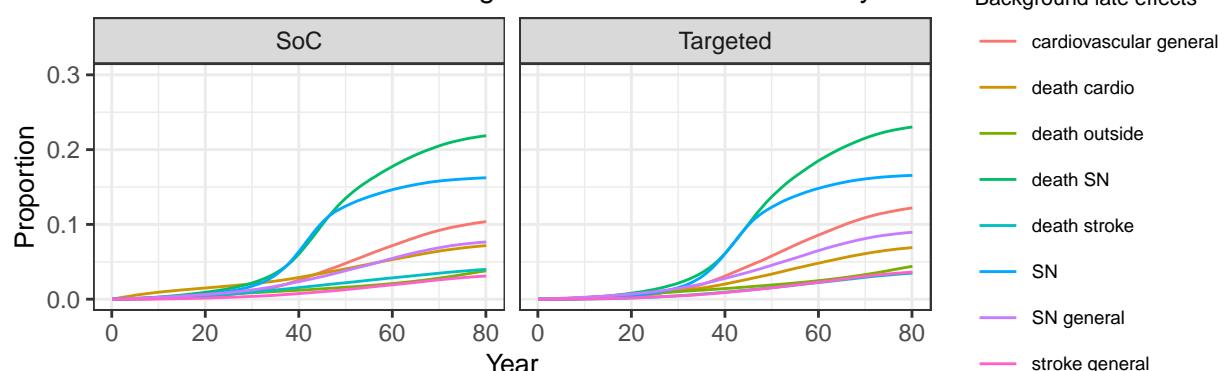
Trace Plot of PLGG States Across Cycles



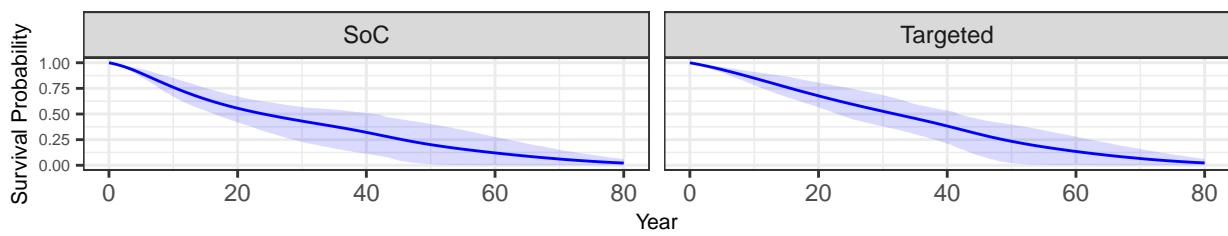
Cumulative Incidence of PLGG-related Late Effects Across Cycles



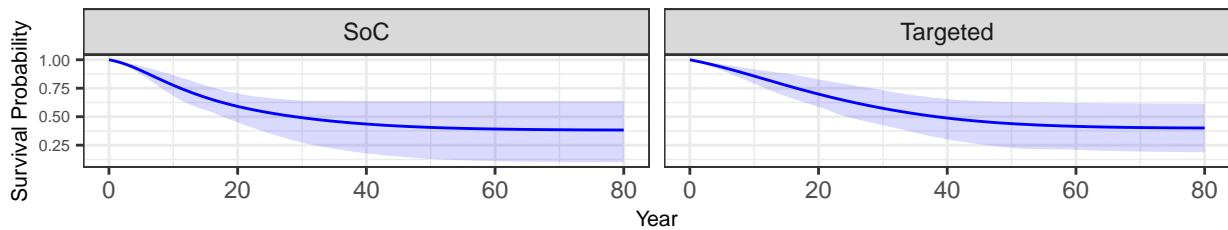
Cumulative Incidence of Background Late Effects Across Cycles



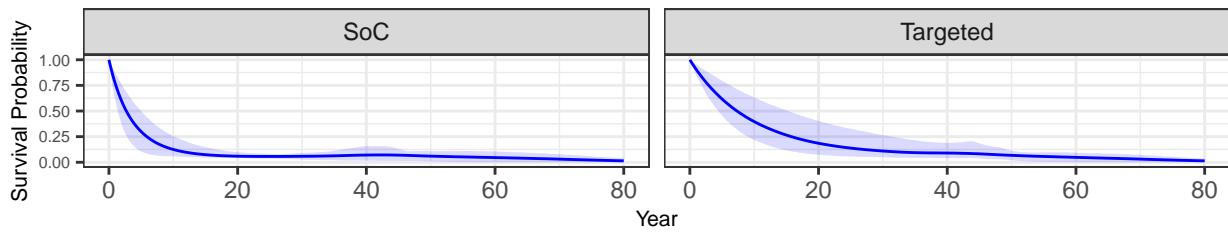
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



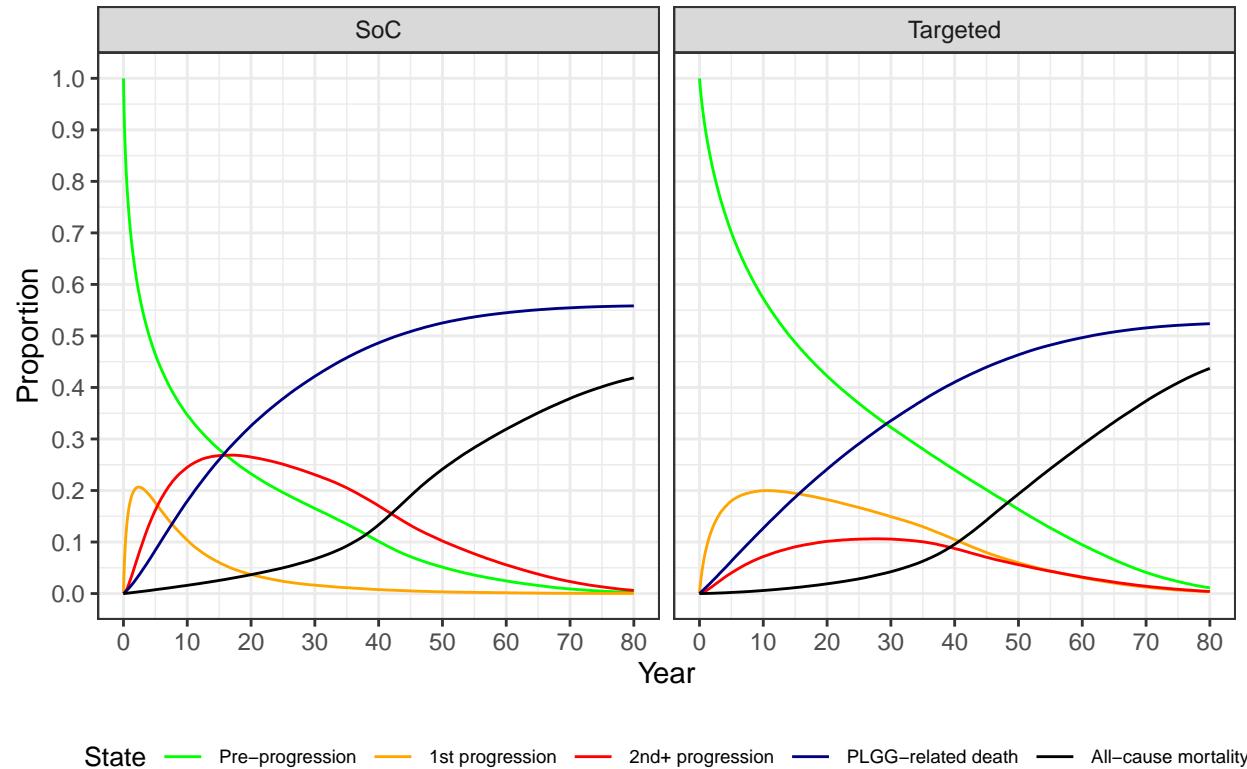
Progression-Free Survival with 95% CI



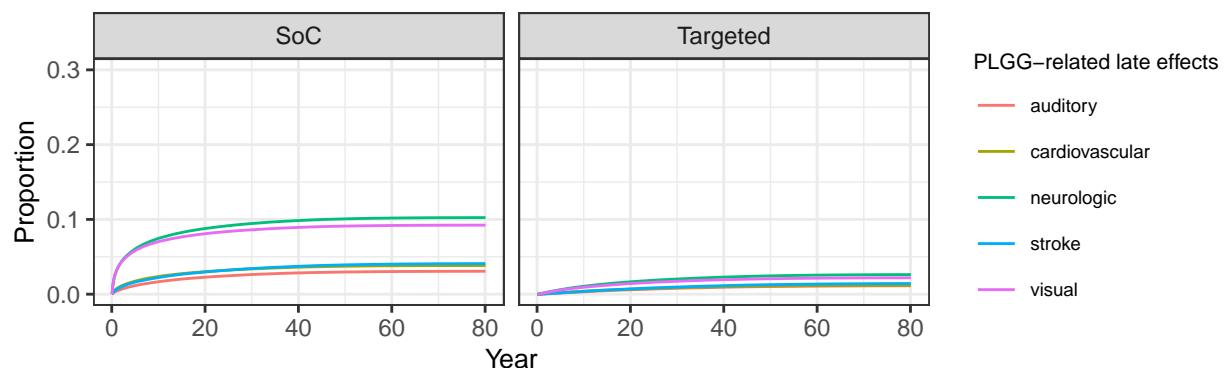
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	31.22 (25.52;36.76)	24.16 (19.35;28.94)	7.06 (2.14;14.24)
Total Cost	\$3,159,304 (\$2,673,249;\$3,627,458)	\$637,609 (\$607,693;\$673,120)	\$2,521,695 (\$2,038,899;\$2,965,030)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$374,113 (\$276,566;\$445,286)	\$-125,666 (\$-223,245;\$-55,768)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$197,787 (\$128,966;\$317,691)	\$-60,384 (\$-109,682;\$-13,918)
General population costs	\$119,998 (\$79,788;\$161,275)	\$65,708 (\$35,900;\$101,890)	\$54,290 (\$24,285;\$96,138)
Targeted costs	\$2,653,455 (\$2,161,994;\$3,133,603)	\$0 (\$0;\$0)	\$2,653,455 (\$2,161,994;\$3,133,603)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

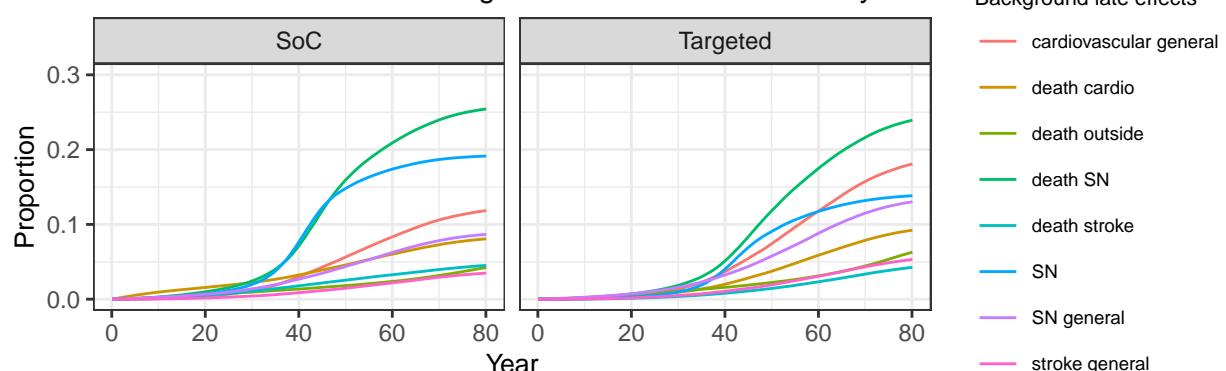
Trace Plot of PLGG States Across Cycles



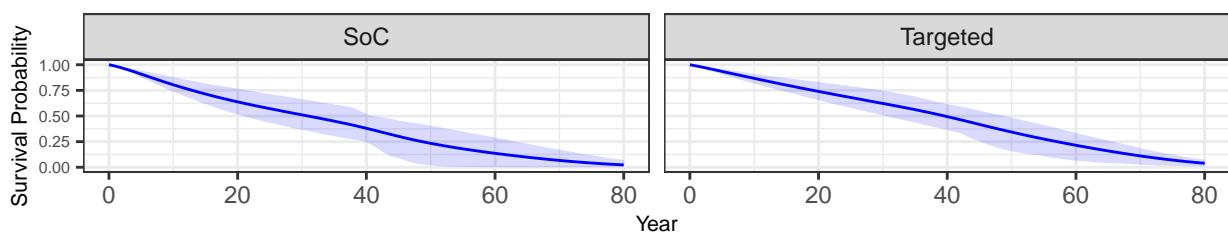
Cumulative Incidence of PLGG-related Late Effects Across Cycles



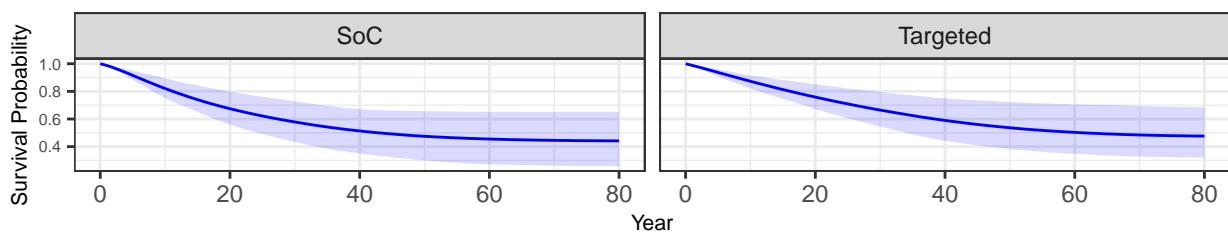
Cumulative Incidence of Background Late Effects Across Cycles



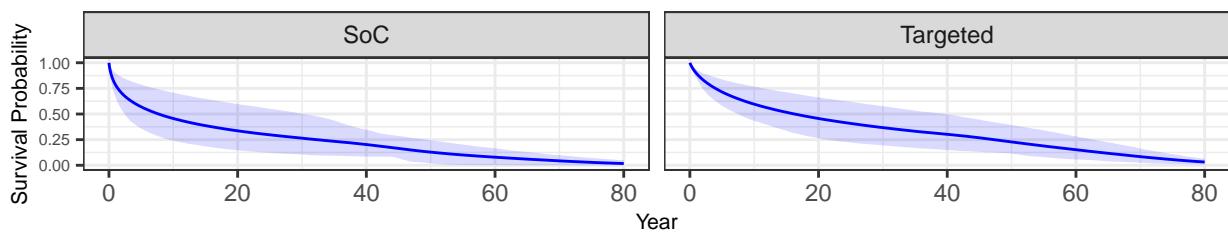
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



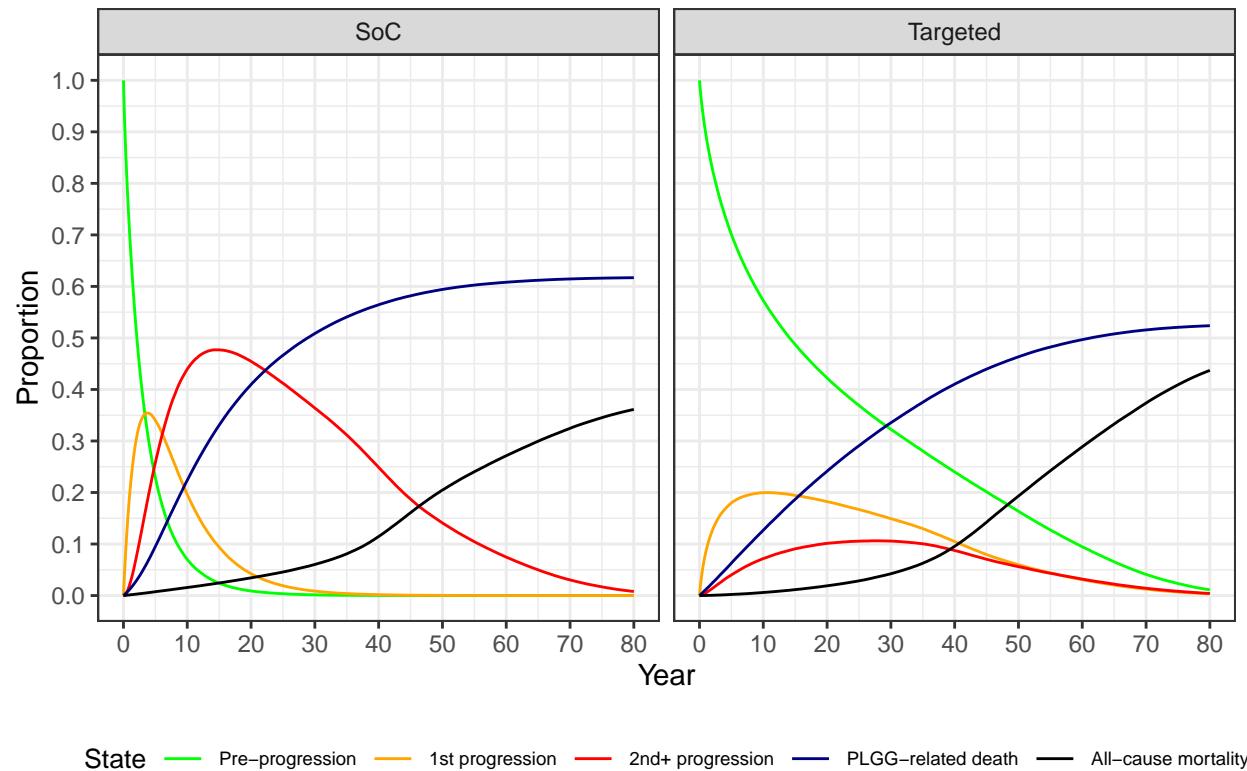
Progression-Free Survival with 95% CI



Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

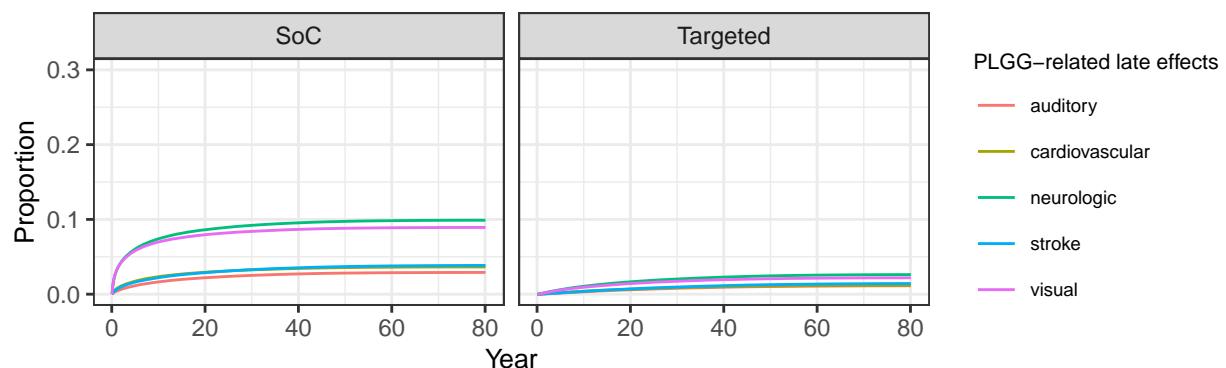
Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	31.22 (25.52;36.76)	21.9 (15.31;27.6)	9.32 (3.51;18.86)
Total Cost	\$3,159,304 (\$2,673,249;\$3,627,458)	\$669,031 (\$618,470;\$713,864)	\$2,490,274 (\$2,012,077;\$2,963,680)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$437,804 (\$344,779;\$532,700)	\$-189,357 (\$-308,775;\$-96,462)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$173,329 (\$69,038;\$304,887)	\$-35,925 (\$-106,871;\$41,692)
General population costs	\$119,998 (\$79,788;\$161,275)	\$57,898 (\$26,185;\$93,891)	\$62,100 (\$33,325;\$107,702)
Targeted costs	\$2,653,455 (\$2,161,994;\$3,133,603)	\$0 (\$0;\$0)	\$2,653,455 (\$2,161,994;\$3,133,603)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

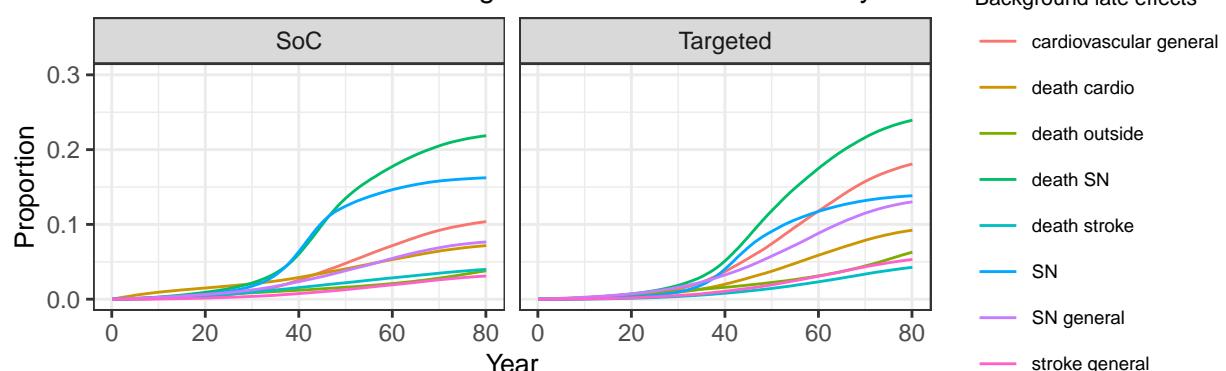


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

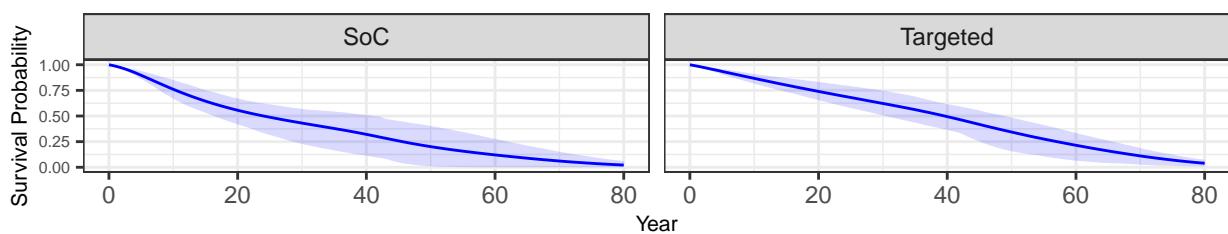
Cumulative Incidence of PLGG-related Late Effects Across Cycles



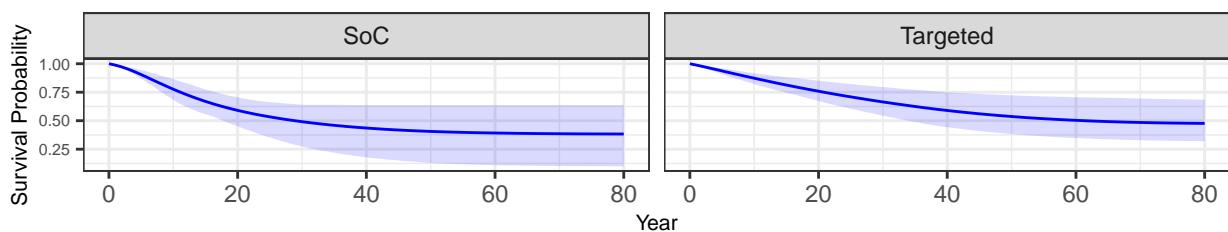
Cumulative Incidence of Background Late Effects Across Cycles



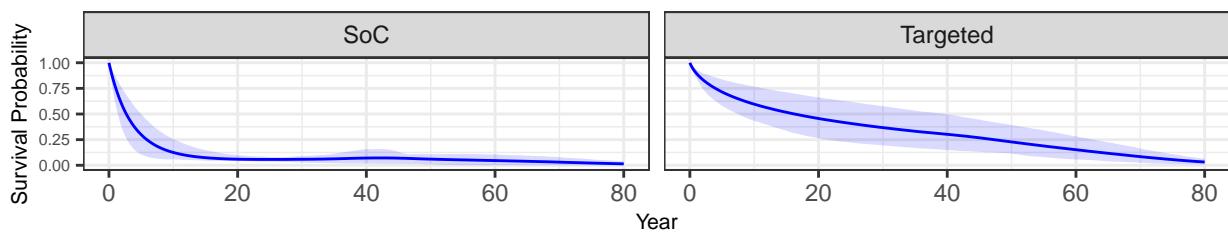
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



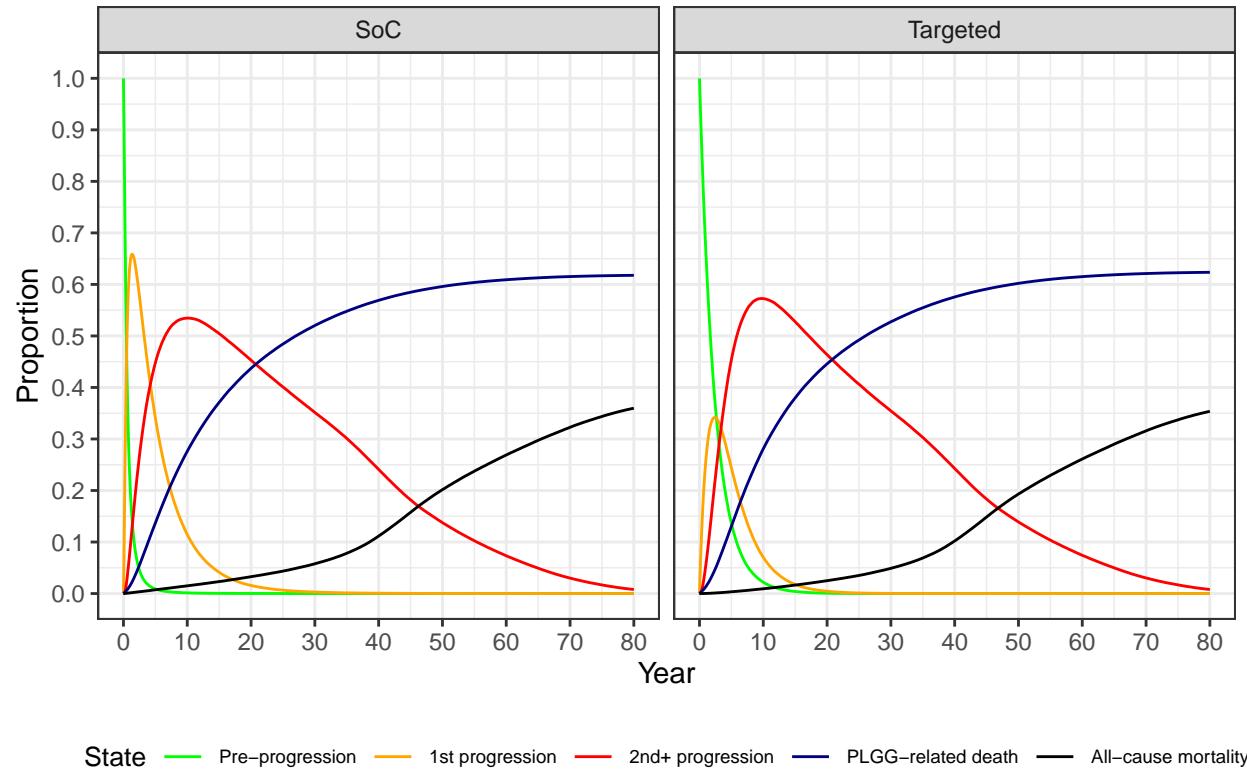
Progression-Free Survival with 95% CI



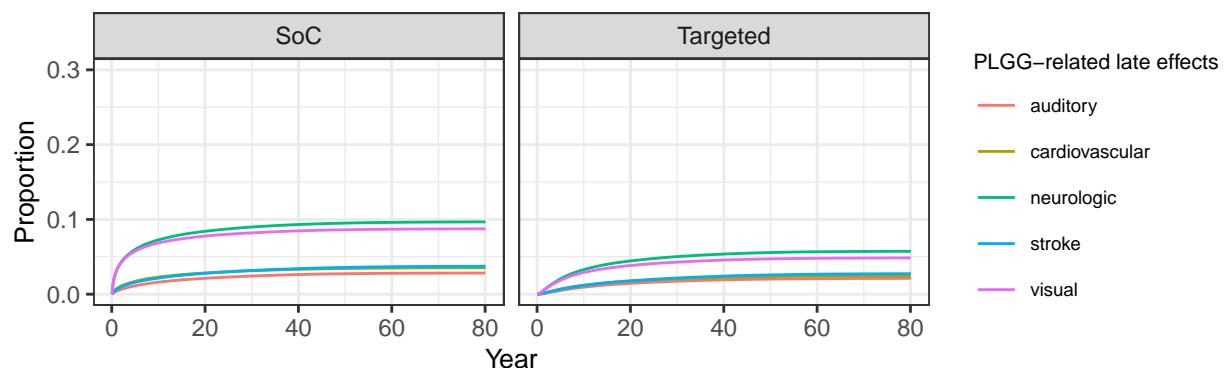
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	22.25 (13.94;29.59)	21.22 (13.13;28.12)	1.03 (-0.36;2.11)
Total Cost	\$2,559,084 (\$1,747,587;\$3,279,085)	\$678,589 (\$627,574;\$726,566)	\$1,880,496 (\$1,125,437;\$2,574,119)
Non-Targeted PLGG related costs	\$397,636 (\$290,330;\$493,089)	\$450,329 (\$344,279;\$545,621)	\$-52,694 (\$-73,926;\$-32,085)
Late effect costs	\$143,101 (\$40,833;\$291,392)	\$171,417 (\$59,221;\$313,821)	\$-28,316 (\$-40,229;\$-17,189)
General population costs	\$66,899 (\$29,702;\$110,339)	\$56,843 (\$22,934;\$96,371)	\$10,056 (\$4,269;\$15,483)
Targeted costs	\$1,951,449 (\$1,186,598;\$2,635,306)	\$0 (\$0;\$0)	\$1,951,449 (\$1,186,598;\$2,635,306)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

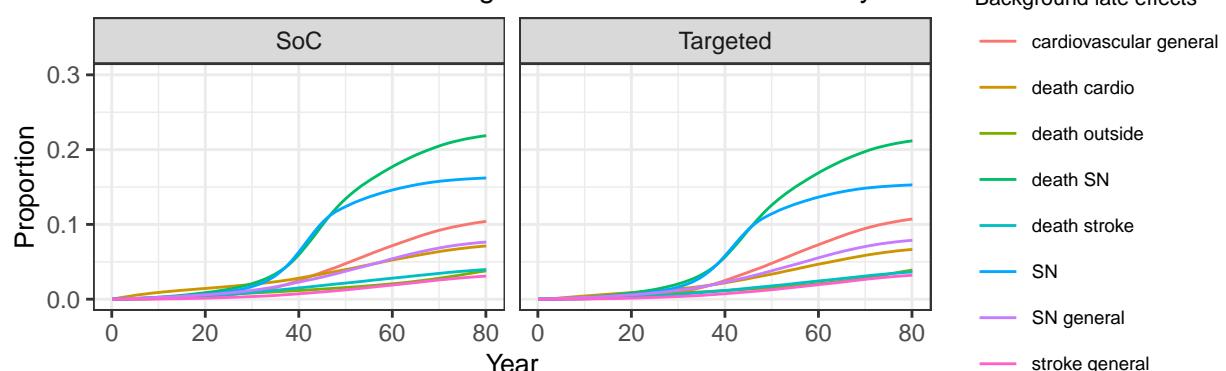
Trace Plot of PLGG States Across Cycles



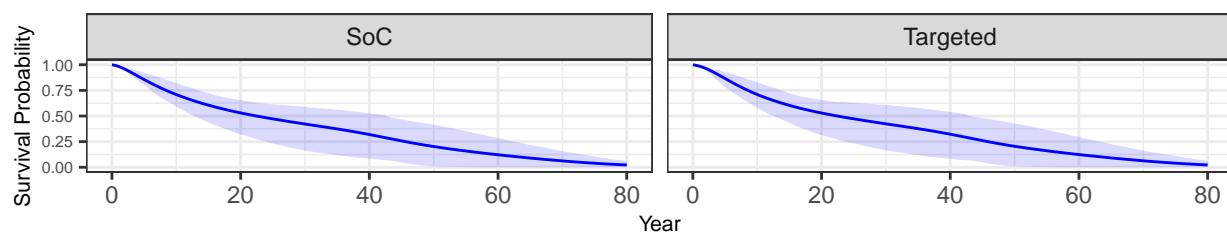
Cumulative Incidence of PLGG-related Late Effects Across Cycles



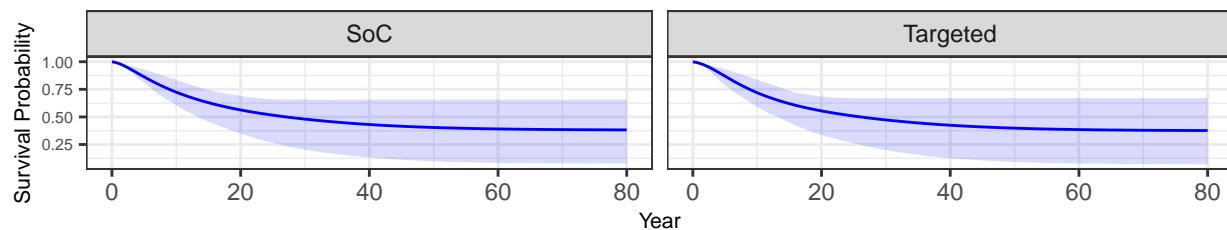
Cumulative Incidence of Background Late Effects Across Cycles



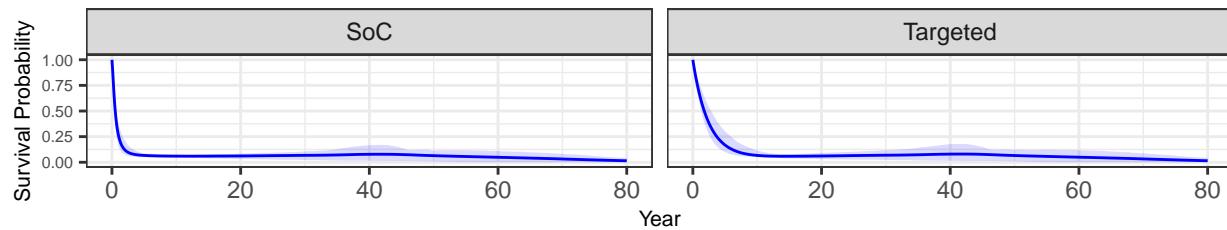
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



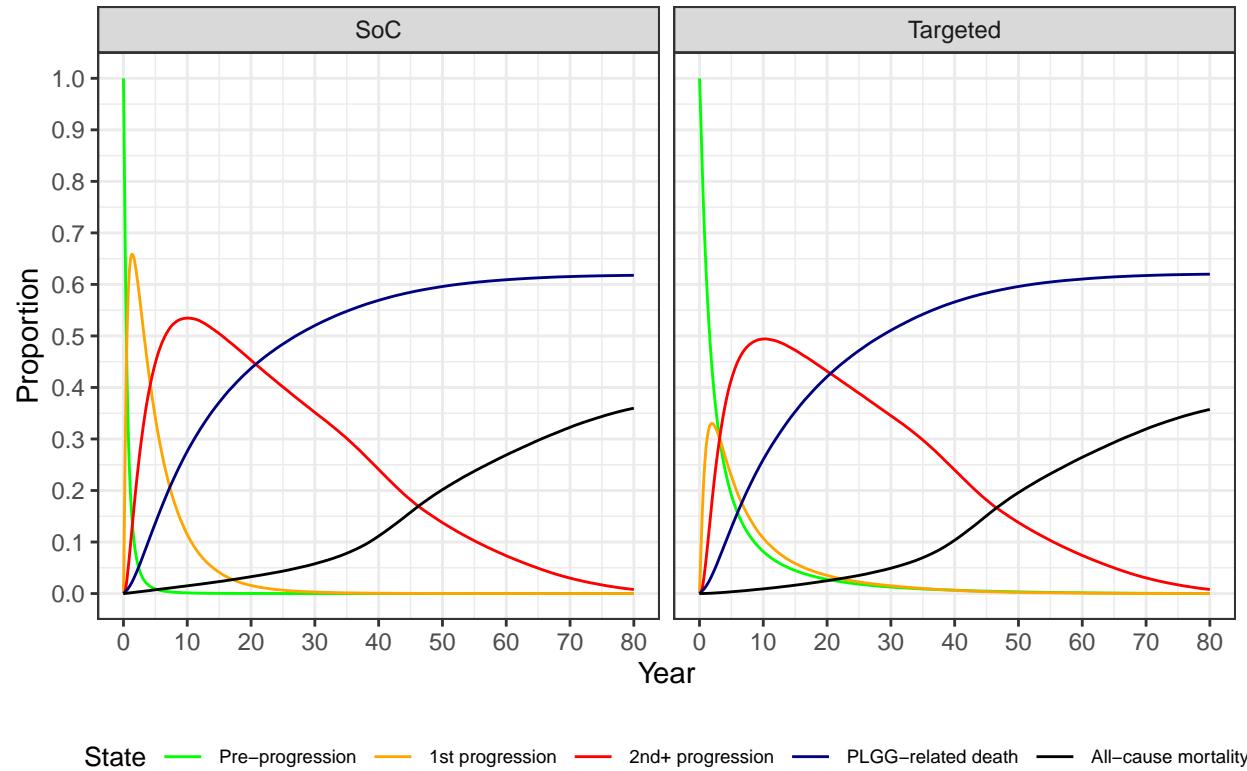
Progression-Free Survival with 95% CI



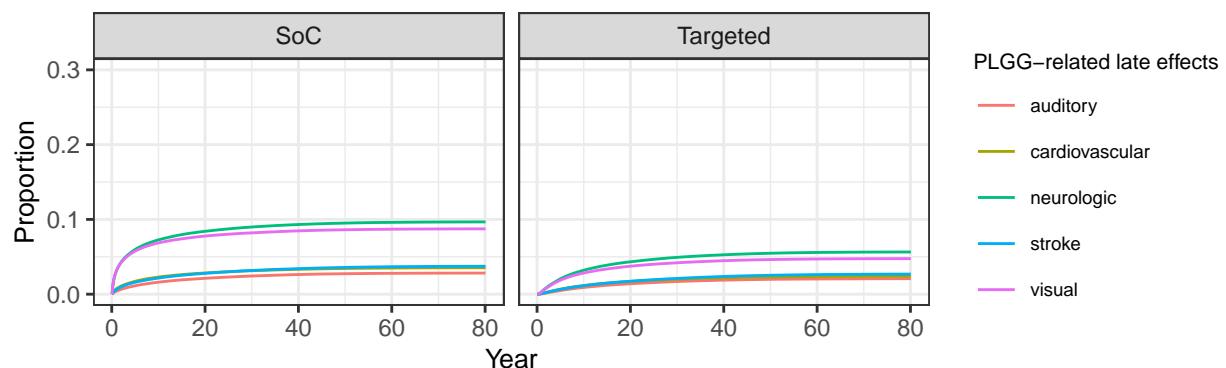
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	22.86 (16.46;29.65)	21.22 (13.13;28.12)	1.64 (0.27;3.07)
Total Cost	\$2,599,704 (\$1,967,430;\$3,283,060)	\$678,589 (\$627,574;\$726,566)	\$1,921,115 (\$1,311,475;\$2,559,883)
Non-Targeted PLGG related costs	\$385,605 (\$279,517;\$478,811)	\$450,329 (\$344,279;\$545,621)	\$-64,724 (\$-87,273;\$-42,861)
Late effect costs	\$143,450 (\$58,686;\$286,967)	\$171,417 (\$59,221;\$313,821)	\$-27,967 (\$-44,034;\$-12,929)
General population costs	\$69,568 (\$35,144;\$111,852)	\$56,843 (\$22,934;\$96,371)	\$12,725 (\$7,158;\$19,831)
Targeted costs	\$2,001,081 (\$1,393,116;\$2,638,940)	\$0 (\$0;\$0)	\$2,001,081 (\$1,393,116;\$2,638,940)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

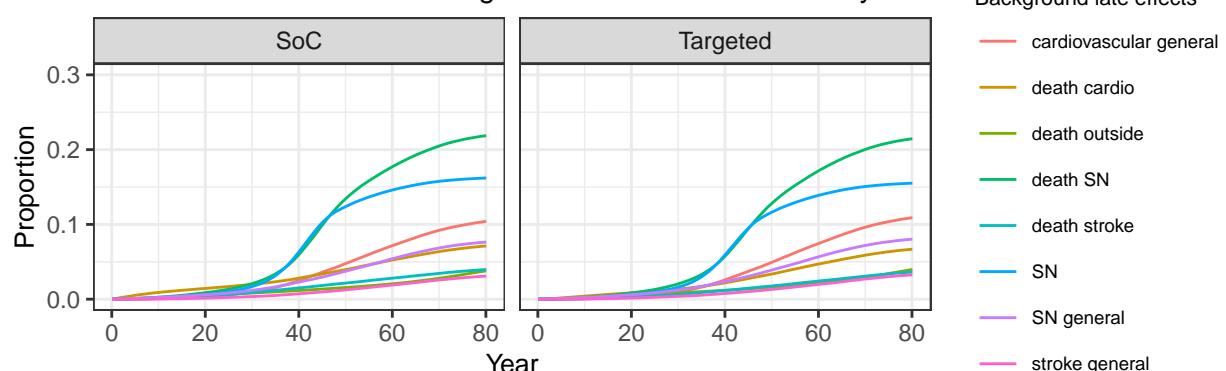
Trace Plot of PLGG States Across Cycles



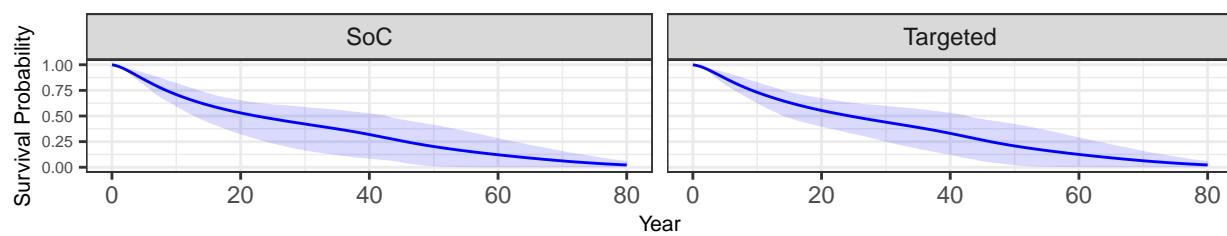
Cumulative Incidence of PLGG-related Late Effects Across Cycles



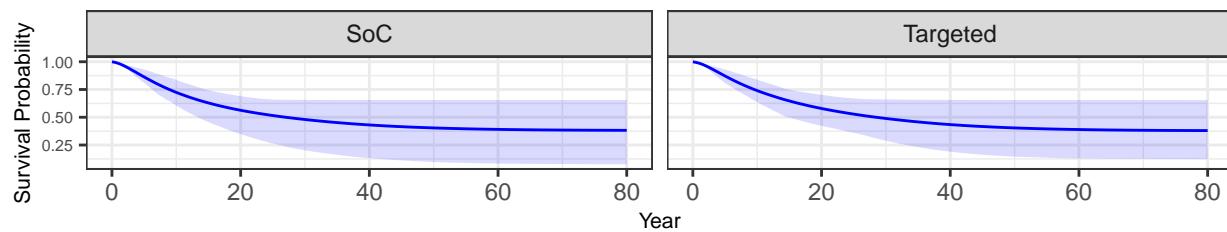
Cumulative Incidence of Background Late Effects Across Cycles



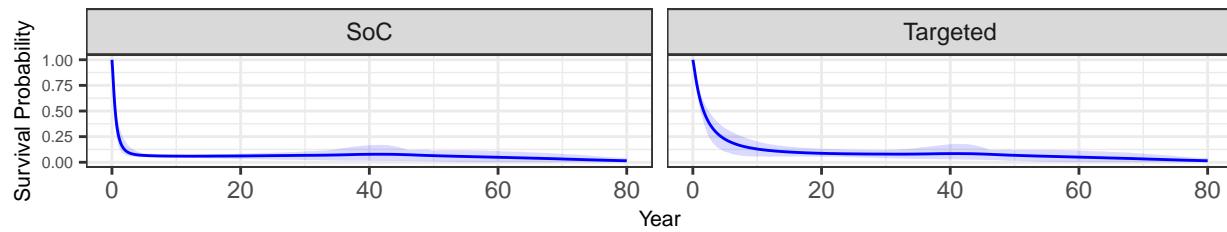
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



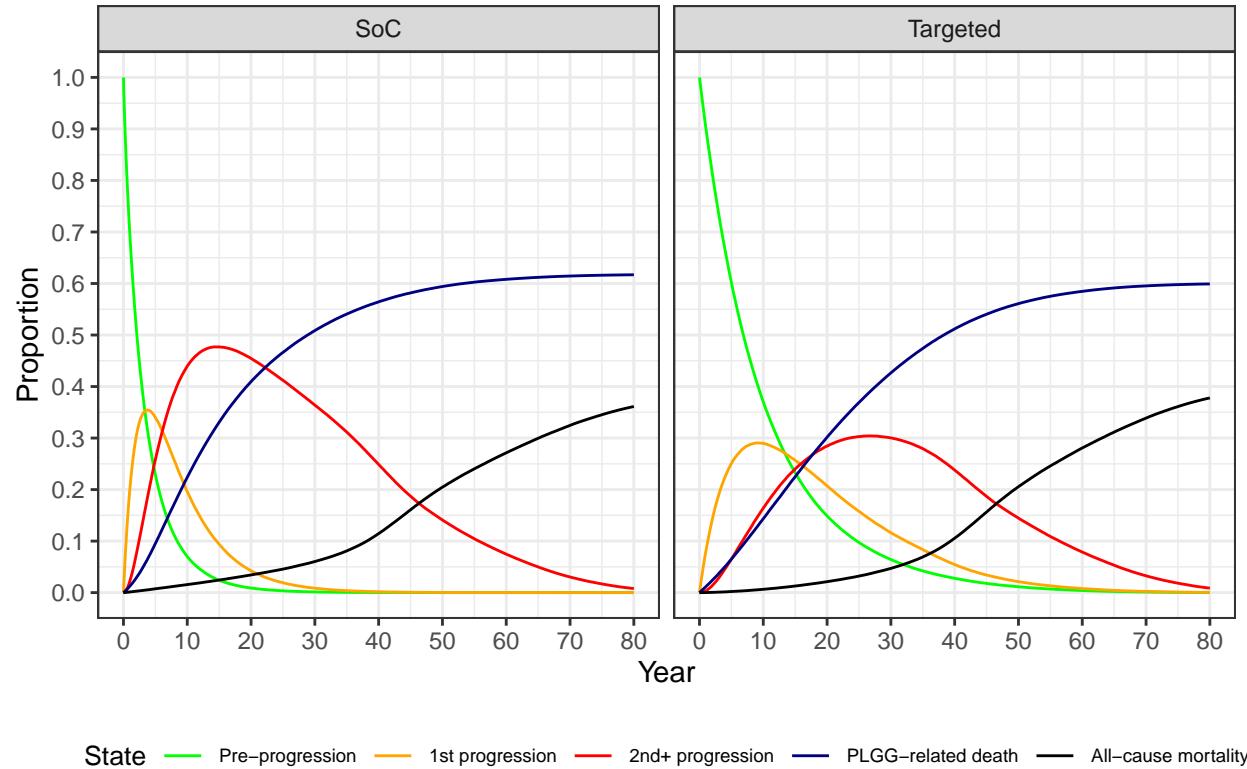
Scenario #1d

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **75% combo price reduction**
- Discount rate: 0
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

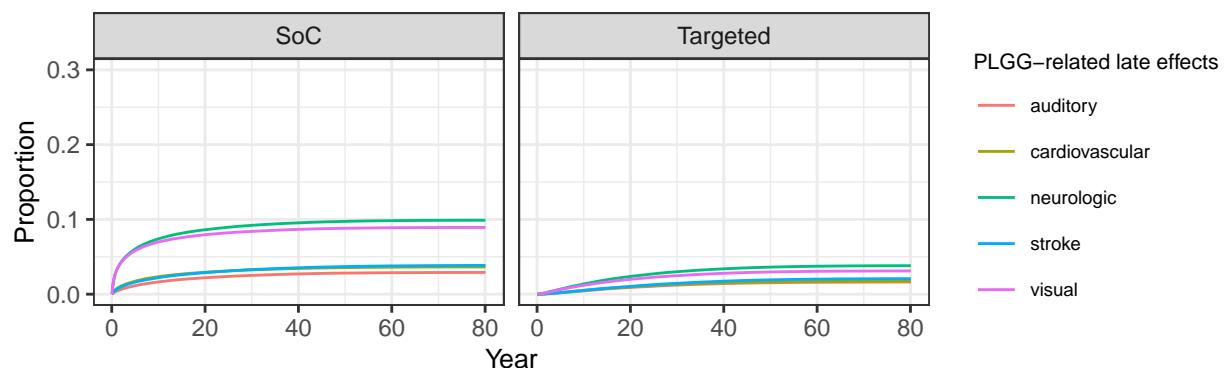
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	26.77 (20.58;33.3)	21.9 (15.31;27.6)	4.87 (1.63;11.18)
Total Cost	\$1,671,344 (\$1,404,949;\$1,922,225)	\$669,031 (\$618,470;\$713,864)	\$1,002,313 (\$735,934;\$1,242,571)
Non-Targeted PLGG related costs	\$302,455 (\$195,734;\$389,915)	\$437,804 (\$344,779;\$532,700)	\$-135,349 (\$-201,858;\$-83,310)
Late effect costs	\$134,485 (\$67,848;\$243,360)	\$173,329 (\$69,038;\$304,887)	\$-38,844 (\$-65,377;\$4,732)
General population costs	\$89,405 (\$49,536;\$130,247)	\$57,898 (\$26,185;\$93,891)	\$31,507 (\$15,887;\$63,026)
Targeted costs	\$1,144,999 (\$867,126;\$1,412,377)	\$0 (\$0;\$0)	\$1,144,999 (\$867,126;\$1,412,377)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

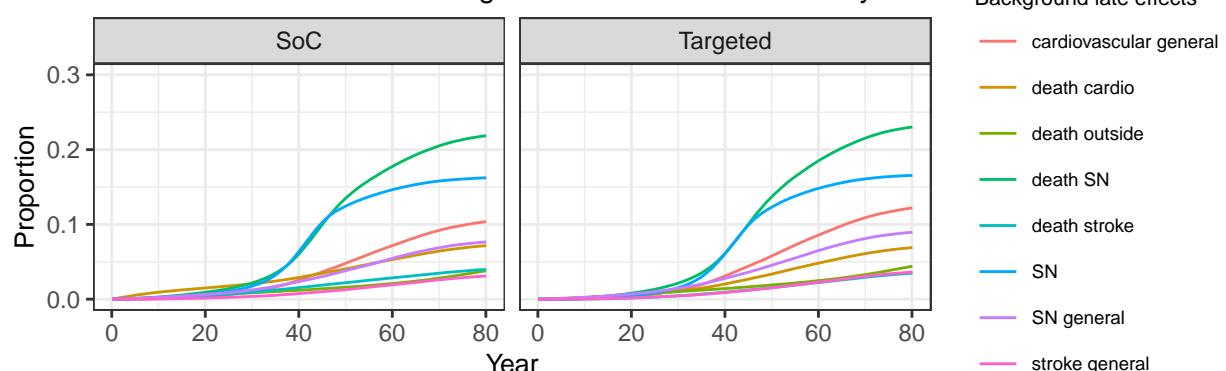
Trace Plot of PLGG States Across Cycles



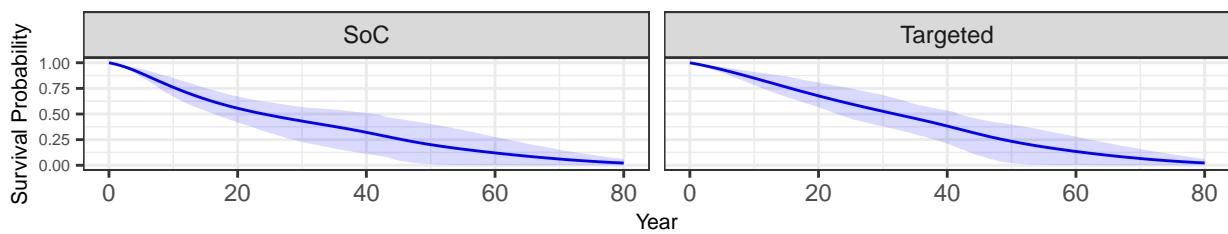
Cumulative Incidence of PLGG-related Late Effects Across Cycles



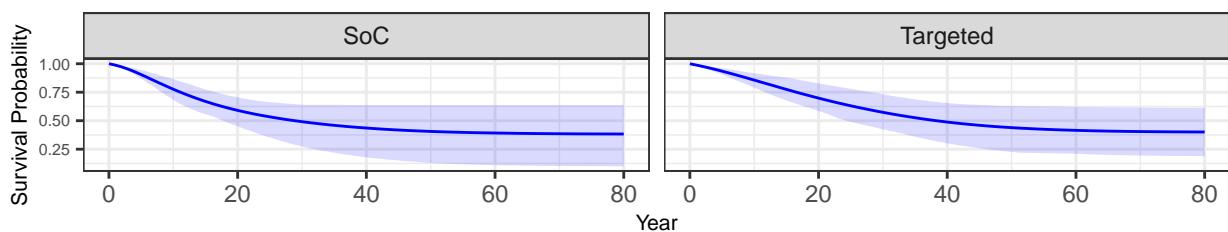
Cumulative Incidence of Background Late Effects Across Cycles



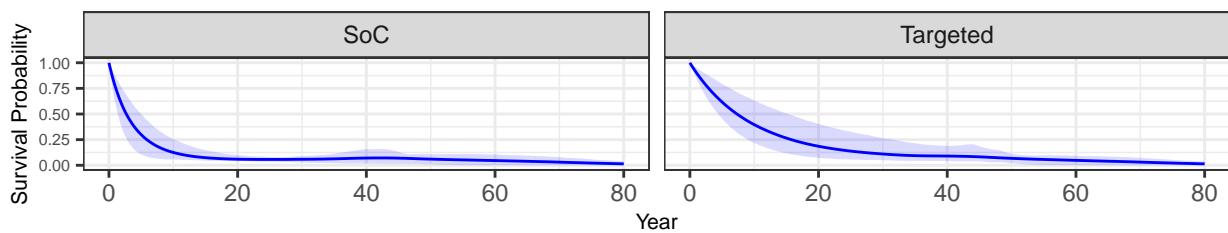
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



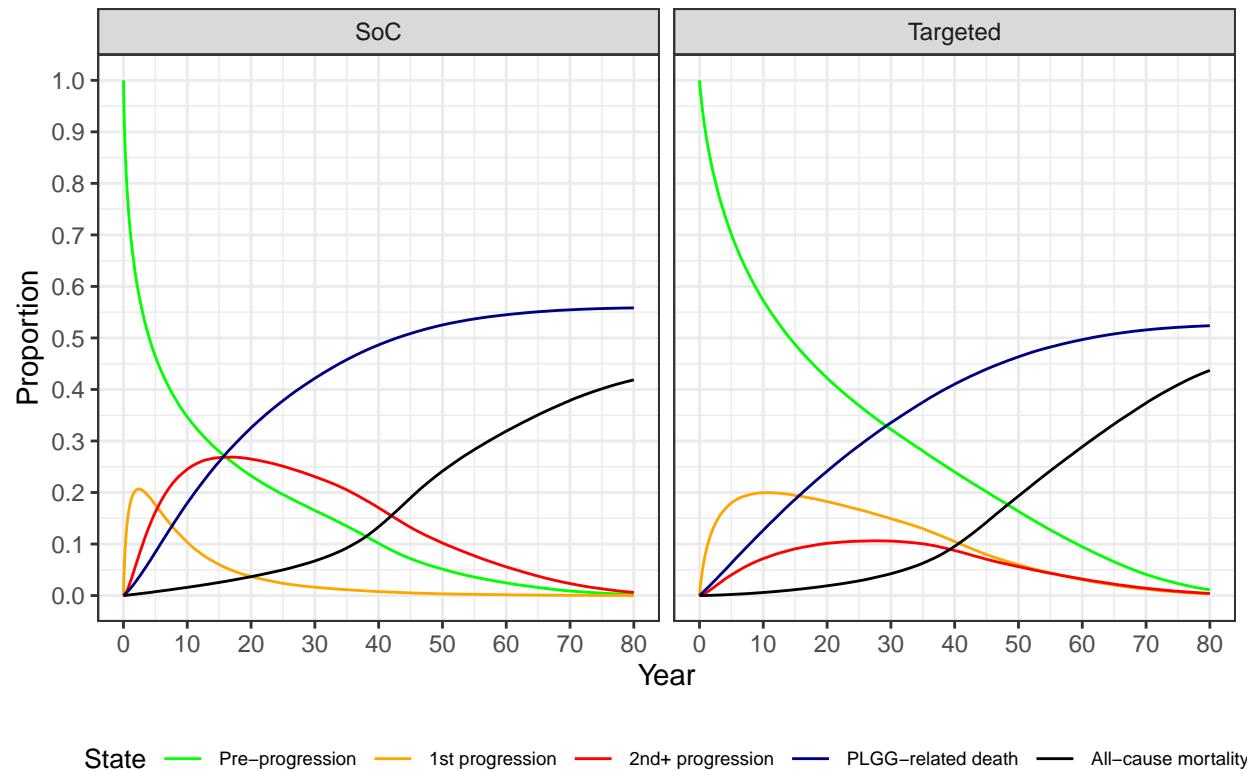
Progression-Free Survival with 95% CI



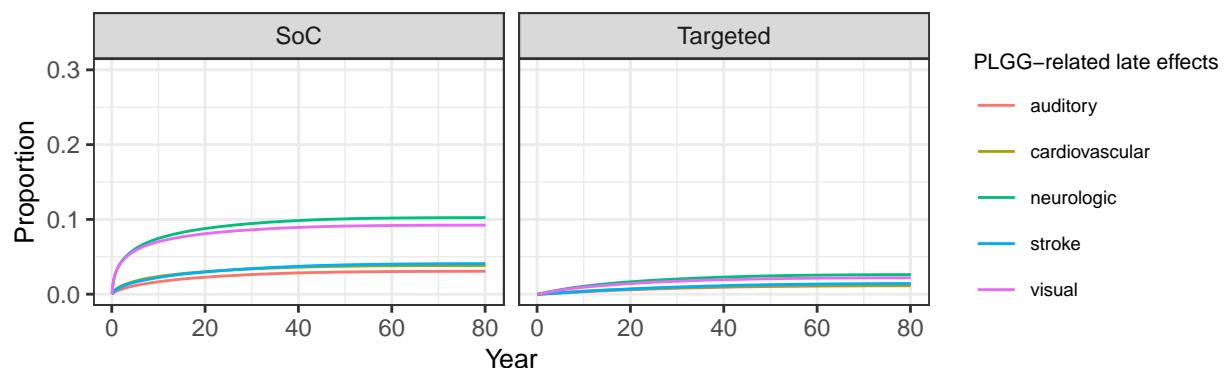
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	31.22 (25.52;36.76)	24.16 (19.35;28.94)	7.06 (2.14;14.24)
Total Cost	\$1,832,577 (\$1,593,631;\$2,060,657)	\$637,609 (\$607,693;\$673,120)	\$1,194,968 (\$957,622;\$1,398,228)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$374,113 (\$276,566;\$445,286)	\$-125,666 (\$-223,245;\$-55,768)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$197,787 (\$128,966;\$317,691)	\$-60,384 (\$-109,682;\$-13,918)
General population costs	\$119,998 (\$79,788;\$161,275)	\$65,708 (\$35,900;\$101,890)	\$54,290 (\$24,285;\$96,138)
Targeted costs	\$1,326,727 (\$1,080,997;\$1,566,801)	\$0 (\$0;\$0)	\$1,326,727 (\$1,080,997;\$1,566,801)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

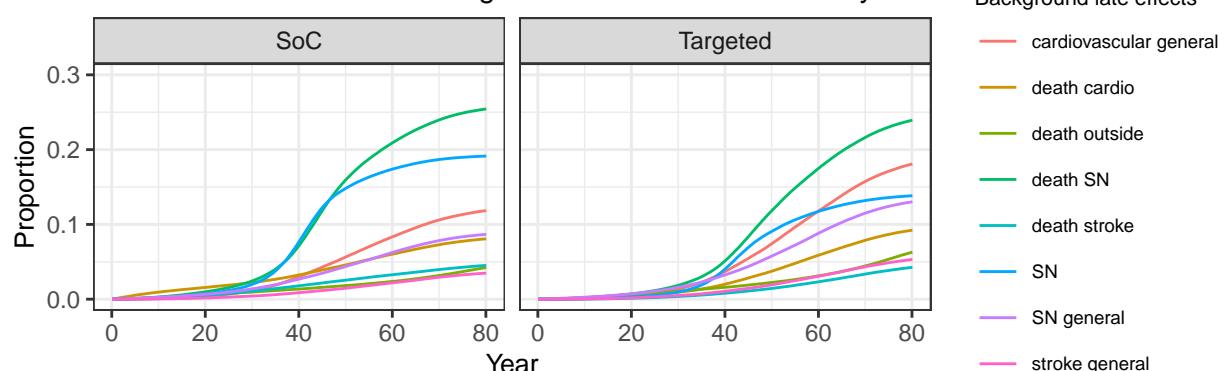
Trace Plot of PLGG States Across Cycles



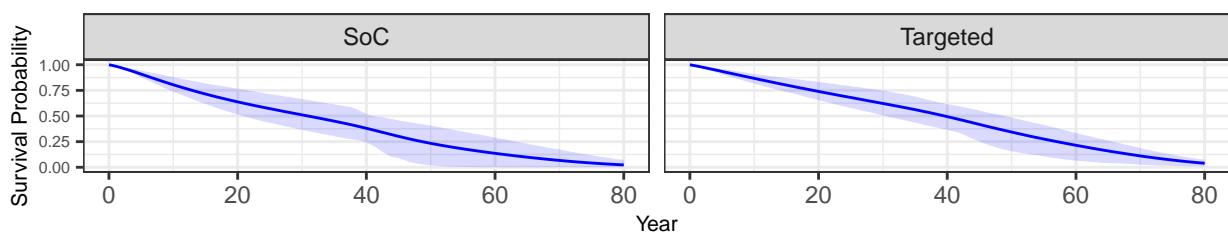
Cumulative Incidence of PLGG-related Late Effects Across Cycles



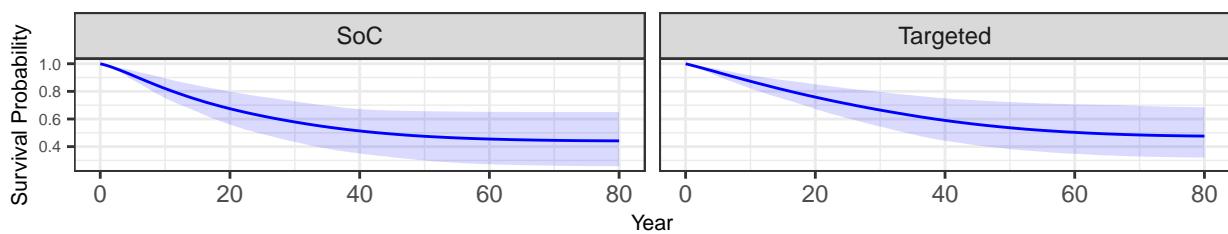
Cumulative Incidence of Background Late Effects Across Cycles



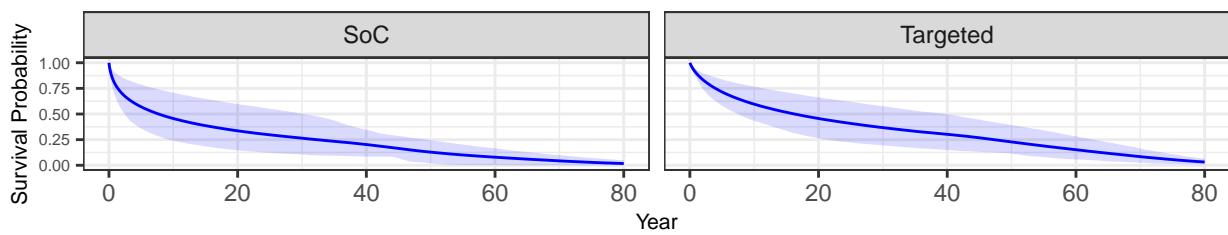
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



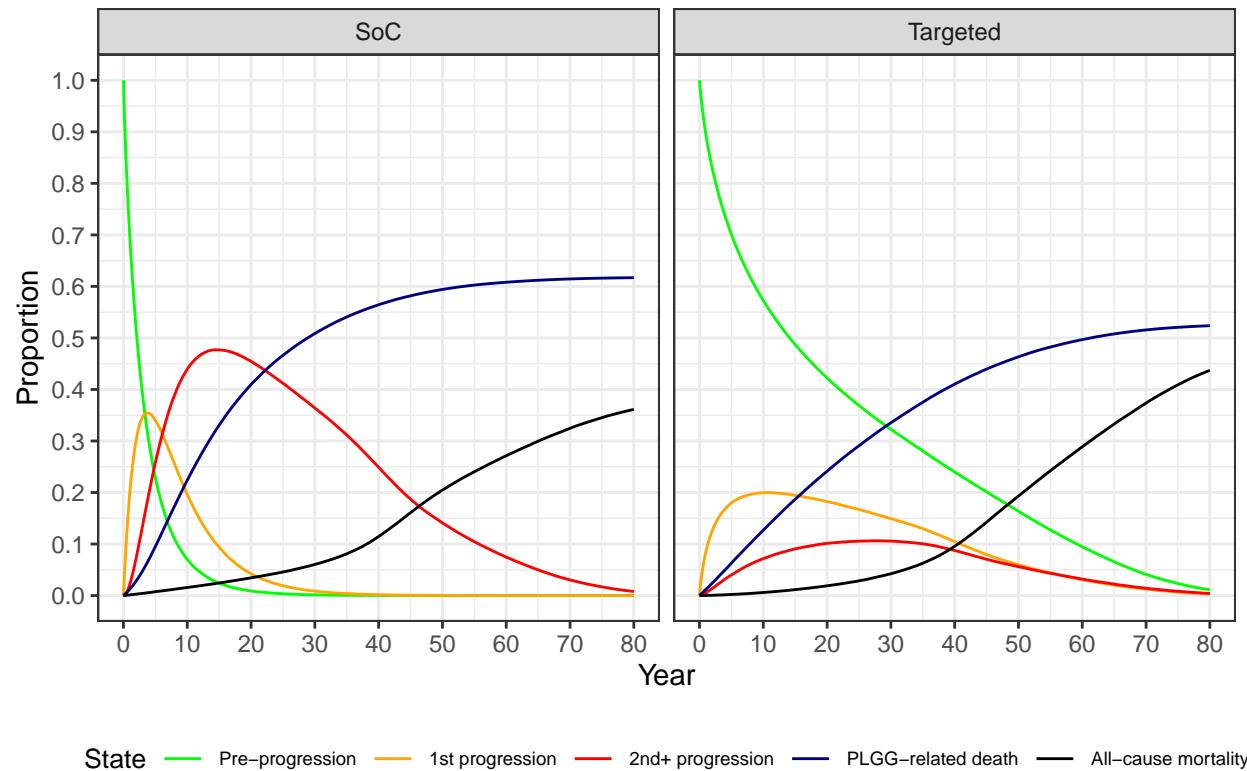
Progression-Free Survival with 95% CI



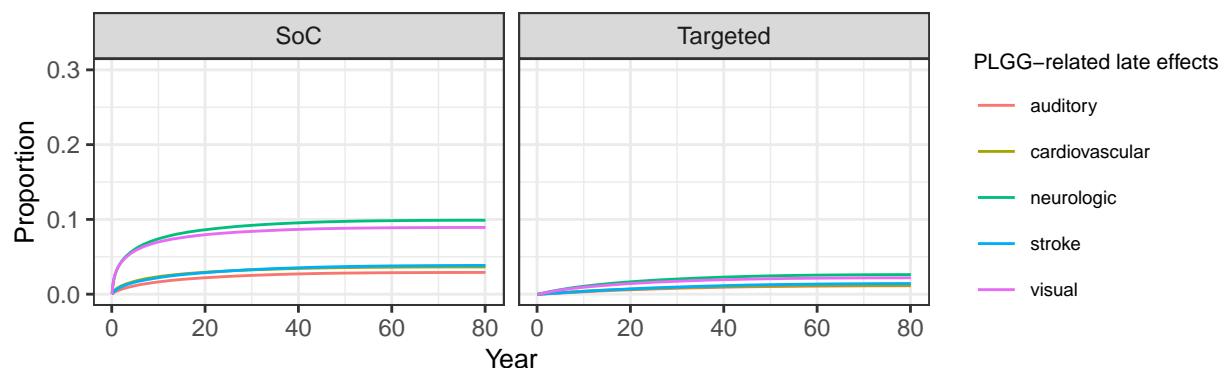
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	31.22 (25.52;36.76)	21.9 (15.31;27.6)	9.32 (3.51;18.86)
Total Cost	\$1,832,577 (\$1,593,631;\$2,060,657)	\$669,031 (\$618,470;\$713,864)	\$1,163,546 (\$913,789;\$1,396,879)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$437,804 (\$344,779;\$532,700)	\$-189,357 (\$-308,775;\$-96,462)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$173,329 (\$69,038;\$304,887)	\$-35,925 (\$-106,871;\$41,692)
General population costs	\$119,998 (\$79,788;\$161,275)	\$57,898 (\$26,185;\$93,891)	\$62,100 (\$33,325;\$107,702)
Targeted costs	\$1,326,727 (\$1,080,997;\$1,566,801)	\$0 (\$0;\$0)	\$1,326,727 (\$1,080,997;\$1,566,801)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

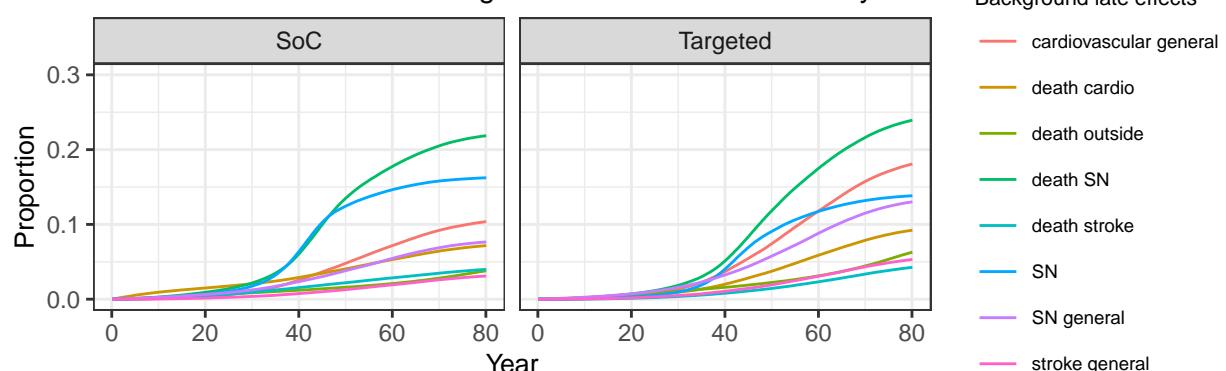
Trace Plot of PLGG States Across Cycles



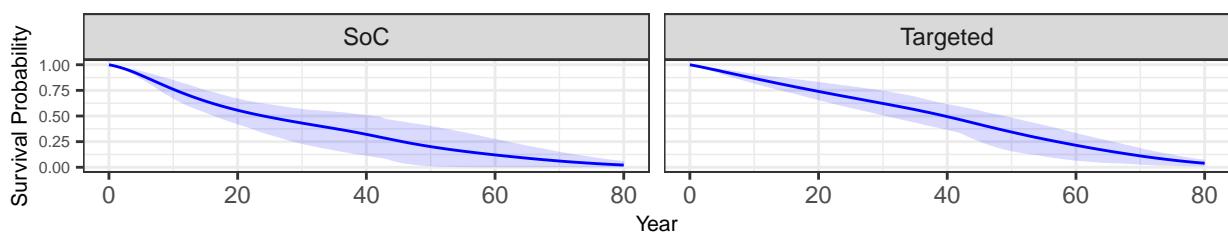
Cumulative Incidence of PLGG-related Late Effects Across Cycles



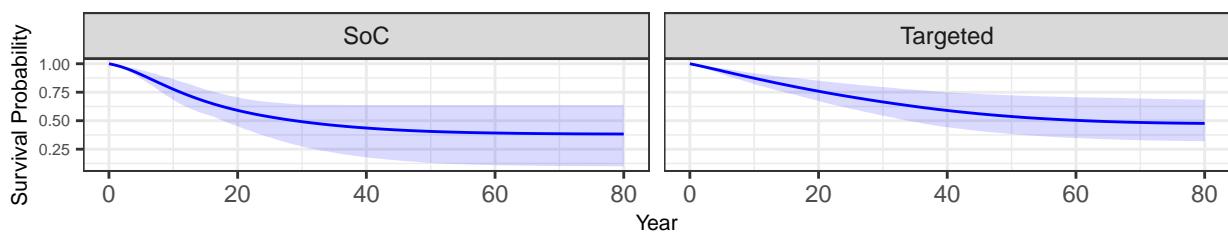
Cumulative Incidence of Background Late Effects Across Cycles



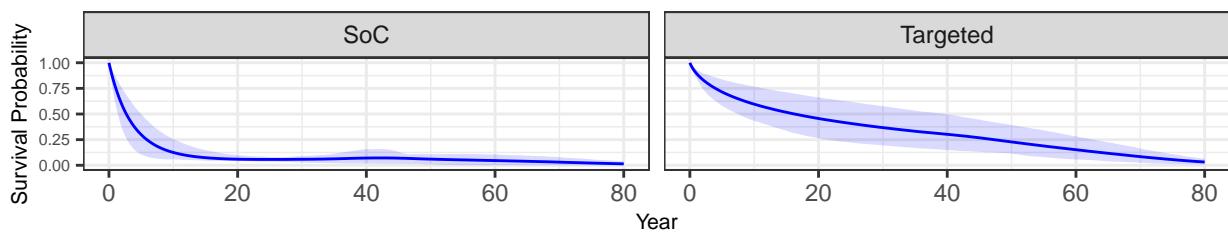
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



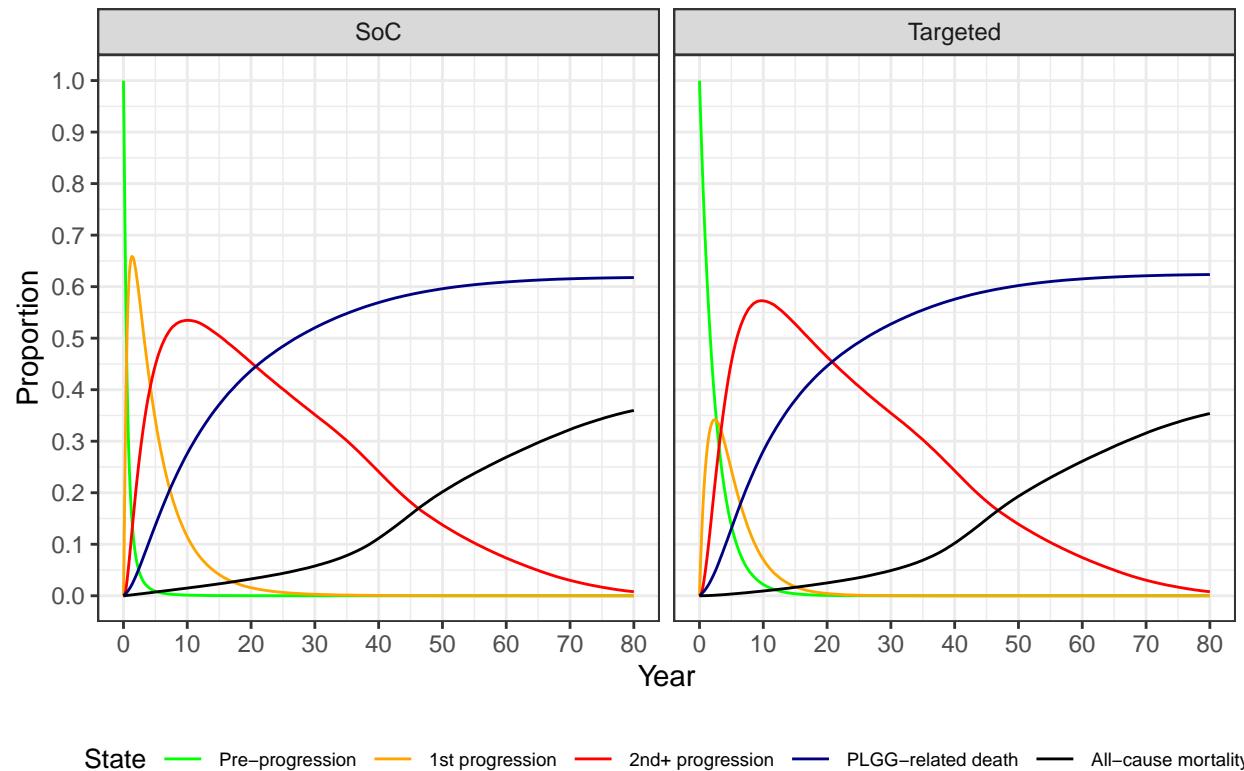
Progression-Free Survival with 95% CI



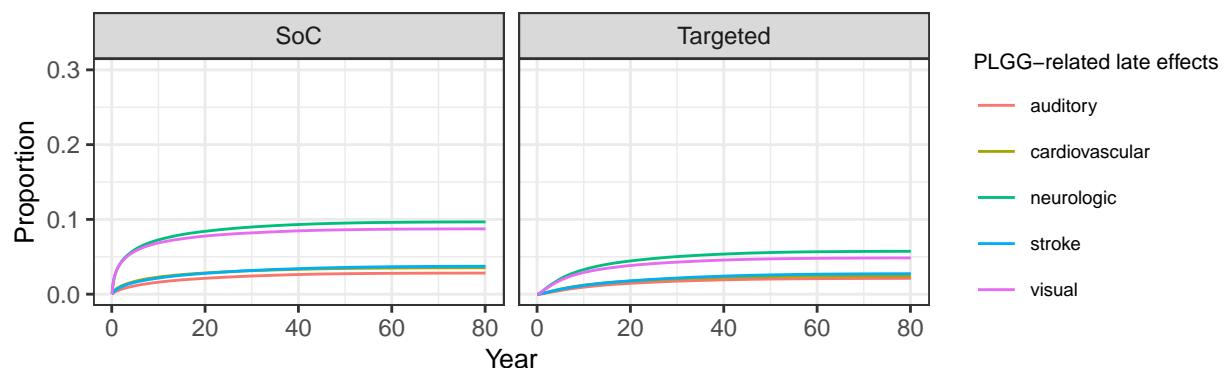
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	22.25 (13.94;29.59)	21.22 (13.13;28.12)	1.03 (-0.36;2.11)
Total Cost	\$1,583,360 (\$1,153,289;\$1,937,706)	\$678,589 (\$627,574;\$726,566)	\$904,771 (\$532,138;\$1,256,466)
Non-Targeted PLGG related costs	\$397,636 (\$290,330;\$493,089)	\$450,329 (\$344,279;\$545,621)	\$-52,694 (\$-73,926;\$-32,085)
Late effect costs	\$143,101 (\$40,833;\$291,392)	\$171,417 (\$59,221;\$313,821)	\$-28,316 (\$-40,229;\$-17,189)
General population costs	\$66,899 (\$29,702;\$110,339)	\$56,843 (\$22,934;\$96,371)	\$10,056 (\$4,269;\$15,483)
Targeted costs	\$975,724 (\$593,299;\$1,317,653)	\$0 (\$0;\$0)	\$975,724 (\$593,299;\$1,317,653)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

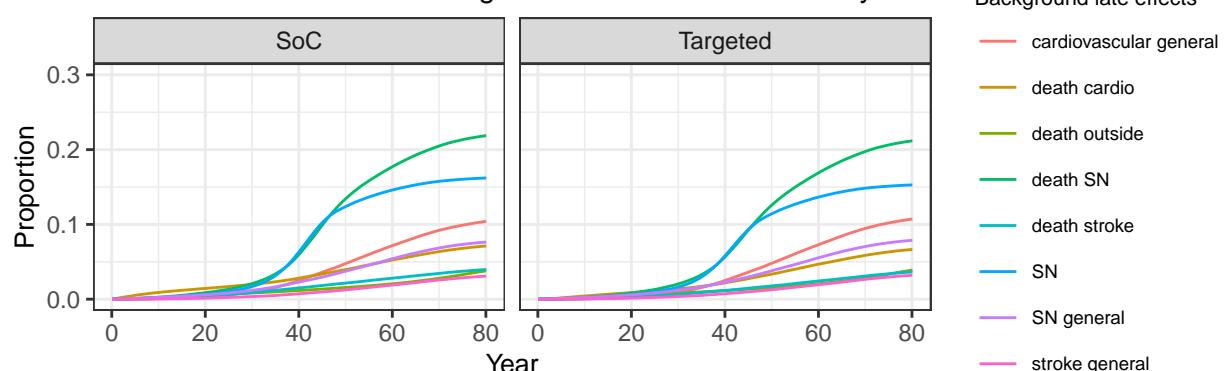
Trace Plot of PLGG States Across Cycles



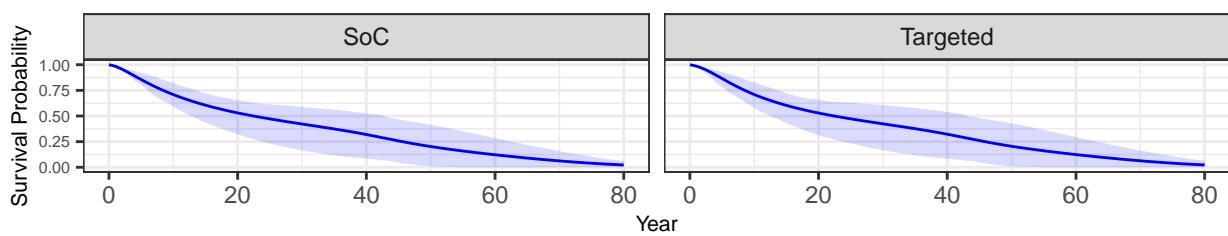
Cumulative Incidence of PLGG-related Late Effects Across Cycles



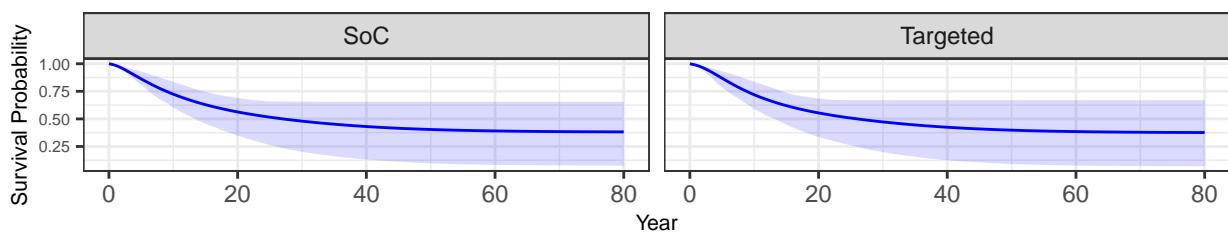
Cumulative Incidence of Background Late Effects Across Cycles



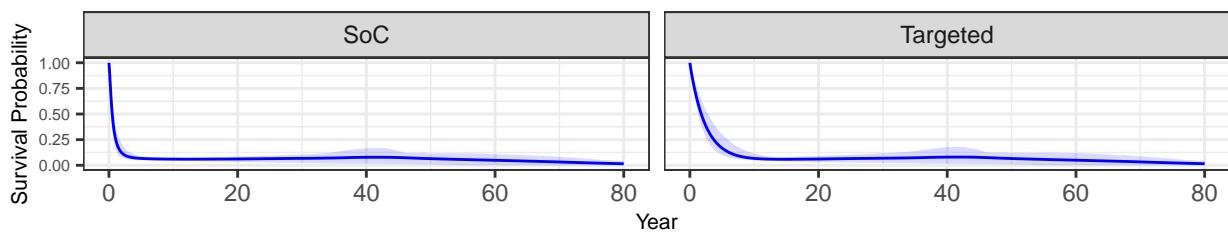
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



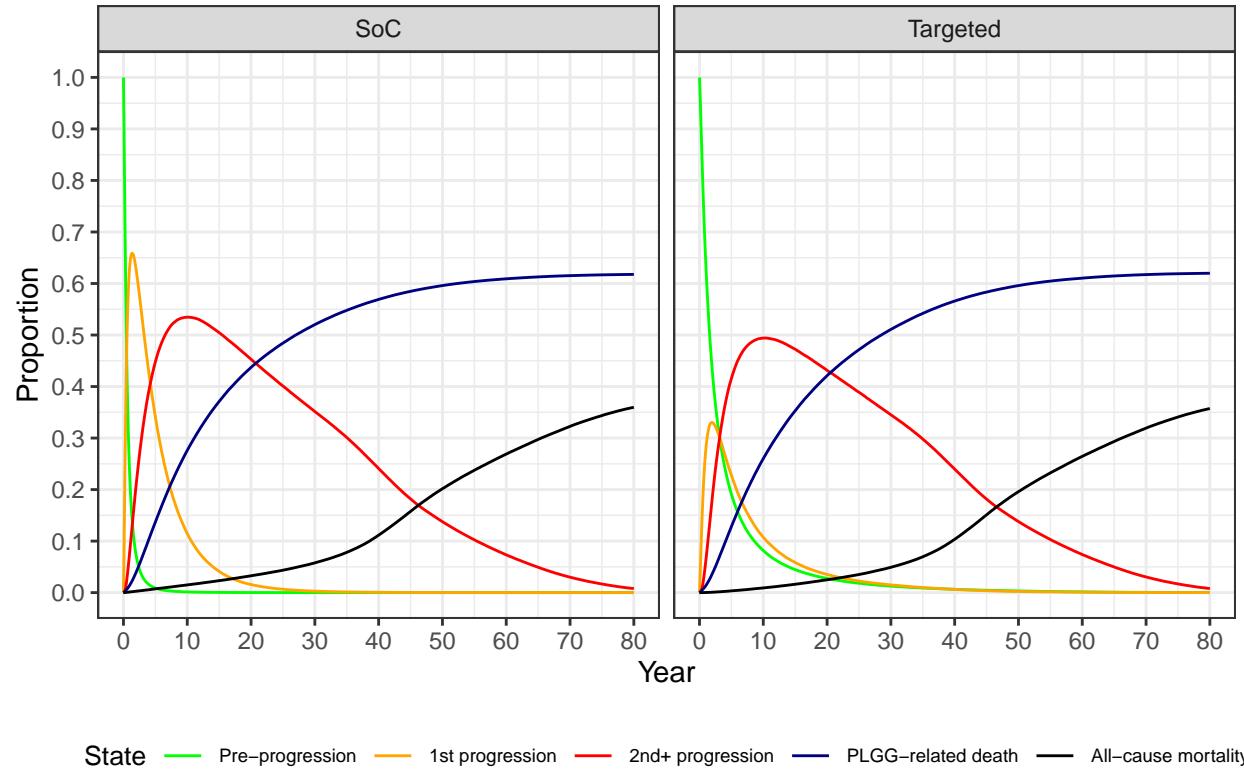
Progression-Free Survival with 95% CI



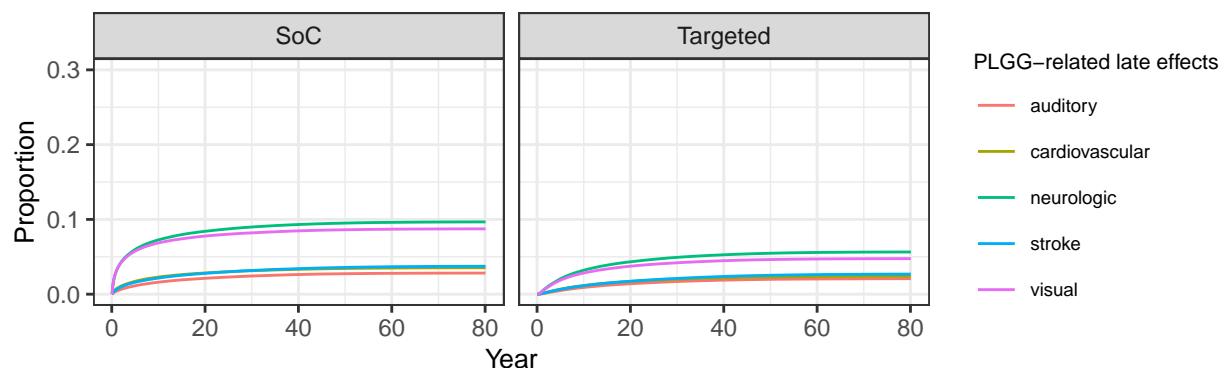
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	22.86 (16.46;29.65)	21.22 (13.13;28.12)	1.64 (0.27;3.07)
Total Cost	\$1,599,164 (\$1,256,892;\$1,933,701)	\$678,589 (\$627,574;\$726,566)	\$920,575 (\$614,909;\$1,241,500)
Non-Targeted PLGG related costs	\$385,605 (\$279,517;\$478,811)	\$450,329 (\$344,279;\$545,621)	\$-64,724 (\$-87,273;\$-42,861)
Late effect costs	\$143,450 (\$58,686;\$286,967)	\$171,417 (\$59,221;\$313,821)	\$-27,967 (\$-44,034;\$-12,929)
General population costs	\$69,568 (\$35,144;\$111,852)	\$56,843 (\$22,934;\$96,371)	\$12,725 (\$7,158;\$19,831)
Targeted costs	\$1,000,540 (\$696,558;\$1,319,470)	\$0 (\$0;\$0)	\$1,000,540 (\$696,558;\$1,319,470)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

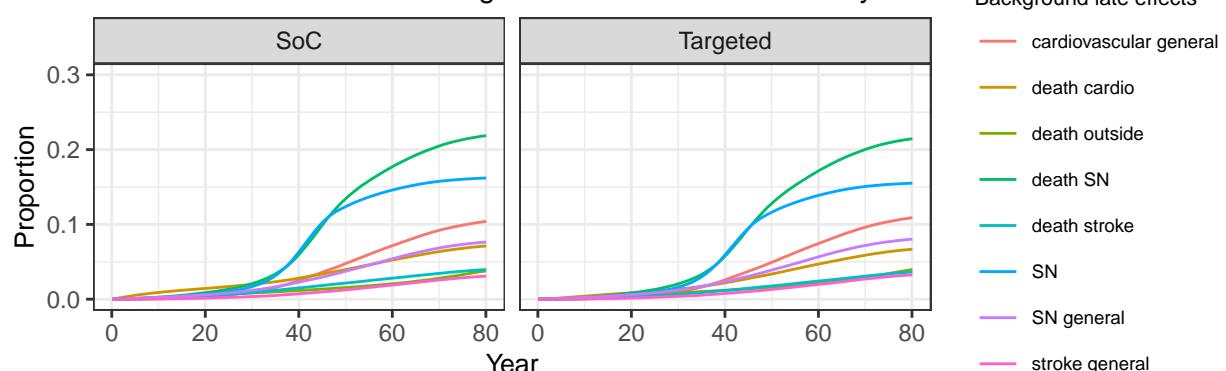
Trace Plot of PLGG States Across Cycles



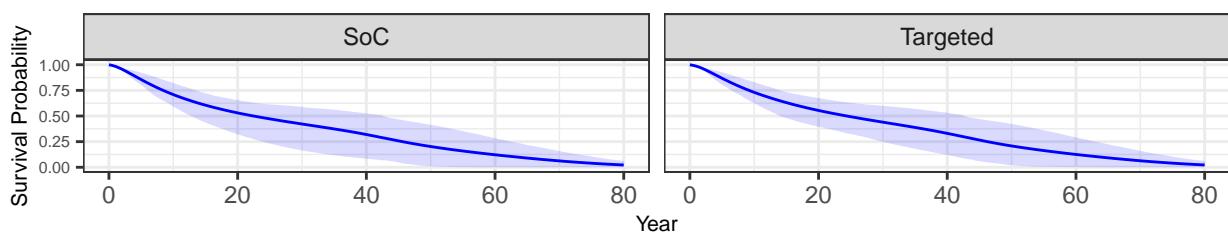
Cumulative Incidence of PLGG-related Late Effects Across Cycles



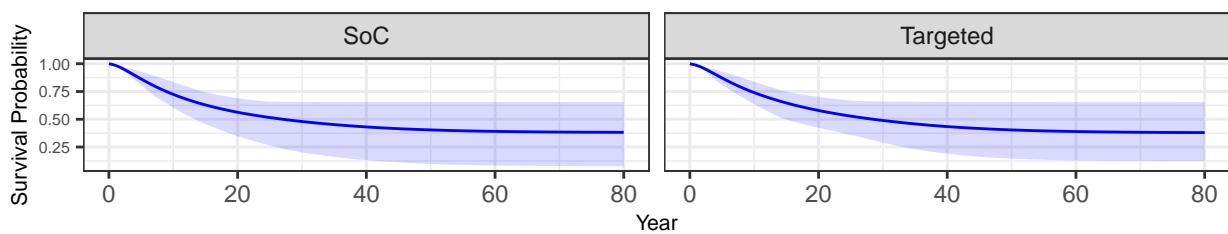
Cumulative Incidence of Background Late Effects Across Cycles



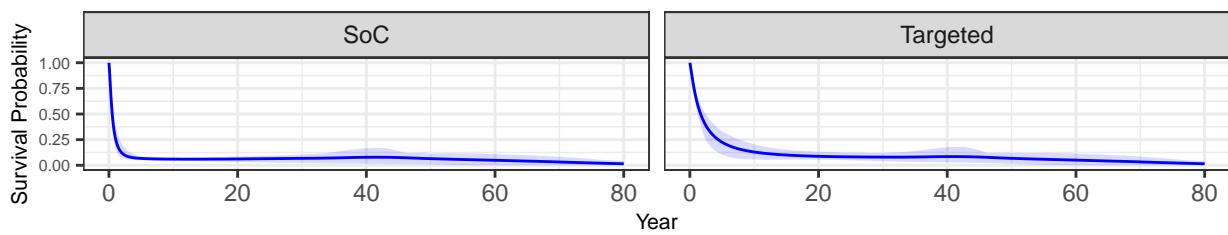
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



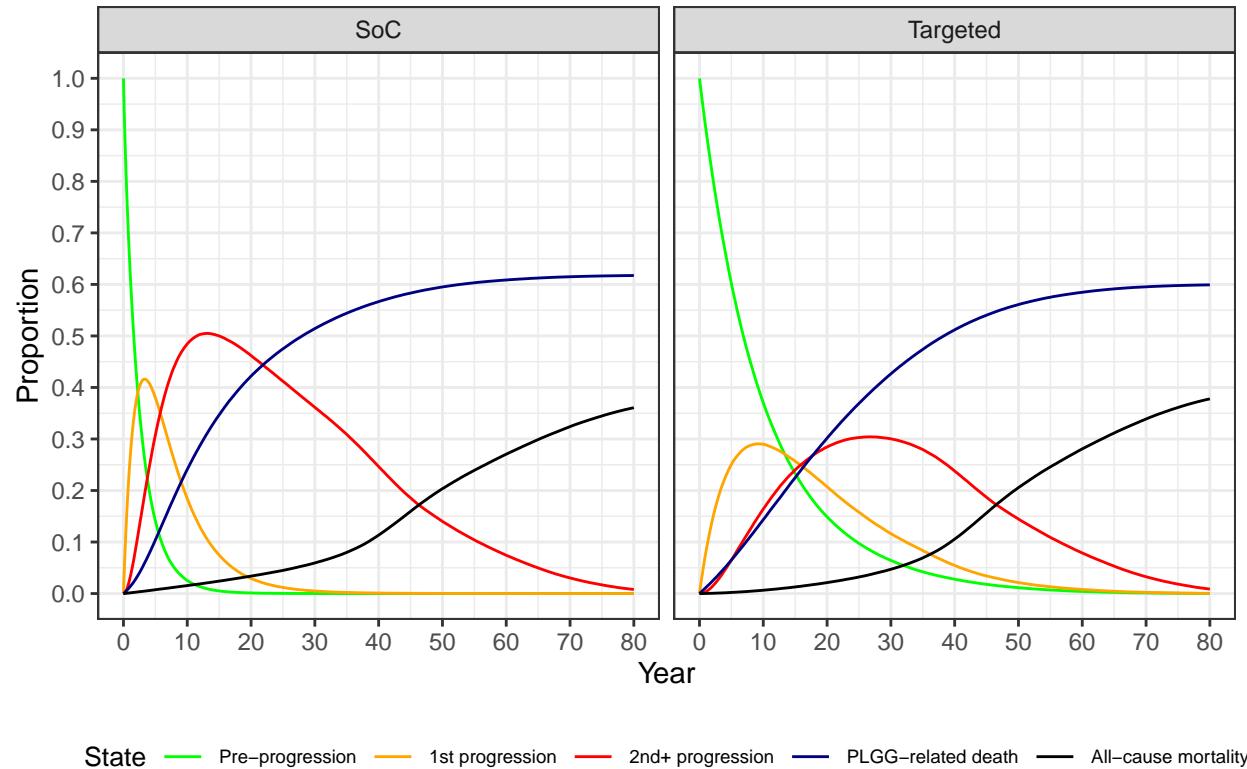
Scenario #1e

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 0
- **Data source for controls: n=34 SickKids controls**
- **Data source for exposed: Investigator assessment - Bouffet et al., NEJM 2023.**
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

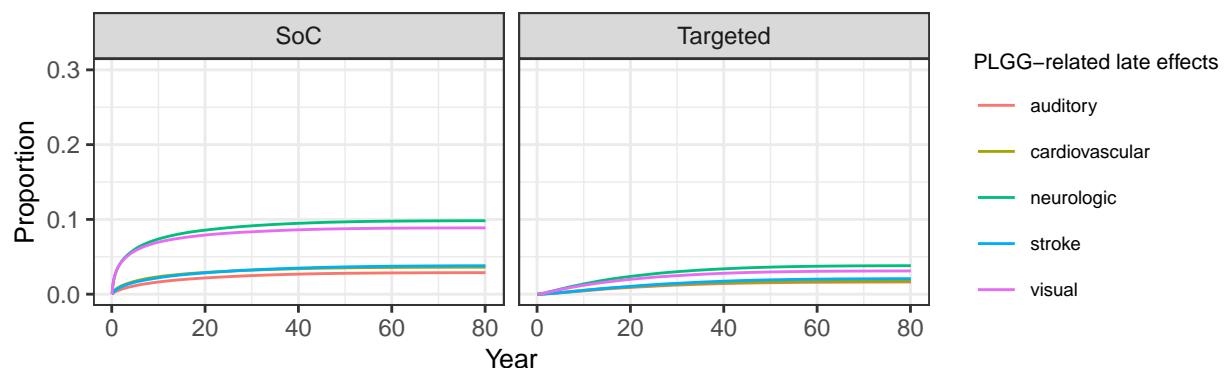
Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.17 (18.71;37.96)	4.54 (0.07;13.37)
QALY	26.77 (20.58;33.3)	21.65 (14.24;27.88)	5.12 (1.56;12.24)
Total Cost	\$5,106,341 (\$4,016,915;\$6,159,355)	\$676,919 (\$631,593;\$719,368)	\$4,429,422 (\$3,355,095;\$5,492,198)
Non-Targeted PLGG related costs	\$302,455 (\$195,734;\$389,915)	\$446,840 (\$347,481;\$546,026)	\$-144,384 (\$-219,956;\$-94,569)
Late effect costs	\$134,485 (\$67,848;\$243,360)	\$172,620 (\$63,433;\$310,211)	\$-38,135 (\$-71,732;\$9,519)
General population costs	\$89,405 (\$49,536;\$130,247)	\$57,459 (\$25,261;\$94,379)	\$31,946 (\$15,729;\$67,514)
Targeted costs	\$4,579,996 (\$3,468,505;\$5,649,507)	\$0 (\$0;\$0)	\$4,579,996 (\$3,468,505;\$5,649,507)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

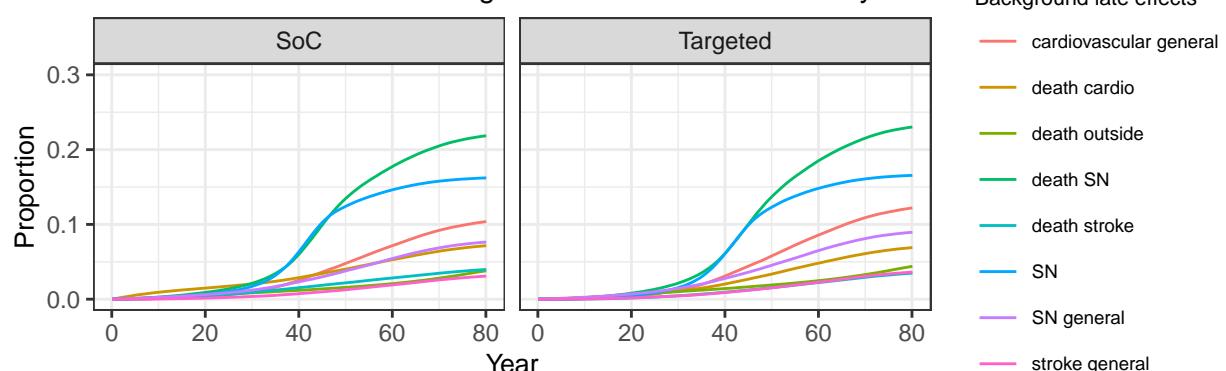
Trace Plot of PLGG States Across Cycles



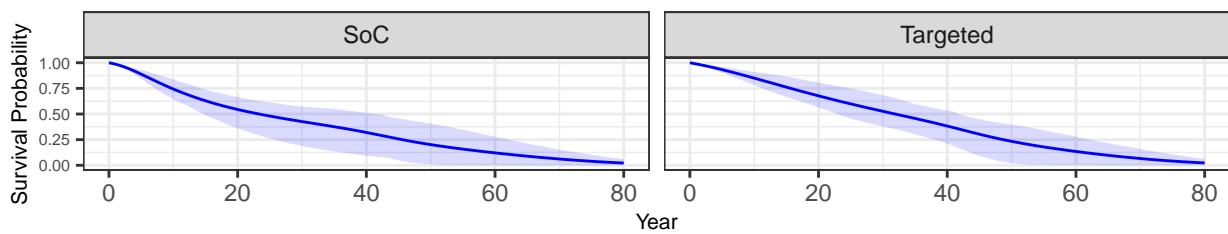
Cumulative Incidence of PLGG-related Late Effects Across Cycles



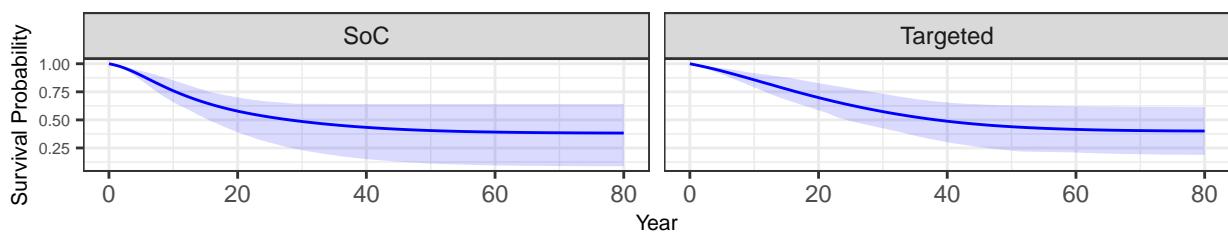
Cumulative Incidence of Background Late Effects Across Cycles



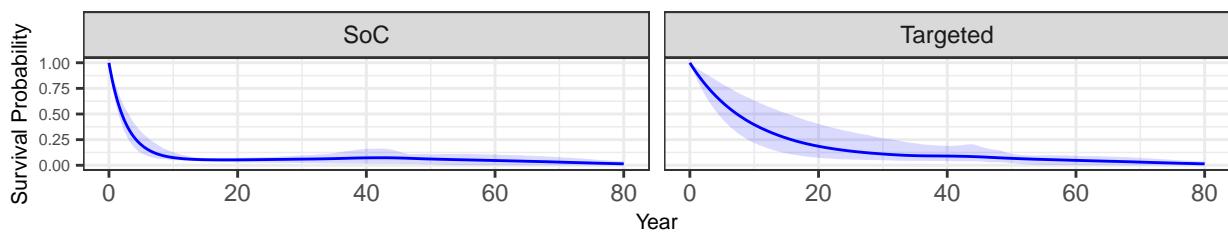
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



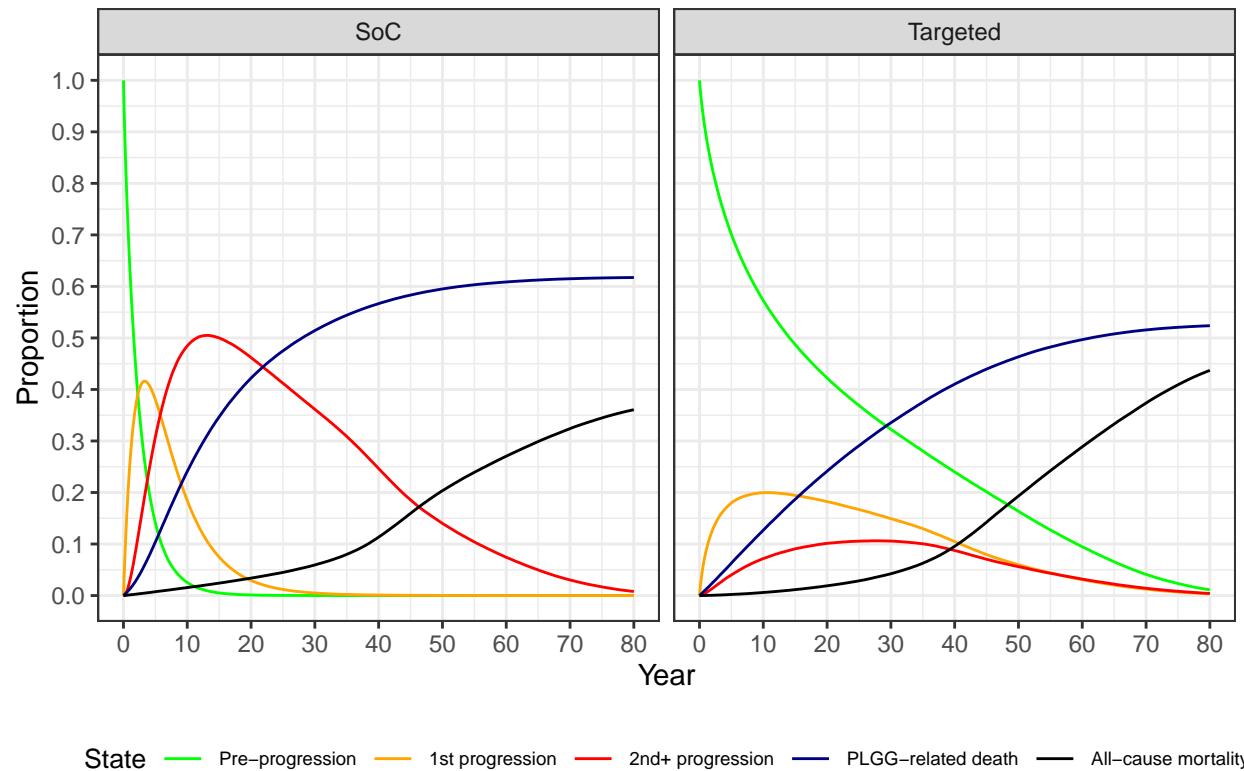
Progression–Free Survival with 95% CI



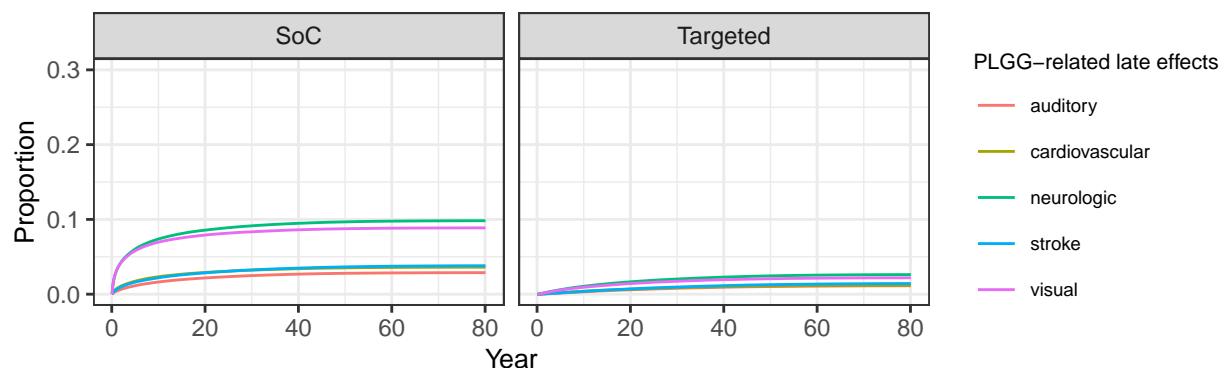
Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.17 (18.71;37.96)	9.85 (1.25;22.84)
QALY	31.22 (25.52;36.76)	21.65 (14.24;27.88)	9.56 (3.44;19.7)
Total Cost	\$5,812,759 (\$4,835,804;\$6,761,060)	\$676,919 (\$631,593;\$719,368)	\$5,135,840 (\$4,162,838;\$6,071,790)
Non-Targeted PLGG related costs	\$248,448 (\$180,882;\$319,703)	\$446,840 (\$347,481;\$546,026)	\$-198,392 (\$-316,299;\$-105,873)
Late effect costs	\$137,404 (\$87,683;\$207,124)	\$172,620 (\$63,433;\$310,211)	\$-35,216 (\$-113,554;\$42,227)
General population costs	\$119,998 (\$79,788;\$161,275)	\$57,459 (\$25,261;\$94,379)	\$62,539 (\$32,656;\$110,372)
Targeted costs	\$5,306,910 (\$4,323,989;\$6,267,205)	\$0 (\$0;\$0)	\$5,306,910 (\$4,323,989;\$6,267,205)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

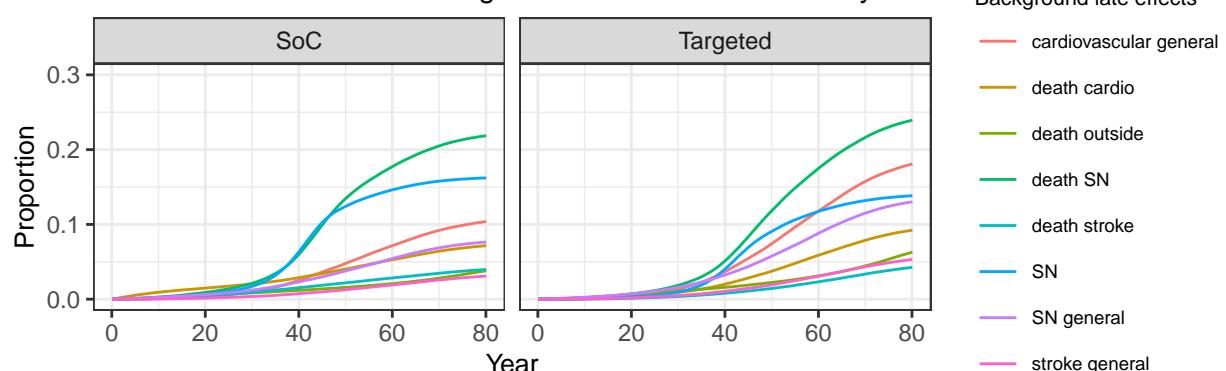
Trace Plot of PLGG States Across Cycles



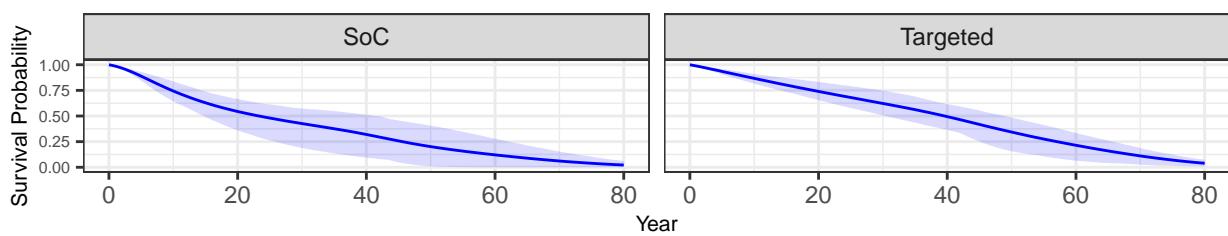
Cumulative Incidence of PLGG-related Late Effects Across Cycles



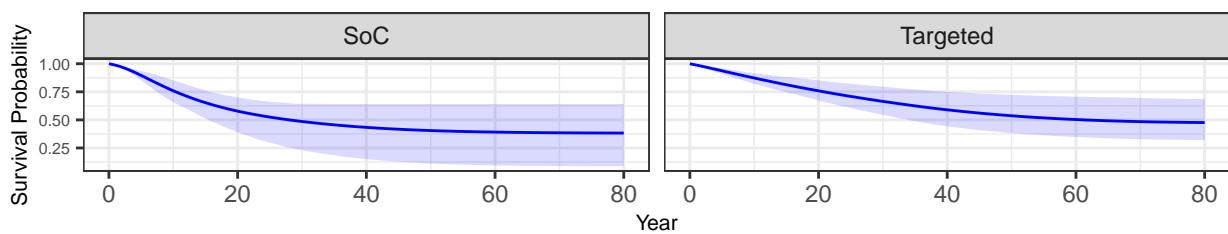
Cumulative Incidence of Background Late Effects Across Cycles



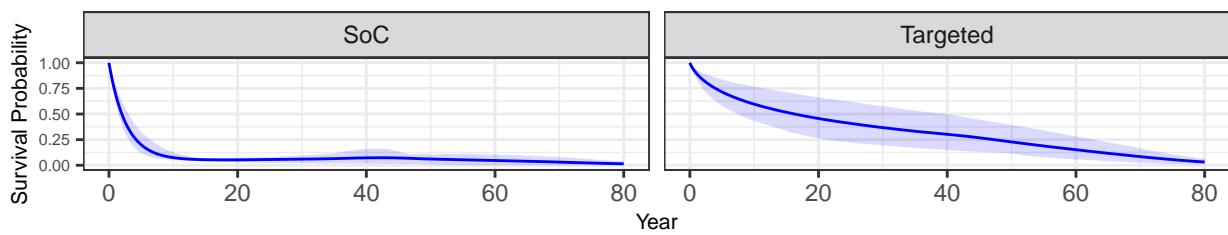
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



3% discount rate

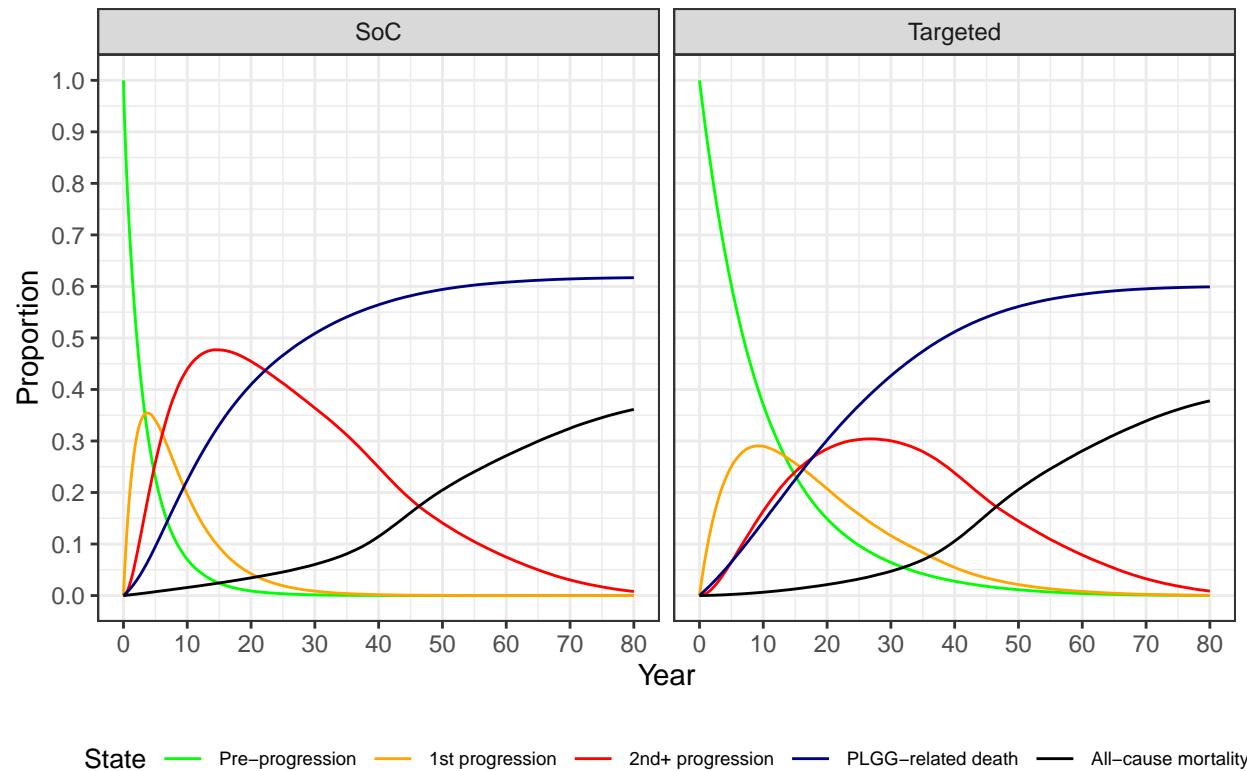
Scenario #1a

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 3
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

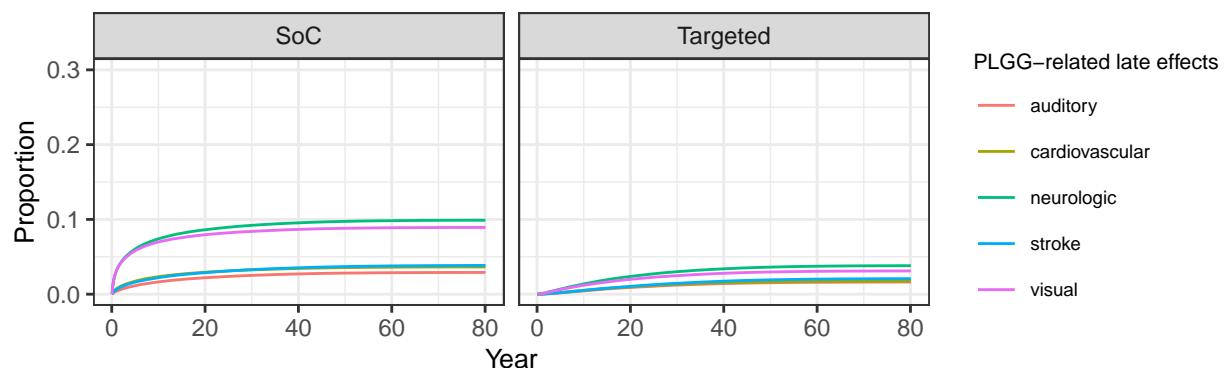
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	10.16 (7.81;12.64)	8.31 (5.81;10.47)	1.85 (0.62;4.24)
Total Cost	\$1,937,613 (\$1,524,296;\$2,337,015)	\$254,006 (\$234,782;\$270,923)	\$1,683,606 (\$1,274,530;\$2,086,283)
Non-Targeted PLGG related costs	\$114,952 (\$74,628;\$147,961)	\$166,281 (\$131,064;\$202,377)	\$-51,328 (\$-76,422;\$-31,472)
Late effect costs	\$51,028 (\$25,734;\$92,366)	\$65,760 (\$26,190;\$115,663)	\$-14,731 (\$-24,769;\$1,823)
General population costs	\$33,919 (\$18,792;\$49,415)	\$21,966 (\$9,936;\$35,622)	\$11,953 (\$6,028;\$23,908)
Targeted costs	\$1,737,713 (\$1,315,964;\$2,143,432)	\$0 (\$0;\$0)	\$1,737,713 (\$1,315,964;\$2,143,432)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

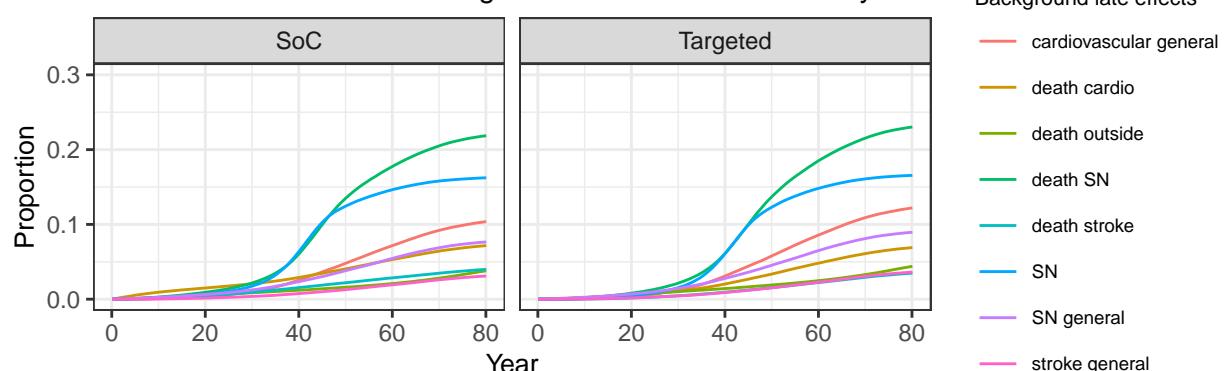
Trace Plot of PLGG States Across Cycles



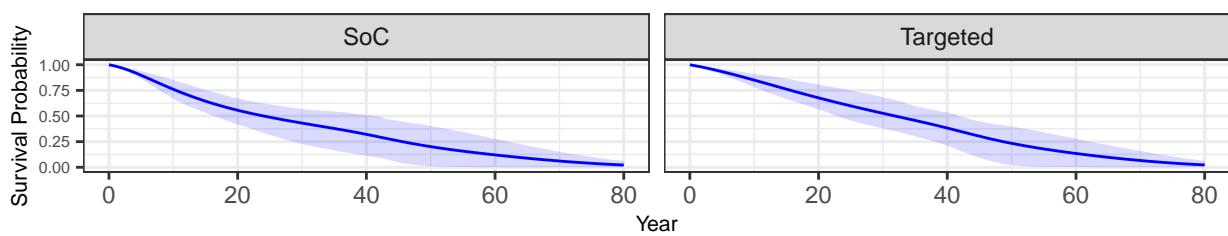
Cumulative Incidence of PLGG-related Late Effects Across Cycles



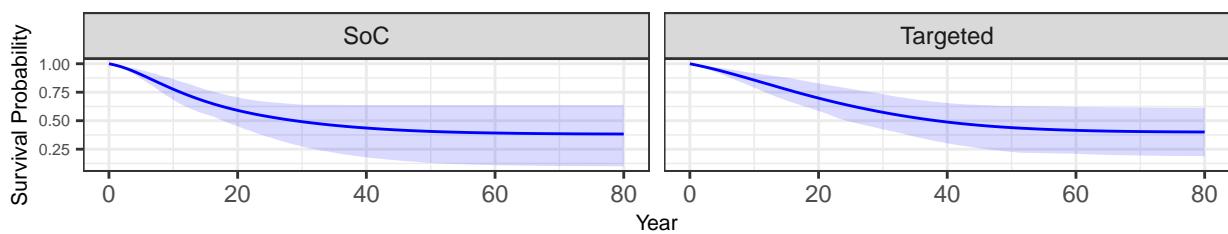
Cumulative Incidence of Background Late Effects Across Cycles



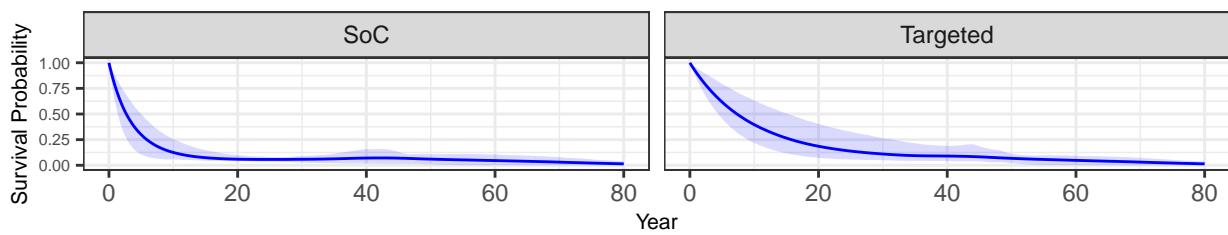
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



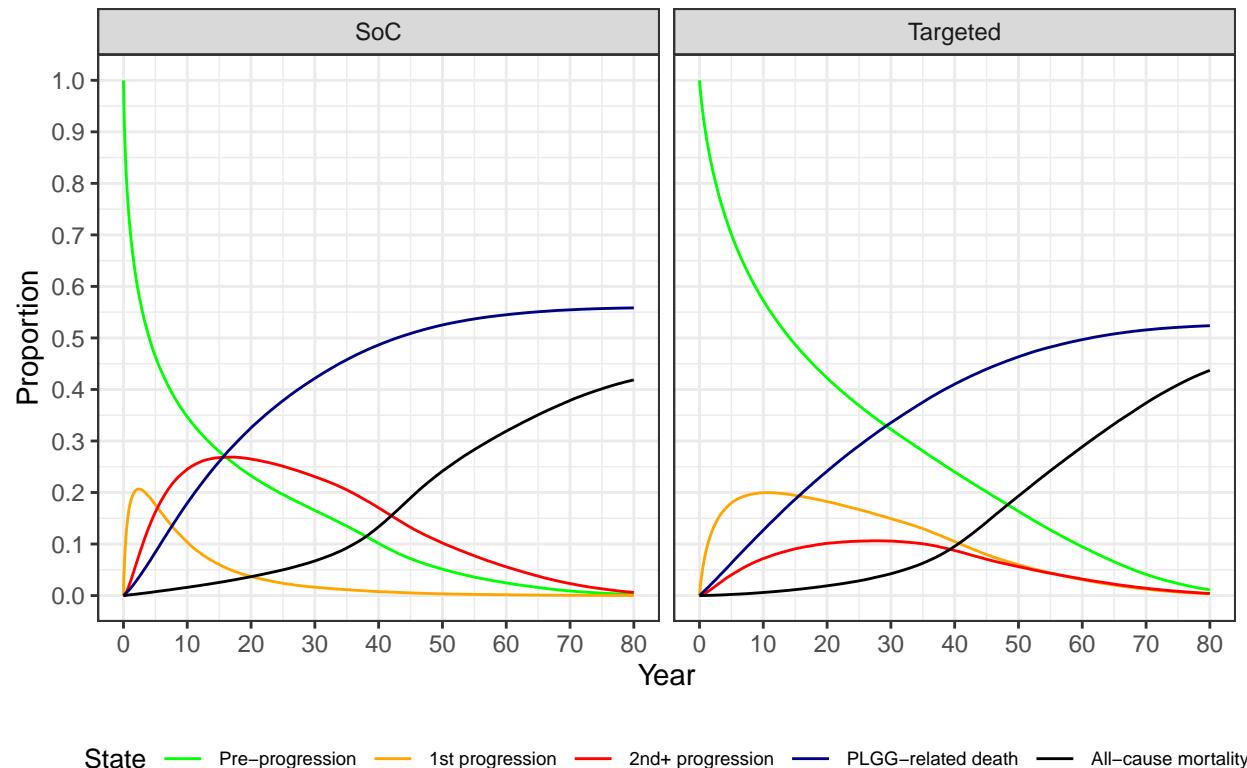
Progression-Free Survival with 95% CI



Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

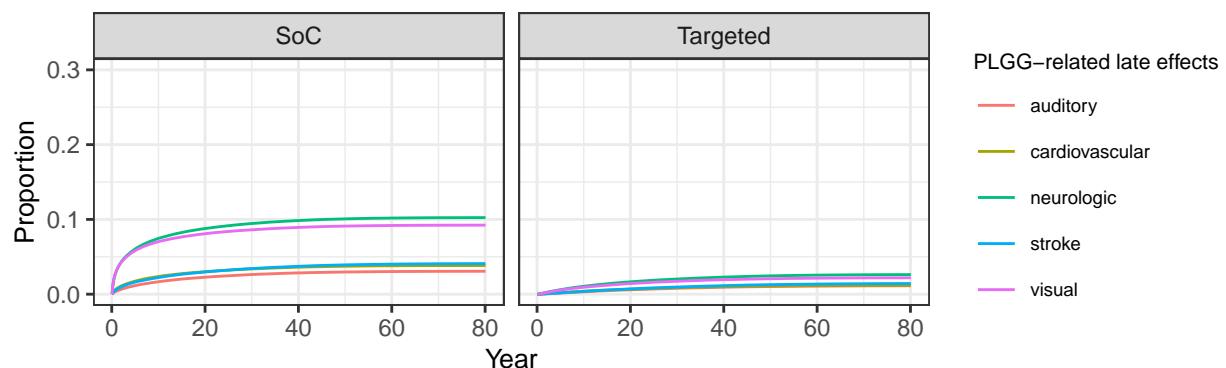
Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	11.84 (9.68;13.95)	9.17 (7.34;10.98)	2.68 (0.81;5.4)
Total Cost	\$2,205,659 (\$1,835,087;\$2,565,352)	\$242,104 (\$230,636;\$255,510)	\$1,963,554 (\$1,594,243;\$2,313,765)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$142,136 (\$105,162;\$169,173)	\$-47,655 (\$-84,811;\$-21,009)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$75,039 (\$48,984;\$120,546)	\$-22,906 (\$-41,637;\$-5,211)
General population costs	\$45,527 (\$30,271;\$61,187)	\$24,930 (\$13,622;\$38,652)	\$20,597 (\$9,213;\$36,475)
Targeted costs	\$2,013,518 (\$1,640,618;\$2,377,825)	\$0 (\$0;\$0)	\$2,013,518 (\$1,640,618;\$2,377,825)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

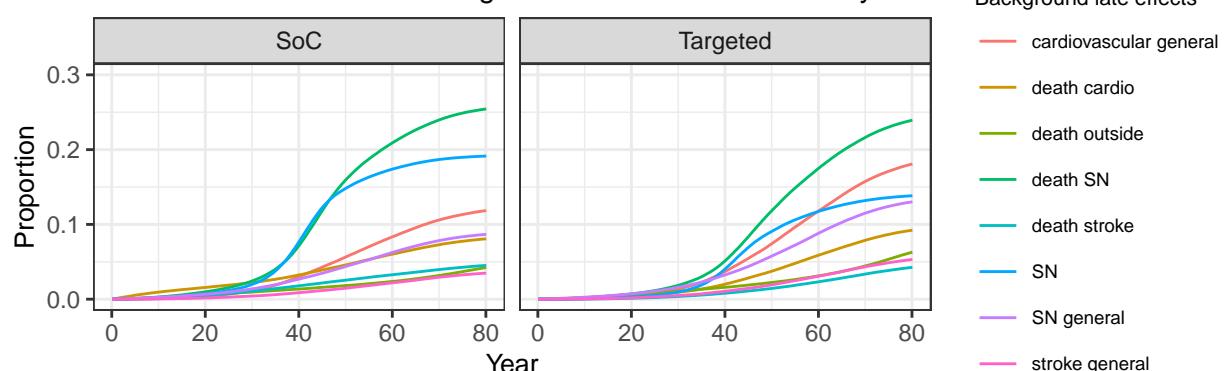


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

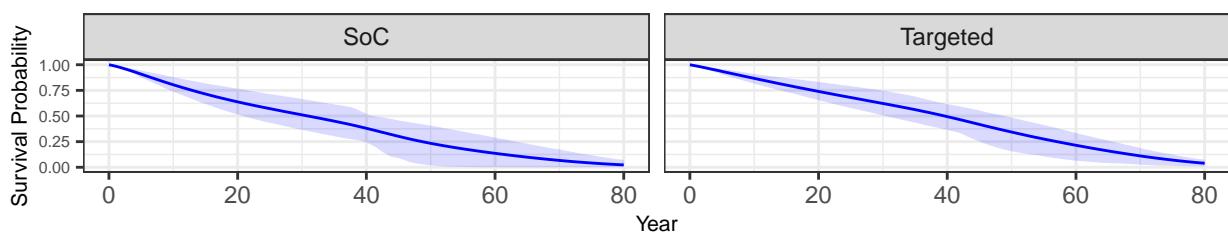
Cumulative Incidence of PLGG-related Late Effects Across Cycles



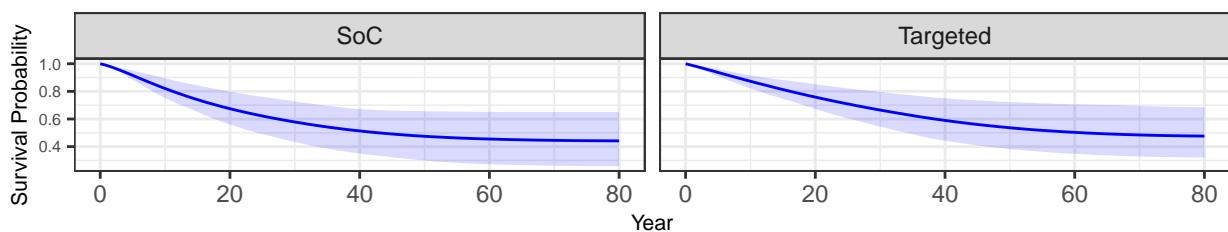
Cumulative Incidence of Background Late Effects Across Cycles



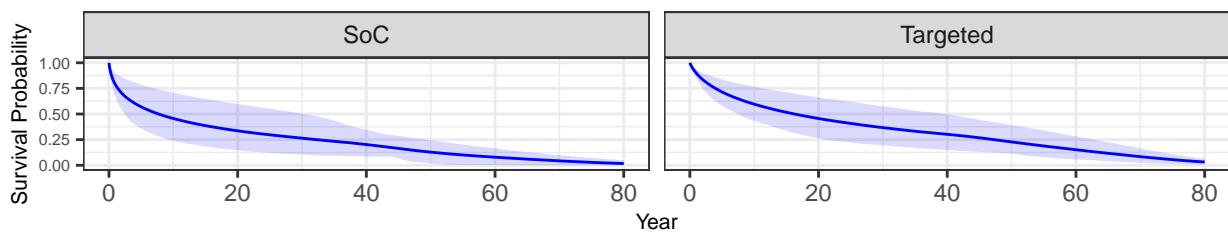
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



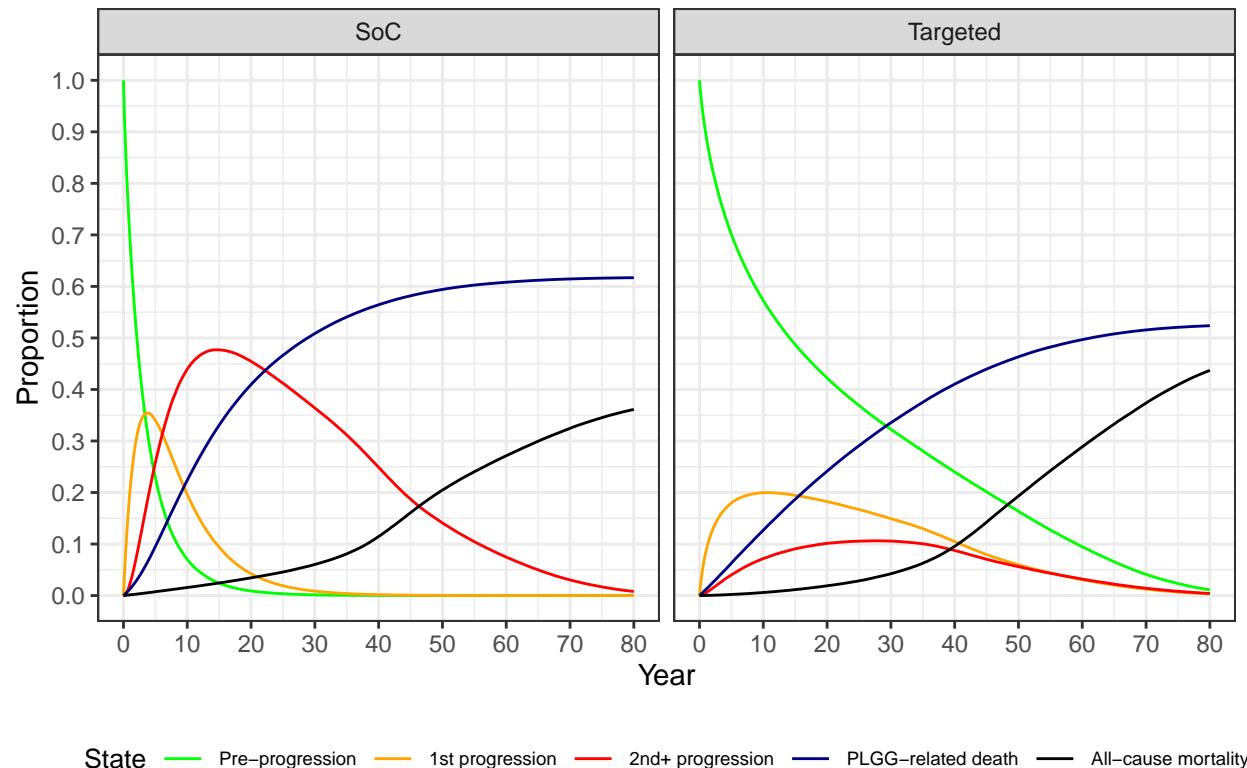
Progression-Free Survival with 95% CI



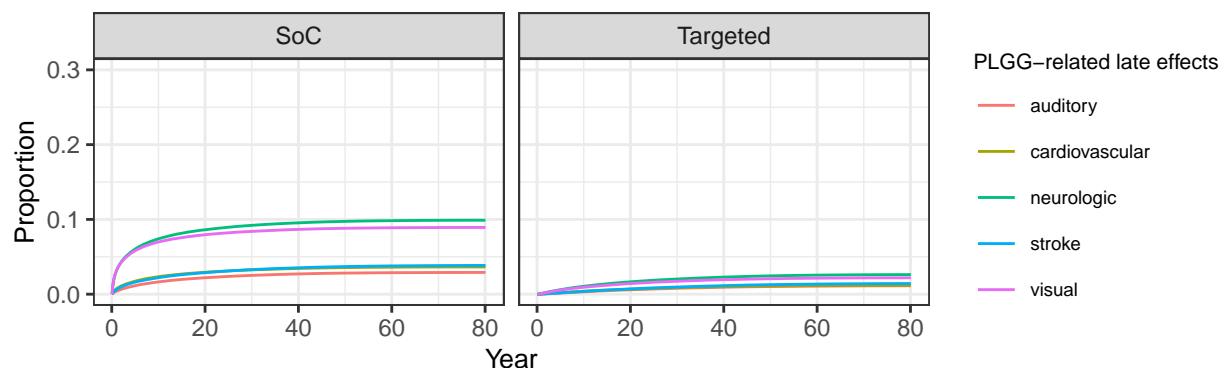
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	11.84 (9.68;13.95)	8.31 (5.81;10.47)	3.54 (1.33;7.15)
Total Cost	\$2,205,659 (\$1,835,087;\$2,565,352)	\$254,006 (\$234,782;\$270,923)	\$1,951,652 (\$1,584,976;\$2,313,331)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$166,281 (\$131,064;\$202,377)	\$-71,799 (\$-117,219;\$-36,530)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$65,760 (\$26,190;\$115,663)	\$-13,627 (\$-40,553;\$15,830)
General population costs	\$45,527 (\$30,271;\$61,187)	\$21,966 (\$9,936;\$35,622)	\$23,561 (\$12,645;\$40,867)
Targeted costs	\$2,013,518 (\$1,640,618;\$2,377,825)	\$0 (\$0;\$0)	\$2,013,518 (\$1,640,618;\$2,377,825)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

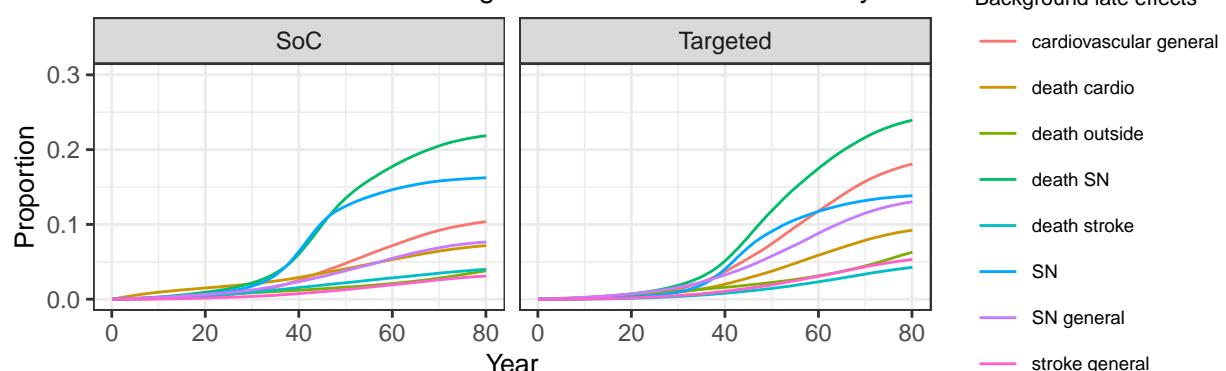
Trace Plot of PLGG States Across Cycles



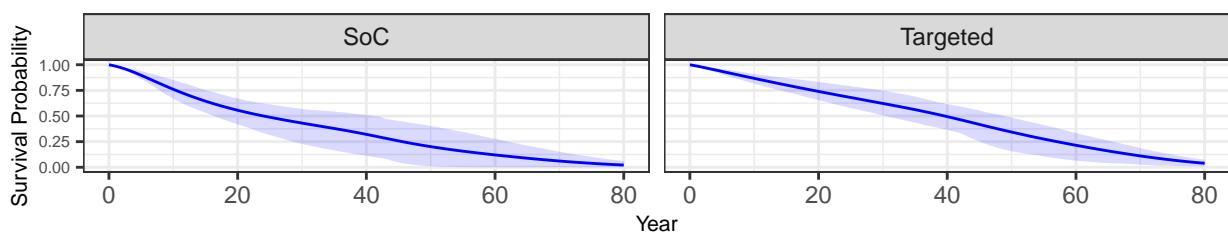
Cumulative Incidence of PLGG-related Late Effects Across Cycles



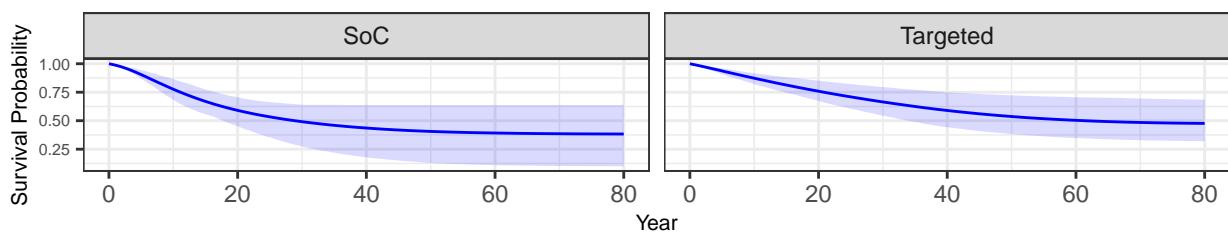
Cumulative Incidence of Background Late Effects Across Cycles



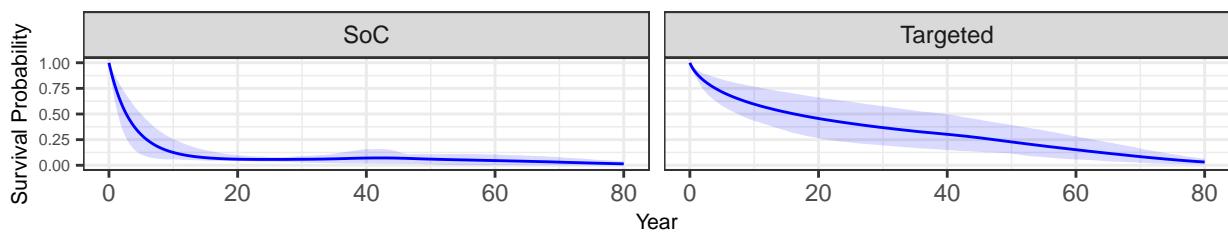
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



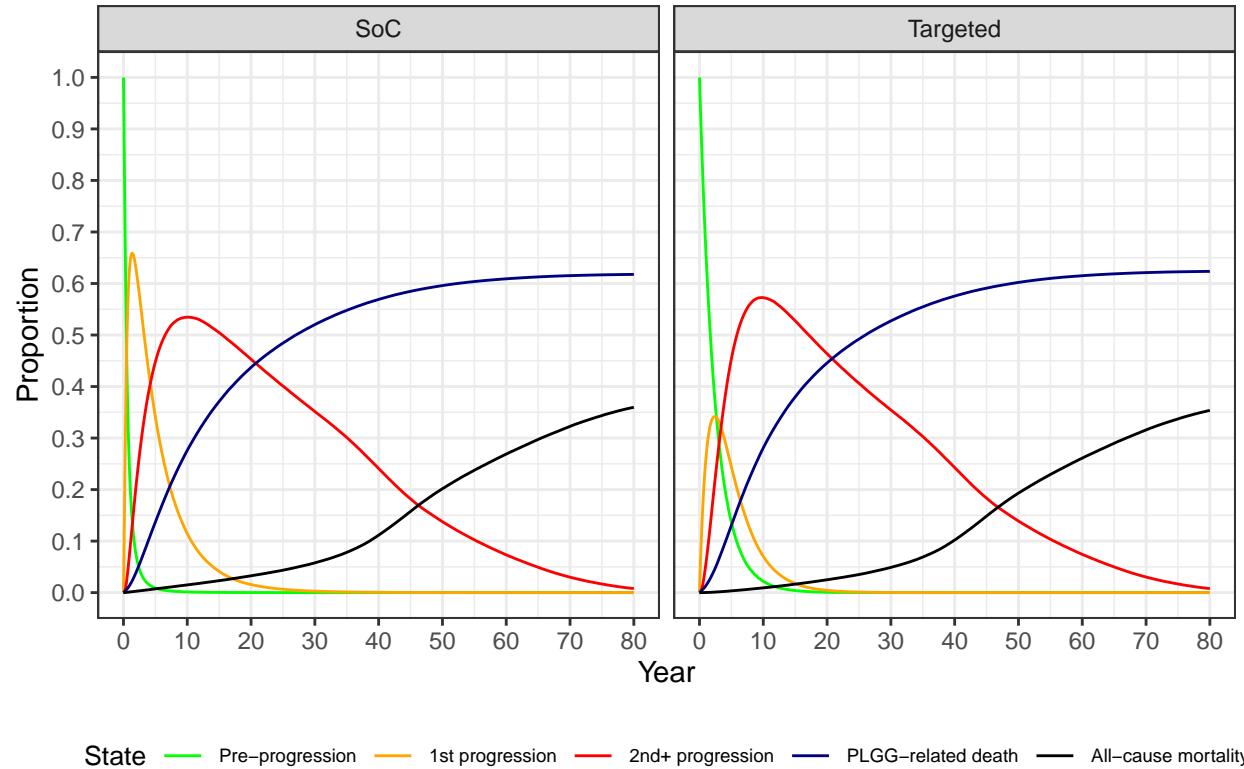
Progression-Free Survival with 95% CI



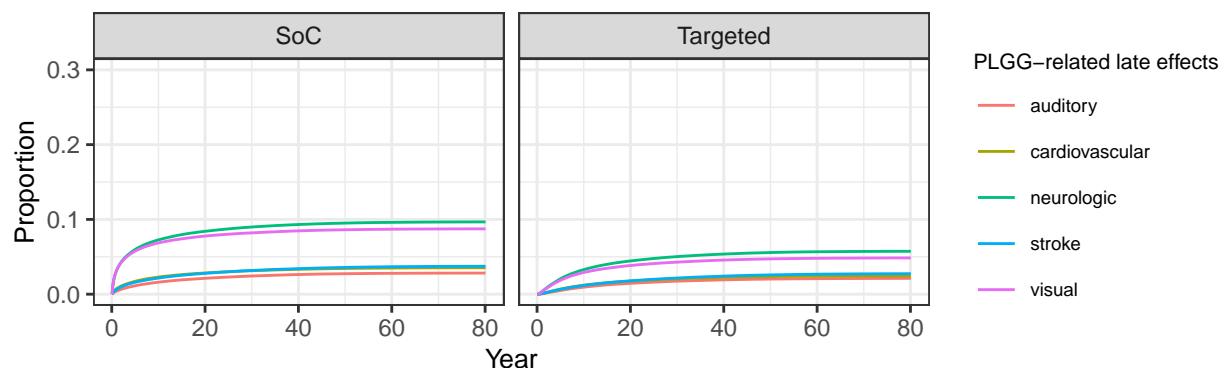
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	8.44 (5.29;11.23)	8.05 (4.98;10.67)	0.39 (-0.13;0.8)
Total Cost	\$1,711,582 (\$1,113,507;\$2,254,921)	\$257,654 (\$238,405;\$275,801)	\$1,453,928 (\$877,132;\$1,976,482)
Non-Targeted PLGG related costs	\$151,084 (\$110,322;\$187,135)	\$171,054 (\$130,791;\$207,080)	\$-19,970 (\$-27,914;\$-12,213)
Late effect costs	\$54,293 (\$15,501;\$110,517)	\$65,034 (\$22,454;\$119,052)	\$-10,741 (\$-15,229;\$-6,510)
General population costs	\$25,381 (\$11,269;\$41,862)	\$21,566 (\$8,702;\$36,563)	\$3,814 (\$1,620;\$5,875)
Targeted costs	\$1,480,825 (\$900,475;\$1,999,734)	\$0 (\$0;\$0)	\$1,480,825 (\$900,475;\$1,999,734)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

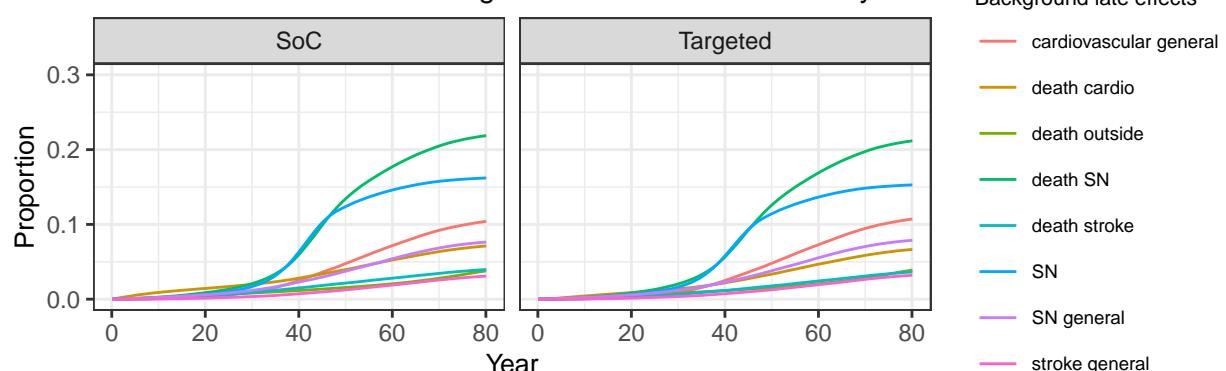
Trace Plot of PLGG States Across Cycles



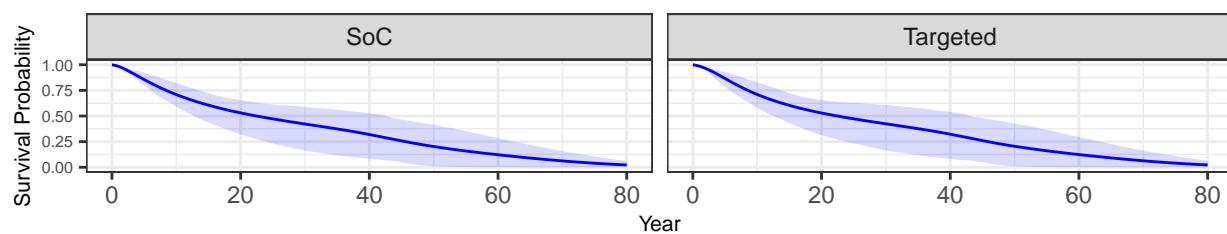
Cumulative Incidence of PLGG-related Late Effects Across Cycles



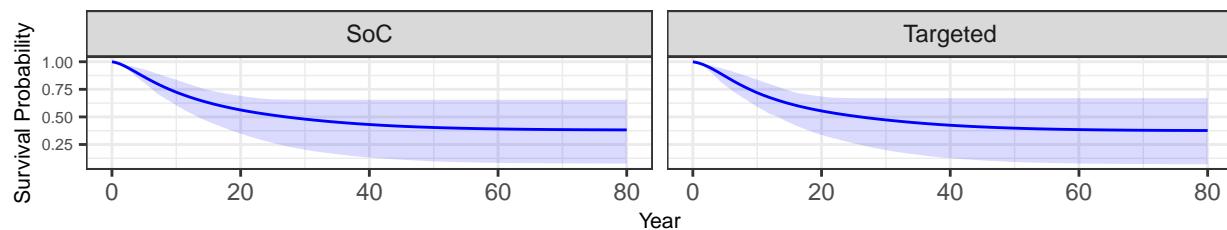
Cumulative Incidence of Background Late Effects Across Cycles



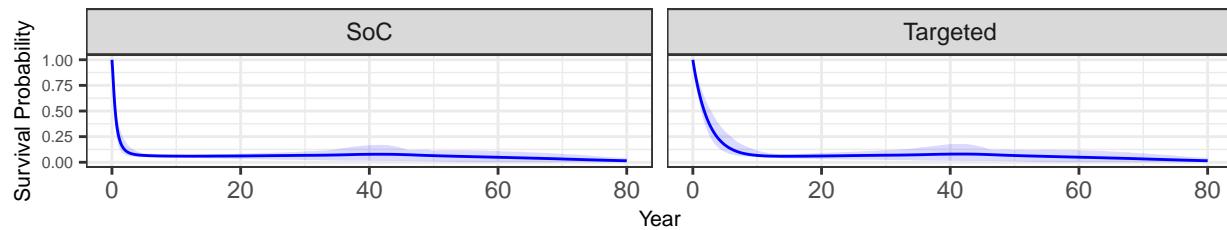
Overall Survival with 95% CI



PLGG-death–related Survival with 95% CI



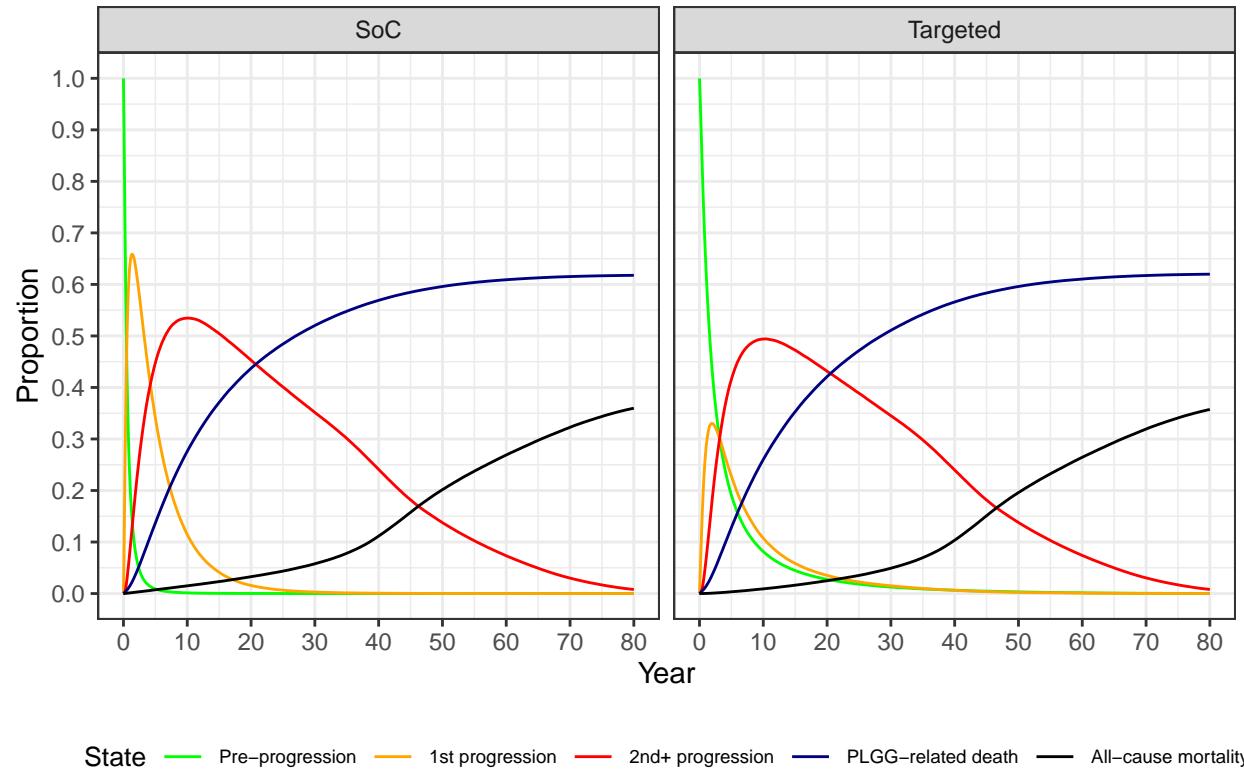
Progression-Free Survival with 95% CI



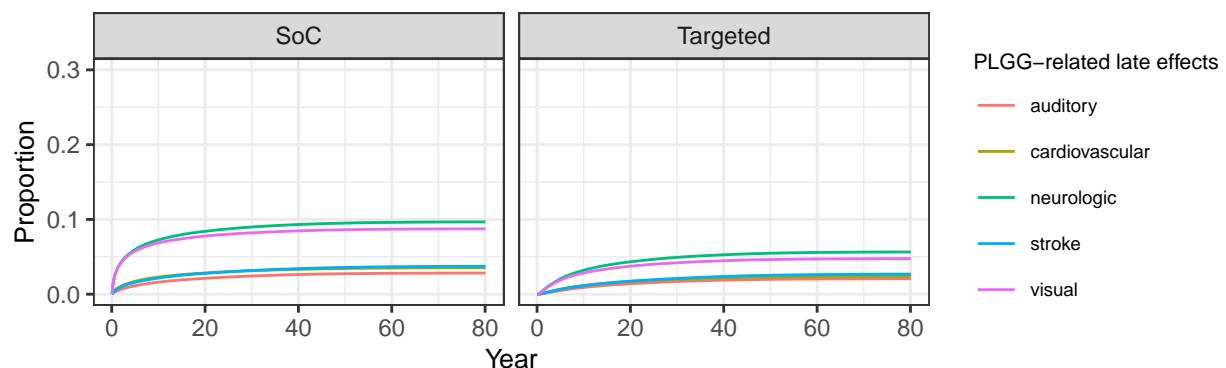
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	8.67 (6.25;11.25)	8.05 (4.98;10.67)	0.62 (0.1;1.16)
Total Cost	\$1,745,816 (\$1,276,181;\$2,237,349)	\$257,654 (\$238,405;\$275,801)	\$1,488,162 (\$1,026,167;\$1,972,538)
Non-Targeted PLGG related costs	\$146,510 (\$106,265;\$181,720)	\$171,054 (\$130,791;\$207,080)	\$-24,544 (\$-33,134;\$-16,257)
Late effect costs	\$54,426 (\$22,289;\$108,860)	\$65,034 (\$22,454;\$119,052)	\$-10,608 (\$-16,716;\$-4,905)
General population costs	\$26,393 (\$13,333;\$42,438)	\$21,566 (\$8,702;\$36,563)	\$4,827 (\$2,715;\$7,522)
Targeted costs	\$1,518,486 (\$1,057,150;\$2,002,501)	\$0 (\$0;\$0)	\$1,518,486 (\$1,057,150;\$2,002,501)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

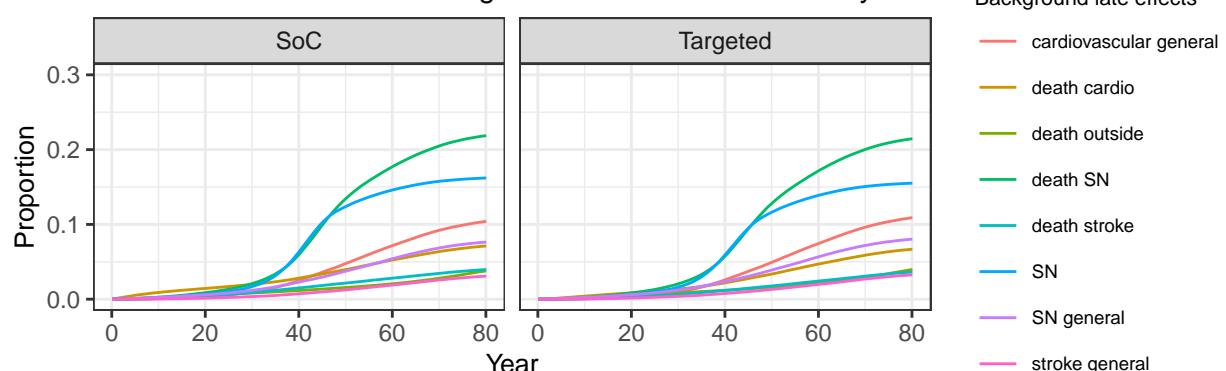
Trace Plot of PLGG States Across Cycles



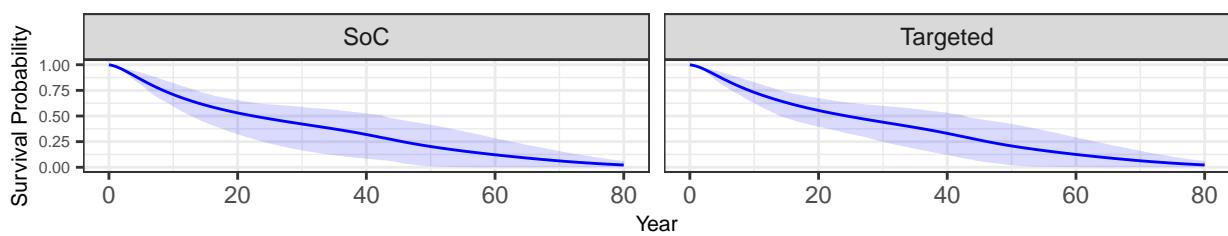
Cumulative Incidence of PLGG-related Late Effects Across Cycles



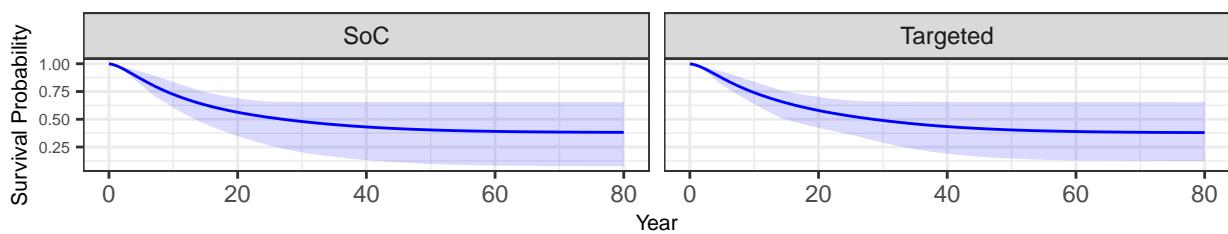
Cumulative Incidence of Background Late Effects Across Cycles



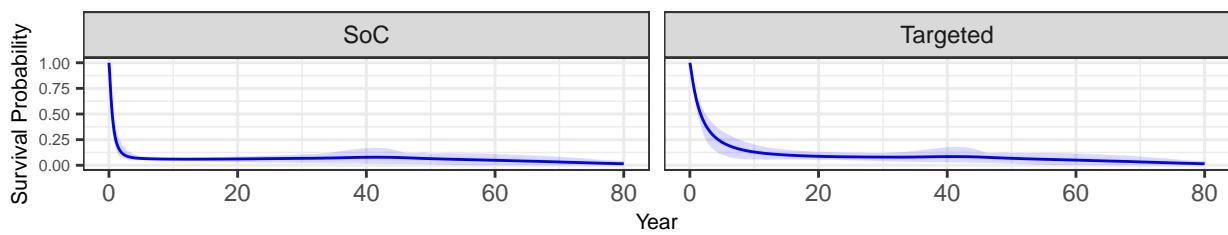
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



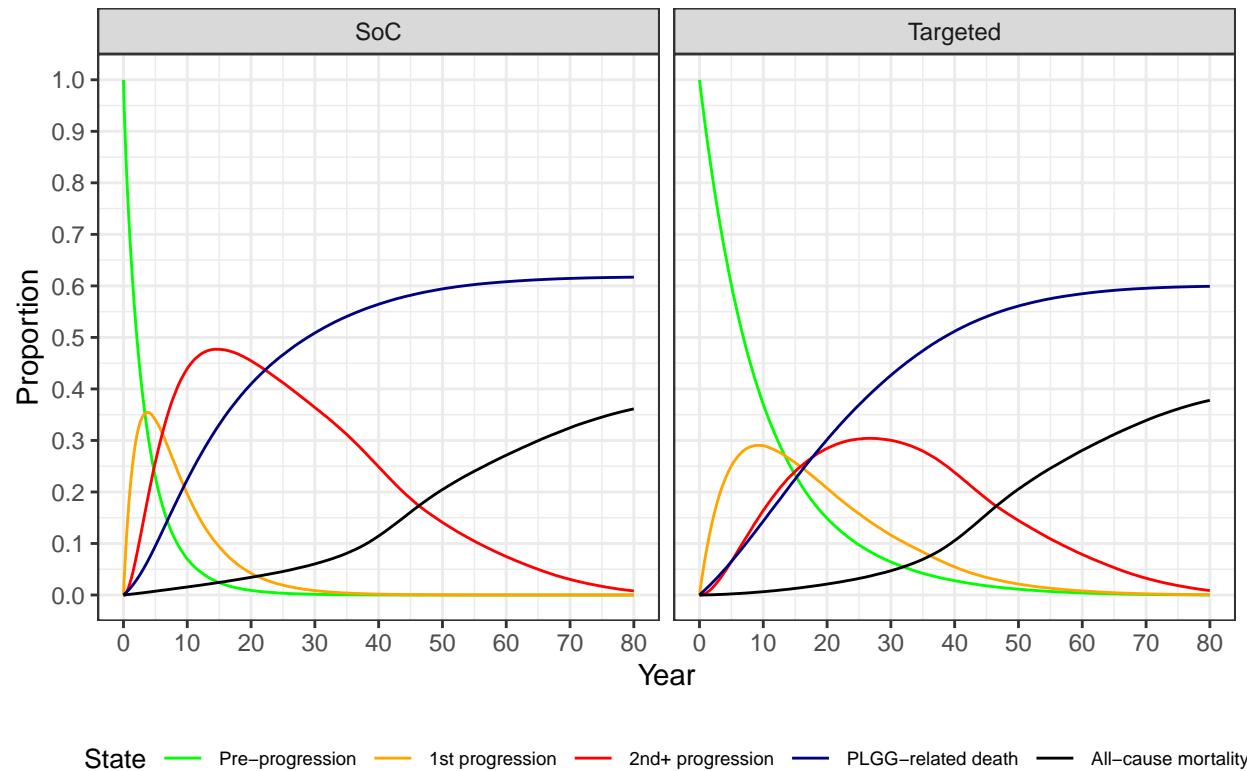
Scenario #1c

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **50% combo price reduction**
- Discount rate: 3
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

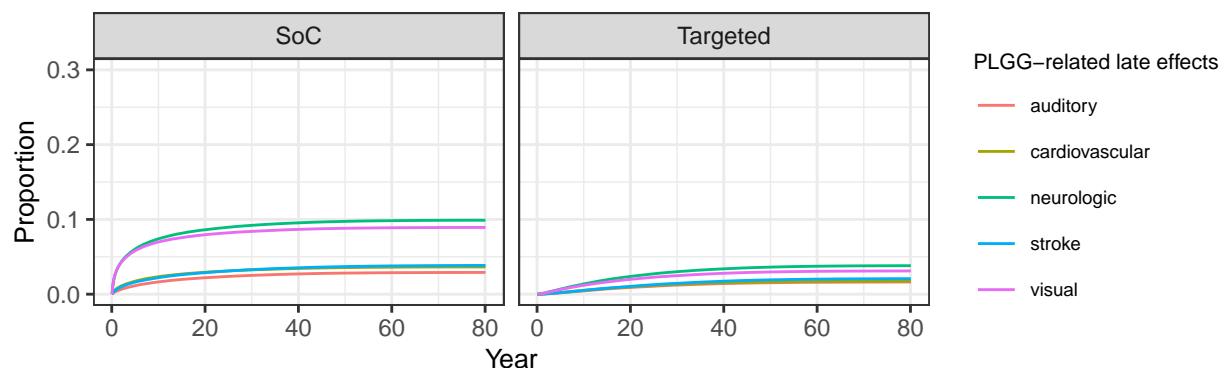
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	10.16 (7.81;12.64)	8.31 (5.81;10.47)	1.85 (0.62;4.24)
Total Cost	\$1,068,756 (\$864,971;\$1,265,299)	\$254,006 (\$234,782;\$270,923)	\$814,750 (\$611,206;\$1,012,437)
Non-Targeted PLGG related costs	\$114,952 (\$74,628;\$147,961)	\$166,281 (\$131,064;\$202,377)	\$-51,328 (\$-76,422;\$-31,472)
Late effect costs	\$51,028 (\$25,734;\$92,366)	\$65,760 (\$26,190;\$115,663)	\$-14,731 (\$-24,769;\$1,823)
General population costs	\$33,919 (\$18,792;\$49,415)	\$21,966 (\$9,936;\$35,622)	\$11,953 (\$6,028;\$23,908)
Targeted costs	\$868,856 (\$657,982;\$1,071,716)	\$0 (\$0;\$0)	\$868,856 (\$657,982;\$1,071,716)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

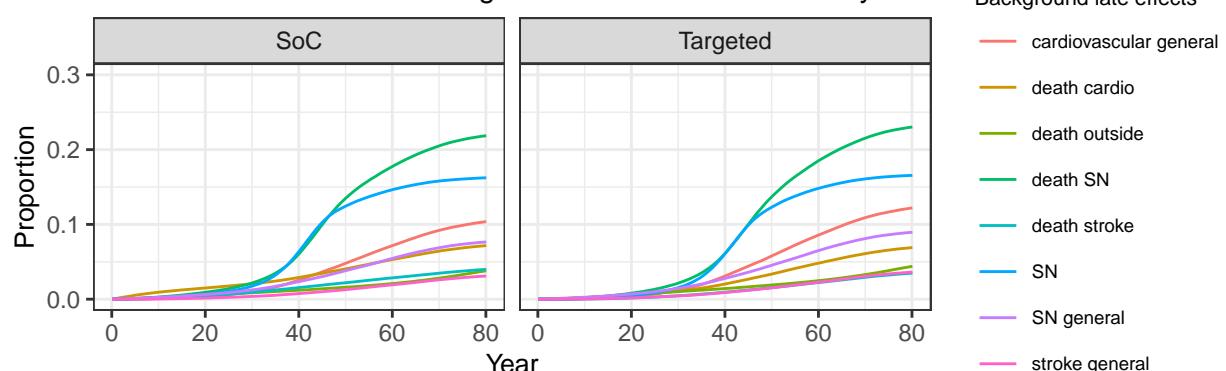
Trace Plot of PLGG States Across Cycles



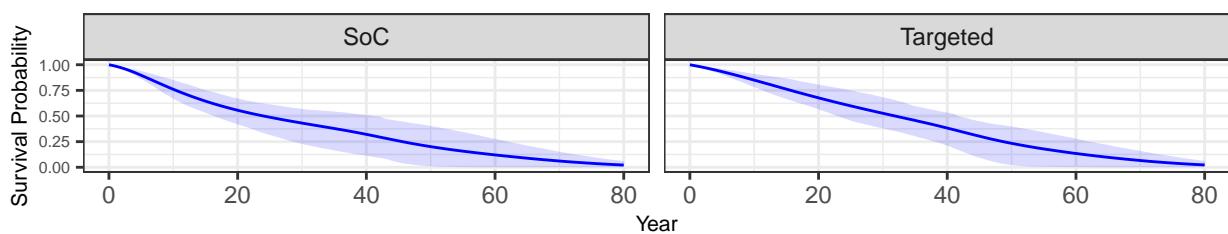
Cumulative Incidence of PLGG-related Late Effects Across Cycles



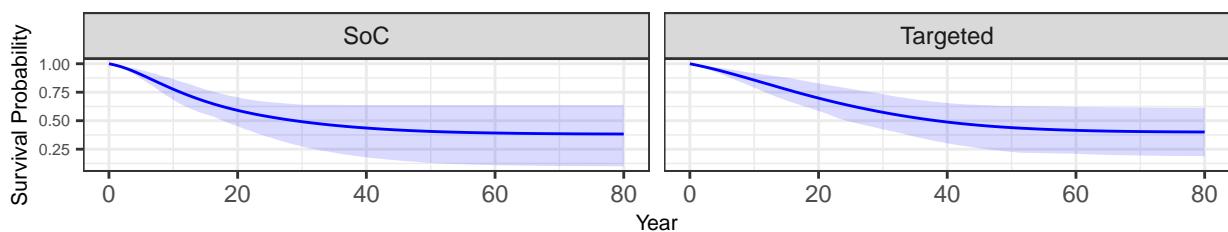
Cumulative Incidence of Background Late Effects Across Cycles



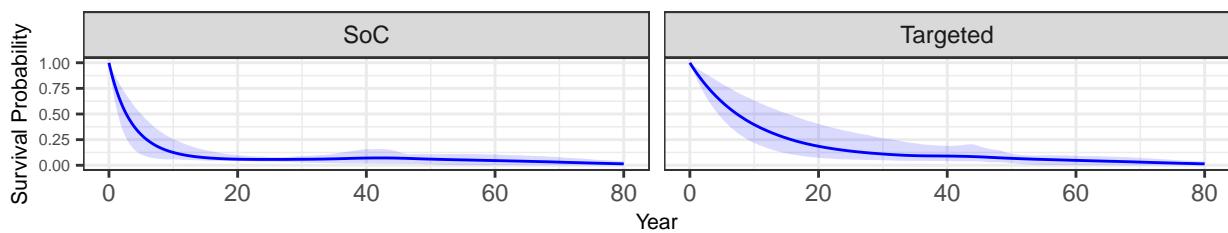
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



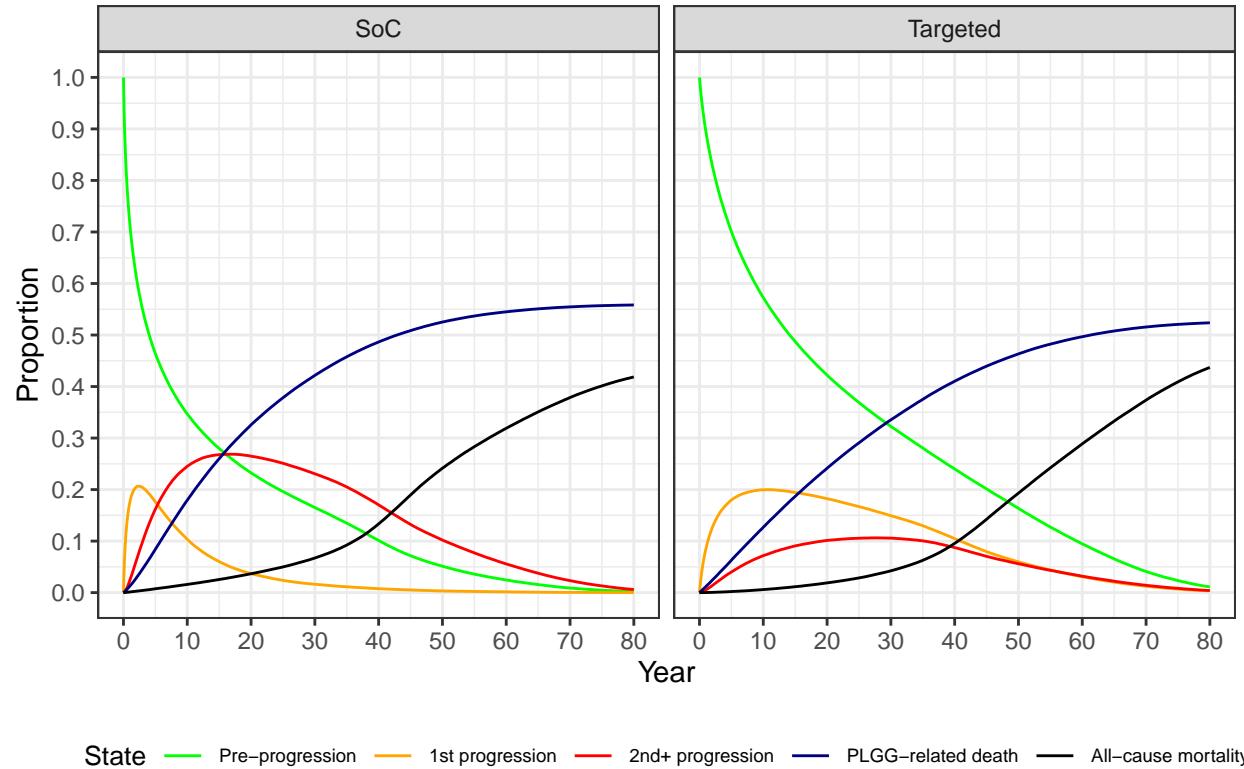
Progression-Free Survival with 95% CI



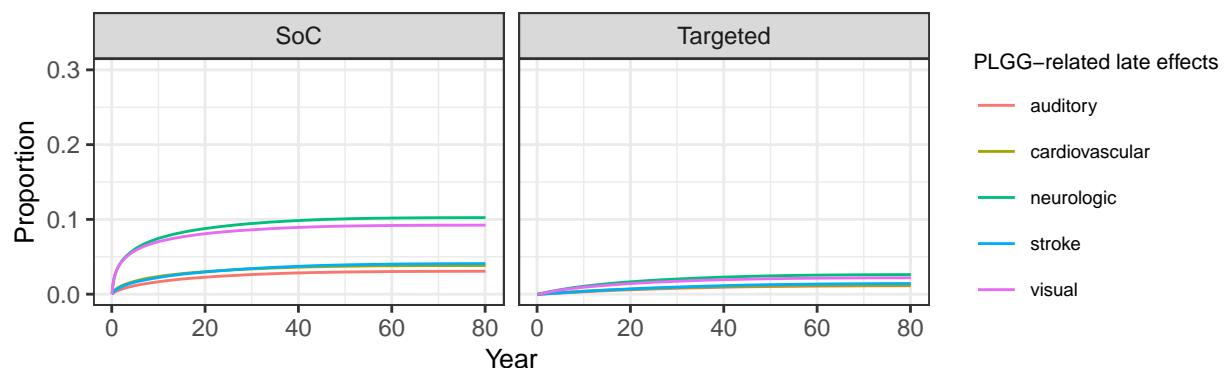
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	11.84 (9.68;13.95)	9.17 (7.34;10.98)	2.68 (0.81;5.4)
Total Cost	\$1,198,900 (\$1,014,566;\$1,376,440)	\$242,104 (\$230,636;\$255,510)	\$956,795 (\$773,722;\$1,124,852)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$142,136 (\$105,162;\$169,173)	\$-47,655 (\$-84,811;\$-21,009)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$75,039 (\$48,984;\$120,546)	\$-22,906 (\$-41,637;\$-5,211)
General population costs	\$45,527 (\$30,271;\$61,187)	\$24,930 (\$13,622;\$38,652)	\$20,597 (\$9,213;\$36,475)
Targeted costs	\$1,006,759 (\$820,309;\$1,188,913)	\$0 (\$0;\$0)	\$1,006,759 (\$820,309;\$1,188,913)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

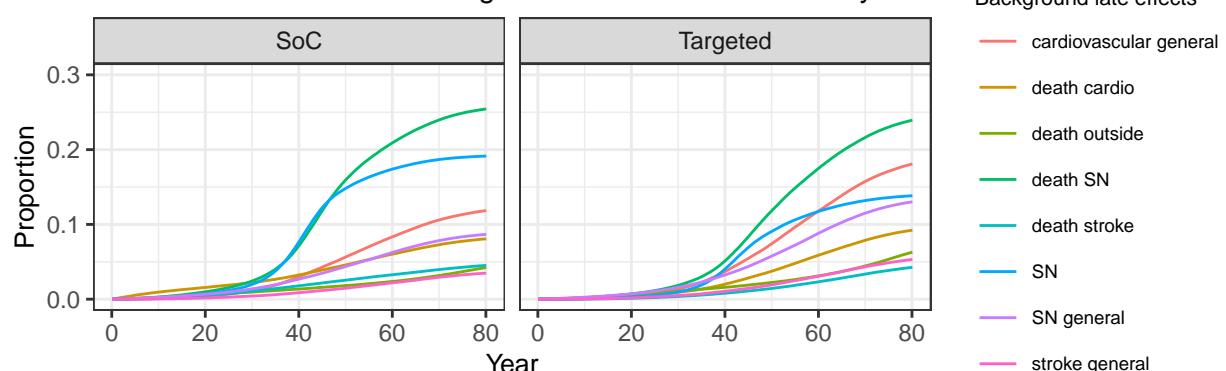
Trace Plot of PLGG States Across Cycles



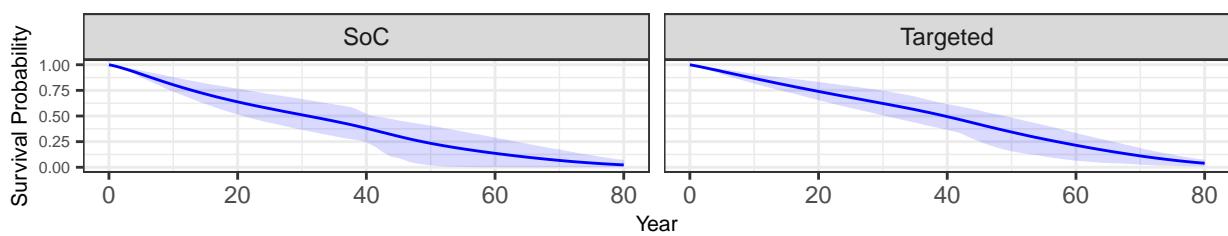
Cumulative Incidence of PLGG-related Late Effects Across Cycles



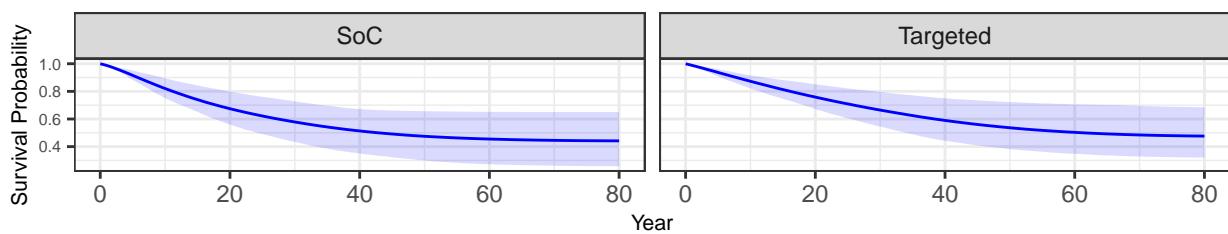
Cumulative Incidence of Background Late Effects Across Cycles



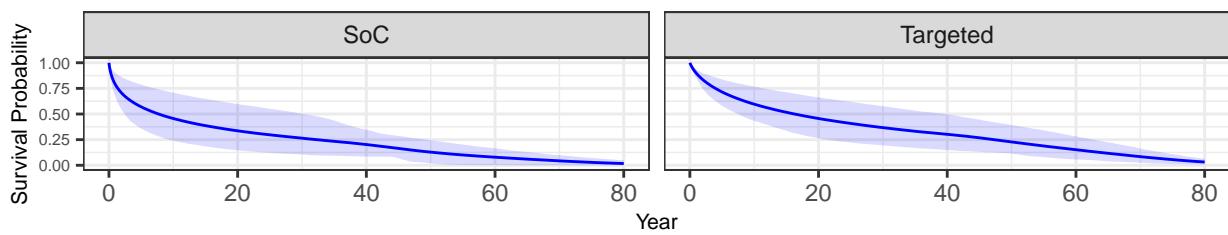
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



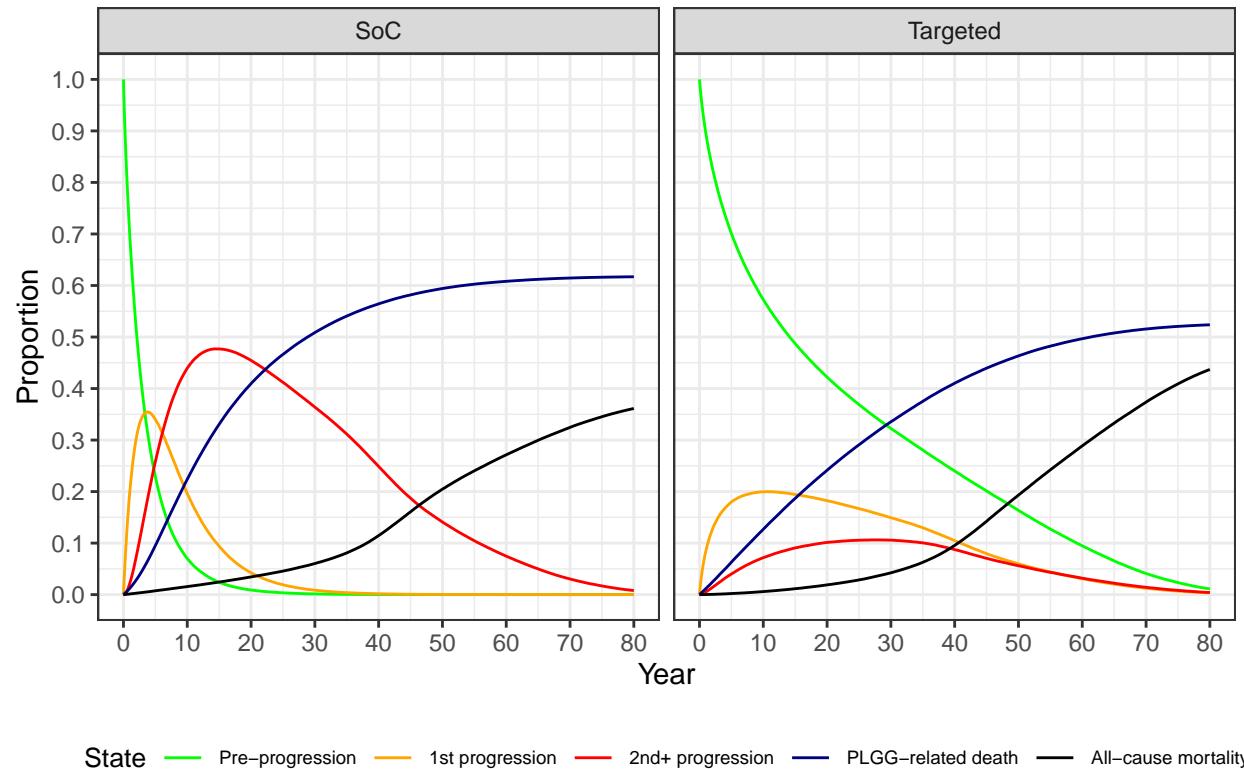
Progression-Free Survival with 95% CI



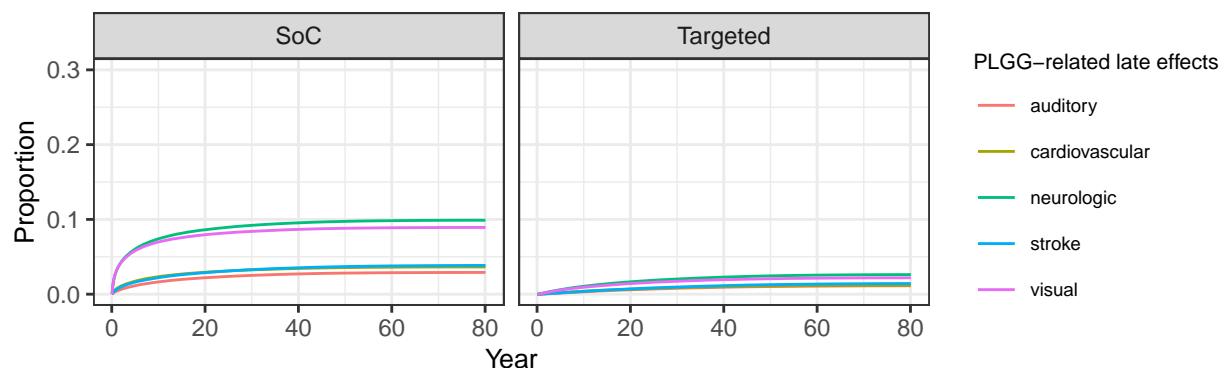
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	11.84 (9.68;13.95)	8.31 (5.81;10.47)	3.54 (1.33;7.15)
Total Cost	\$1,198,900 (\$1,014,566;\$1,376,440)	\$254,006 (\$234,782;\$270,923)	\$944,893 (\$763,629;\$1,124,418)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$166,281 (\$131,064;\$202,377)	\$-71,799 (\$-117,219;\$-36,530)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$65,760 (\$26,190;\$115,663)	\$-13,627 (\$-40,553;\$15,830)
General population costs	\$45,527 (\$30,271;\$61,187)	\$21,966 (\$9,936;\$35,622)	\$23,561 (\$12,645;\$40,867)
Targeted costs	\$1,006,759 (\$820,309;\$1,188,913)	\$0 (\$0;\$0)	\$1,006,759 (\$820,309;\$1,188,913)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

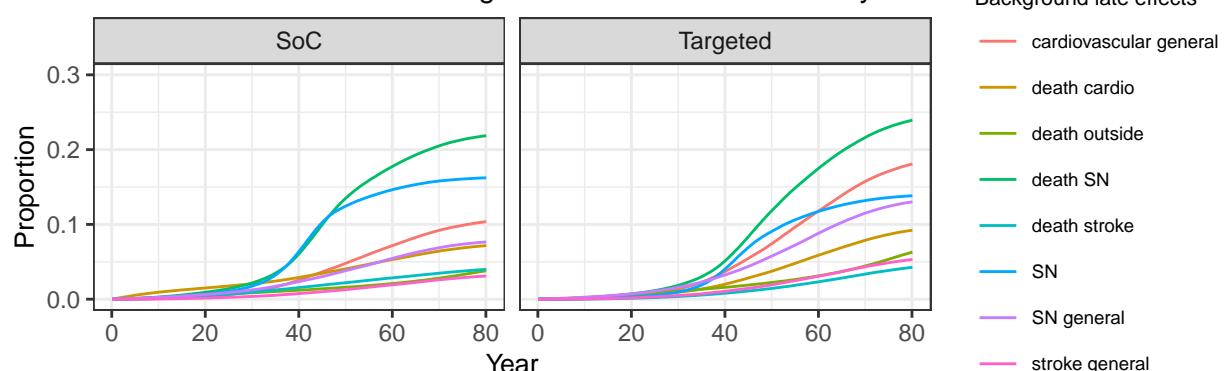
Trace Plot of PLGG States Across Cycles



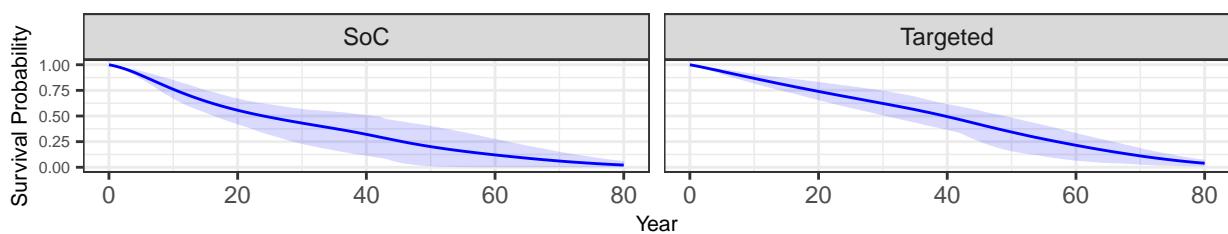
Cumulative Incidence of PLGG-related Late Effects Across Cycles



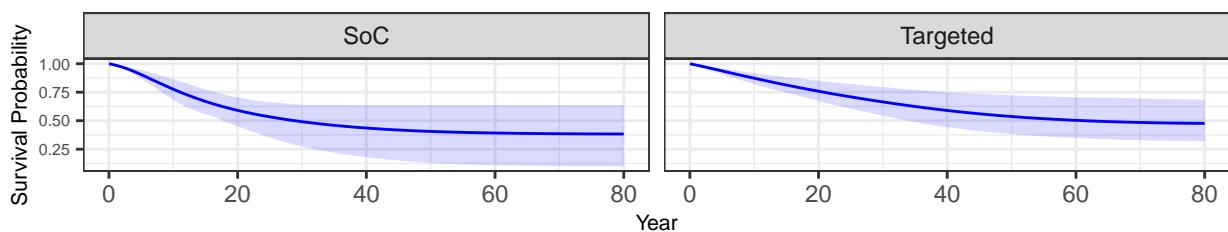
Cumulative Incidence of Background Late Effects Across Cycles



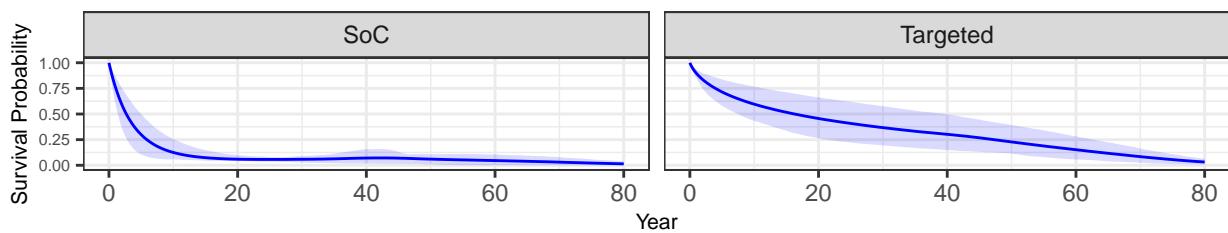
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



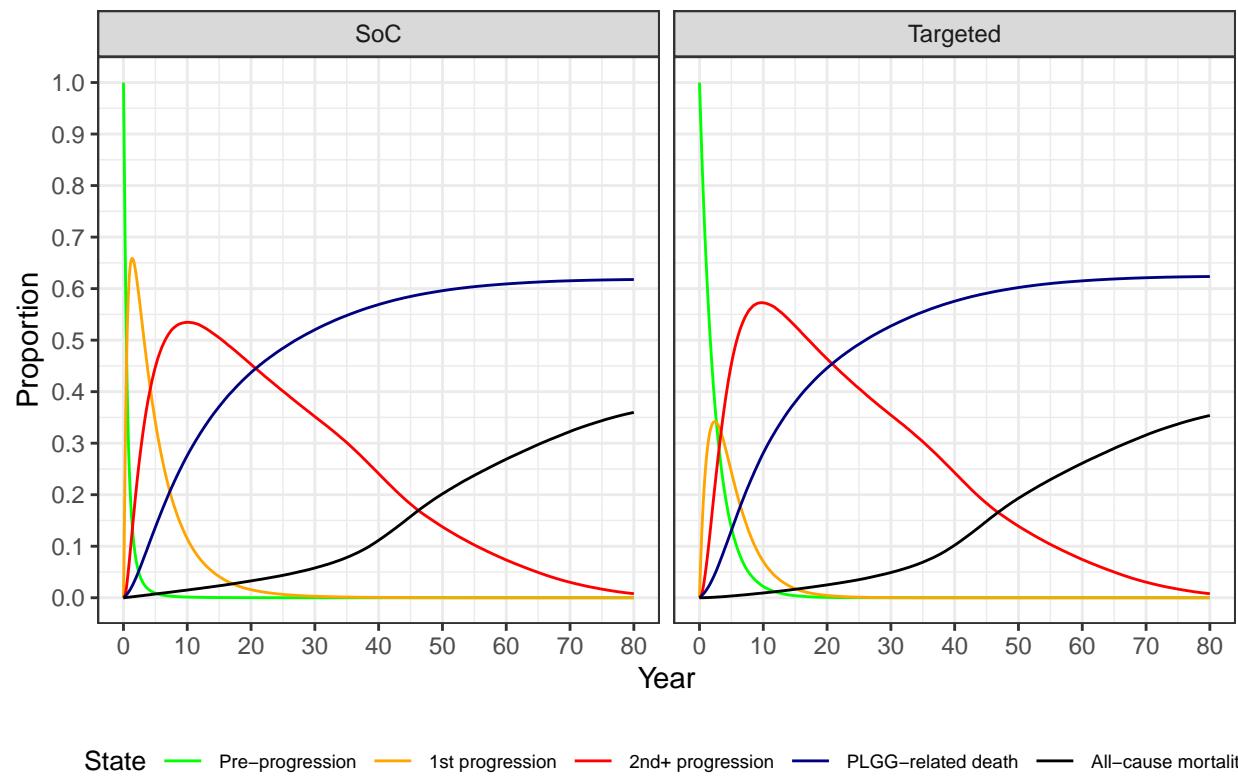
Progression-Free Survival with 95% CI



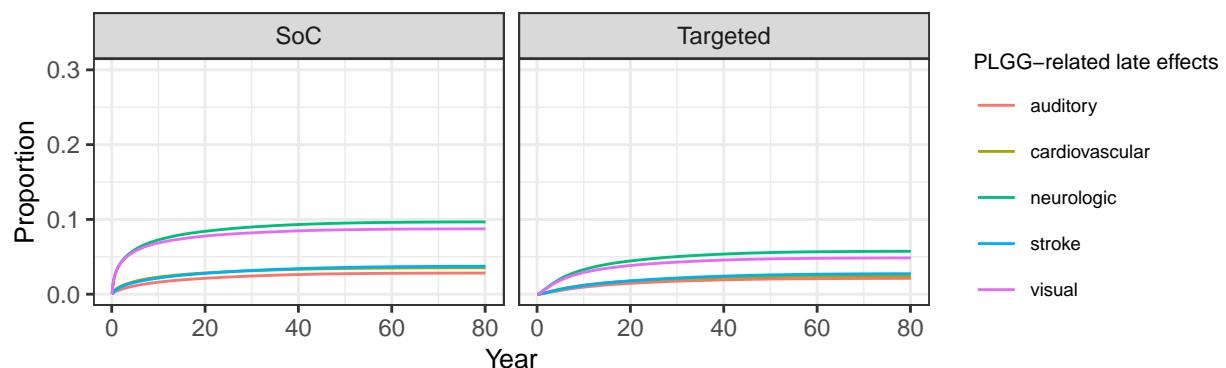
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	8.44 (5.29;11.23)	8.05 (4.98;10.67)	0.39 (-0.13;0.8)
Total Cost	\$971,170 (\$663,269;\$1,244,315)	\$257,654 (\$238,405;\$275,801)	\$713,516 (\$426,894;\$976,615)
Non-Targeted PLGG related costs	\$151,084 (\$110,322;\$187,135)	\$171,054 (\$130,791;\$207,080)	\$-19,970 (\$-27,914;\$-12,213)
Late effect costs	\$54,293 (\$15,501;\$110,517)	\$65,034 (\$22,454;\$119,052)	\$-10,741 (\$-15,229;\$-6,510)
General population costs	\$25,381 (\$11,269;\$41,862)	\$21,566 (\$8,702;\$36,563)	\$3,814 (\$1,620;\$5,875)
Targeted costs	\$740,412 (\$450,238;\$999,867)	\$0 (\$0;\$0)	\$740,412 (\$450,238;\$999,867)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

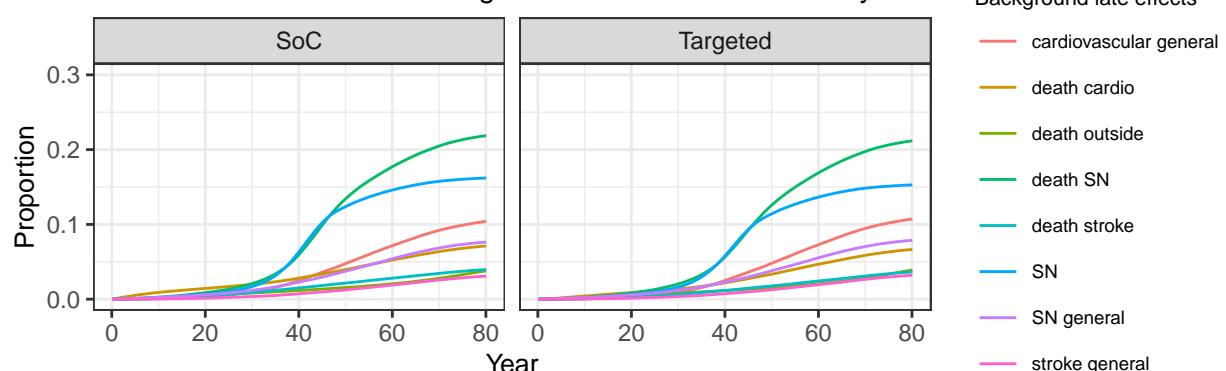
Trace Plot of PLGG States Across Cycles



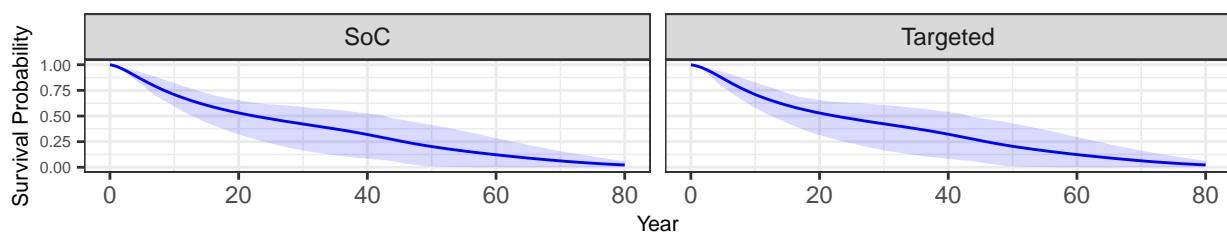
Cumulative Incidence of PLGG-related Late Effects Across Cycles



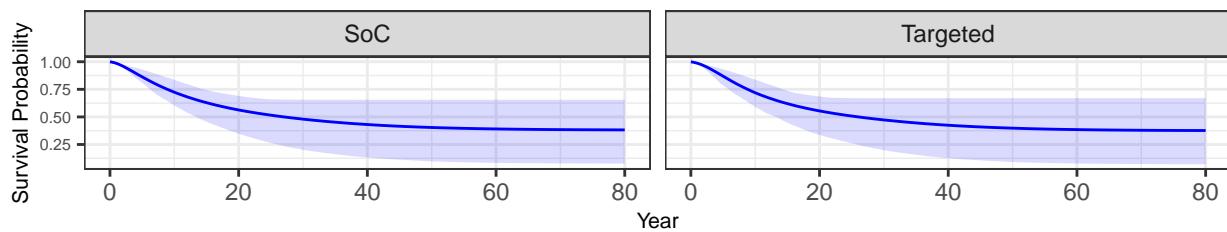
Cumulative Incidence of Background Late Effects Across Cycles



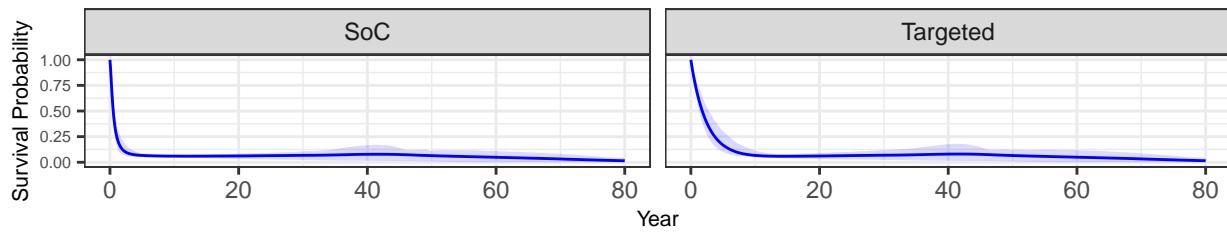
Overall Survival with 95% CI



PLGG-death–related Survival with 95% CI



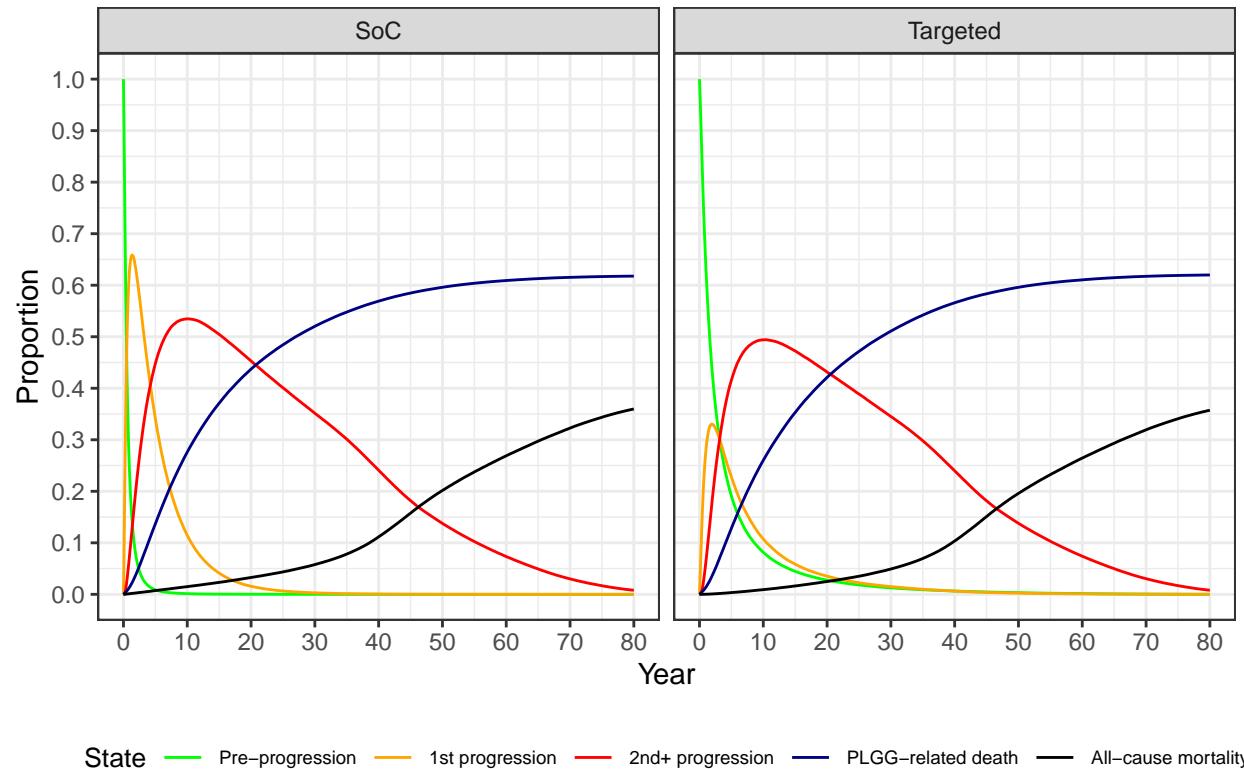
Progression-Free Survival with 95% CI



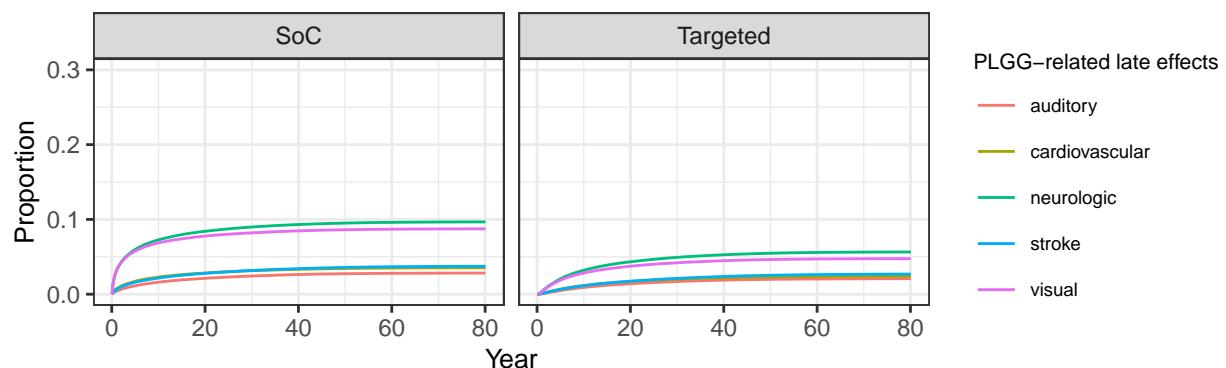
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	8.67 (6.25;11.25)	8.05 (4.98;10.67)	0.62 (0.1;1.16)
Total Cost	\$986,573 (\$746,827;\$1,245,891)	\$257,654 (\$238,405;\$275,801)	\$728,918 (\$497,569;\$971,287)
Non-Targeted PLGG related costs	\$146,510 (\$106,265;\$181,720)	\$171,054 (\$130,791;\$207,080)	\$-24,544 (\$-33,134;\$-16,257)
Late effect costs	\$54,426 (\$22,289;\$108,860)	\$65,034 (\$22,454;\$119,052)	\$-10,608 (\$-16,716;\$-4,905)
General population costs	\$26,393 (\$13,333;\$42,438)	\$21,566 (\$8,702;\$36,563)	\$4,827 (\$2,715;\$7,522)
Targeted costs	\$759,243 (\$528,575;\$1,001,250)	\$0 (\$0;\$0)	\$759,243 (\$528,575;\$1,001,250)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

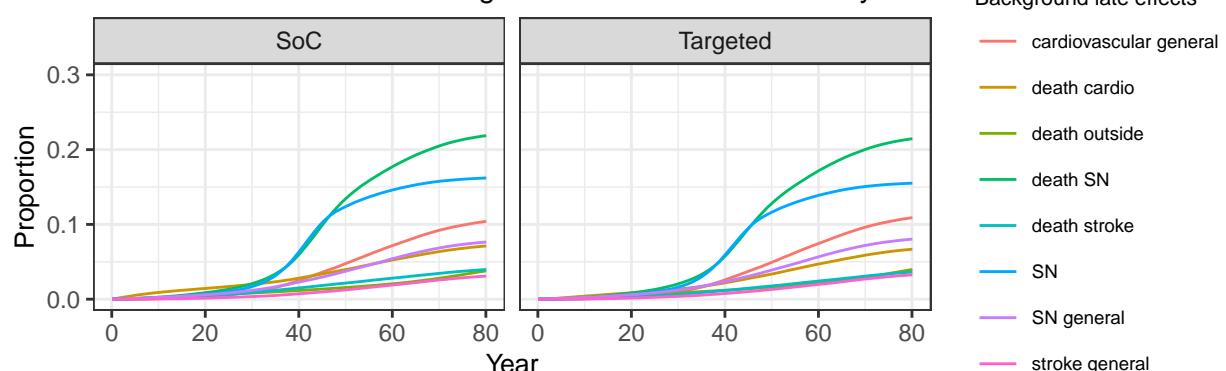
Trace Plot of PLGG States Across Cycles



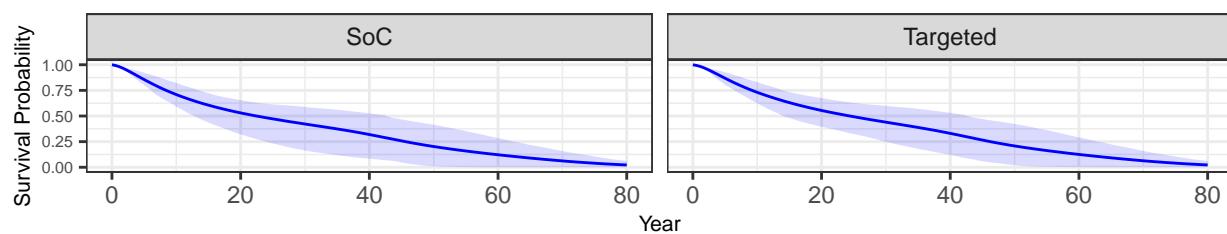
Cumulative Incidence of PLGG-related Late Effects Across Cycles



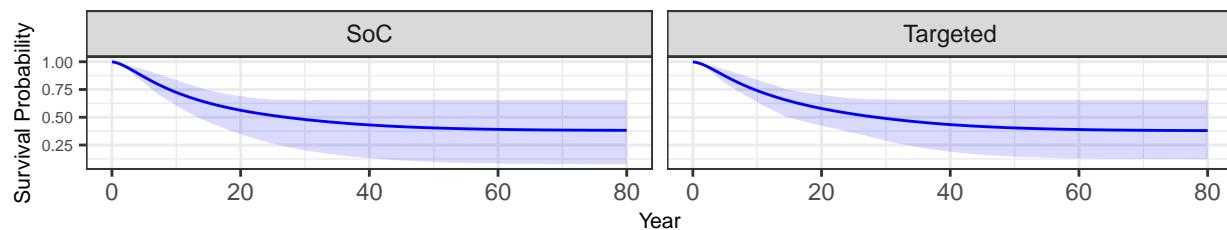
Cumulative Incidence of Background Late Effects Across Cycles



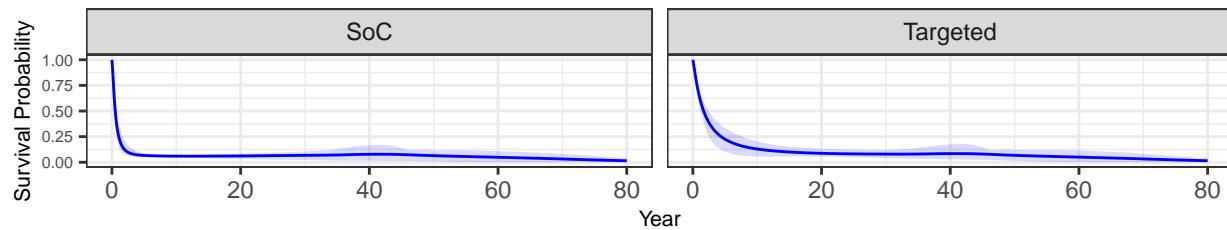
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



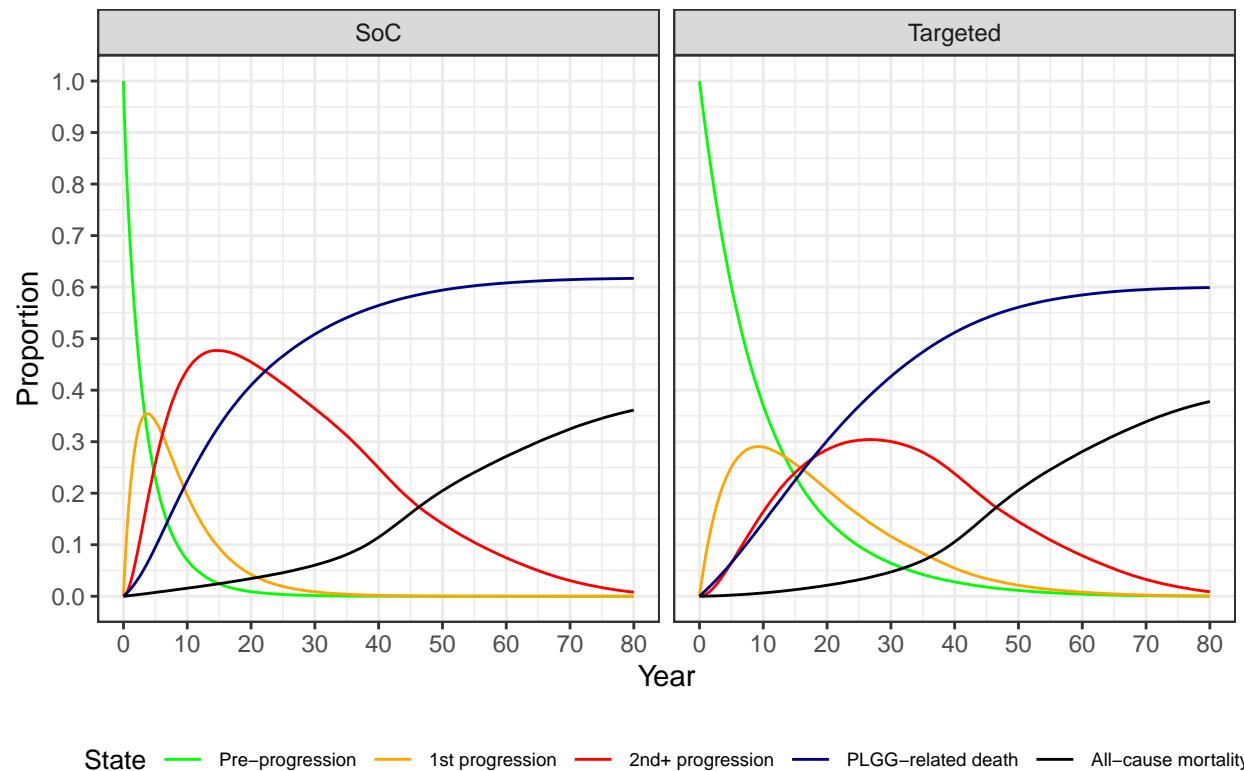
Scenario #1d

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **75% combo price reduction**
- Discount rate: 3
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

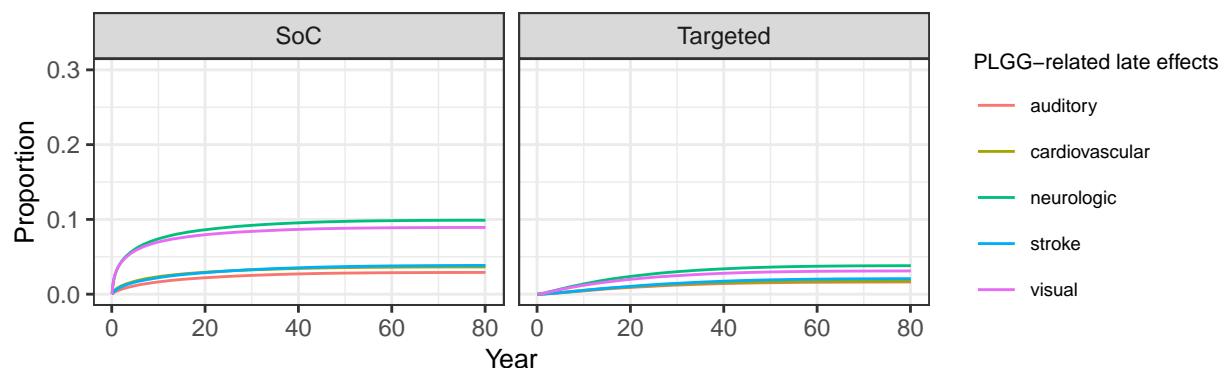
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.5 (20.11;37.73)	4.2 (0.24;12.65)
QALY	10.16 (7.81;12.64)	8.31 (5.81;10.47)	1.85 (0.62;4.24)
Total Cost	\$634,328 (\$533,267;\$729,441)	\$254,006 (\$234,782;\$270,923)	\$380,322 (\$279,182;\$471,551)
Non-Targeted PLGG related costs	\$114,952 (\$74,628;\$147,961)	\$166,281 (\$131,064;\$202,377)	\$-51,328 (\$-76,422;\$-31,472)
Late effect costs	\$51,028 (\$25,734;\$92,366)	\$65,760 (\$26,190;\$115,663)	\$-14,731 (\$-24,769;\$1,823)
General population costs	\$33,919 (\$18,792;\$49,415)	\$21,966 (\$9,936;\$35,622)	\$11,953 (\$6,028;\$23,908)
Targeted costs	\$434,428 (\$328,991;\$535,858)	\$0 (\$0;\$0)	\$434,428 (\$328,991;\$535,858)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

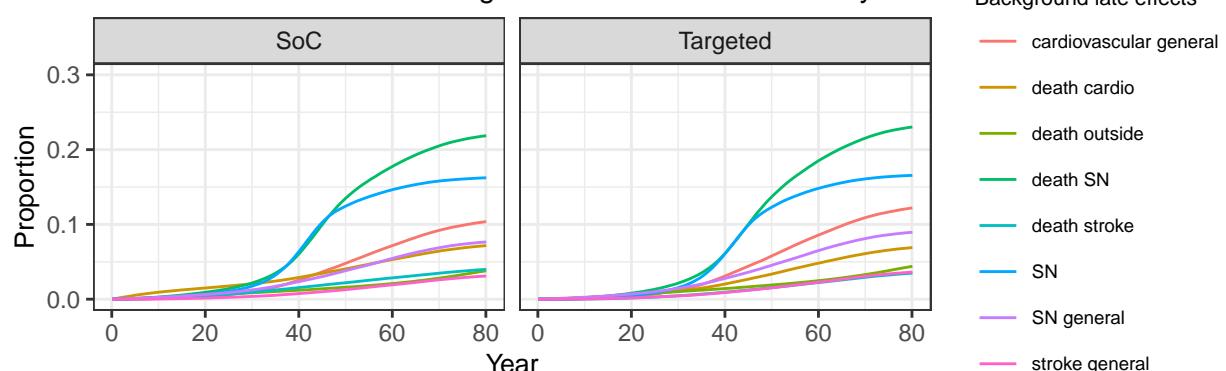
Trace Plot of PLGG States Across Cycles



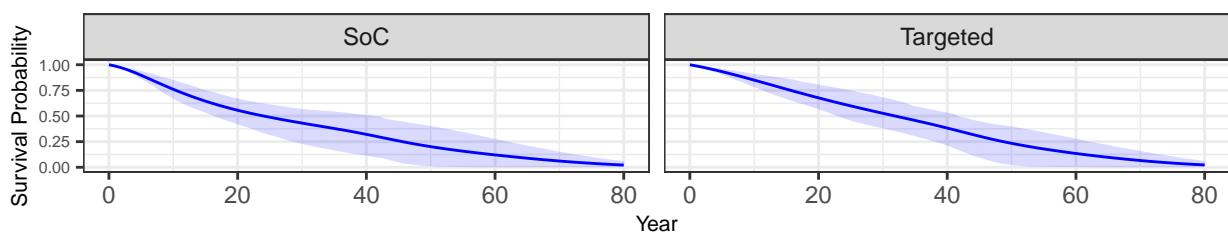
Cumulative Incidence of PLGG-related Late Effects Across Cycles



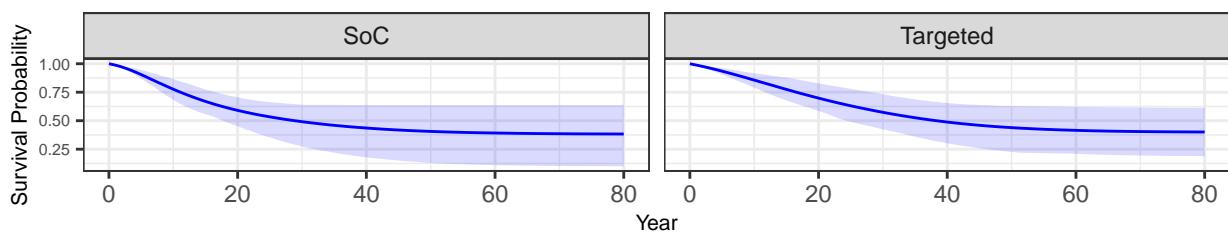
Cumulative Incidence of Background Late Effects Across Cycles



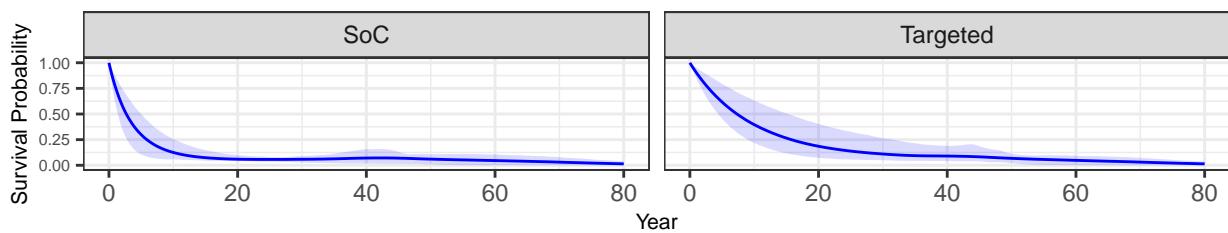
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



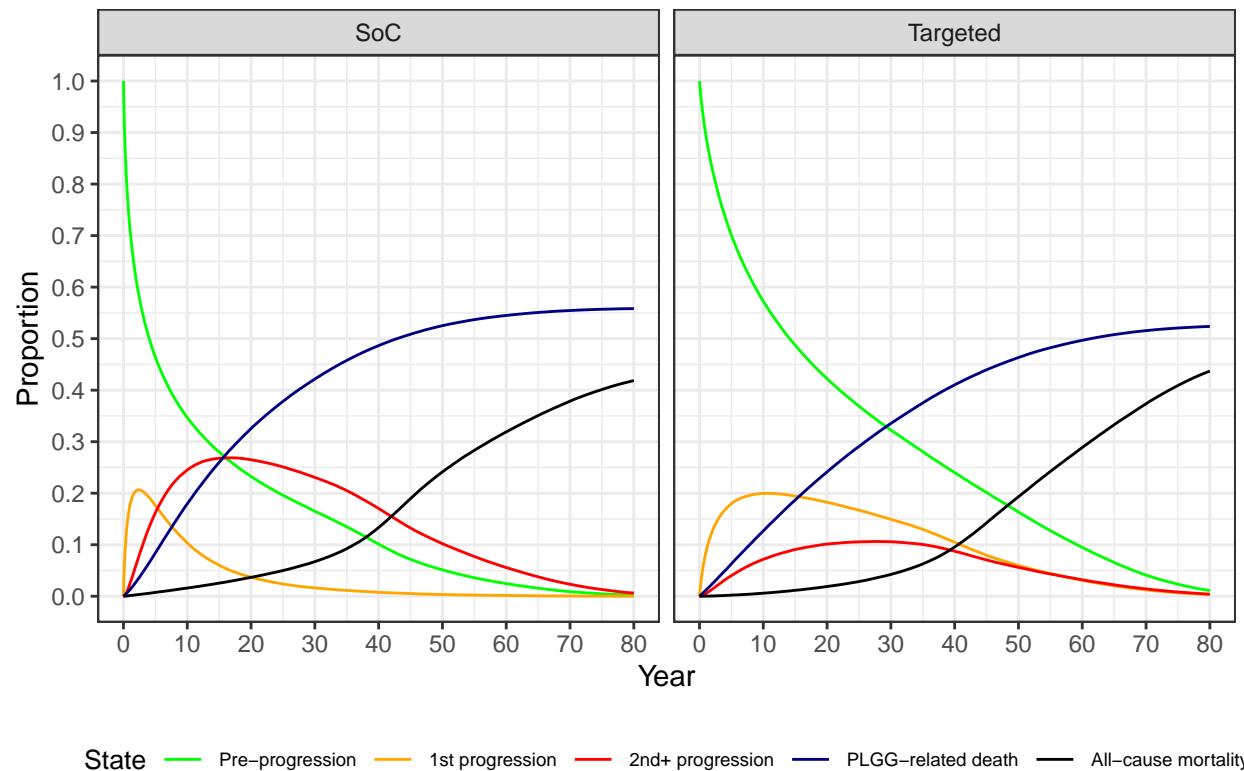
Progression-Free Survival with 95% CI



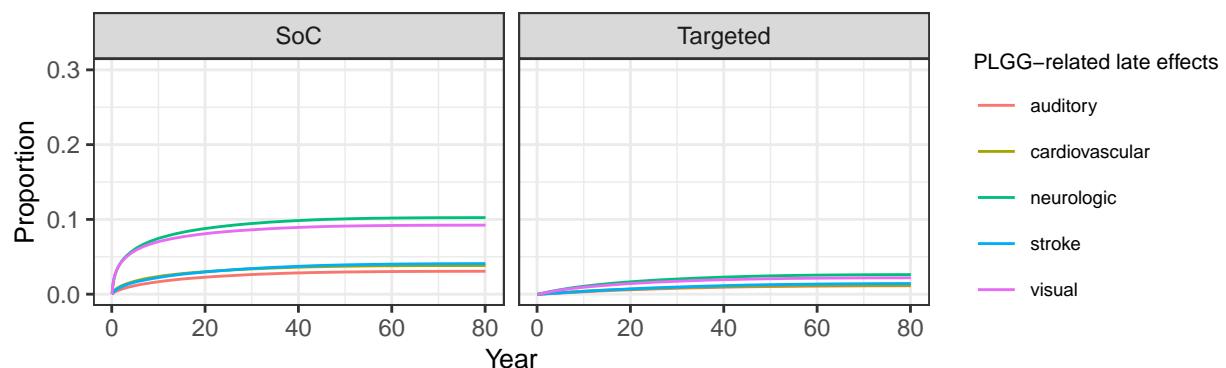
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	32.68 (26.31;39.54)	6.34 (0.38;14.98)
QALY	11.84 (9.68;13.95)	9.17 (7.34;10.98)	2.68 (0.81;5.4)
Total Cost	\$695,520 (\$604,925;\$781,983)	\$242,104 (\$230,636;\$255,510)	\$453,416 (\$363,462;\$530,396)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$142,136 (\$105,162;\$169,173)	\$-47,655 (\$-84,811;\$-21,009)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$75,039 (\$48,984;\$120,546)	\$-22,906 (\$-41,637;\$-5,211)
General population costs	\$45,527 (\$30,271;\$61,187)	\$24,930 (\$13,622;\$38,652)	\$20,597 (\$9,213;\$36,475)
Targeted costs	\$503,379 (\$410,154;\$594,456)	\$0 (\$0;\$0)	\$503,379 (\$410,154;\$594,456)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

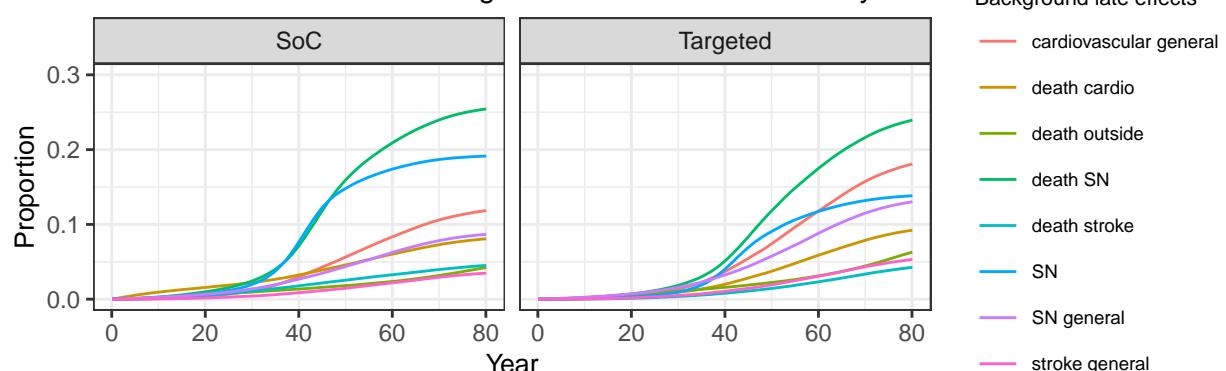
Trace Plot of PLGG States Across Cycles



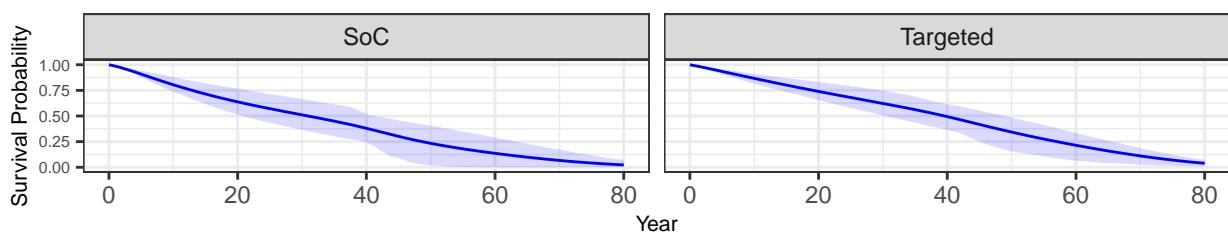
Cumulative Incidence of PLGG-related Late Effects Across Cycles



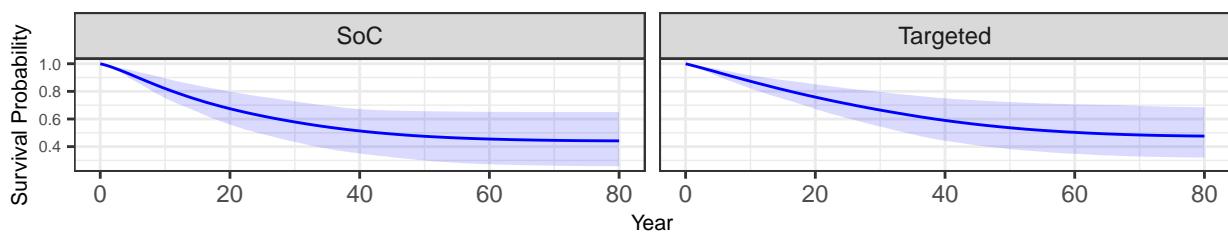
Cumulative Incidence of Background Late Effects Across Cycles



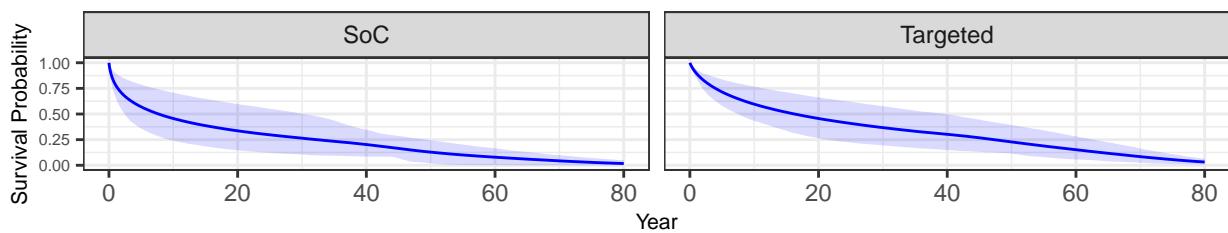
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



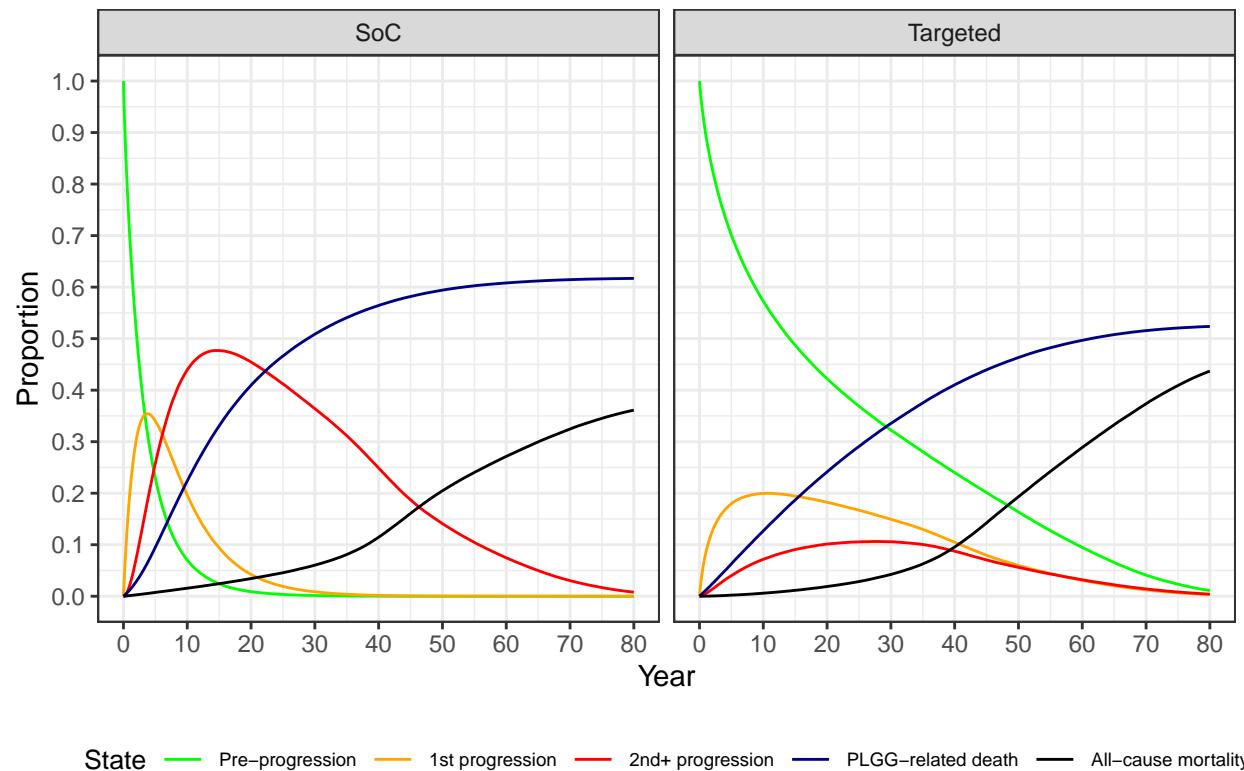
Progression-Free Survival with 95% CI



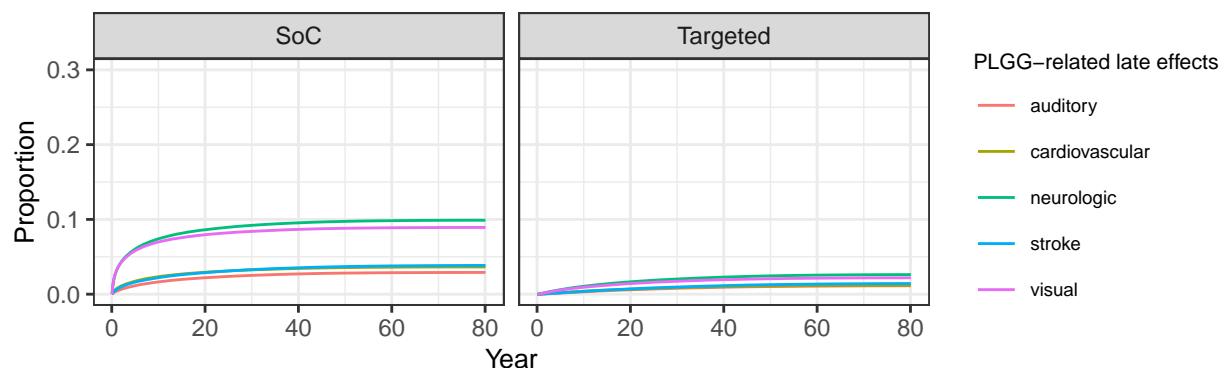
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.5 (20.11;37.73)	9.51 (1.35;21.73)
QALY	11.84 (9.68;13.95)	8.31 (5.81;10.47)	3.54 (1.33;7.15)
Total Cost	\$695,520 (\$604,925;\$781,983)	\$254,006 (\$234,782;\$270,923)	\$441,514 (\$346,988;\$529,962)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$166,281 (\$131,064;\$202,377)	\$-71,799 (\$-117,219;\$-36,530)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$65,760 (\$26,190;\$115,663)	\$-13,627 (\$-40,553;\$15,830)
General population costs	\$45,527 (\$30,271;\$61,187)	\$21,966 (\$9,936;\$35,622)	\$23,561 (\$12,645;\$40,867)
Targeted costs	\$503,379 (\$410,154;\$594,456)	\$0 (\$0;\$0)	\$503,379 (\$410,154;\$594,456)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

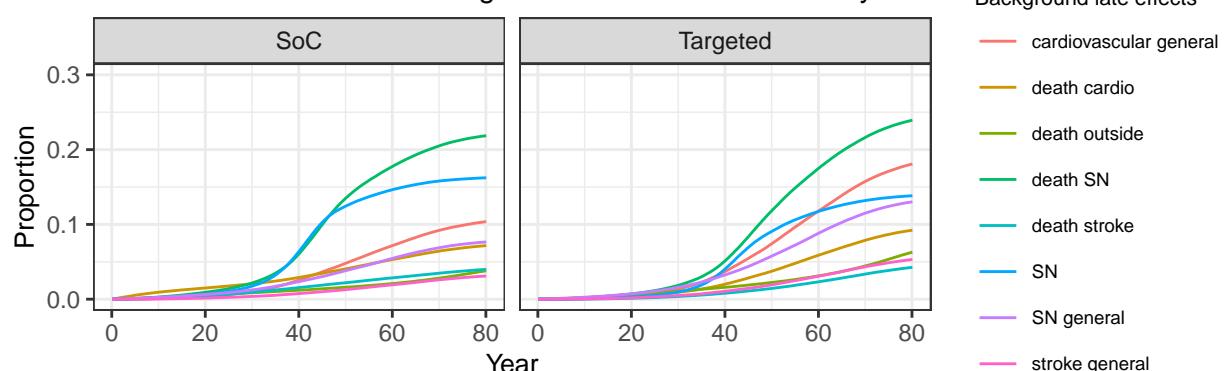
Trace Plot of PLGG States Across Cycles



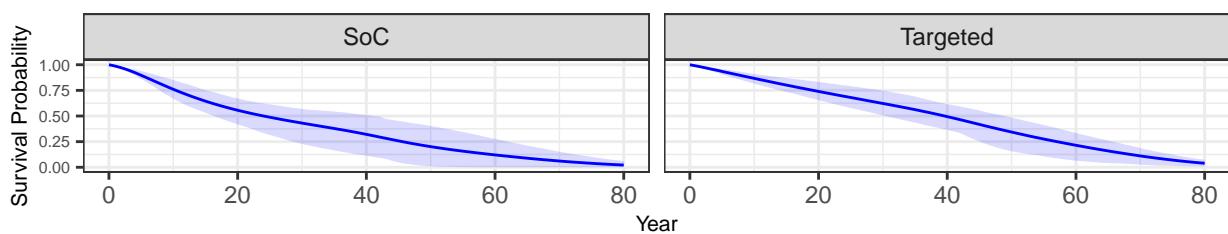
Cumulative Incidence of PLGG-related Late Effects Across Cycles



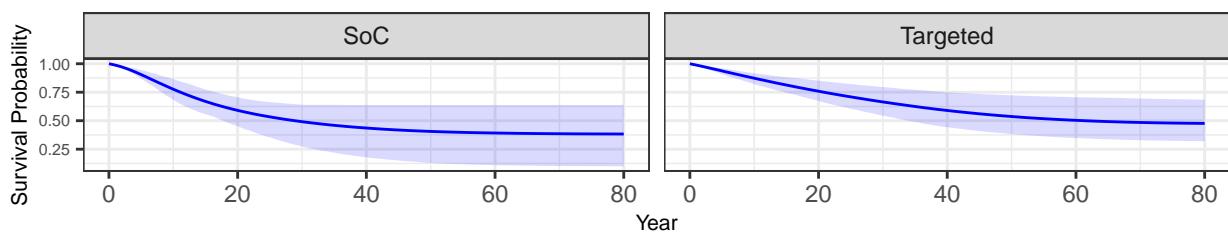
Cumulative Incidence of Background Late Effects Across Cycles



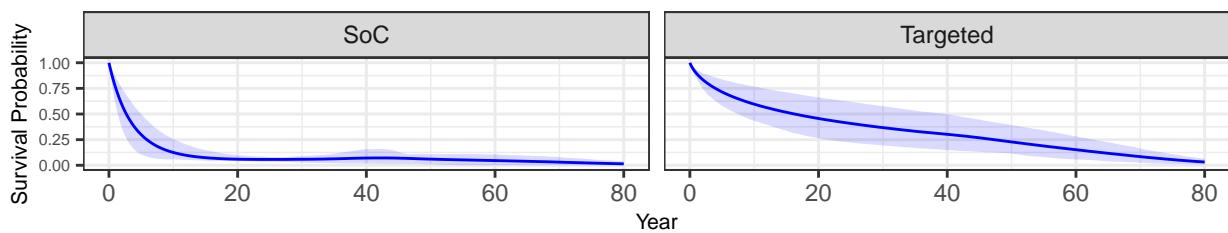
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



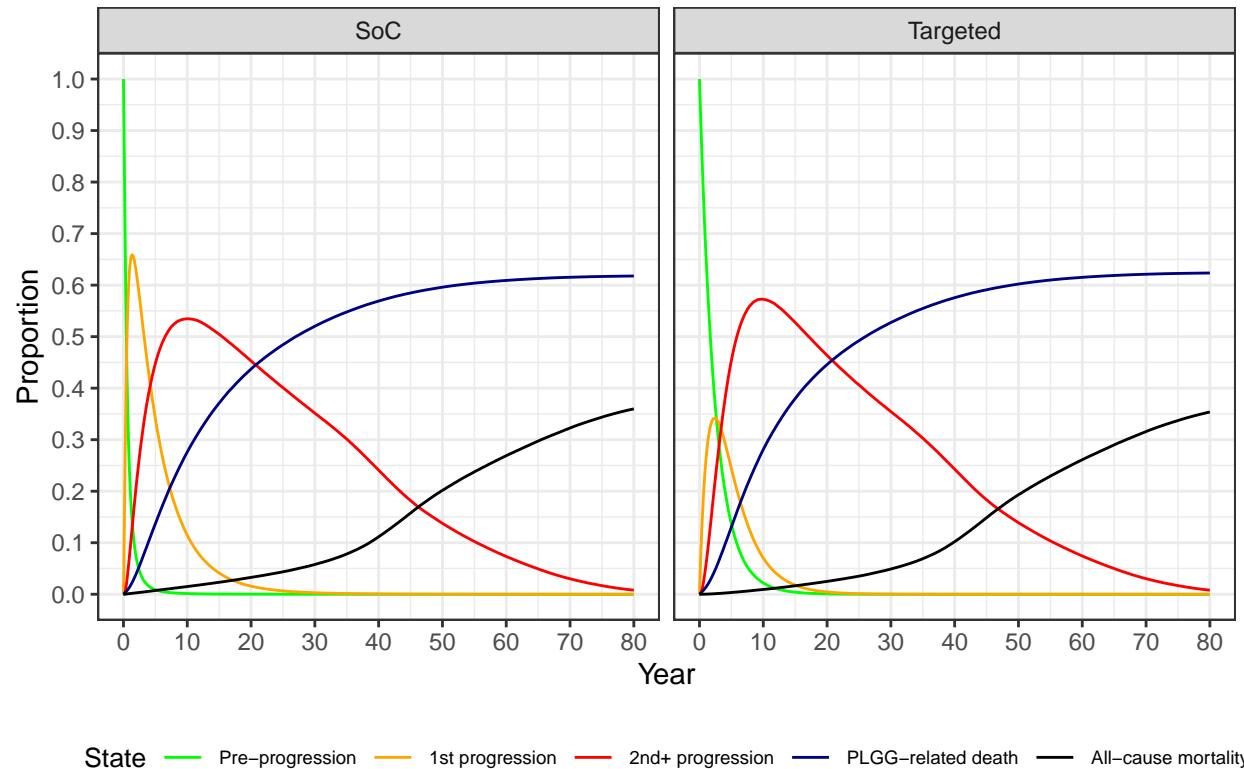
Progression-Free Survival with 95% CI



Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

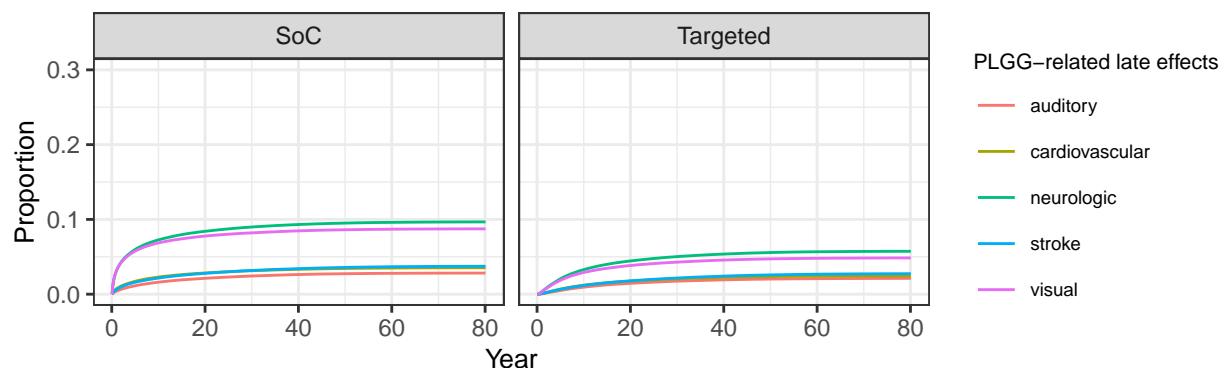
Variable	intervention	control	Delta
Life-years	28.75 (17.56;38.73)	28.6 (17.23;38.19)	0.15 (-1.43;1.37)
QALY	8.44 (5.29;11.23)	8.05 (4.98;10.67)	0.39 (-0.13;0.8)
Total Cost	\$600,964 (\$437,702;\$735,335)	\$257,654 (\$238,405;\$275,801)	\$343,310 (\$201,775;\$476,682)
Non-Targeted PLGG related costs	\$151,084 (\$110,322;\$187,135)	\$171,054 (\$130,791;\$207,080)	\$-19,970 (\$-27,914;\$-12,213)
Late effect costs	\$54,293 (\$15,501;\$110,517)	\$65,034 (\$22,454;\$119,052)	\$-10,741 (\$-15,229;\$-6,510)
General population costs	\$25,381 (\$11,269;\$41,862)	\$21,566 (\$8,702;\$36,563)	\$3,814 (\$1,620;\$5,875)
Targeted costs	\$370,206 (\$225,119;\$499,934)	\$0 (\$0;\$0)	\$370,206 (\$225,119;\$499,934)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

Trace Plot of PLGG States Across Cycles

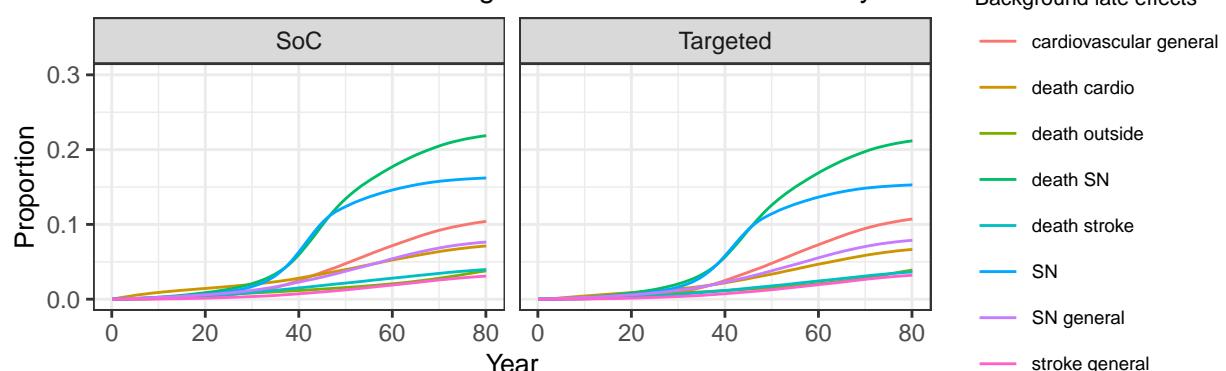


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

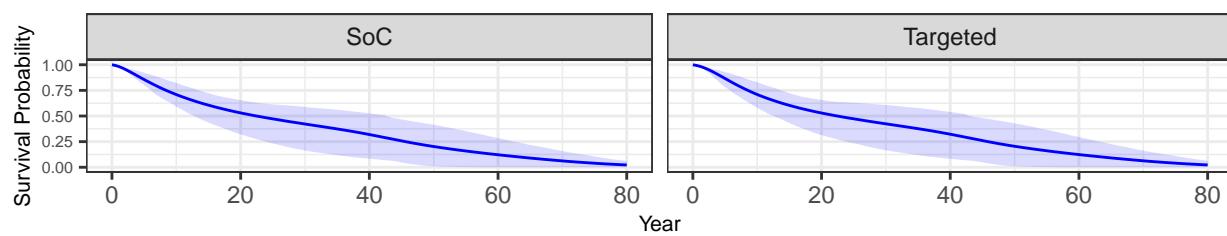
Cumulative Incidence of PLGG-related Late Effects Across Cycles



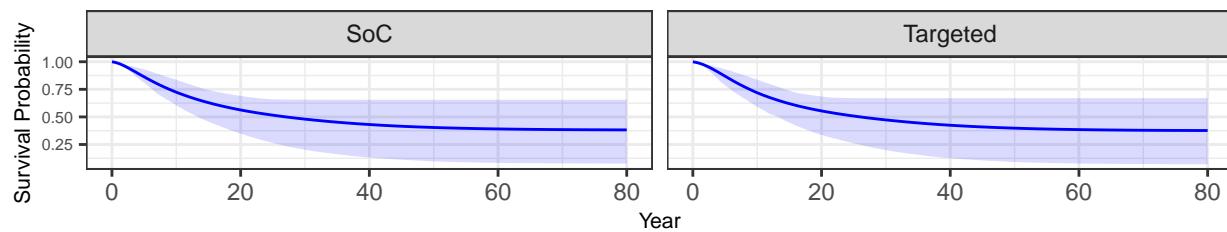
Cumulative Incidence of Background Late Effects Across Cycles



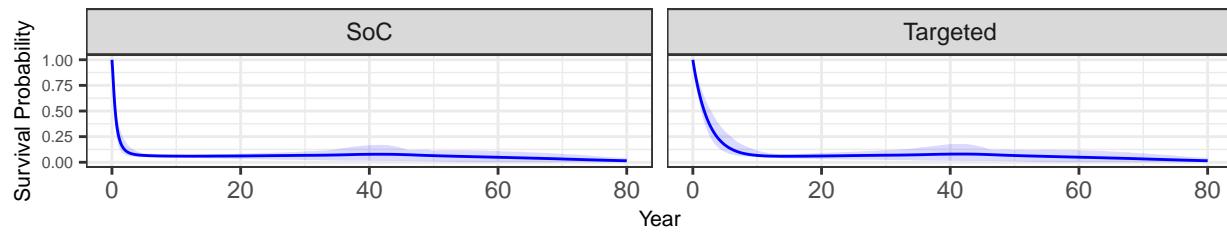
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



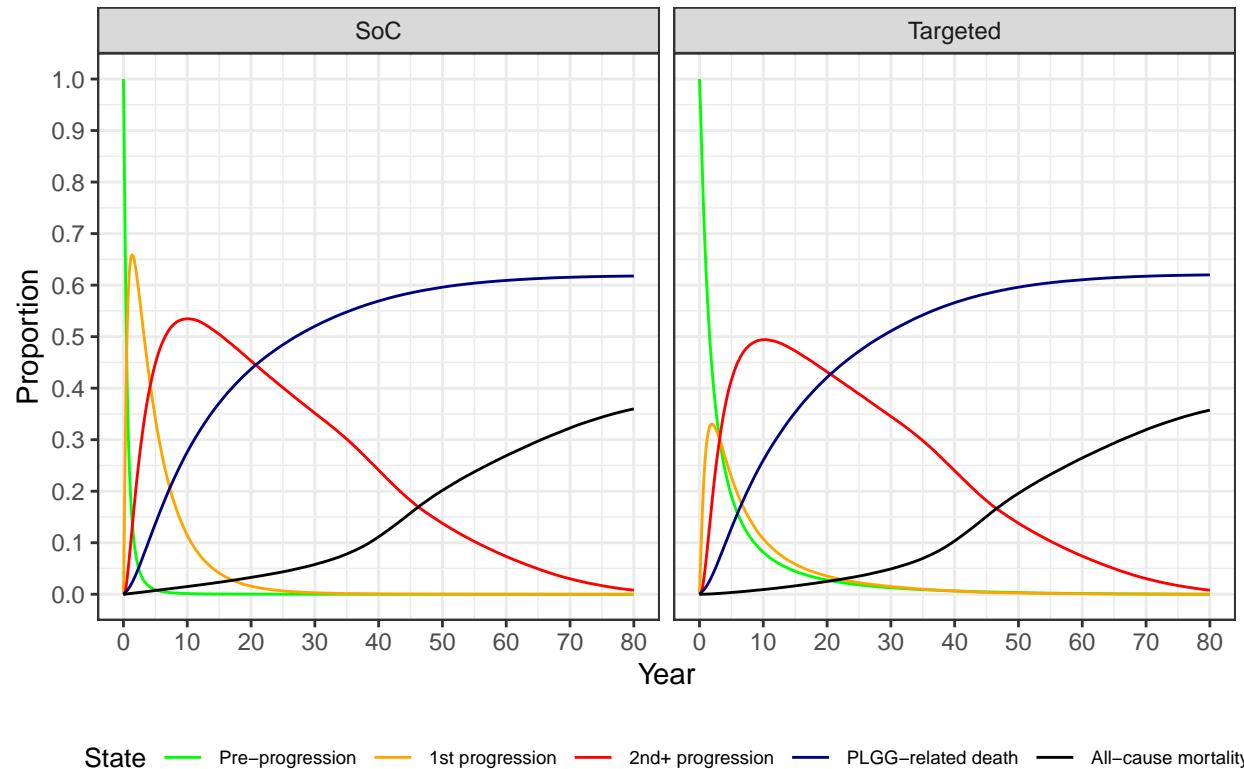
Progression-Free Survival with 95% CI



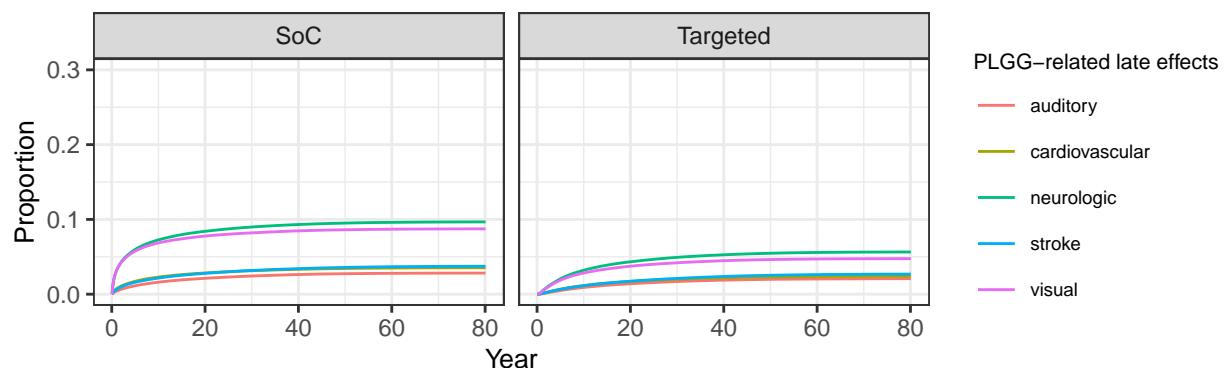
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	29.47 (20.58;38.79)	28.6 (17.23;38.19)	0.87 (-0.71;2.23)
QALY	8.67 (6.25;11.25)	8.05 (4.98;10.67)	0.62 (0.1;1.16)
Total Cost	\$606,951 (\$477,218;\$733,873)	\$257,654 (\$238,405;\$275,801)	\$349,297 (\$233,270;\$471,090)
Non-Targeted PLGG related costs	\$146,510 (\$106,265;\$181,720)	\$171,054 (\$130,791;\$207,080)	\$-24,544 (\$-33,134;\$-16,257)
Late effect costs	\$54,426 (\$22,289;\$108,860)	\$65,034 (\$22,454;\$119,052)	\$-10,608 (\$-16,716;\$-4,905)
General population costs	\$26,393 (\$13,333;\$42,438)	\$21,566 (\$8,702;\$36,563)	\$4,827 (\$2,715;\$7,522)
Targeted costs	\$379,622 (\$264,288;\$500,625)	\$0 (\$0;\$0)	\$379,622 (\$264,288;\$500,625)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

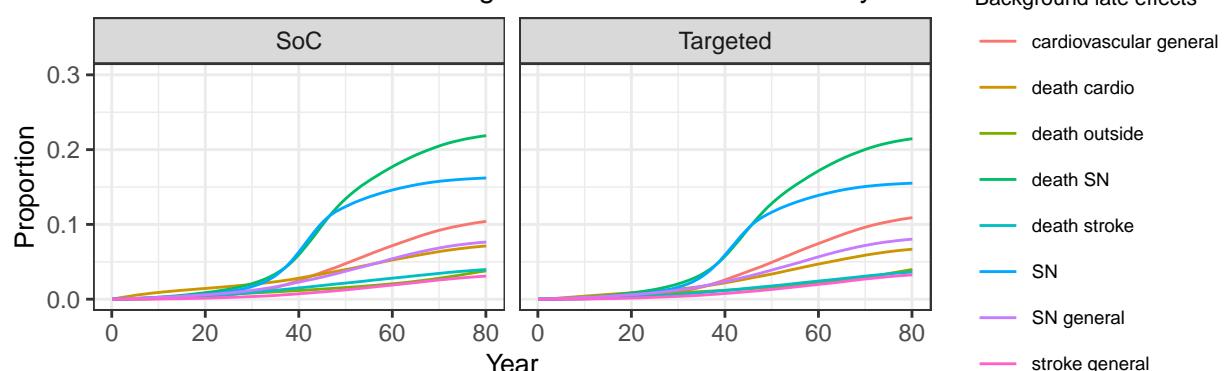
Trace Plot of PLGG States Across Cycles



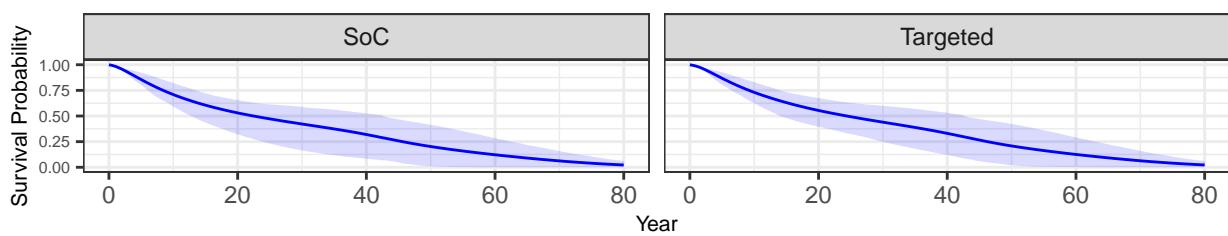
Cumulative Incidence of PLGG-related Late Effects Across Cycles



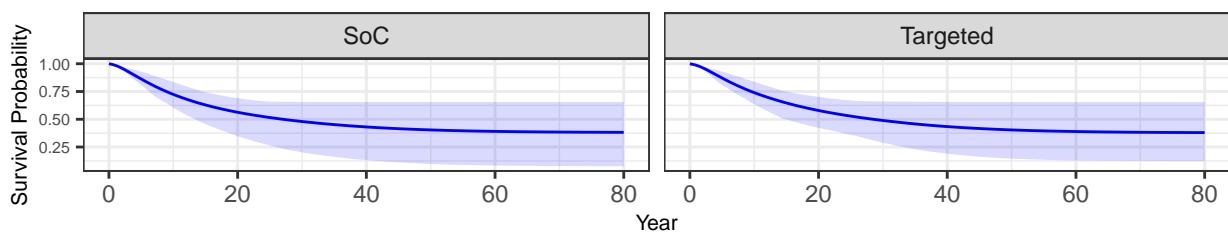
Cumulative Incidence of Background Late Effects Across Cycles



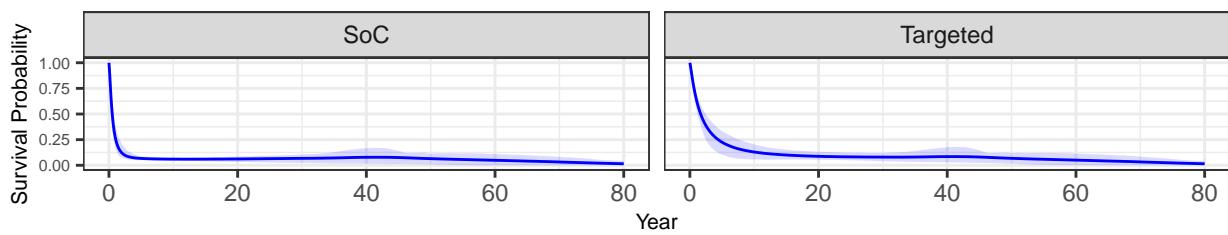
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



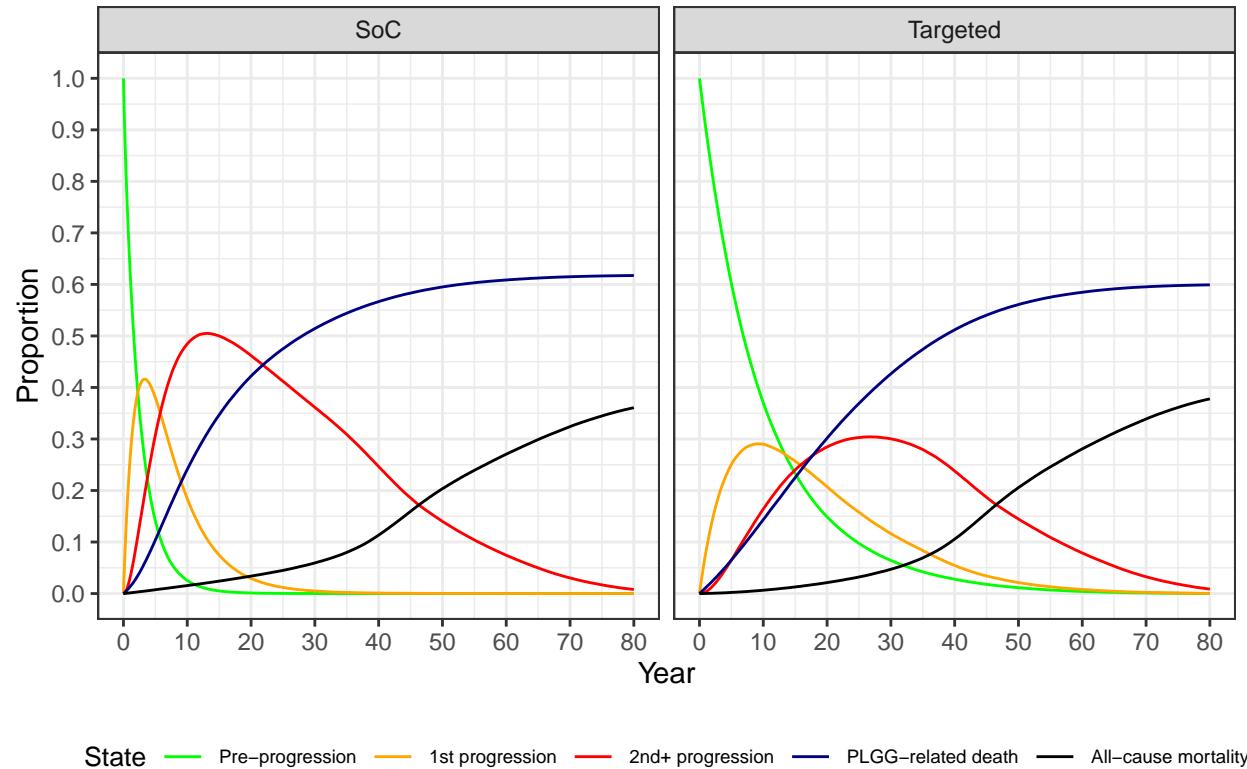
Scenario #1e

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 3
- **Data source for controls: n=34 SickKids controls**
- **Data source for exposed: Investigator assessment - Bouffet et al., NEJM 2023.**
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

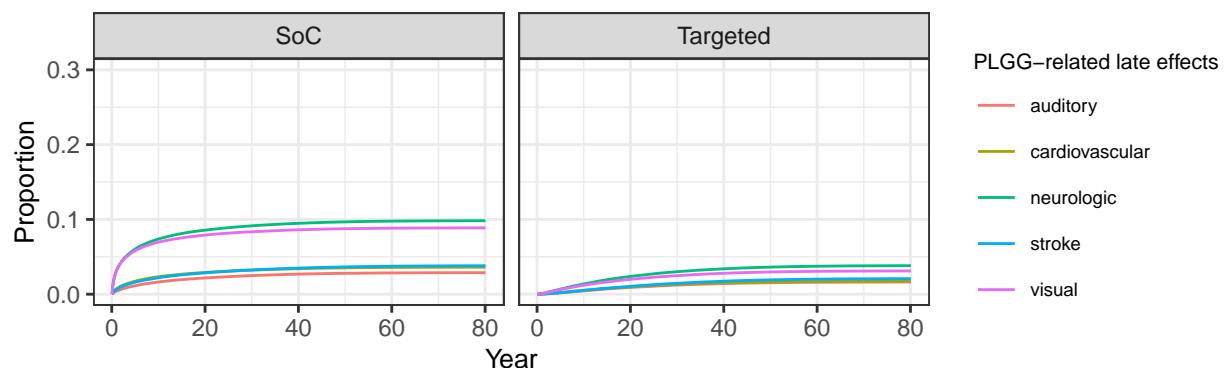
Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	33.7 (25.57;41.53)	29.17 (18.71;37.96)	4.54 (0.07;13.37)
QALY	10.16 (7.81;12.64)	8.22 (5.4;10.58)	1.94 (0.59;4.64)
Total Cost	\$1,937,613 (\$1,524,296;\$2,337,015)	\$257,014 (\$239,978;\$273,111)	\$1,680,599 (\$1,272,924;\$2,083,617)
Non-Targeted PLGG related costs	\$114,952 (\$74,628;\$147,961)	\$169,724 (\$132,059;\$207,284)	\$-54,772 (\$-83,395;\$-35,821)
Late effect costs	\$51,028 (\$25,734;\$92,366)	\$65,490 (\$24,055;\$117,669)	\$-14,461 (\$-27,162;\$3,614)
General population costs	\$33,919 (\$18,792;\$49,415)	\$21,800 (\$9,585;\$35,806)	\$12,119 (\$5,967;\$25,610)
Targeted costs	\$1,737,713 (\$1,315,964;\$2,143,432)	\$0 (\$0;\$0)	\$1,737,713 (\$1,315,964;\$2,143,432)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

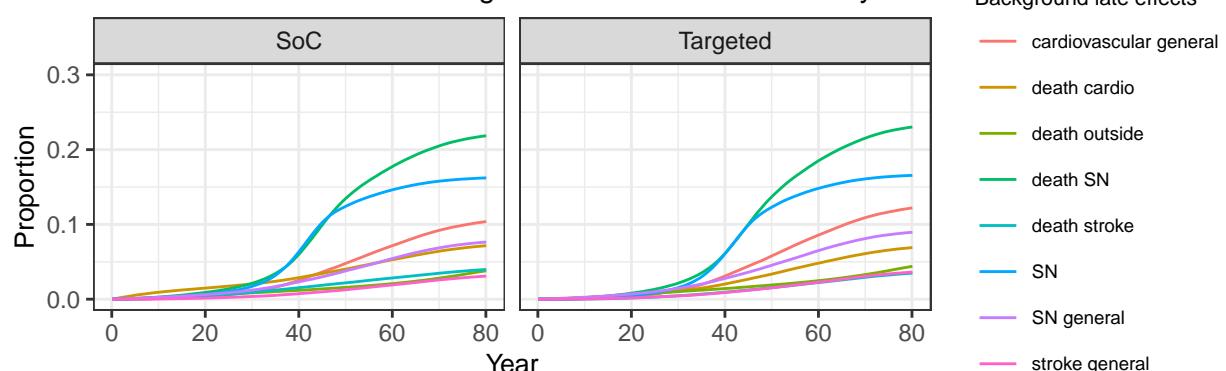
Trace Plot of PLGG States Across Cycles



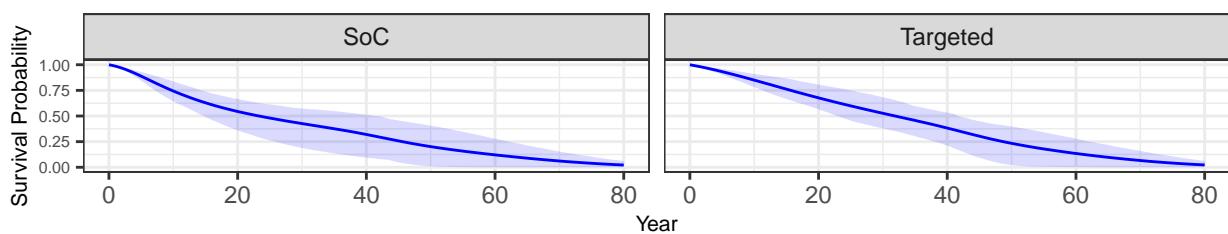
Cumulative Incidence of PLGG-related Late Effects Across Cycles



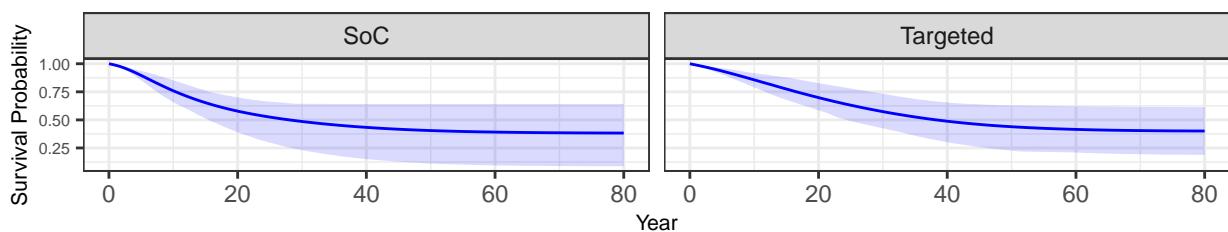
Cumulative Incidence of Background Late Effects Across Cycles



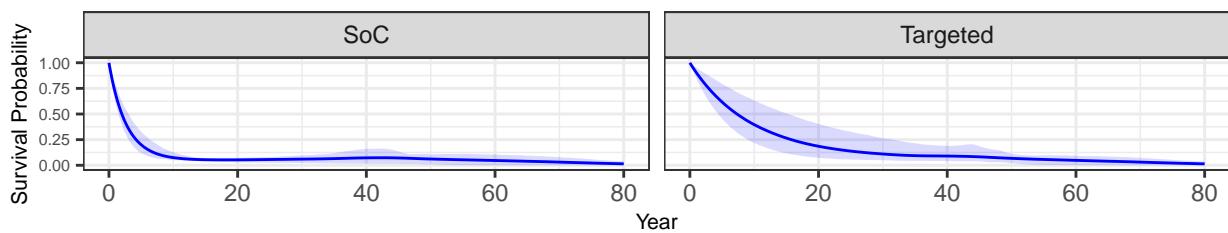
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



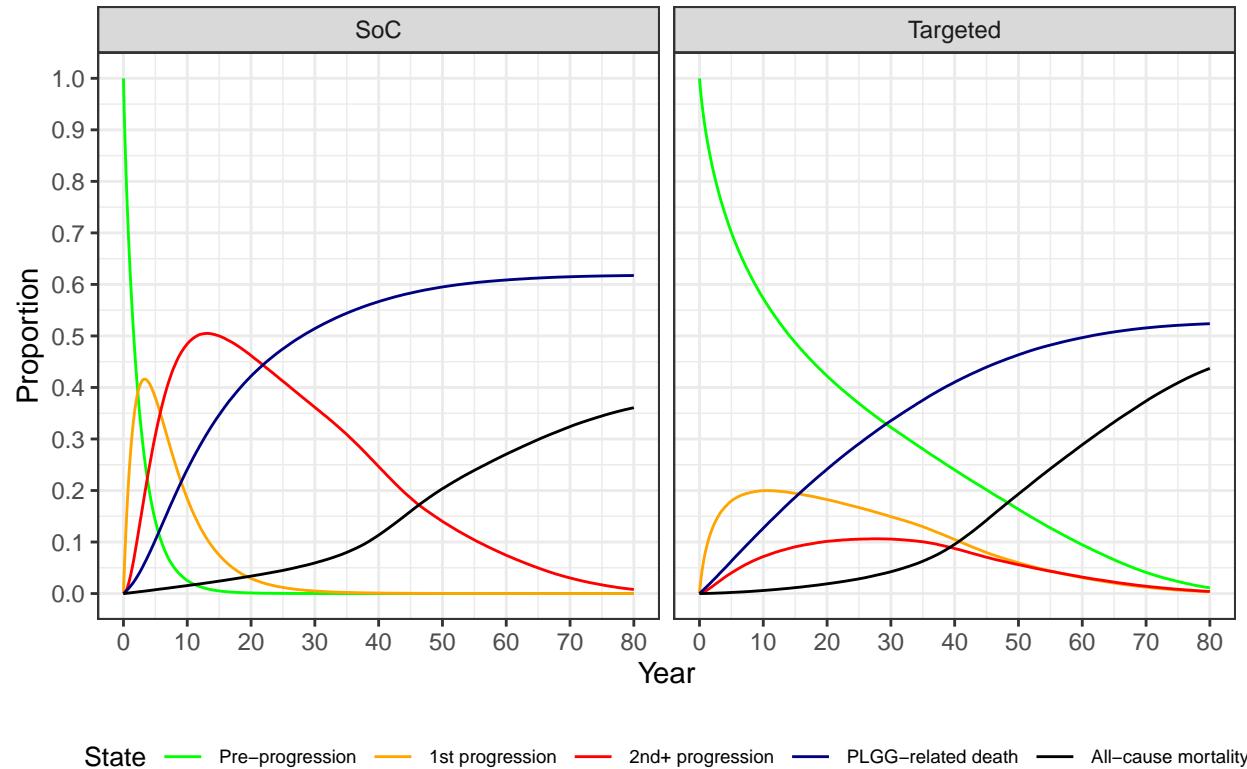
Progression–Free Survival with 95% CI



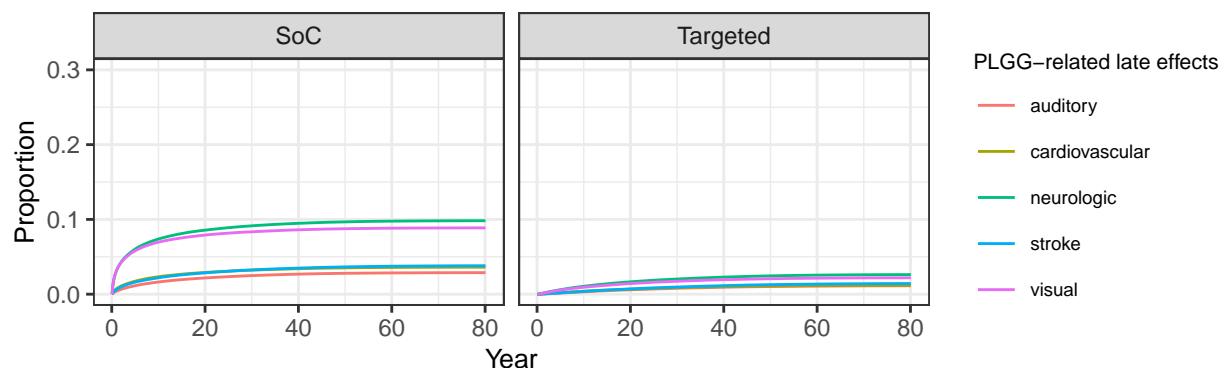
Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	39.02 (31.82;46.04)	29.17 (18.71;37.96)	9.85 (1.25;22.84)
QALY	11.84 (9.68;13.95)	8.22 (5.4;10.58)	3.63 (1.31;7.47)
Total Cost	\$2,205,659 (\$1,835,087;\$2,565,352)	\$257,014 (\$239,978;\$273,111)	\$1,948,645 (\$1,579,660;\$2,303,611)
Non-Targeted PLGG related costs	\$94,481 (\$69,019;\$121,396)	\$169,724 (\$132,059;\$207,284)	\$-75,243 (\$-120,100;\$-40,185)
Late effect costs	\$52,132 (\$33,270;\$78,610)	\$65,490 (\$24,055;\$117,669)	\$-13,357 (\$-43,070;\$16,011)
General population costs	\$45,527 (\$30,271;\$61,187)	\$21,800 (\$9,585;\$35,806)	\$23,727 (\$12,392;\$41,879)
Targeted costs	\$2,013,518 (\$1,640,618;\$2,377,825)	\$0 (\$0;\$0)	\$2,013,518 (\$1,640,618;\$2,377,825)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

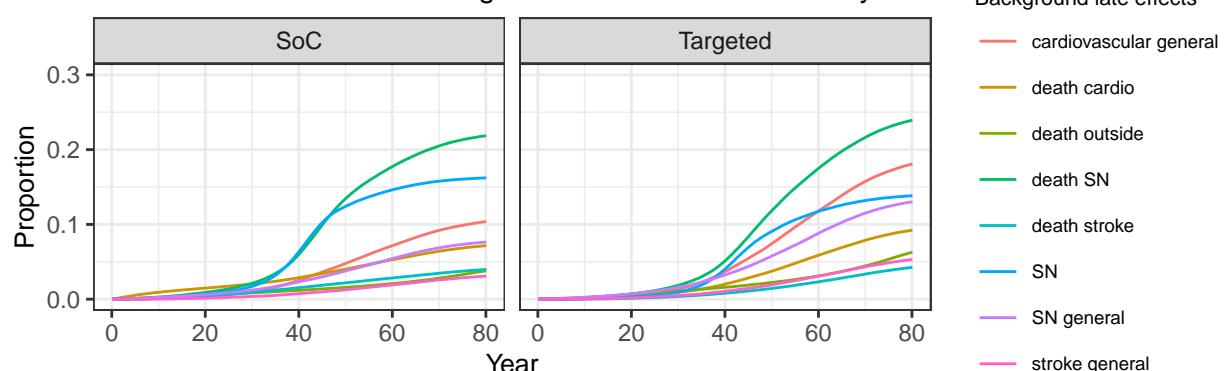
Trace Plot of PLGG States Across Cycles



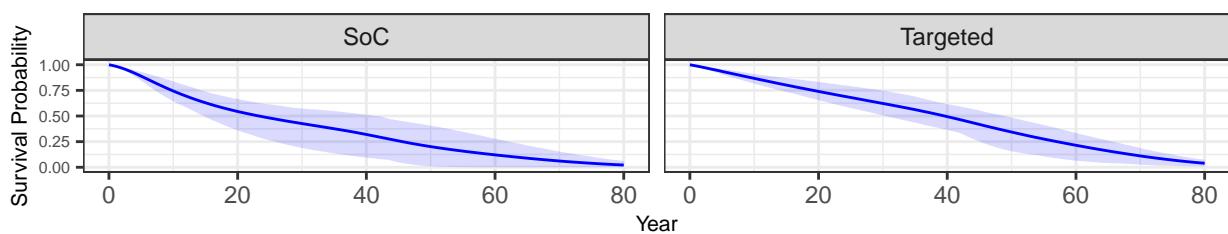
Cumulative Incidence of PLGG-related Late Effects Across Cycles



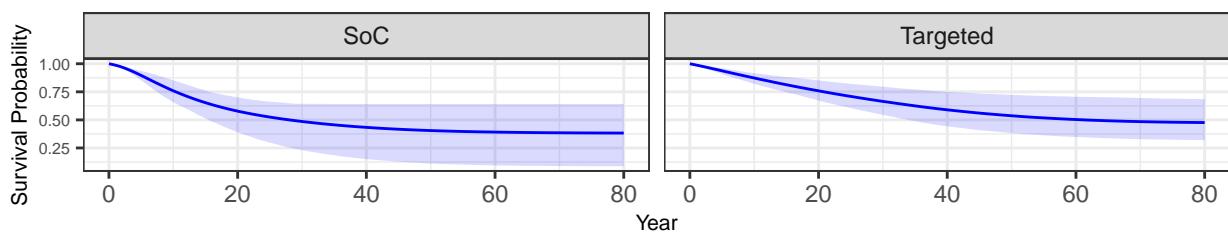
Cumulative Incidence of Background Late Effects Across Cycles



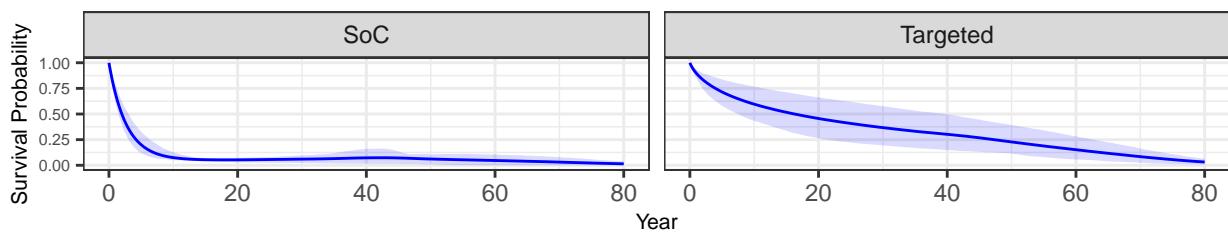
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



20% radiated at subsequent progression

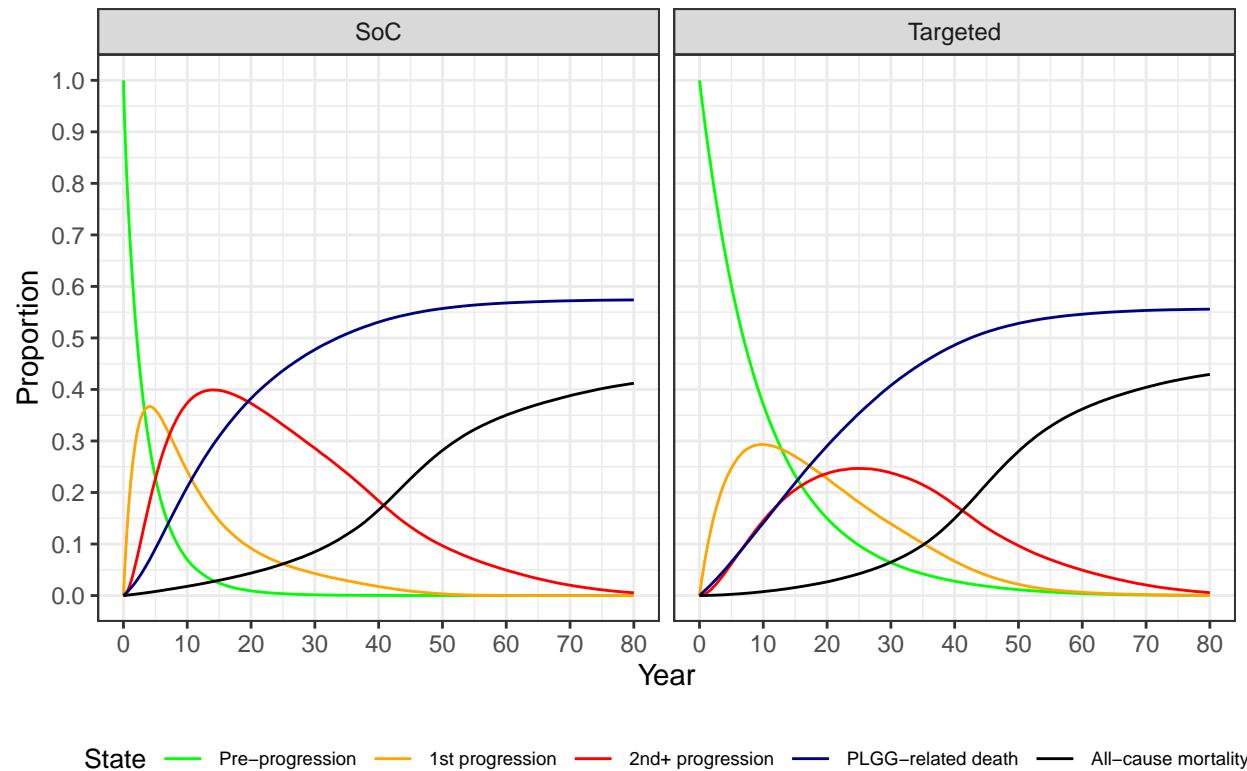
Scenario #1a

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 20% radiation at progression
- 100% combo price
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

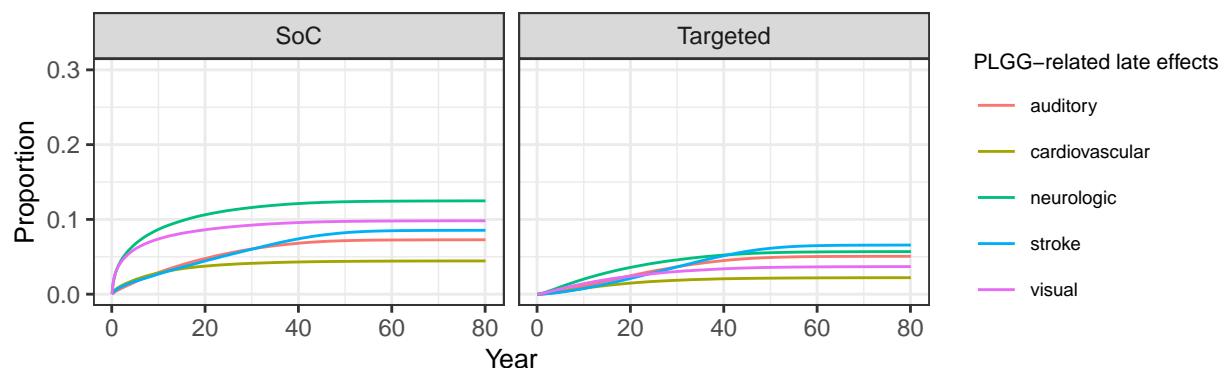
Variable	intervention	control	Delta
Life-years	32.48 (25.96;39.25)	28.64 (20.97;35.16)	3.84 (0.27;11.06)
QALY	14.83 (11.84;18.04)	12.11 (9.06;14.63)	2.72 (1.01;6.03)
Total Cost	\$2,403,280 (\$1,879,717;\$3,012,999)	\$395,261 (\$365,504;\$416,998)	\$2,008,018 (\$1,505,681;\$2,613,128)
Non-Targeted PLGG related costs	\$166,697 (\$112,032;\$211,304)	\$243,921 (\$200,740;\$292,397)	\$-77,225 (\$-113,406;\$-49,081)
Late effect costs	\$98,249 (\$64,144;\$143,861)	\$122,042 (\$64,189;\$179,418)	\$-23,794 (\$-40,221;\$729)
General population costs	\$45,481 (\$28,493;\$64,999)	\$27,976 (\$14,665;\$42,065)	\$17,506 (\$9,088;\$34,448)
Targeted costs	\$2,091,605 (\$1,576,380;\$2,713,489)	\$0 (\$0;\$0)	\$2,091,605 (\$1,576,380;\$2,713,489)
Radiation costs	\$1,247 (\$1,029;\$1,363)	\$1,322 (\$1,243;\$1,392)	\$-75 (\$-329;\$81)

Trace Plot of PLGG States Across Cycles

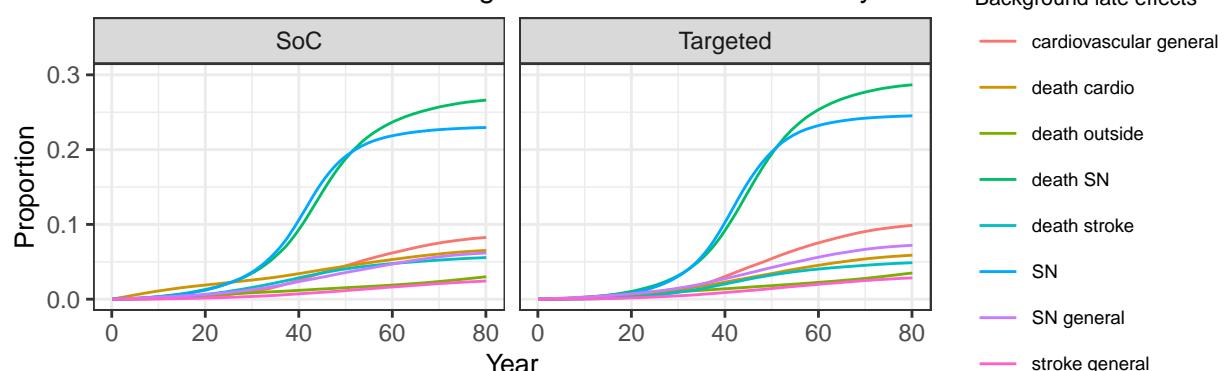


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

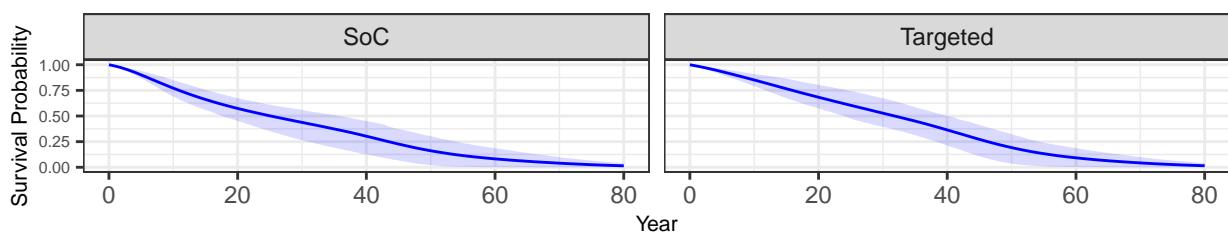
Cumulative Incidence of PLGG-related Late Effects Across Cycles



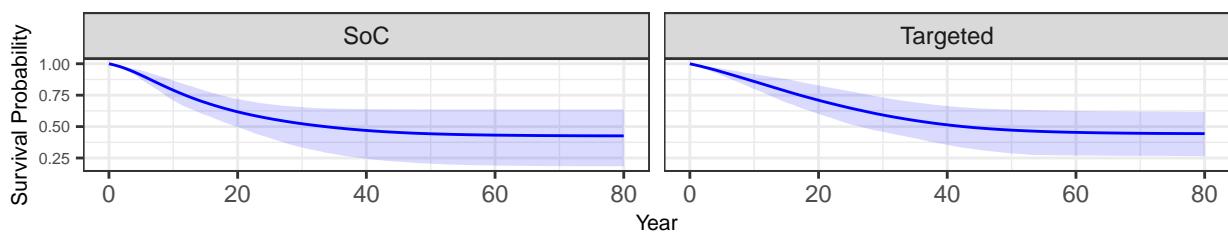
Cumulative Incidence of Background Late Effects Across Cycles



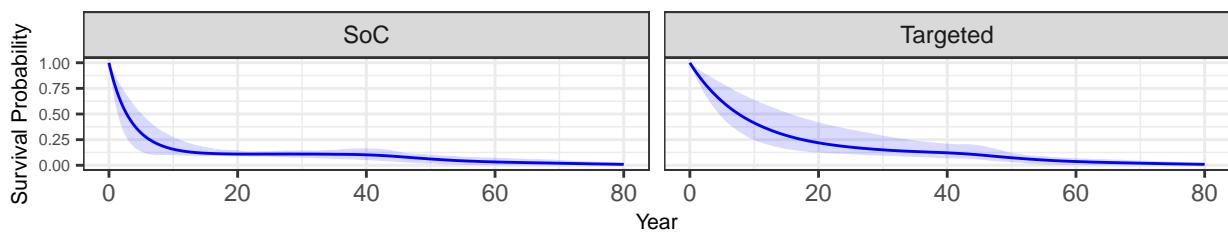
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



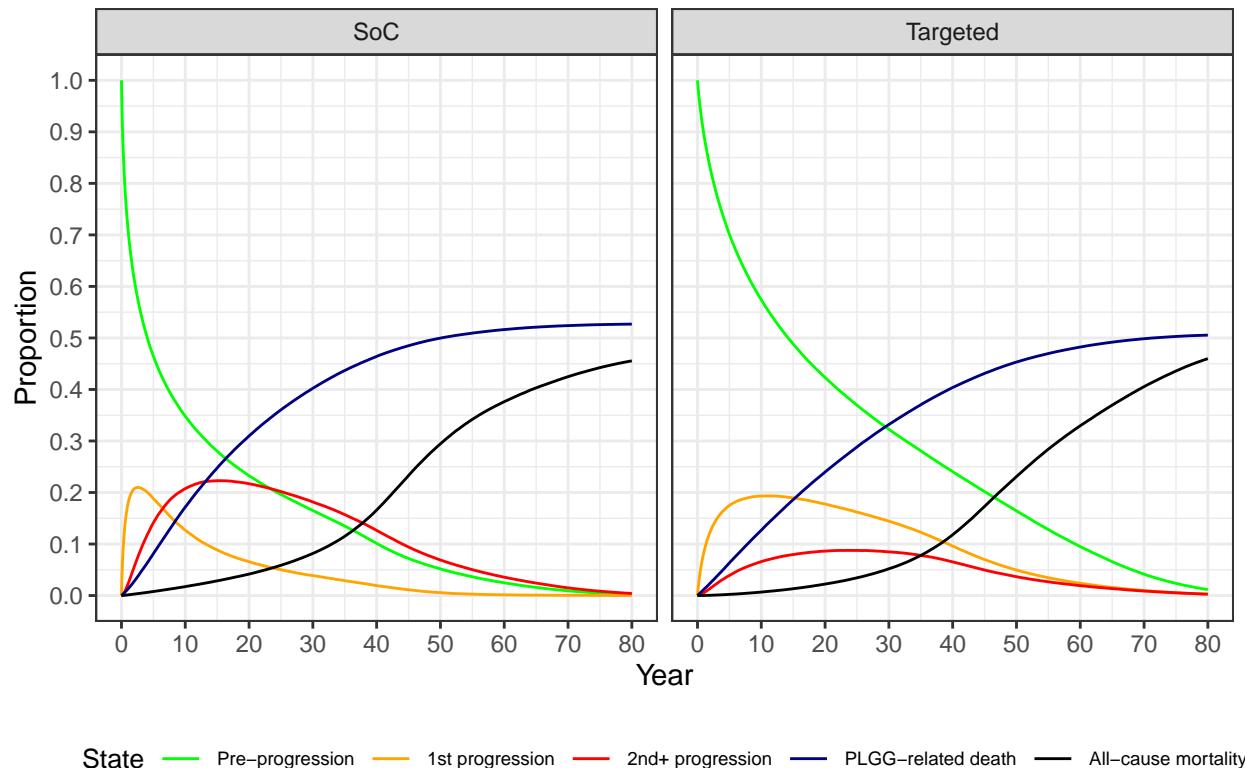
Progression-Free Survival with 95% CI



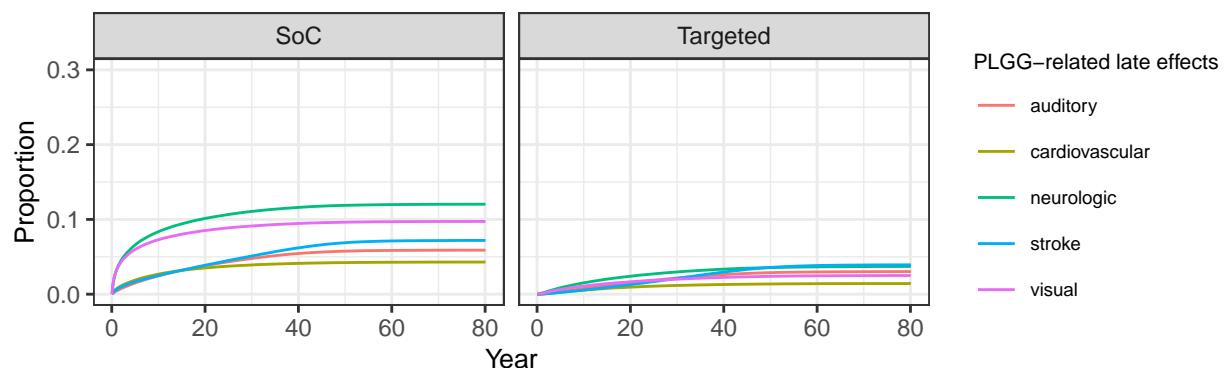
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	32.04 (26.37;37.48)	6.01 (-0.38;14.37)
QALY	17.64 (14.54;21.11)	13.63 (11.27;15.83)	4.01 (0.86;8.14)
Total Cost	\$3,045,842 (\$2,446,468;\$3,738,489)	\$375,954 (\$356,889;\$392,667)	\$2,669,888 (\$2,079,515;\$3,352,454)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$210,099 (\$157,944;\$246,665)	\$-69,234 (\$-120,666;\$-35,229)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$130,725 (\$94,124;\$187,424)	\$-40,999 (\$-64,774;\$-16,602)
General population costs	\$65,694 (\$45,261;\$91,539)	\$34,221 (\$21,047;\$48,447)	\$31,473 (\$11,076;\$54,489)
Targeted costs	\$2,748,871 (\$2,145,824;\$3,452,211)	\$0 (\$0;\$0)	\$2,748,871 (\$2,145,824;\$3,452,211)
Radiation costs	\$686 (\$315;\$1,036)	\$909 (\$469;\$1,256)	\$-223 (\$-735;\$402)

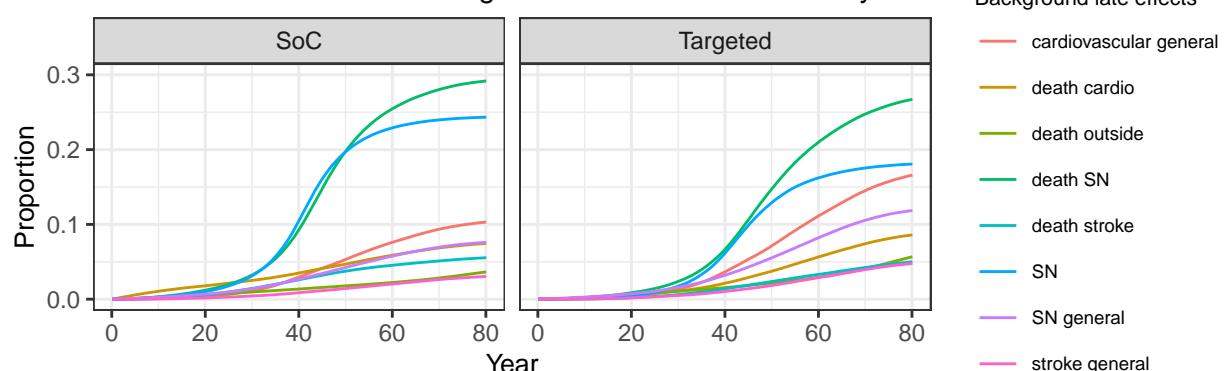
Trace Plot of PLGG States Across Cycles



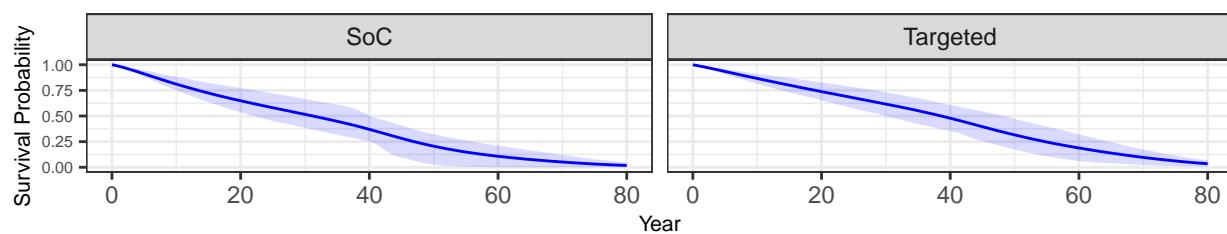
Cumulative Incidence of PLGG-related Late Effects Across Cycles



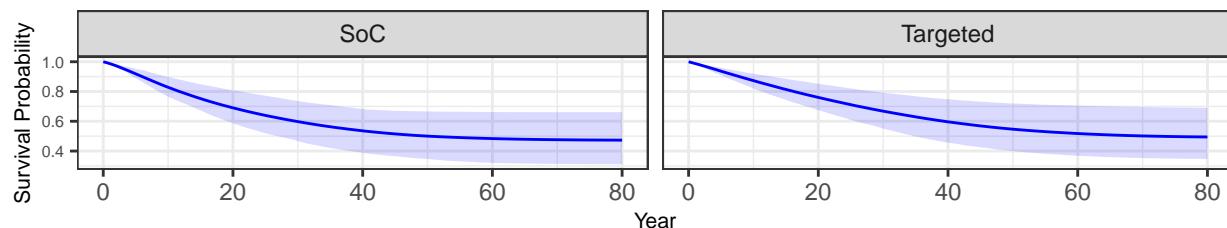
Cumulative Incidence of Background Late Effects Across Cycles



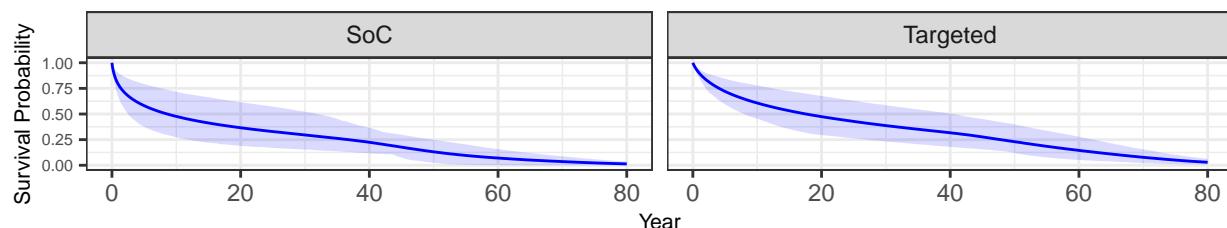
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



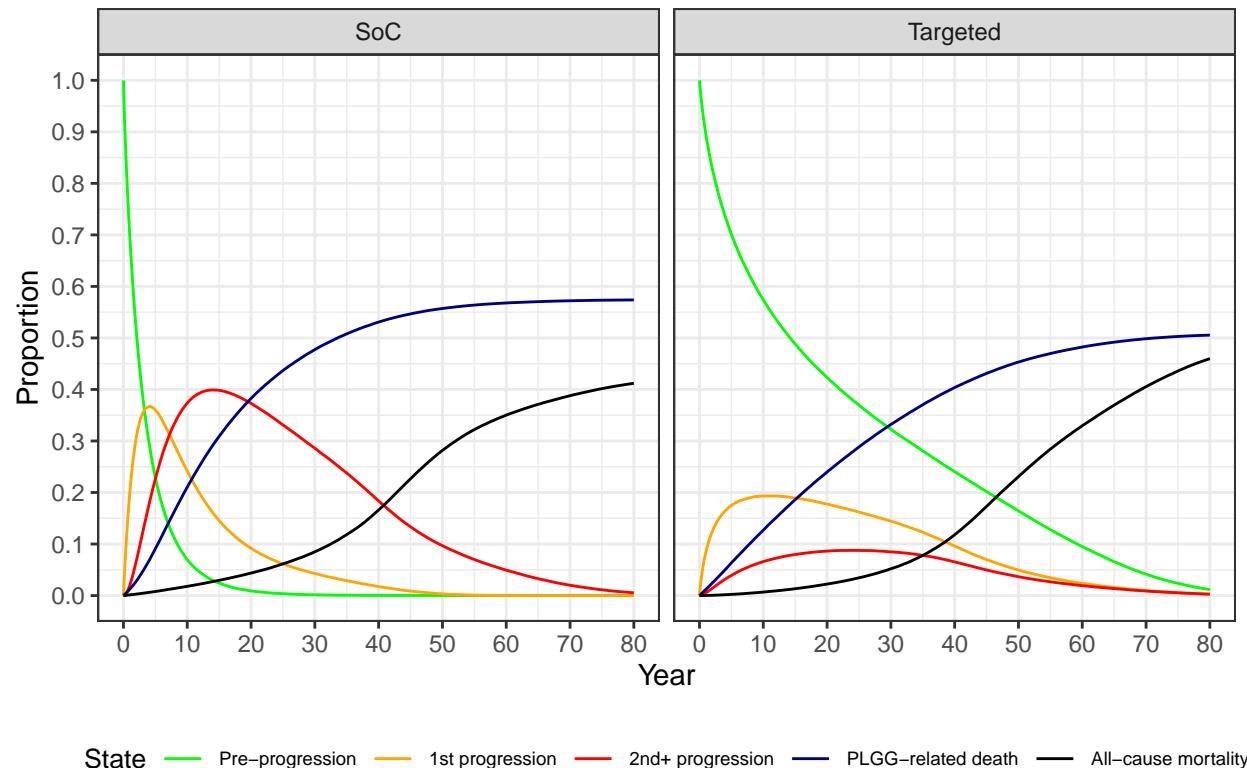
Progression-Free Survival with 95% CI



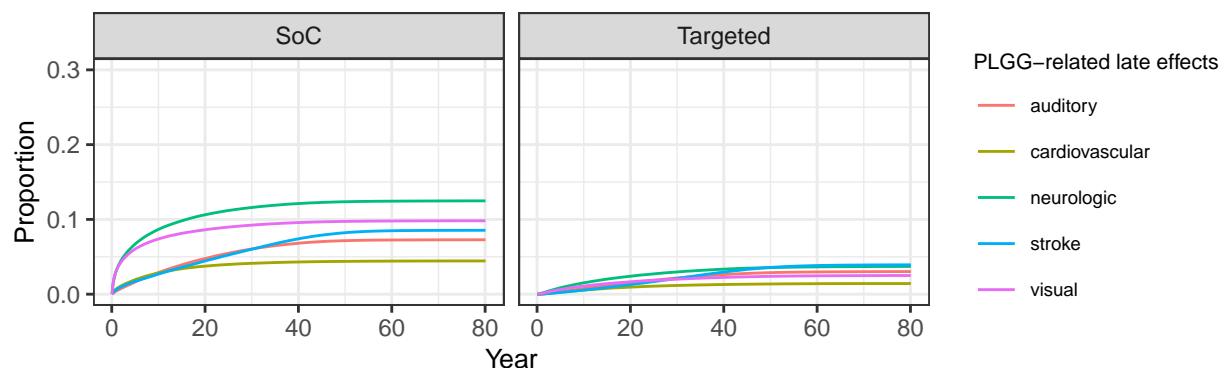
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	28.64 (20.97;35.16)	9.42 (2.37;20.78)
QALY	17.64 (14.54;21.11)	12.11 (9.06;14.63)	5.52 (2.55;10.4)
Total Cost	\$3,045,842 (\$2,446,468;\$3,738,489)	\$395,261 (\$365,504;\$416,998)	\$2,650,581 (\$2,057,884;\$3,345,983)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$243,921 (\$200,740;\$292,397)	\$-103,056 (\$-165,421;\$-57,455)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$122,042 (\$64,189;\$179,418)	\$-32,317 (\$-69,470;\$6,205)
General population costs	\$65,694 (\$45,261;\$91,539)	\$27,976 (\$14,665;\$42,065)	\$37,718 (\$20,440;\$61,663)
Targeted costs	\$2,748,871 (\$2,145,824;\$3,452,211)	\$0 (\$0;\$0)	\$2,748,871 (\$2,145,824;\$3,452,211)
Radiation costs	\$686 (\$315;\$1,036)	\$1,322 (\$1,243;\$1,392)	\$-636 (\$-1,005;\$-283)

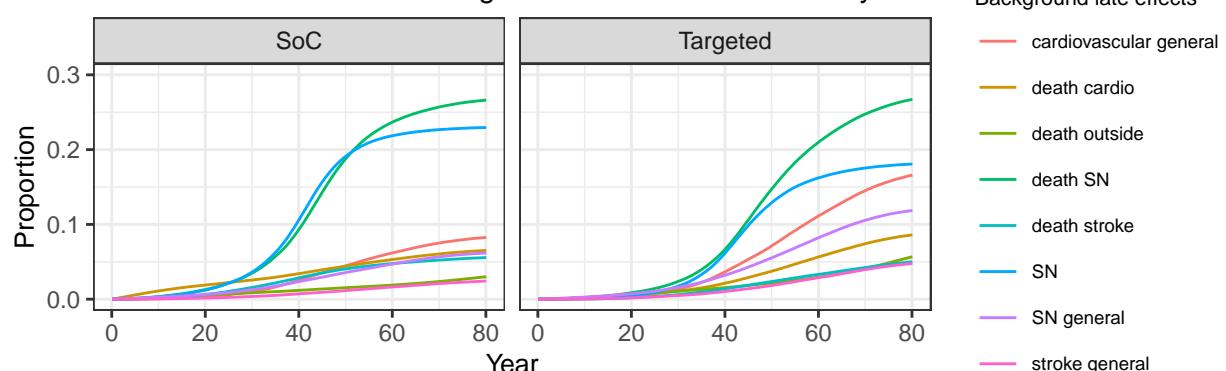
Trace Plot of PLGG States Across Cycles



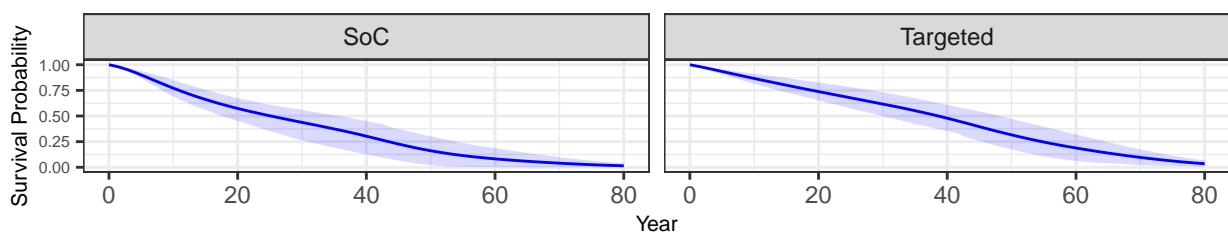
Cumulative Incidence of PLGG-related Late Effects Across Cycles



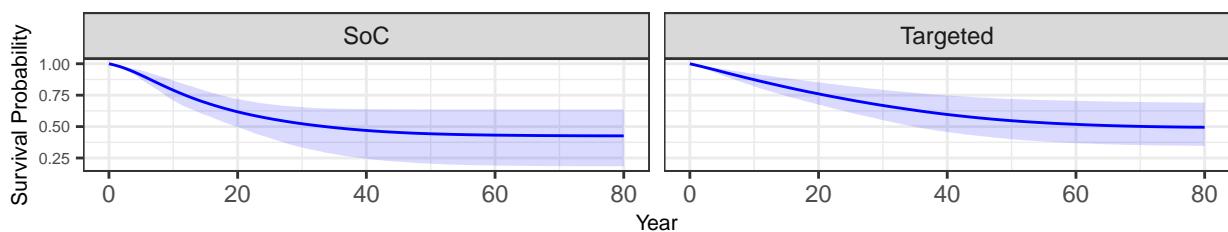
Cumulative Incidence of Background Late Effects Across Cycles



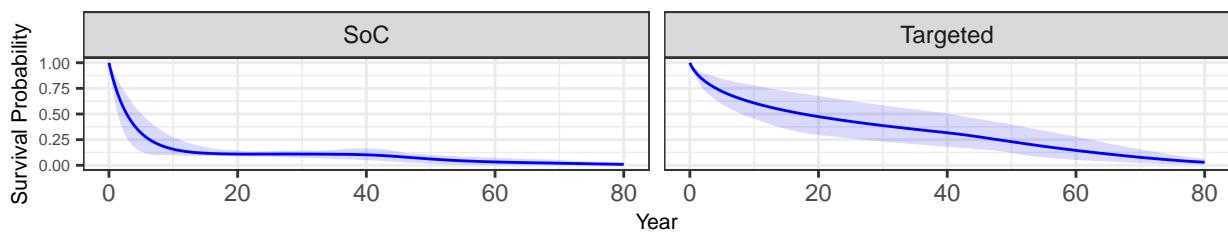
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



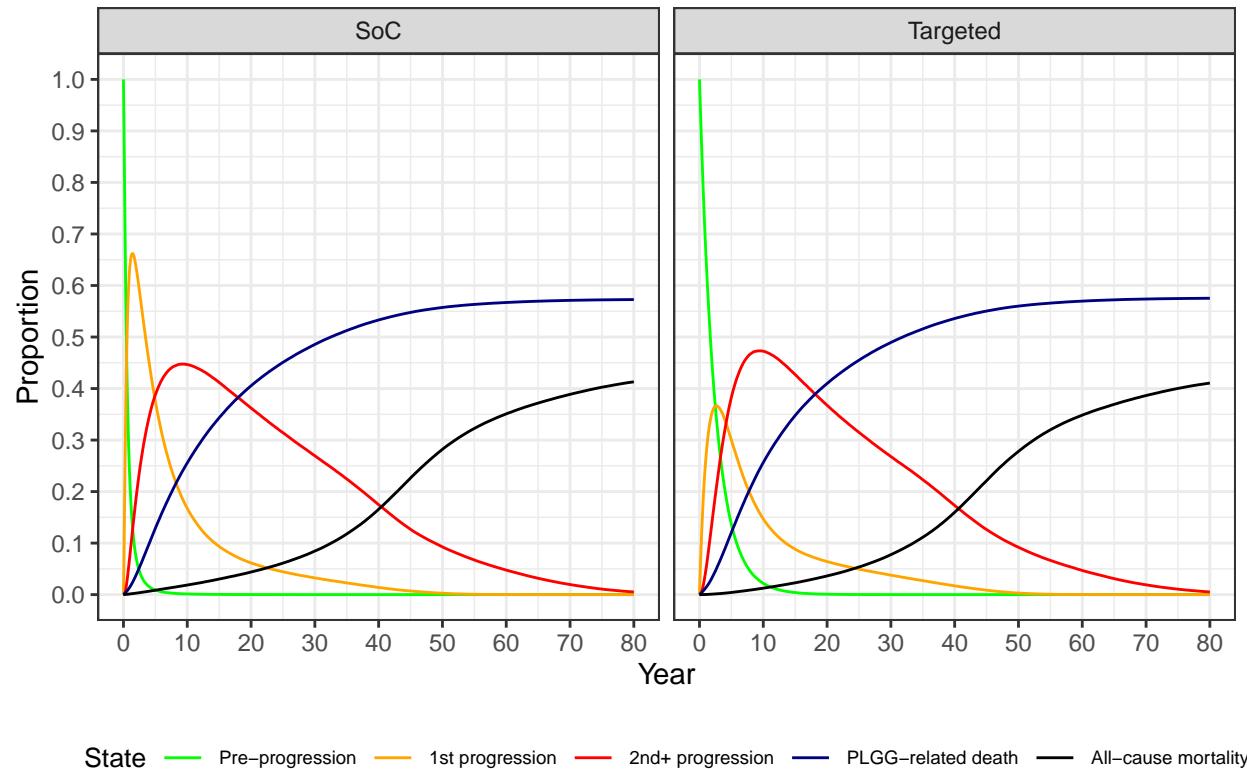
Progression-Free Survival with 95% CI



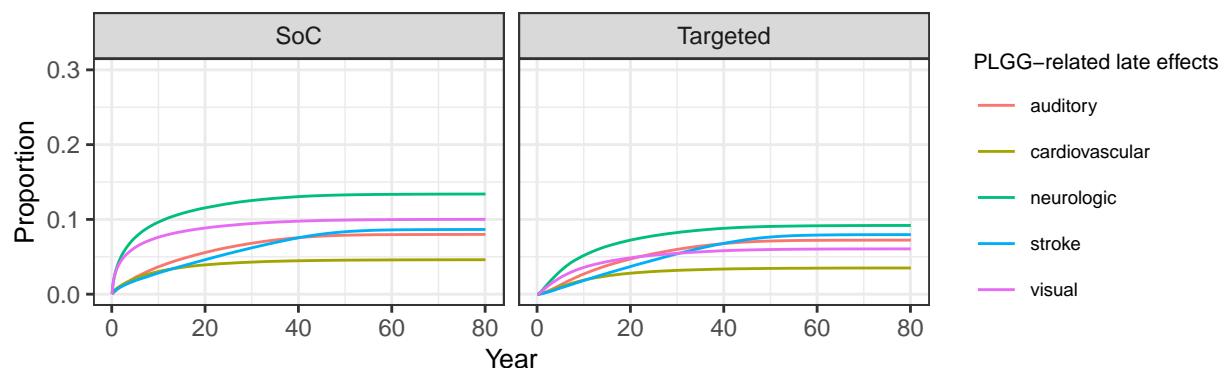
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	27.99 (18.78;35.49)	27.78 (18.5;35.33)	0.2 (-1.14;1.56)
QALY	12.27 (8.35;15.37)	11.64 (7.87;14.59)	0.63 (-0.11;1.42)
Total Cost	\$1,913,469 (\$1,319,975;\$2,448,214)	\$403,893 (\$374,906;\$430,537)	\$1,509,577 (\$943,855;\$2,008,789)
Non-Targeted PLGG related costs	\$218,040 (\$166,683;\$266,961)	\$249,796 (\$198,221;\$298,290)	\$-31,756 (\$-44,279;\$-21,347)
Late effect costs	\$109,237 (\$50,606;\$176,066)	\$125,975 (\$64,219;\$191,430)	\$-16,738 (\$-24,260;\$-10,108)
General population costs	\$32,278 (\$16,459;\$49,131)	\$26,731 (\$12,396;\$42,032)	\$5,547 (\$2,697;\$8,623)
Targeted costs	\$1,552,472 (\$982,485;\$2,056,012)	\$0 (\$0;\$0)	\$1,552,472 (\$982,485;\$2,056,012)
Radiation costs	\$1,443 (\$1,419;\$1,474)	\$1,391 (\$1,354;\$1,426)	\$52 (\$14;\$89)

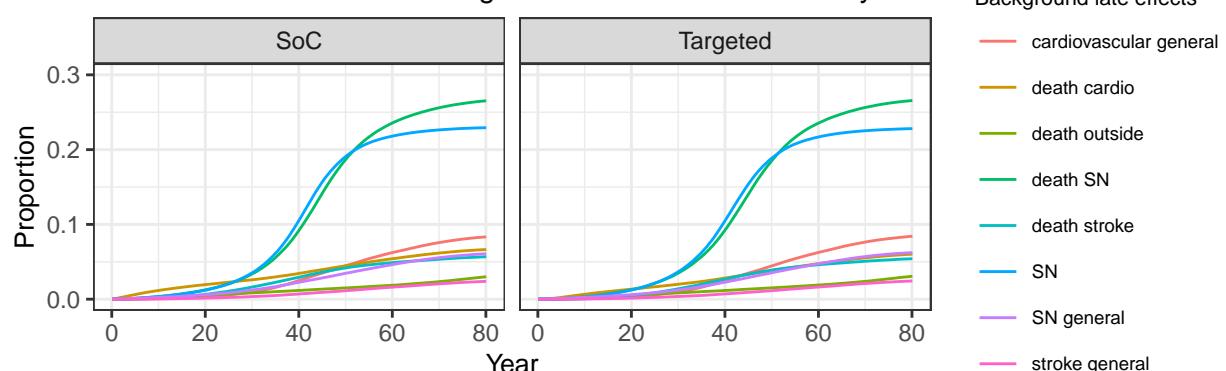
Trace Plot of PLGG States Across Cycles



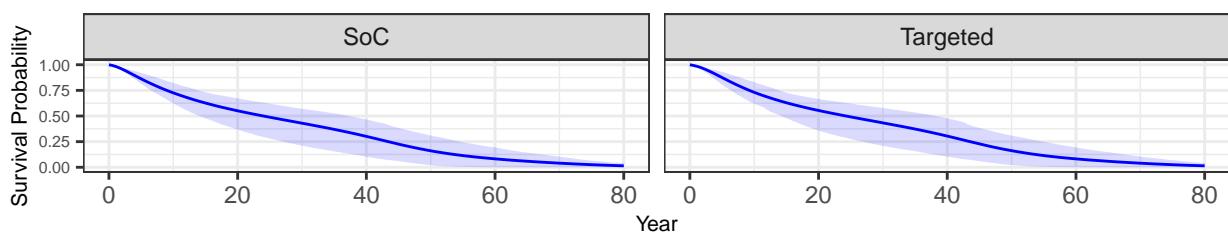
Cumulative Incidence of PLGG-related Late Effects Across Cycles



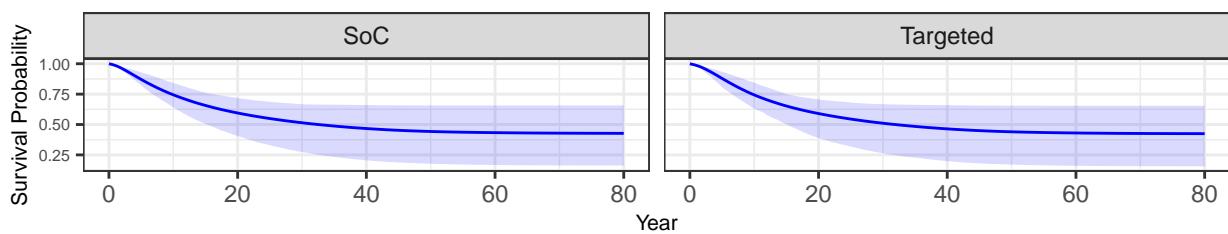
Cumulative Incidence of Background Late Effects Across Cycles



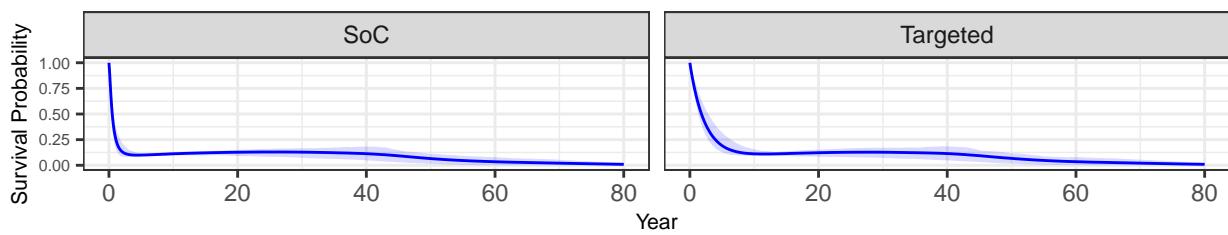
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



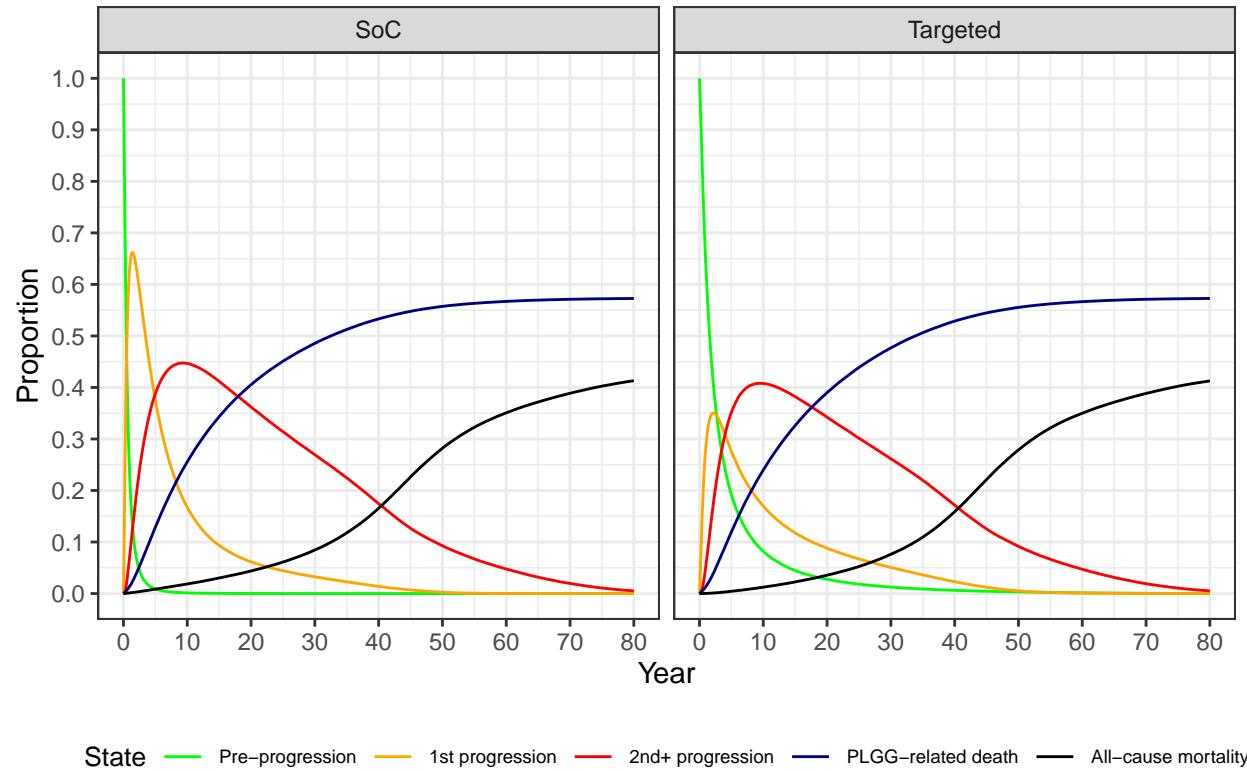
Progression-Free Survival with 95% CI



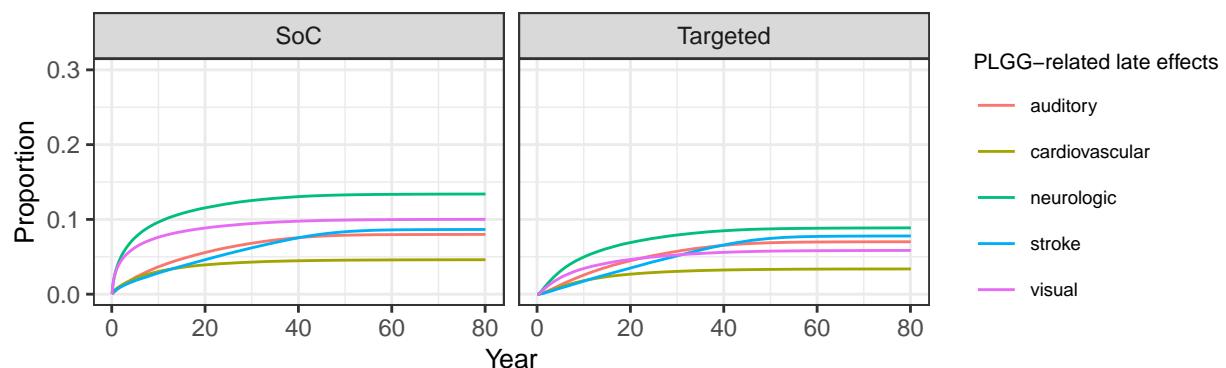
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.62 (21.5;36.23)	27.78 (18.5;35.33)	0.83 (-0.32;1.92)
QALY	12.61 (9.73;15.84)	11.64 (7.87;14.59)	0.96 (0.36;1.66)
Total Cost	\$1,982,857 (\$1,497,259;\$2,501,453)	\$403,893 (\$374,906;\$430,537)	\$1,578,964 (\$1,106,569;\$2,080,034)
Non-Targeted PLGG related costs	\$211,765 (\$160,443;\$258,180)	\$249,796 (\$198,221;\$298,290)	\$-38,031 (\$-50,985;\$-26,026)
Late effect costs	\$108,106 (\$59,451;\$173,533)	\$125,975 (\$64,219;\$191,430)	\$-17,869 (\$-29,204;\$-8,286)
General population costs	\$33,883 (\$19,754;\$50,082)	\$26,731 (\$12,396;\$42,032)	\$7,152 (\$4,135;\$11,217)
Targeted costs	\$1,627,680 (\$1,151,569;\$2,138,682)	\$0 (\$0;\$0)	\$1,627,680 (\$1,151,569;\$2,138,682)
Radiation costs	\$1,423 (\$1,335;\$1,482)	\$1,391 (\$1,354;\$1,426)	\$32 (\$-40;\$86)

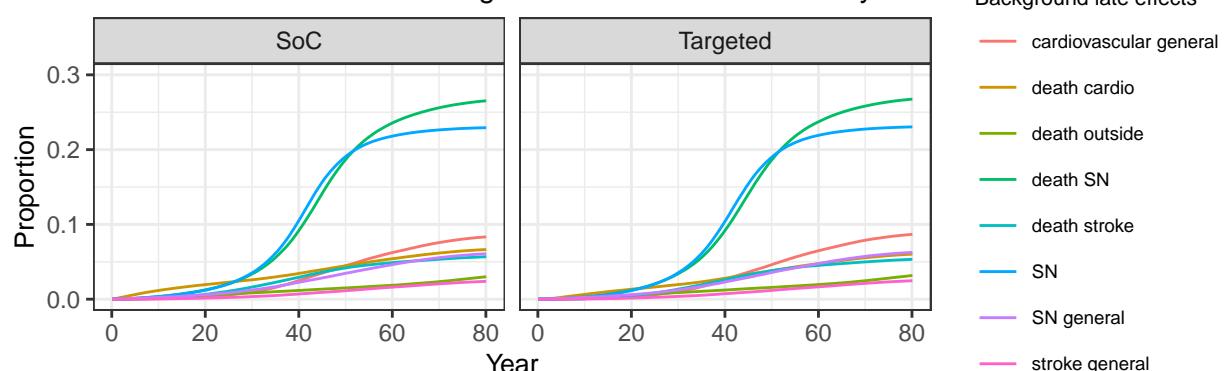
Trace Plot of PLGG States Across Cycles



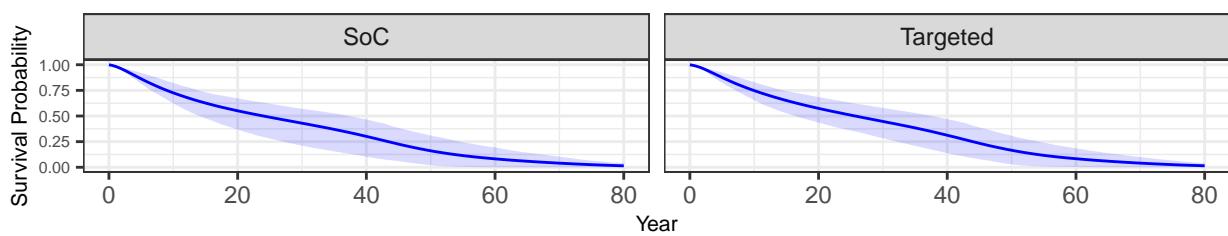
Cumulative Incidence of PLGG-related Late Effects Across Cycles



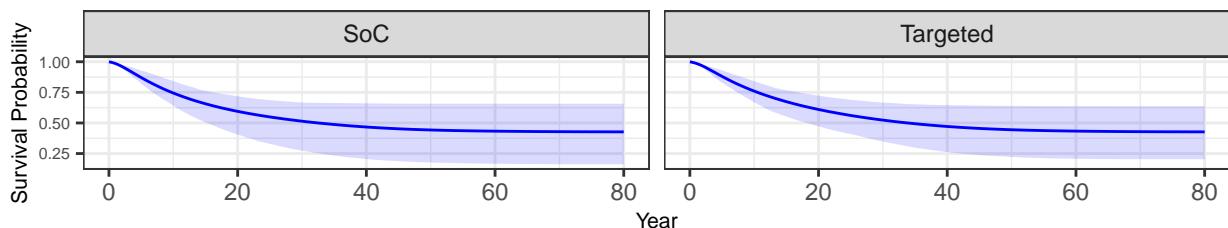
Cumulative Incidence of Background Late Effects Across Cycles



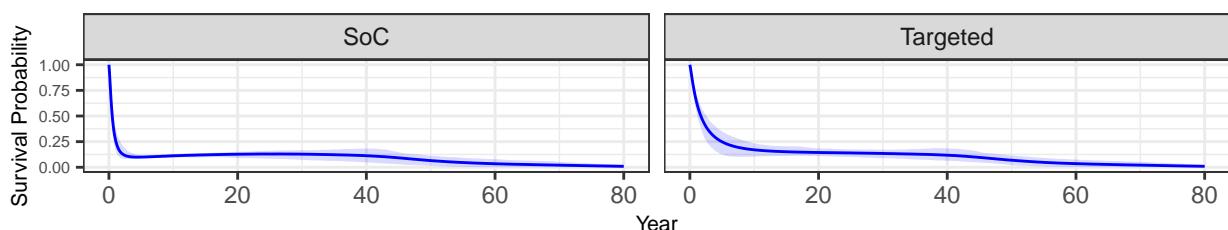
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



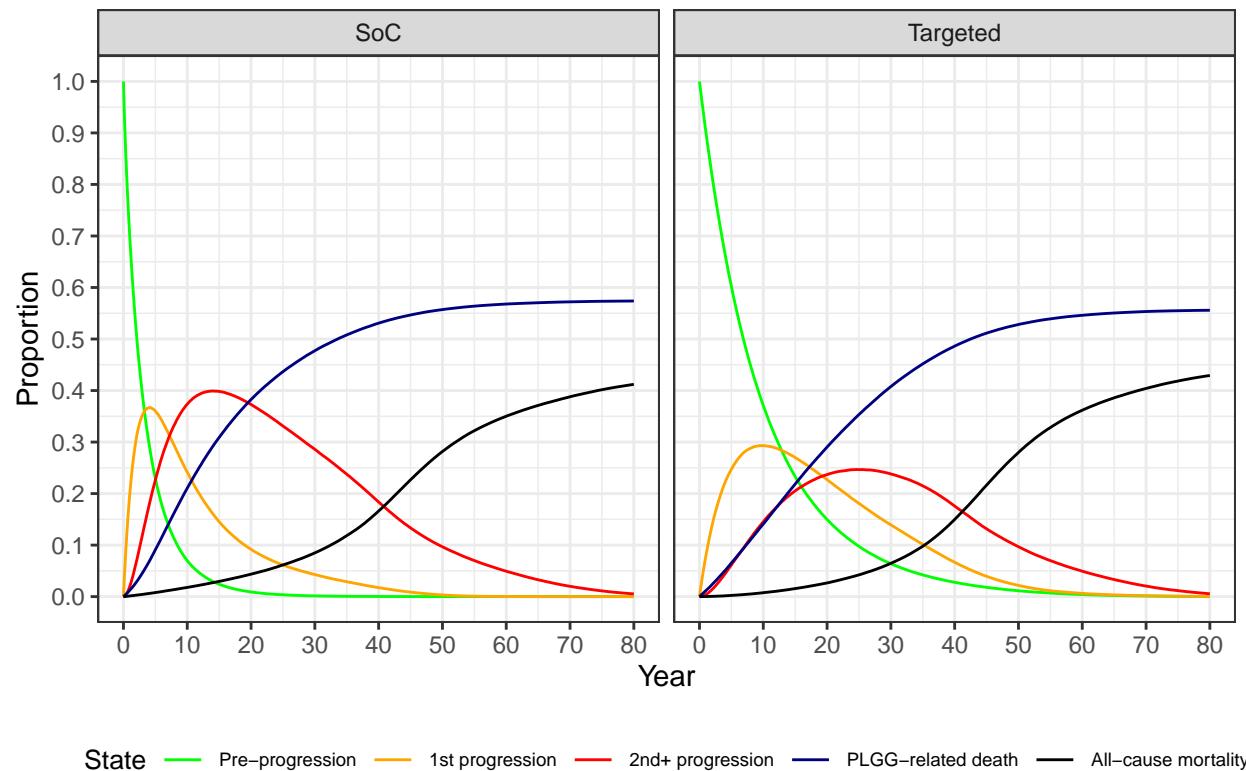
Scenario #1c

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 20% radiation at progression
- **50% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

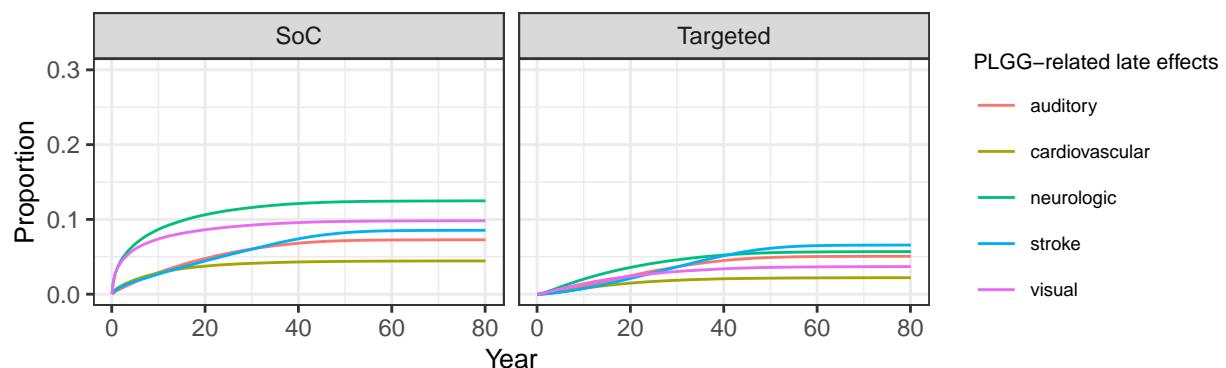
Variable	intervention	control	Delta
Life-years	32.48 (25.96;39.25)	28.64 (20.97;35.16)	3.84 (0.27;11.06)
QALY	14.83 (11.84;18.04)	12.11 (9.06;14.63)	2.72 (1.01;6.03)
Total Cost	\$1,357,477 (\$1,091,891;\$1,654,708)	\$395,261 (\$365,504;\$416,998)	\$962,215 (\$716,413;\$1,254,837)
Non-Targeted PLGG related costs	\$166,697 (\$112,032;\$211,304)	\$243,921 (\$200,740;\$292,397)	\$-77,225 (\$-113,406;\$-49,081)
Late effect costs	\$98,249 (\$64,144;\$143,861)	\$122,042 (\$64,189;\$179,418)	\$-23,794 (\$-40,221;\$729)
General population costs	\$45,481 (\$28,493;\$64,999)	\$27,976 (\$14,665;\$42,065)	\$17,506 (\$9,088;\$34,448)
Targeted costs	\$1,045,803 (\$788,190;\$1,356,745)	\$0 (\$0;\$0)	\$1,045,803 (\$788,190;\$1,356,745)
Radiation costs	\$1,247 (\$1,029;\$1,363)	\$1,322 (\$1,243;\$1,392)	\$-75 (\$-329;\$81)

Trace Plot of PLGG States Across Cycles

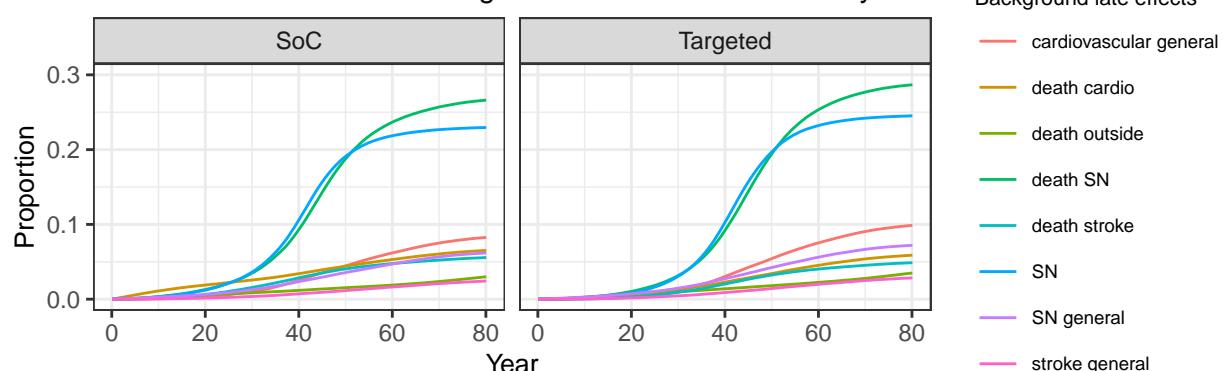


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

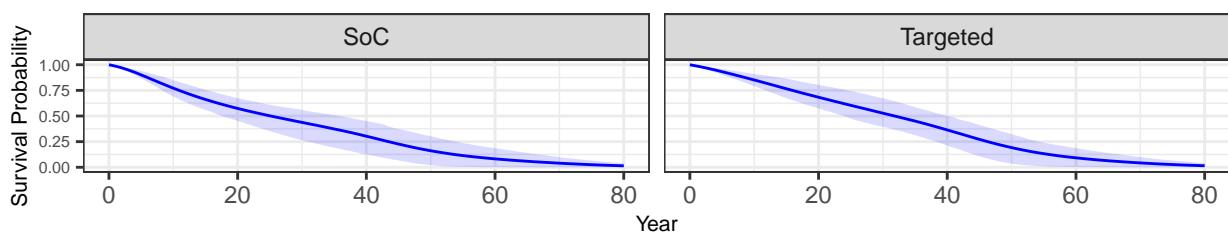
Cumulative Incidence of PLGG-related Late Effects Across Cycles



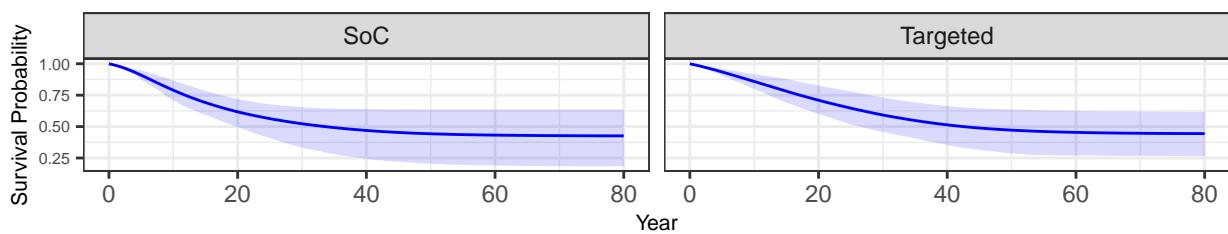
Cumulative Incidence of Background Late Effects Across Cycles



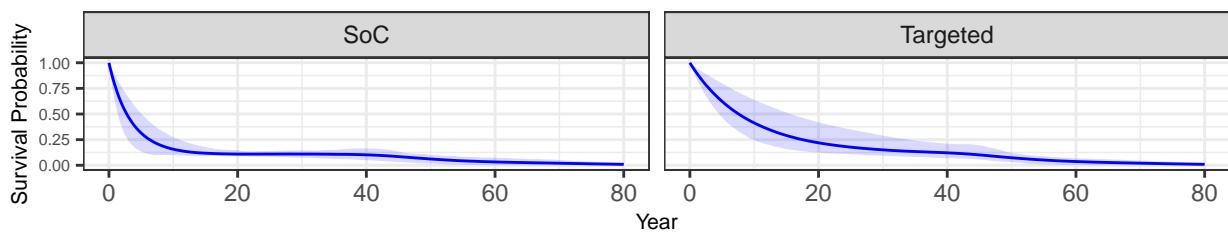
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



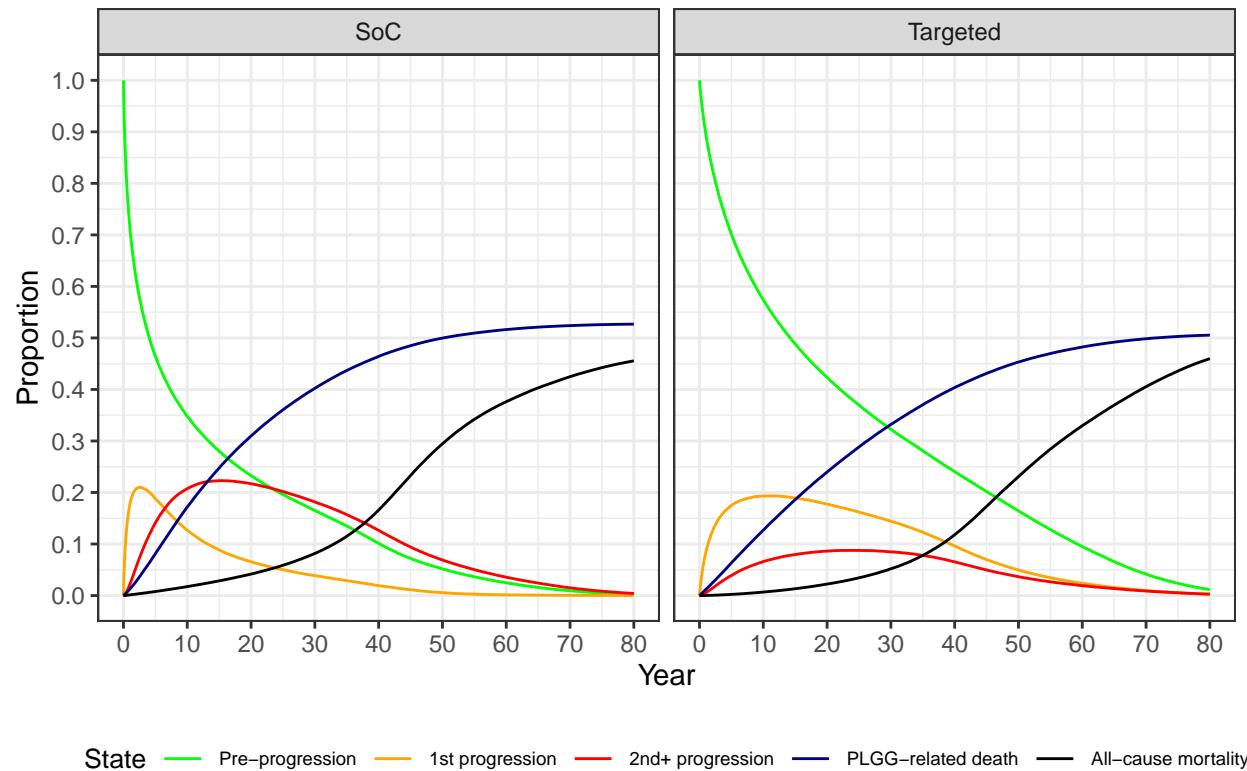
Progression-Free Survival with 95% CI



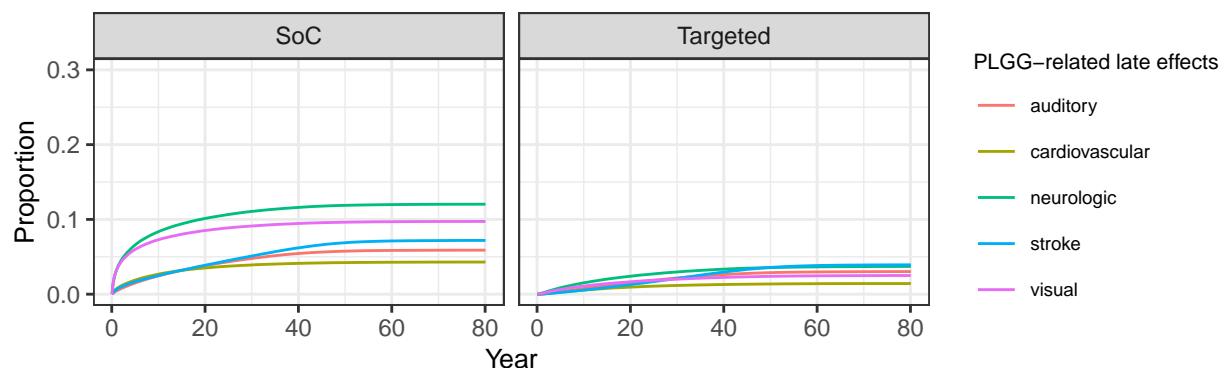
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	32.04 (26.37;37.48)	6.01 (-0.38;14.37)
QALY	17.64 (14.54;21.11)	13.63 (11.27;15.83)	4.01 (0.86;8.14)
Total Cost	\$1,671,407 (\$1,376,645;\$2,012,384)	\$375,954 (\$356,889;\$392,667)	\$1,295,453 (\$1,006,185;\$1,626,349)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$210,099 (\$157,944;\$246,665)	\$-69,234 (\$-120,666;\$-35,229)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$130,725 (\$94,124;\$187,424)	\$-40,999 (\$-64,774;\$-16,602)
General population costs	\$65,694 (\$45,261;\$91,539)	\$34,221 (\$21,047;\$48,447)	\$31,473 (\$11,076;\$54,489)
Targeted costs	\$1,374,436 (\$1,072,912;\$1,726,105)	\$0 (\$0;\$0)	\$1,374,436 (\$1,072,912;\$1,726,105)
Radiation costs	\$686 (\$315;\$1,036)	\$909 (\$469;\$1,256)	\$-223 (\$-735;\$402)

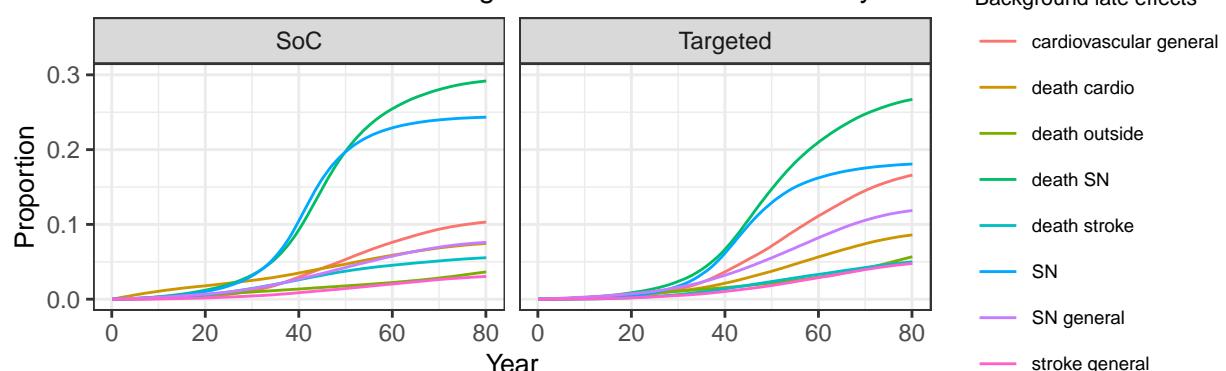
Trace Plot of PLGG States Across Cycles



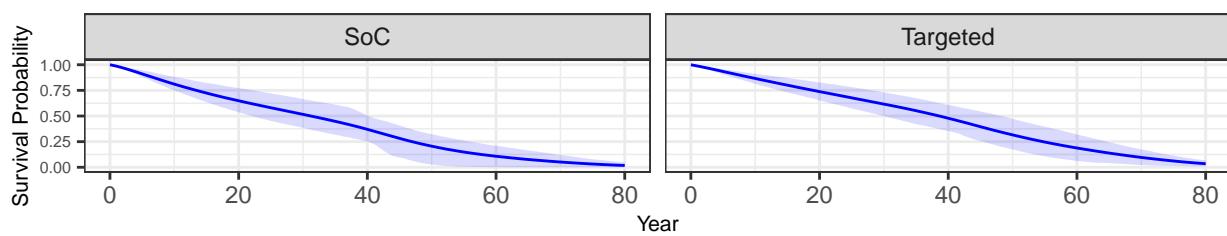
Cumulative Incidence of PLGG-related Late Effects Across Cycles



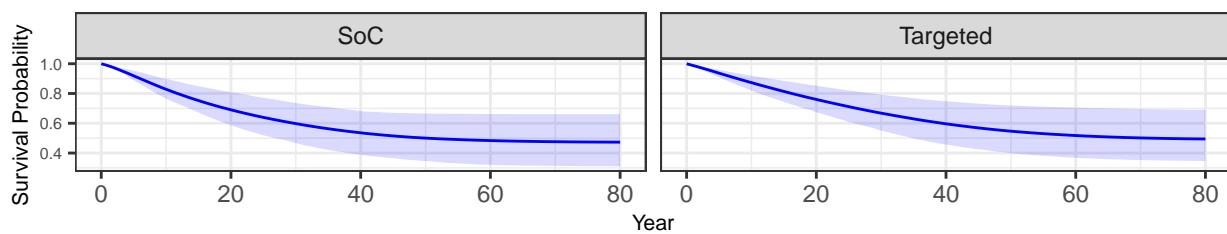
Cumulative Incidence of Background Late Effects Across Cycles



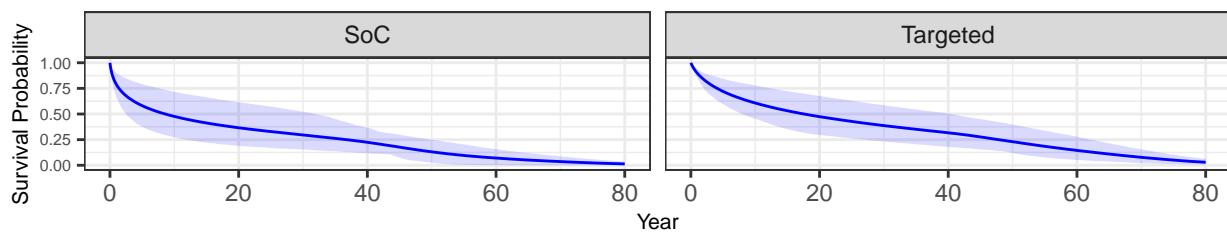
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



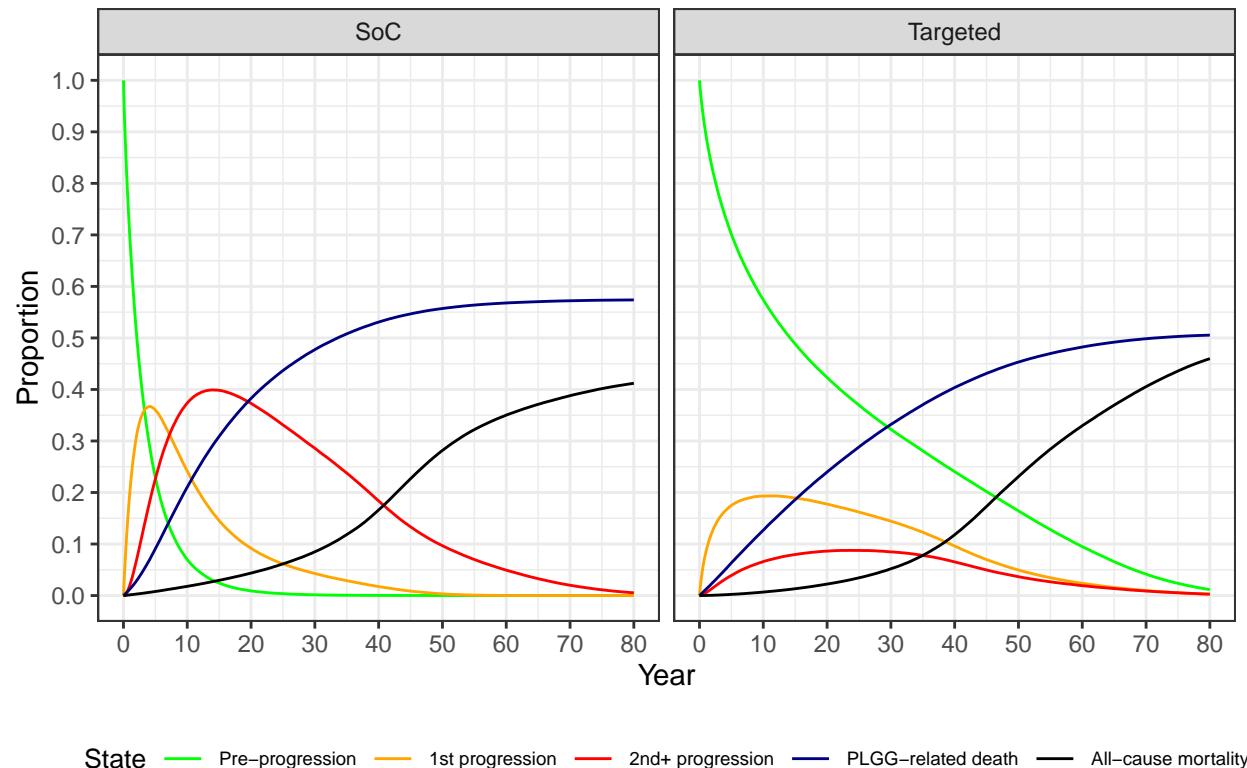
Progression-Free Survival with 95% CI



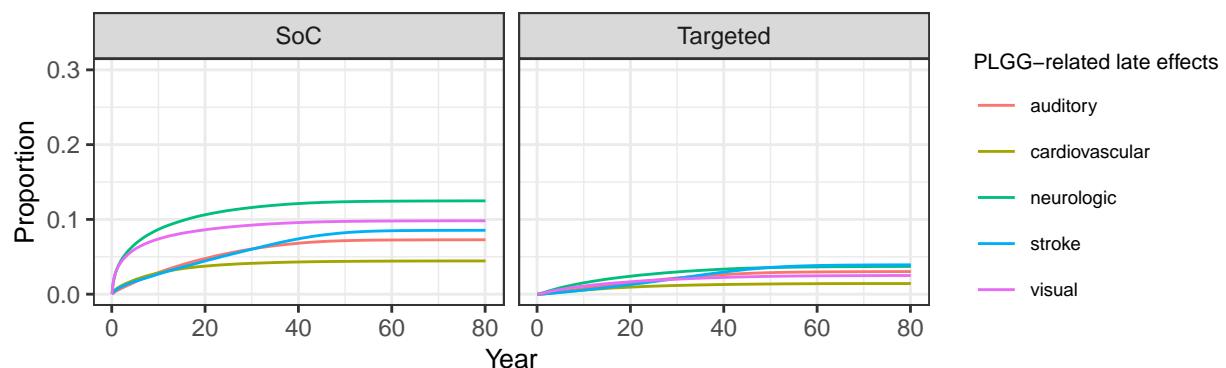
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	28.64 (20.97;35.16)	9.42 (2.37;20.78)
QALY	17.64 (14.54;21.11)	12.11 (9.06;14.63)	5.52 (2.55;10.4)
Total Cost	\$1,671,407 (\$1,376,645;\$2,012,384)	\$395,261 (\$365,504;\$416,998)	\$1,276,145 (\$984,555;\$1,621,052)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$243,921 (\$200,740;\$292,397)	\$-103,056 (\$-165,421;\$-57,455)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$122,042 (\$64,189;\$179,418)	\$-32,317 (\$-69,470;\$6,205)
General population costs	\$65,694 (\$45,261;\$91,539)	\$27,976 (\$14,665;\$42,065)	\$37,718 (\$20,440;\$61,663)
Targeted costs	\$1,374,436 (\$1,072,912;\$1,726,105)	\$0 (\$0;\$0)	\$1,374,436 (\$1,072,912;\$1,726,105)
Radiation costs	\$686 (\$315;\$1,036)	\$1,322 (\$1,243;\$1,392)	\$-636 (\$-1,005;\$-283)

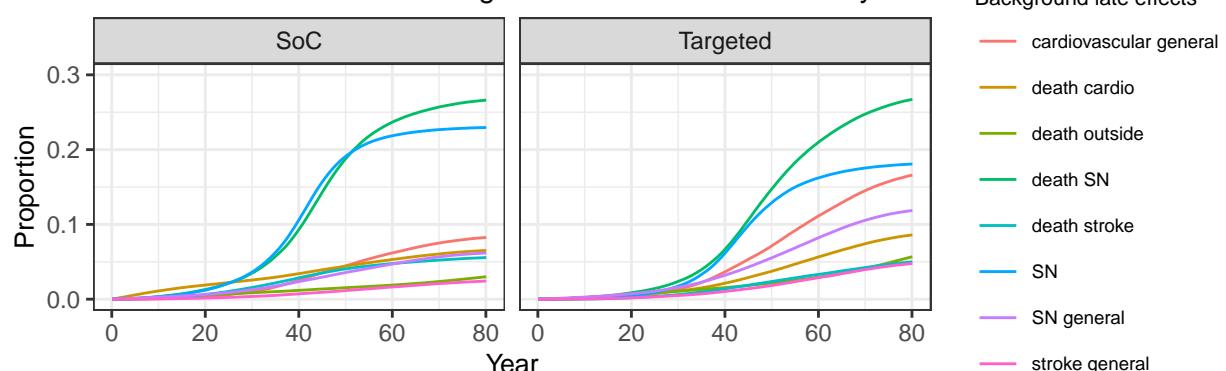
Trace Plot of PLGG States Across Cycles



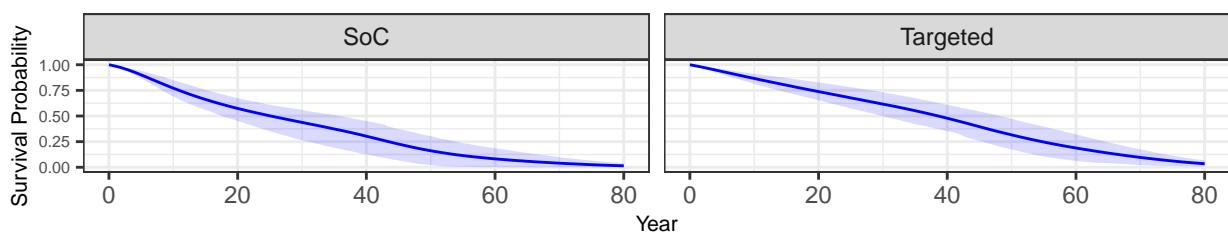
Cumulative Incidence of PLGG-related Late Effects Across Cycles



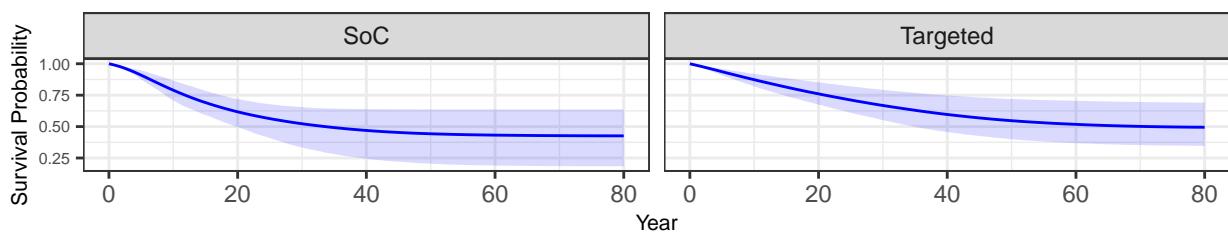
Cumulative Incidence of Background Late Effects Across Cycles



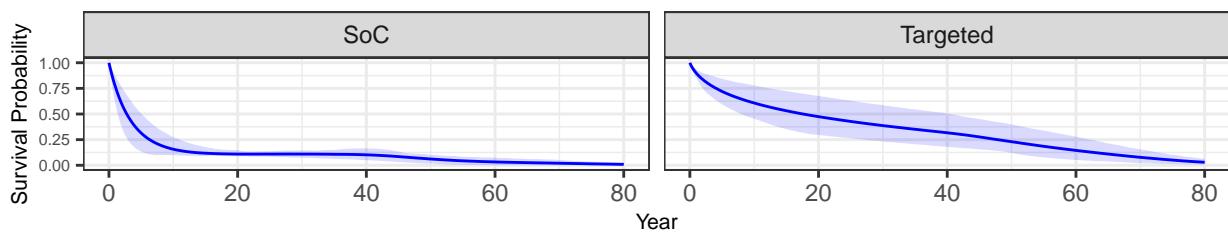
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



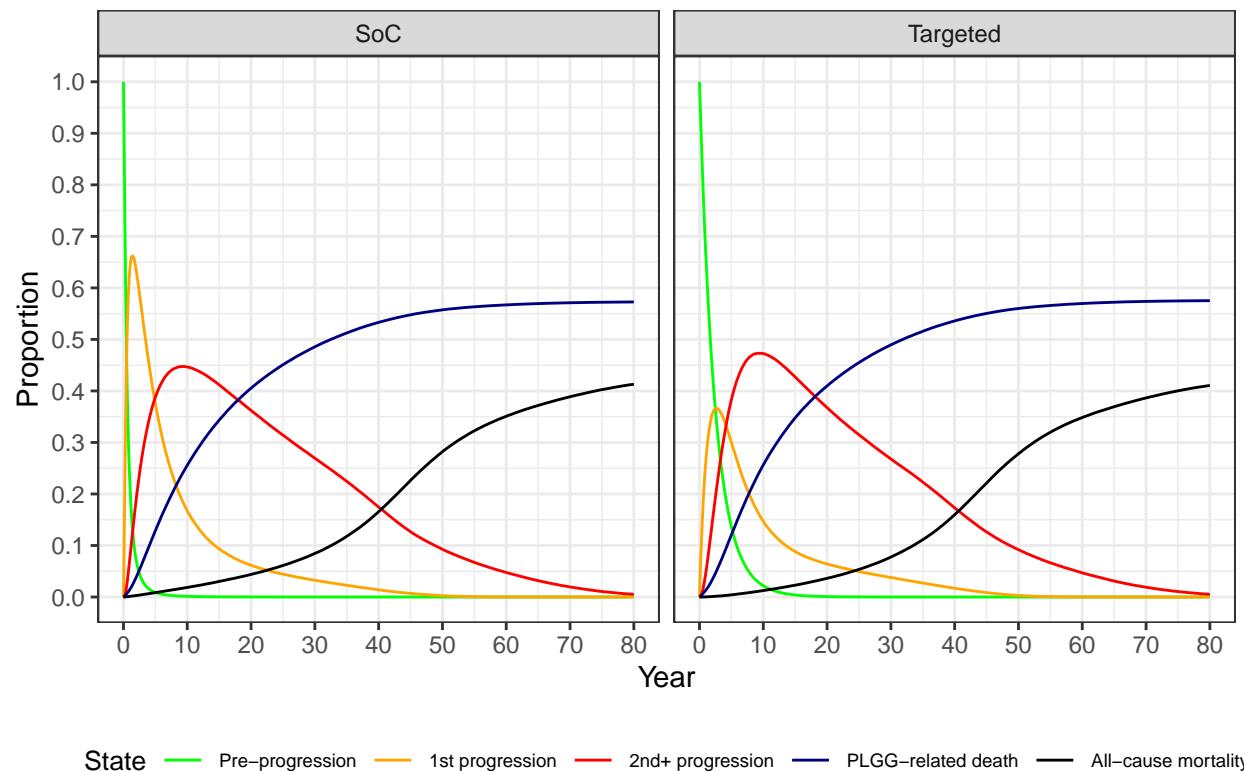
Progression-Free Survival with 95% CI



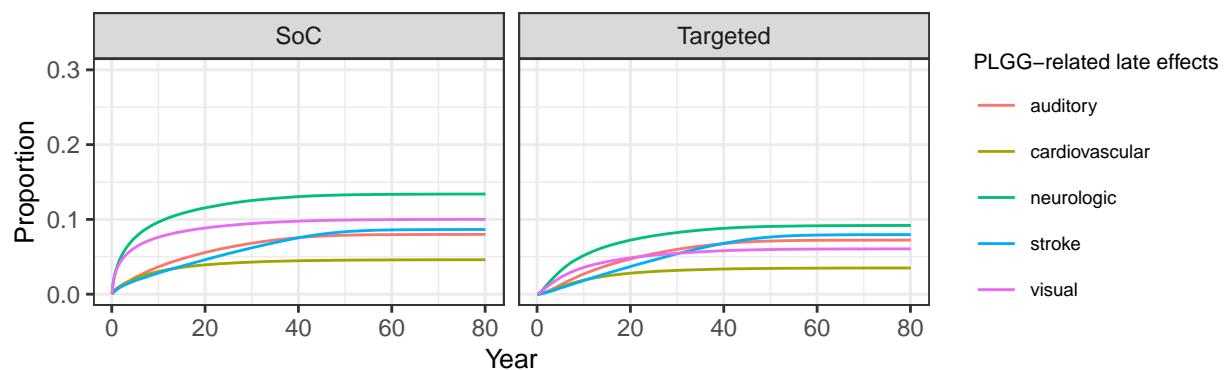
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	27.99 (18.78;35.49)	27.78 (18.5;35.33)	0.2 (-1.14;1.56)
QALY	12.27 (8.35;15.37)	11.64 (7.87;14.59)	0.63 (-0.11;1.42)
Total Cost	\$1,137,233 (\$828,732;\$1,402,676)	\$403,893 (\$374,906;\$430,537)	\$733,341 (\$452,612;\$982,911)
Non-Targeted PLGG related costs	\$218,040 (\$166,683;\$266,961)	\$249,796 (\$198,221;\$298,290)	\$-31,756 (\$-44,279;\$-21,347)
Late effect costs	\$109,237 (\$50,606;\$176,066)	\$125,975 (\$64,219;\$191,430)	\$-16,738 (\$-24,260;\$-10,108)
General population costs	\$32,278 (\$16,459;\$49,131)	\$26,731 (\$12,396;\$42,032)	\$5,547 (\$2,697;\$8,623)
Targeted costs	\$776,236 (\$491,242;\$1,028,006)	\$0 (\$0;\$0)	\$776,236 (\$491,242;\$1,028,006)
Radiation costs	\$1,443 (\$1,419;\$1,474)	\$1,391 (\$1,354;\$1,426)	\$52 (\$14;\$89)

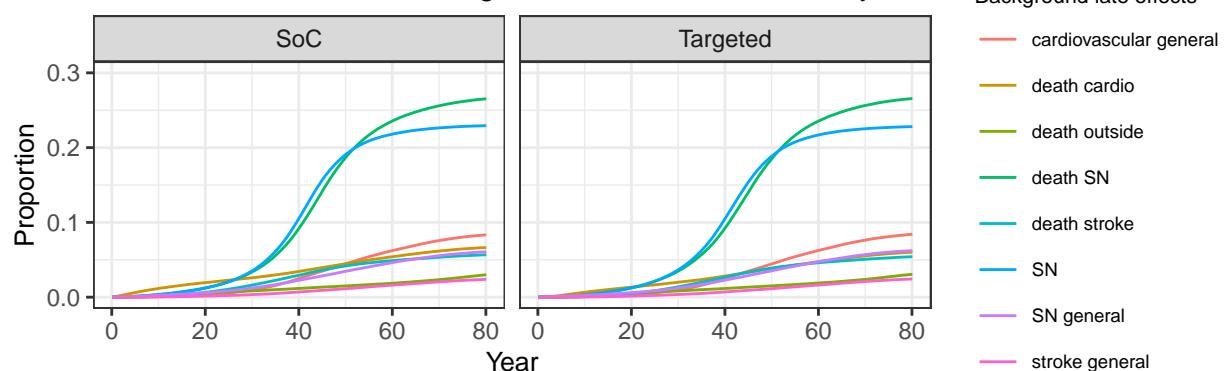
Trace Plot of PLGG States Across Cycles



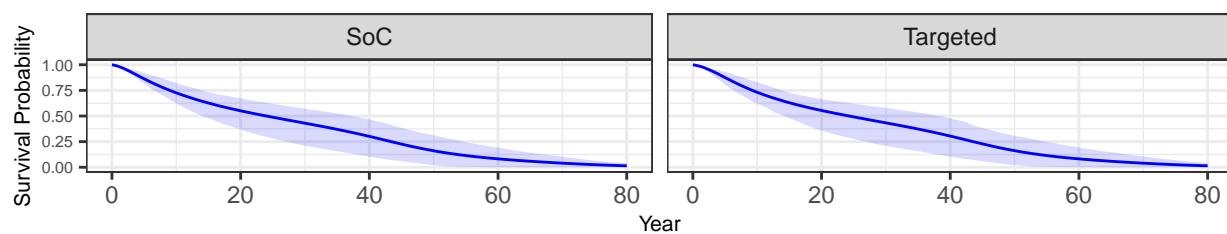
Cumulative Incidence of PLGG-related Late Effects Across Cycles



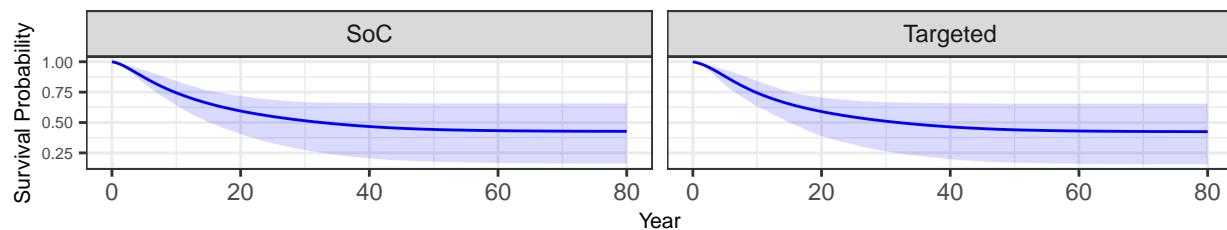
Cumulative Incidence of Background Late Effects Across Cycles



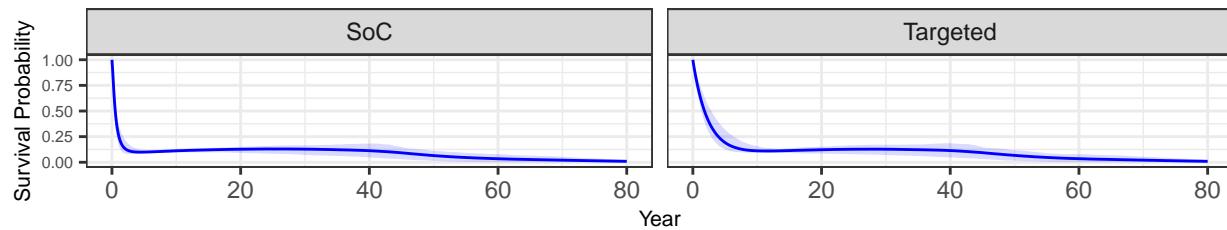
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



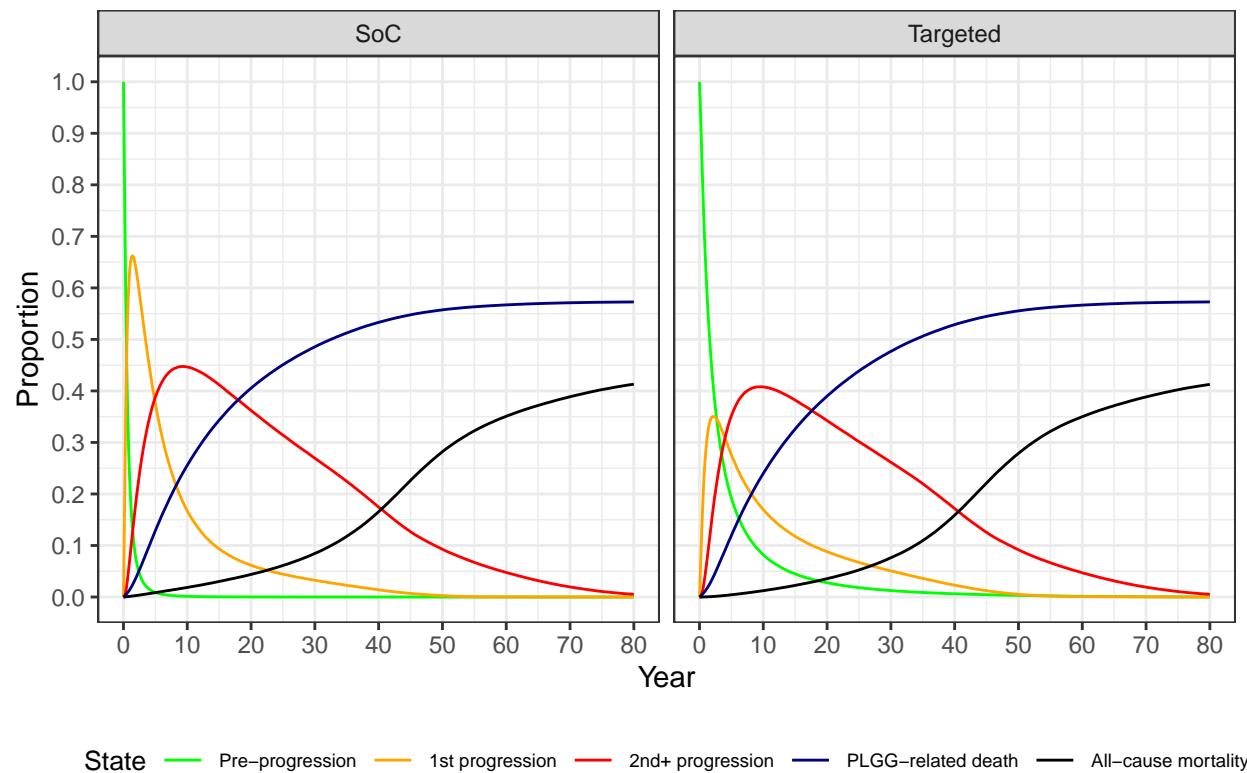
Progression-Free Survival with 95% CI



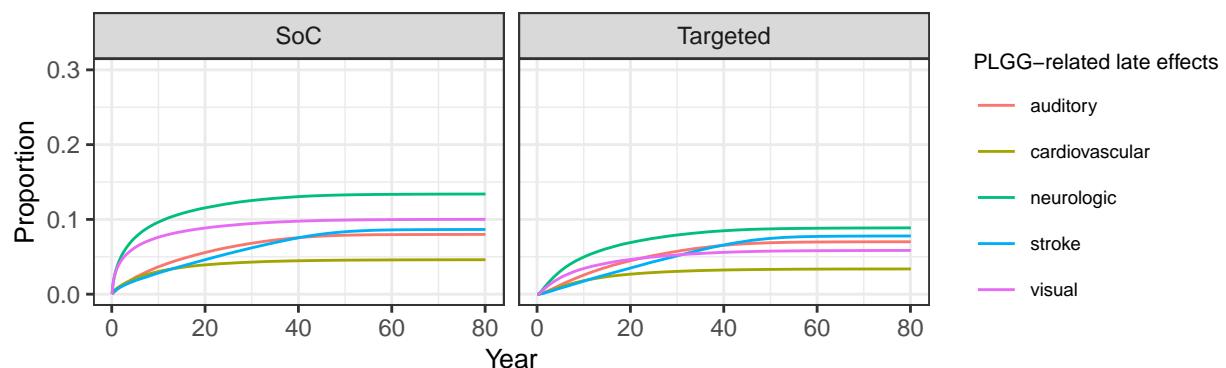
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.62 (21.5;36.23)	27.78 (18.5;35.33)	0.83 (-0.32;1.92)
QALY	12.61 (9.73;15.84)	11.64 (7.87;14.59)	0.96 (0.36;1.66)
Total Cost	\$1,169,017 (\$921,475;\$1,444,241)	\$403,893 (\$374,906;\$430,537)	\$765,124 (\$530,785;\$1,010,693)
Non-Targeted PLGG related costs	\$211,765 (\$160,443;\$258,180)	\$249,796 (\$198,221;\$298,290)	\$-38,031 (\$-50,985;\$-26,026)
Late effect costs	\$108,106 (\$59,451;\$173,533)	\$125,975 (\$64,219;\$191,430)	\$-17,869 (\$-29,204;\$-8,286)
General population costs	\$33,883 (\$19,754;\$50,082)	\$26,731 (\$12,396;\$42,032)	\$7,152 (\$4,135;\$11,217)
Targeted costs	\$813,840 (\$575,784;\$1,069,341)	\$0 (\$0;\$0)	\$813,840 (\$575,784;\$1,069,341)
Radiation costs	\$1,423 (\$1,335;\$1,482)	\$1,391 (\$1,354;\$1,426)	\$32 (\$-40;\$86)

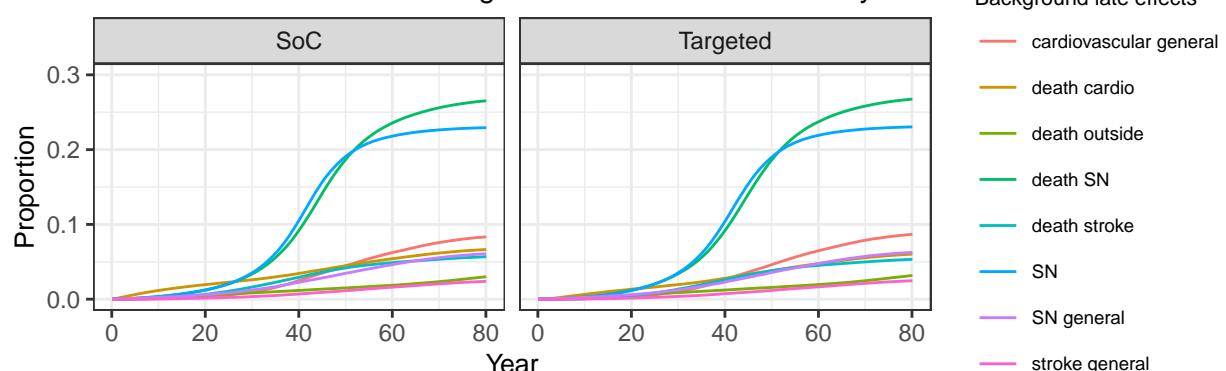
Trace Plot of PLGG States Across Cycles



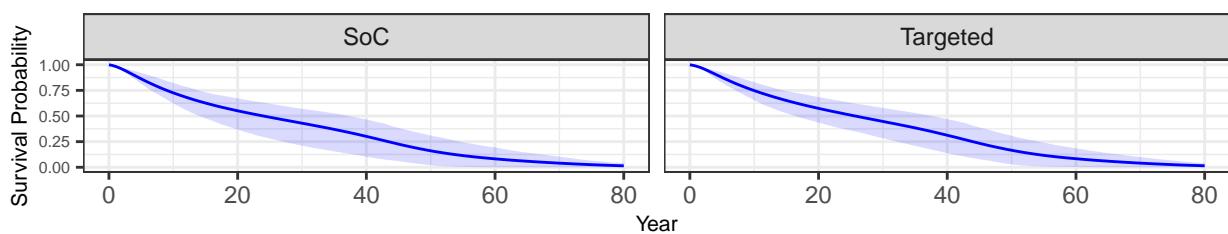
Cumulative Incidence of PLGG-related Late Effects Across Cycles



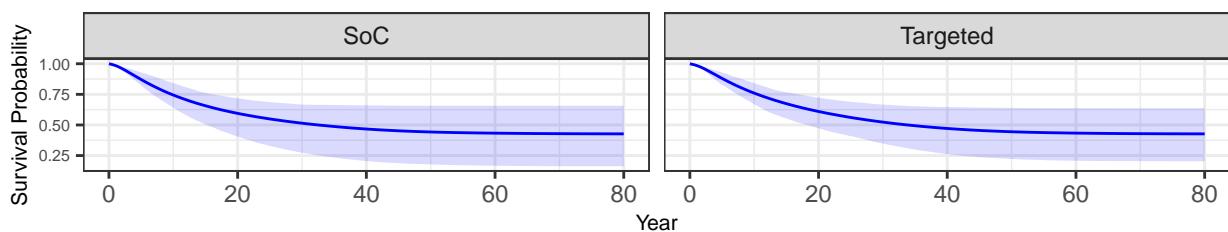
Cumulative Incidence of Background Late Effects Across Cycles



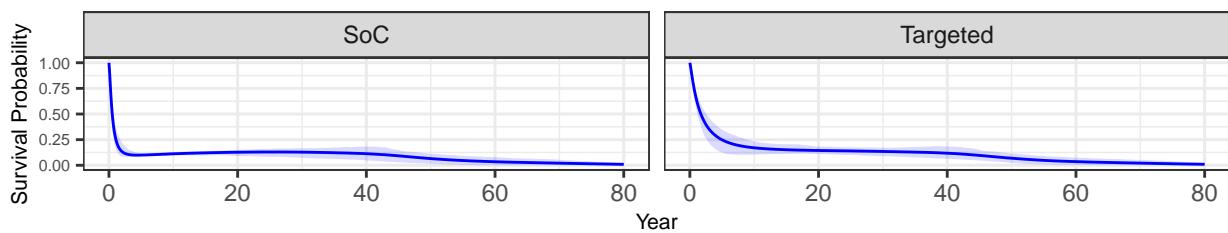
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI

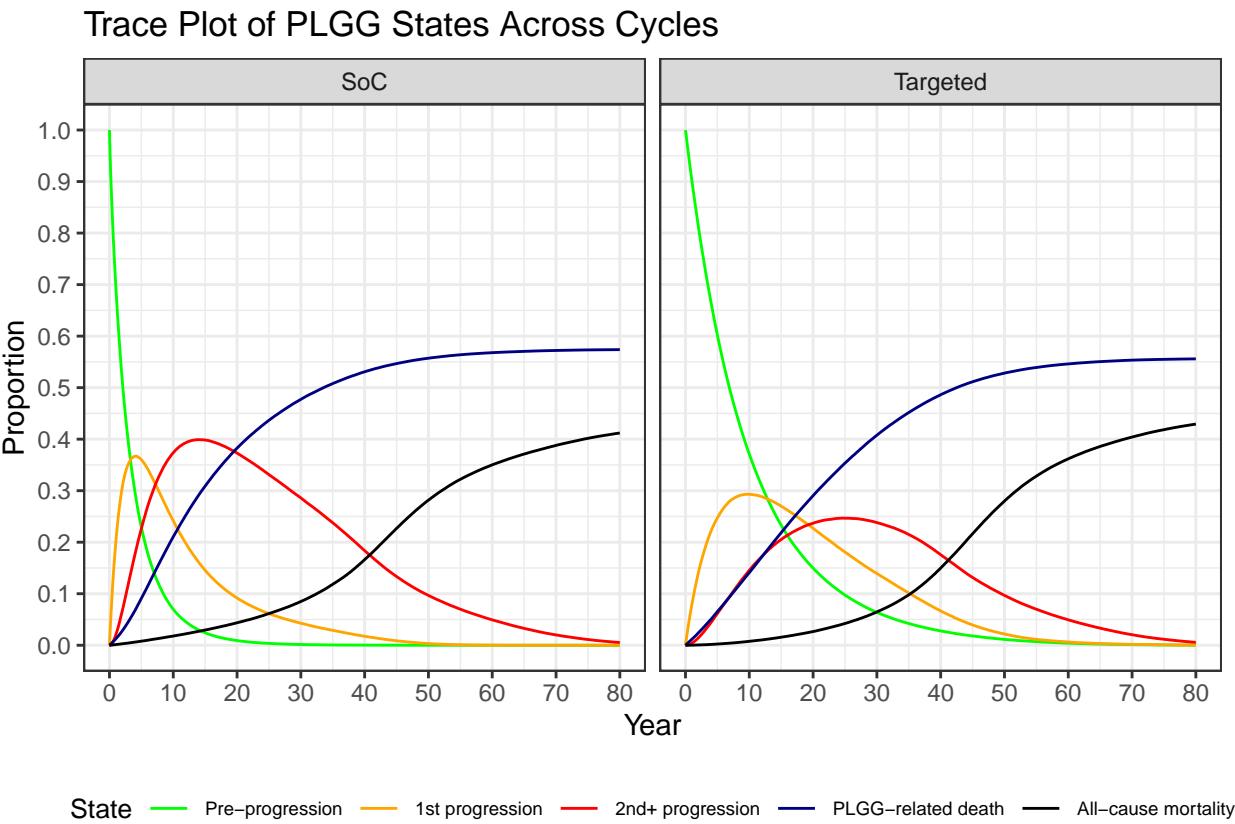


Scenario #1d

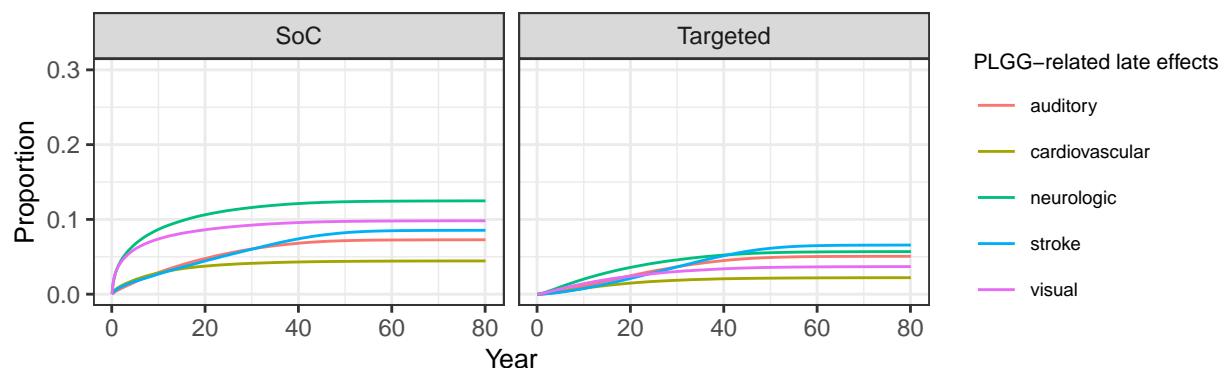
- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 20% radiation at progression
- **75% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

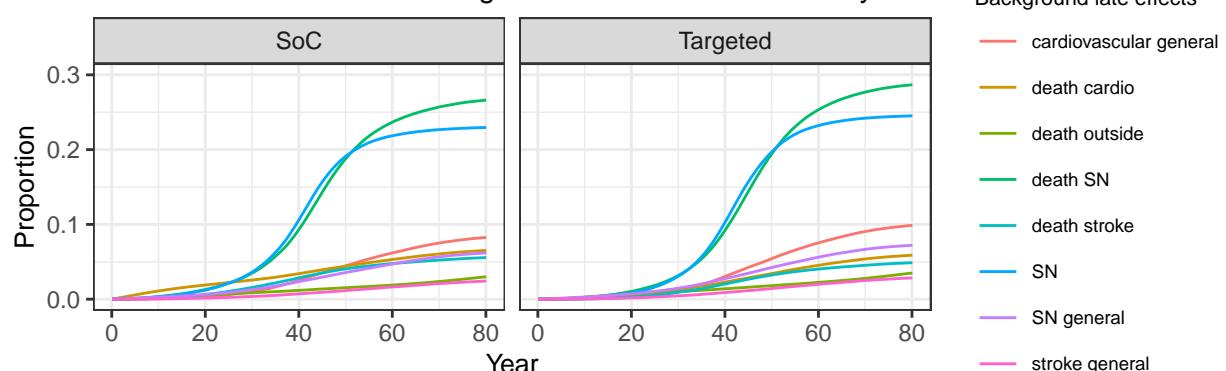
Variable	intervention	control	Delta
Life-years	32.48 (25.96;39.25)	28.64 (20.97;35.16)	3.84 (0.27;11.06)
QALY	14.83 (11.84;18.04)	12.11 (9.06;14.63)	2.72 (1.01;6.03)
Total Cost	\$834,575 (\$708,425;\$975,562)	\$395,261 (\$365,504;\$416,998)	\$439,314 (\$321,123;\$575,691)
Non-Targeted PLGG related costs	\$166,697 (\$112,032;\$211,304)	\$243,921 (\$200,740;\$292,397)	\$-77,225 (\$-113,406;\$-49,081)
Late effect costs	\$98,249 (\$64,144;\$143,861)	\$122,042 (\$64,189;\$179,418)	\$-23,794 (\$-40,221;\$729)
General population costs	\$45,481 (\$28,493;\$64,999)	\$27,976 (\$14,665;\$42,065)	\$17,506 (\$9,088;\$34,448)
Targeted costs	\$522,901 (\$394,095;\$678,372)	\$0 (\$0;\$0)	\$522,901 (\$394,095;\$678,372)
Radiation costs	\$1,247 (\$1,029;\$1,363)	\$1,322 (\$1,243;\$1,392)	\$-75 (\$-329;\$81)



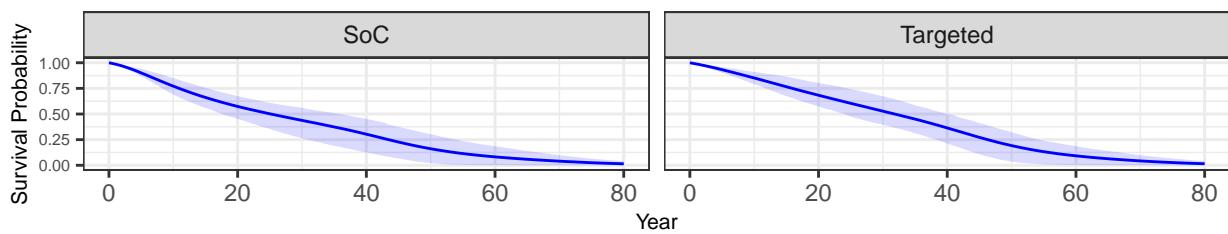
Cumulative Incidence of PLGG-related Late Effects Across Cycles



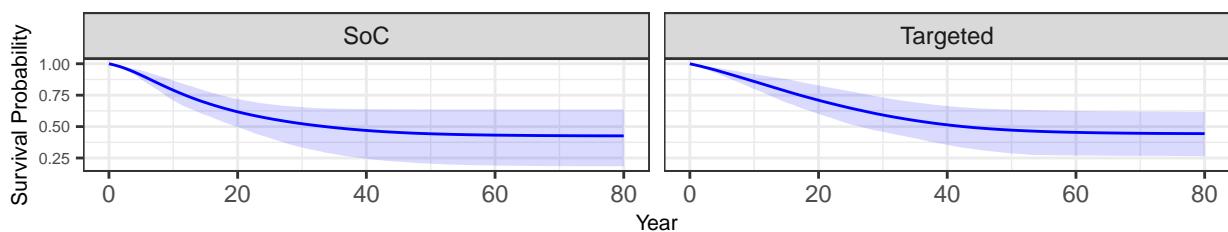
Cumulative Incidence of Background Late Effects Across Cycles



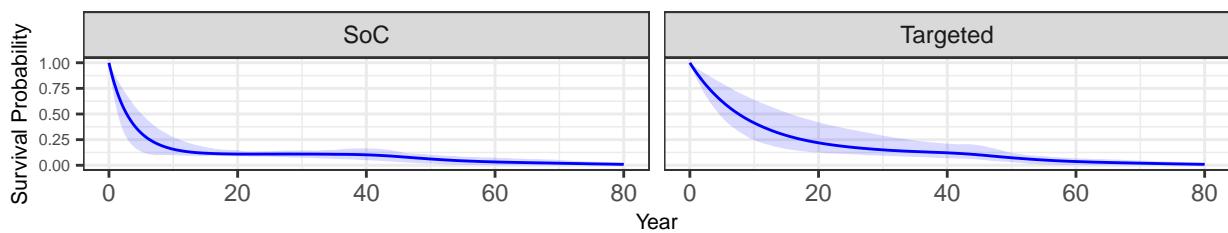
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



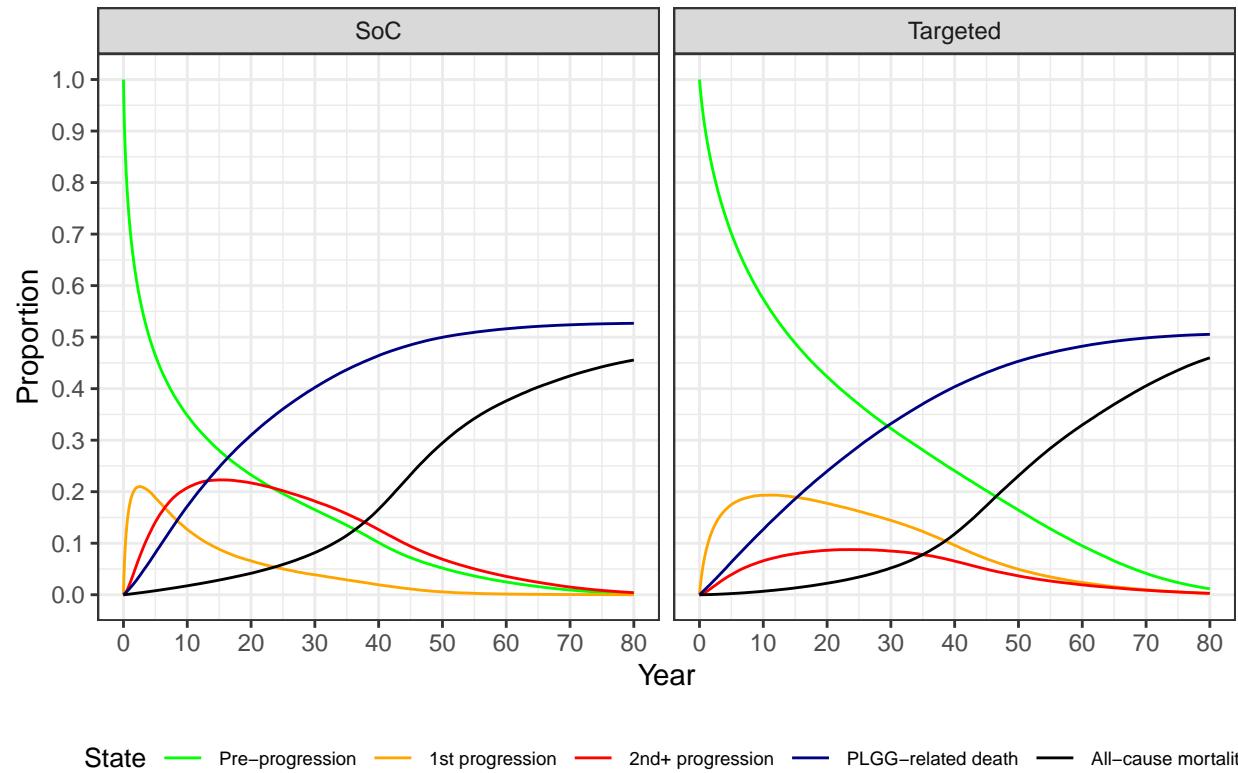
Progression-Free Survival with 95% CI



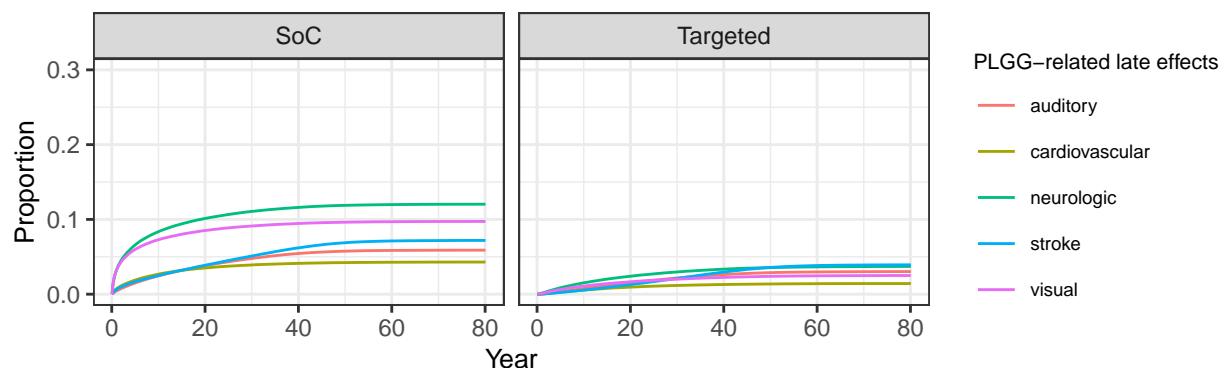
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	32.04 (26.37;37.48)	6.01 (-0.38;14.37)
QALY	17.64 (14.54;21.11)	13.63 (11.27;15.83)	4.01 (0.86;8.14)
Total Cost	\$984,189 (\$841,734;\$1,149,331)	\$375,954 (\$356,889;\$392,667)	\$608,235 (\$469,520;\$763,296)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$210,099 (\$157,944;\$246,665)	\$-69,234 (\$-120,666;\$-35,229)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$130,725 (\$94,124;\$187,424)	\$-40,999 (\$-64,774;\$-16,602)
General population costs	\$65,694 (\$45,261;\$91,539)	\$34,221 (\$21,047;\$48,447)	\$31,473 (\$11,076;\$54,489)
Targeted costs	\$687,218 (\$536,456;\$863,053)	\$0 (\$0;\$0)	\$687,218 (\$536,456;\$863,053)
Radiation costs	\$686 (\$315;\$1,036)	\$909 (\$469;\$1,256)	\$-223 (\$-735;\$402)

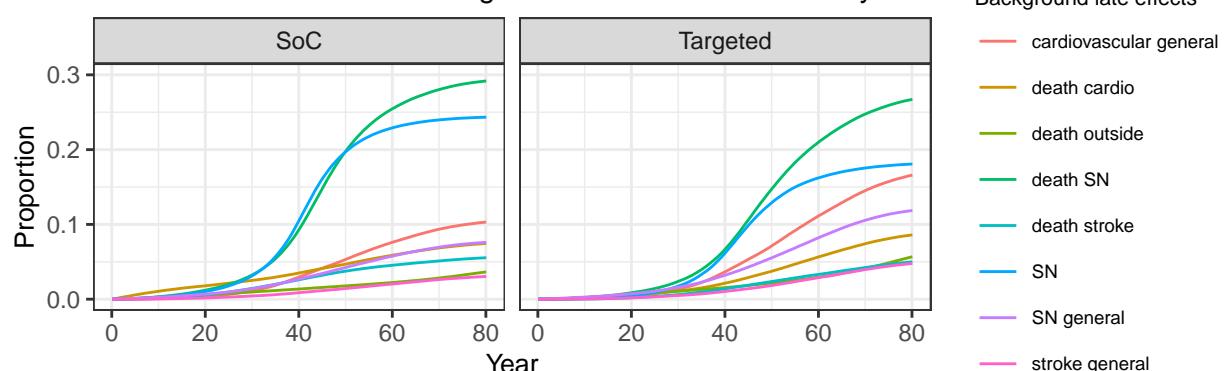
Trace Plot of PLGG States Across Cycles



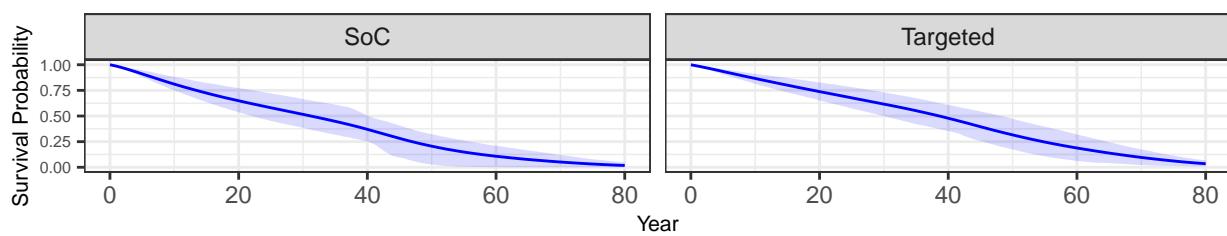
Cumulative Incidence of PLGG-related Late Effects Across Cycles



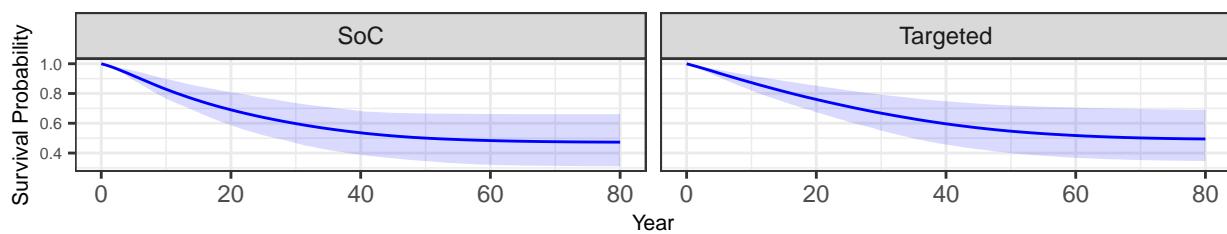
Cumulative Incidence of Background Late Effects Across Cycles



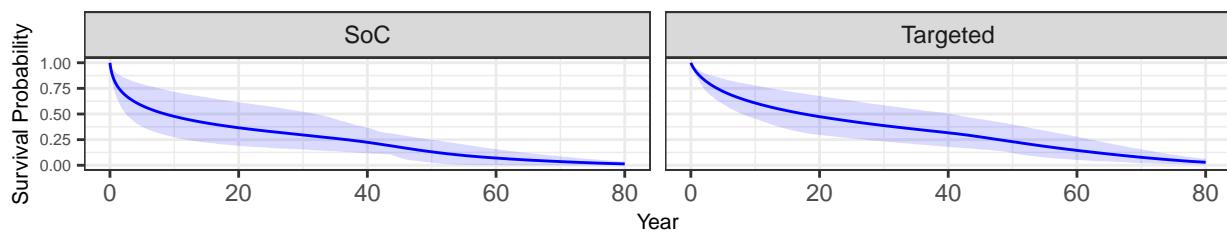
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



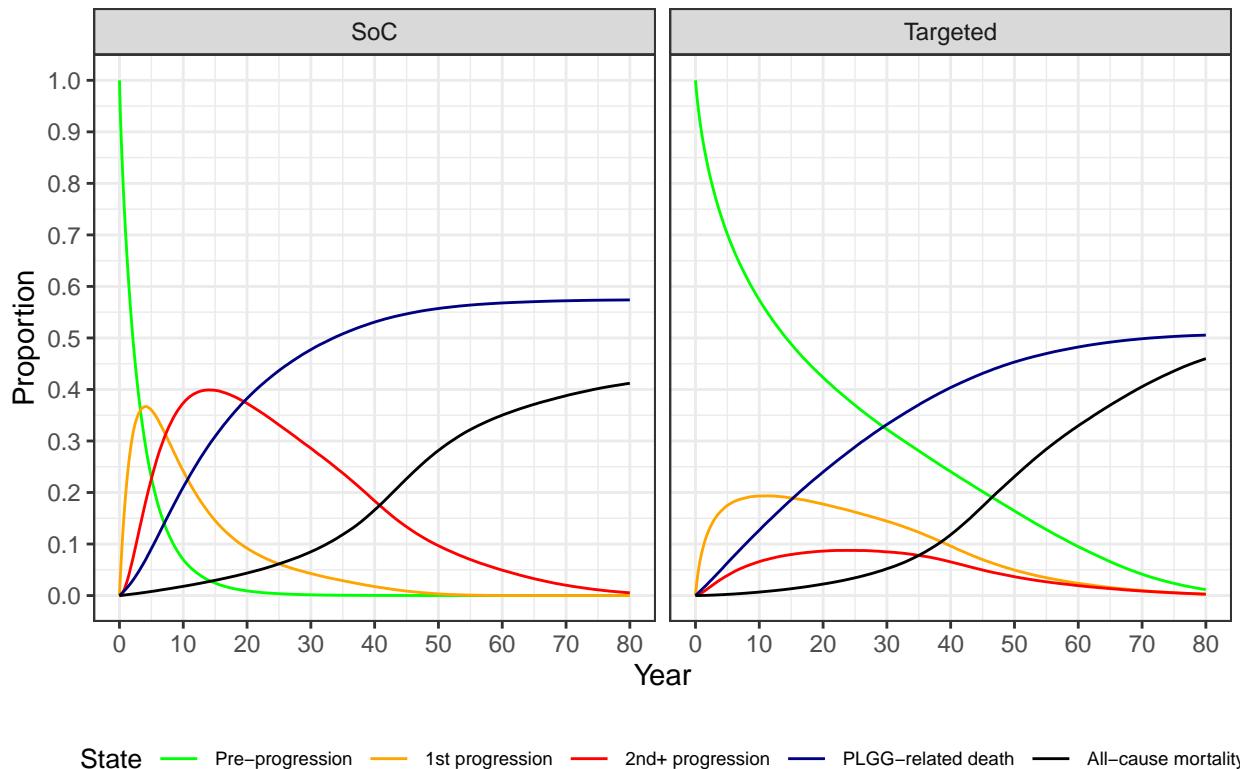
Progression-Free Survival with 95% CI



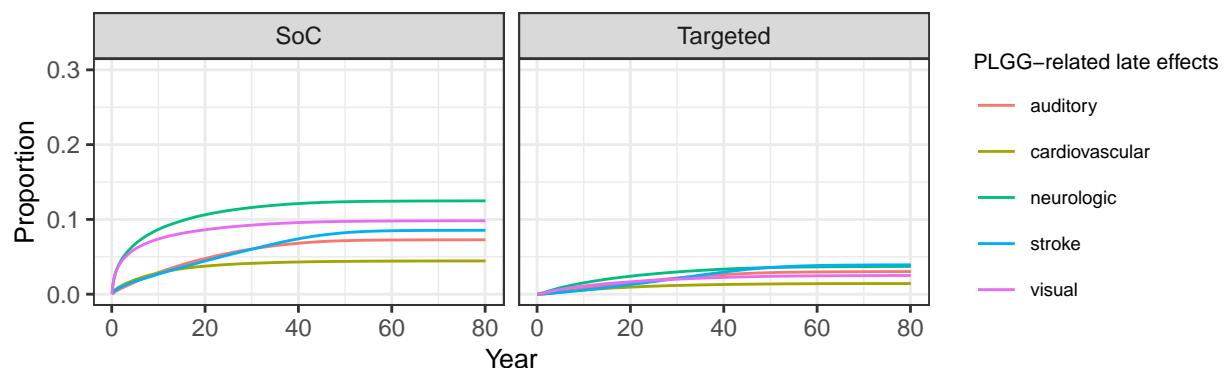
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	28.64 (20.97;35.16)	9.42 (2.37;20.78)
QALY	17.64 (14.54;21.11)	12.11 (9.06;14.63)	5.52 (2.55;10.4)
Total Cost	\$984,189 (\$841,734;\$1,149,331)	\$395,261 (\$365,504;\$416,998)	\$588,928 (\$446,357;\$758,607)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$243,921 (\$200,740;\$292,397)	\$-103,056 (\$-165,421;\$-57,455)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$122,042 (\$64,189;\$179,418)	\$-32,317 (\$-69,470;\$6,205)
General population costs	\$65,694 (\$45,261;\$91,539)	\$27,976 (\$14,665;\$42,065)	\$37,718 (\$20,440;\$61,663)
Targeted costs	\$687,218 (\$536,456;\$863,053)	\$0 (\$0;\$0)	\$687,218 (\$536,456;\$863,053)
Radiation costs	\$686 (\$315;\$1,036)	\$1,322 (\$1,243;\$1,392)	\$-636 (\$-1,005;\$-283)

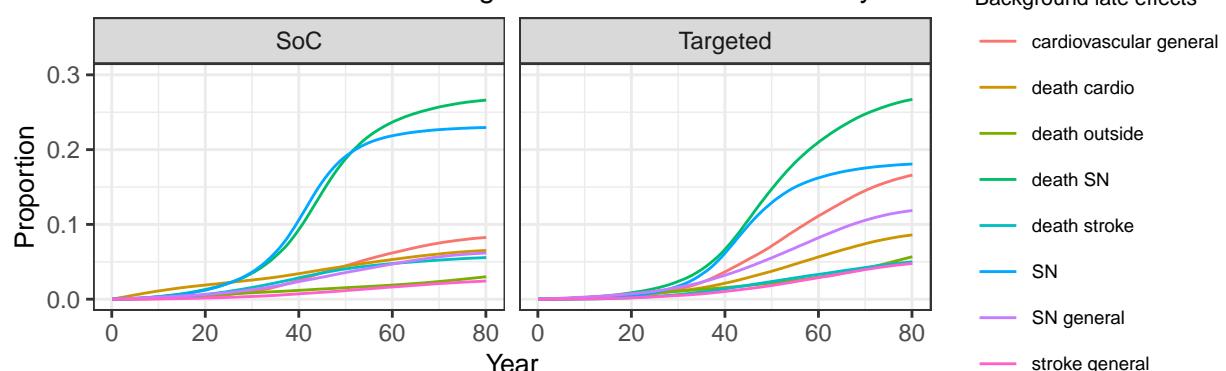
Trace Plot of PLGG States Across Cycles



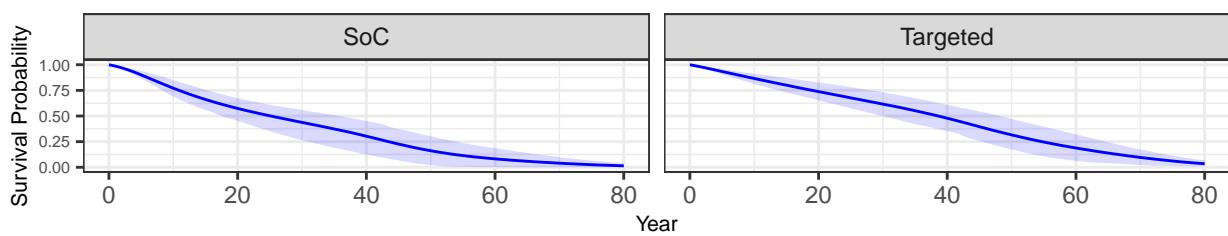
Cumulative Incidence of PLGG-related Late Effects Across Cycles



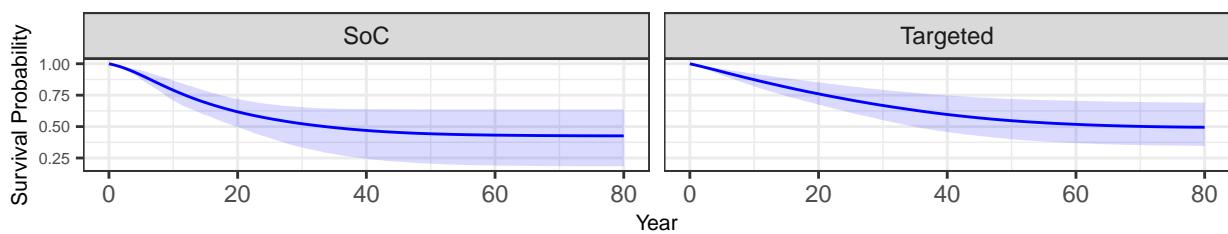
Cumulative Incidence of Background Late Effects Across Cycles



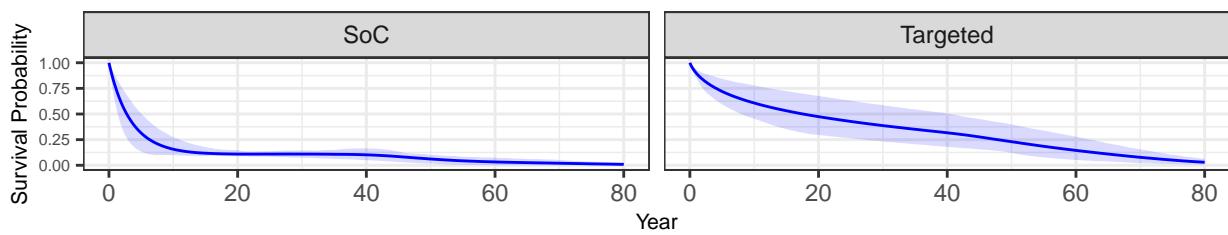
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



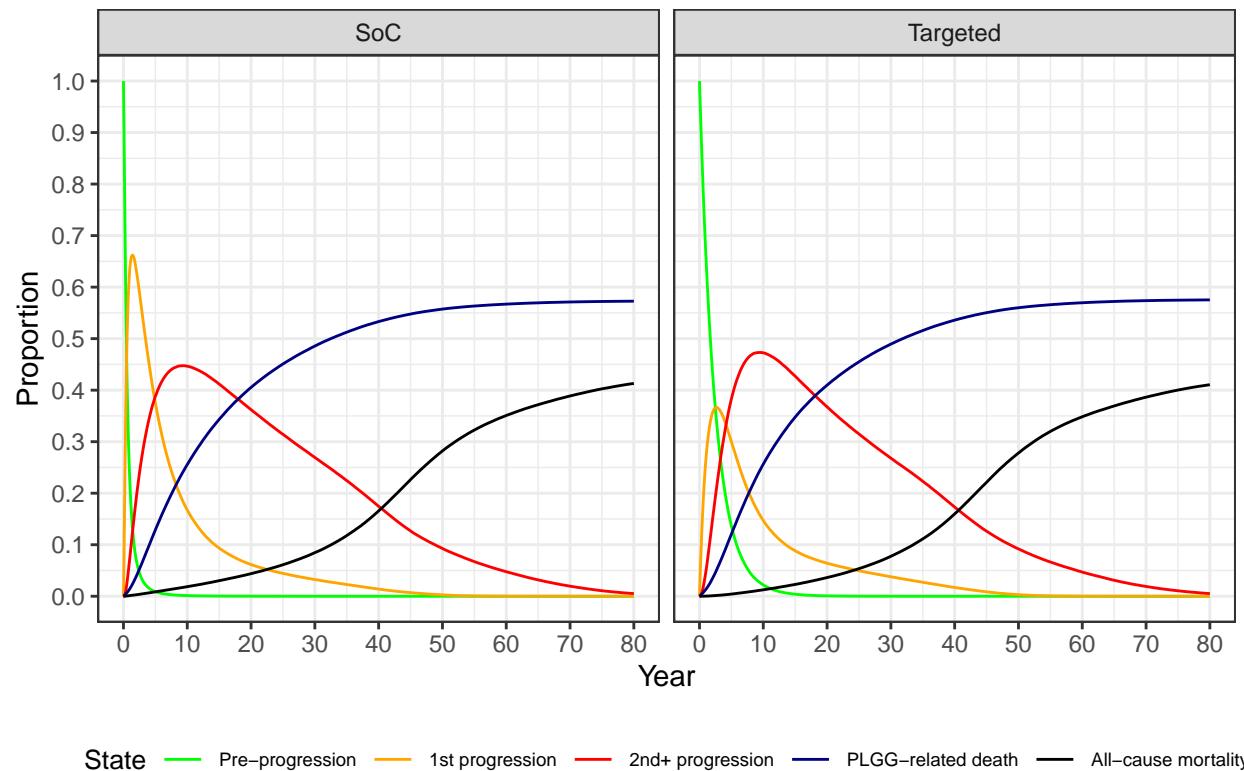
Progression-Free Survival with 95% CI



Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

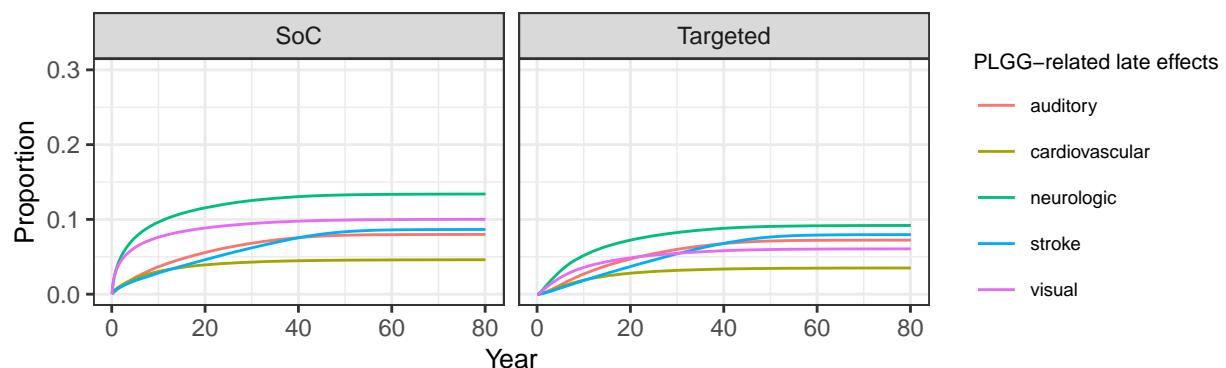
Variable	intervention	control	Delta
Life-years	27.99 (18.78;35.49)	27.78 (18.5;35.33)	0.2 (-1.14;1.56)
QALY	12.27 (8.35;15.37)	11.64 (7.87;14.59)	0.63 (-0.11;1.42)
Total Cost	\$749,115 (\$583,111;\$879,908)	\$403,893 (\$374,906;\$430,537)	\$345,223 (\$206,991;\$470,918)
Non-Targeted PLGG related costs	\$218,040 (\$166,683;\$266,961)	\$249,796 (\$198,221;\$298,290)	\$-31,756 (\$-44,279;\$-21,347)
Late effect costs	\$109,237 (\$50,606;\$176,066)	\$125,975 (\$64,219;\$191,430)	\$-16,738 (\$-24,260;\$-10,108)
General population costs	\$32,278 (\$16,459;\$49,131)	\$26,731 (\$12,396;\$42,032)	\$5,547 (\$2,697;\$8,623)
Targeted costs	\$388,118 (\$245,621;\$514,003)	\$0 (\$0;\$0)	\$388,118 (\$245,621;\$514,003)
Radiation costs	\$1,443 (\$1,419;\$1,474)	\$1,391 (\$1,354;\$1,426)	\$52 (\$14;\$89)

Trace Plot of PLGG States Across Cycles

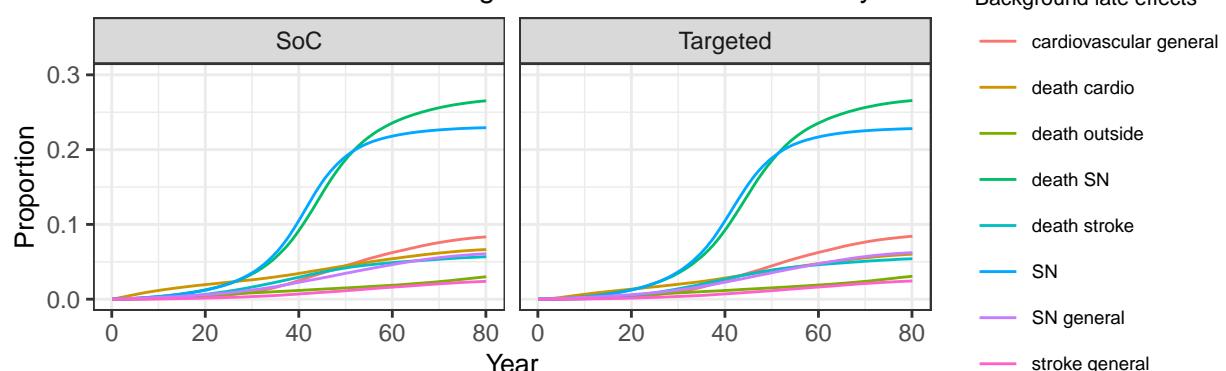


State — Pre-progression — 1st progression — 2nd+ progression — PLGG-related death — All-cause mortality

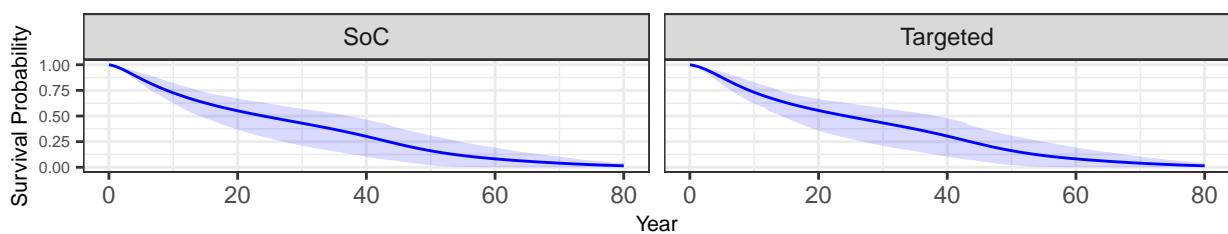
Cumulative Incidence of PLGG-related Late Effects Across Cycles



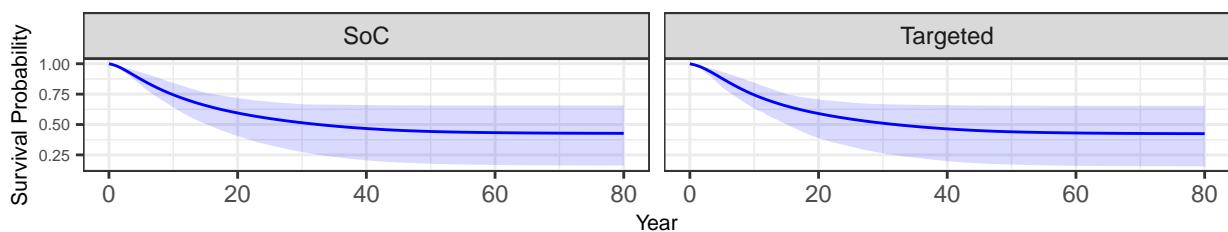
Cumulative Incidence of Background Late Effects Across Cycles



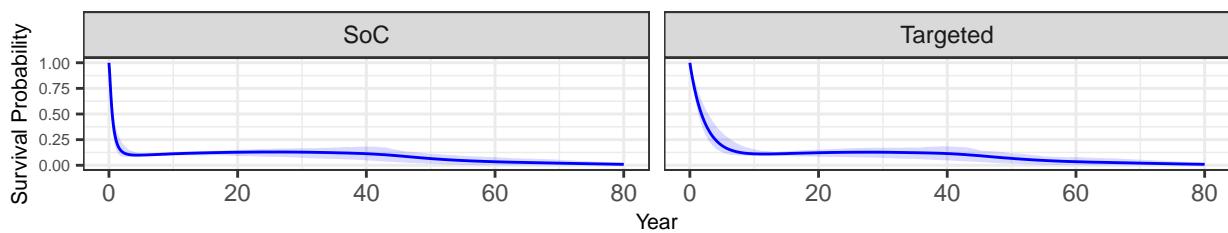
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



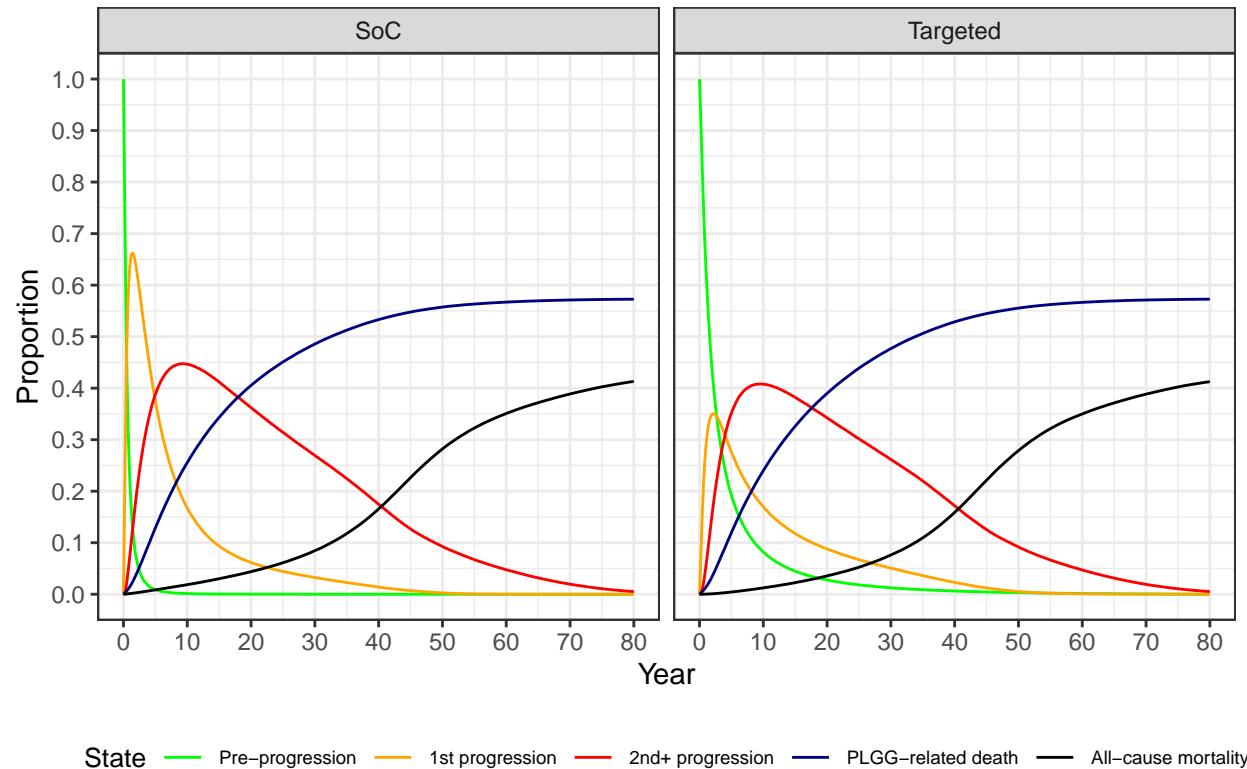
Progression-Free Survival with 95% CI



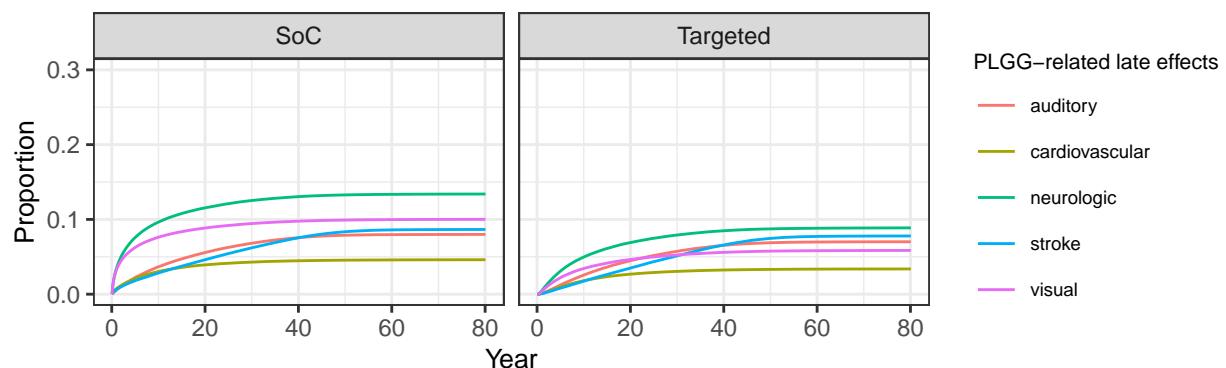
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.62 (21.5;36.23)	27.78 (18.5;35.33)	0.83 (-0.32;1.92)
QALY	12.61 (9.73;15.84)	11.64 (7.87;14.59)	0.96 (0.36;1.66)
Total Cost	\$762,097 (\$633,583;\$905,253)	\$403,893 (\$374,906;\$430,537)	\$358,204 (\$242,893;\$476,022)
Non-Targeted PLGG related costs	\$211,765 (\$160,443;\$258,180)	\$249,796 (\$198,221;\$298,290)	\$-38,031 (\$-50,985;\$-26,026)
Late effect costs	\$108,106 (\$59,451;\$173,533)	\$125,975 (\$64,219;\$191,430)	\$-17,869 (\$-29,204;\$-8,286)
General population costs	\$33,883 (\$19,754;\$50,082)	\$26,731 (\$12,396;\$42,032)	\$7,152 (\$4,135;\$11,217)
Targeted costs	\$406,920 (\$287,892;\$534,670)	\$0 (\$0;\$0)	\$406,920 (\$287,892;\$534,670)
Radiation costs	\$1,423 (\$1,335;\$1,482)	\$1,391 (\$1,354;\$1,426)	\$32 (\$-40;\$86)

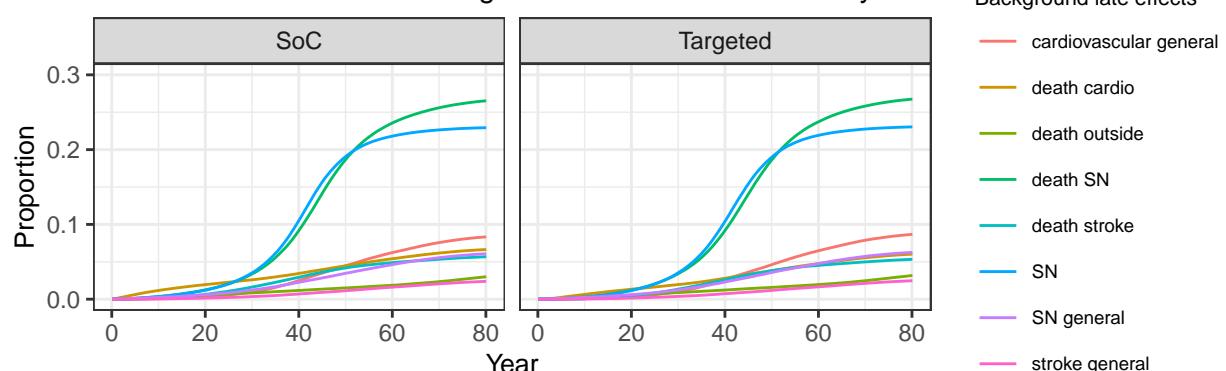
Trace Plot of PLGG States Across Cycles



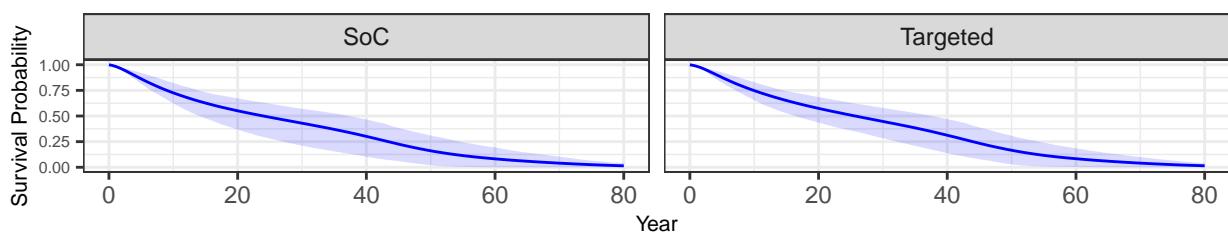
Cumulative Incidence of PLGG-related Late Effects Across Cycles



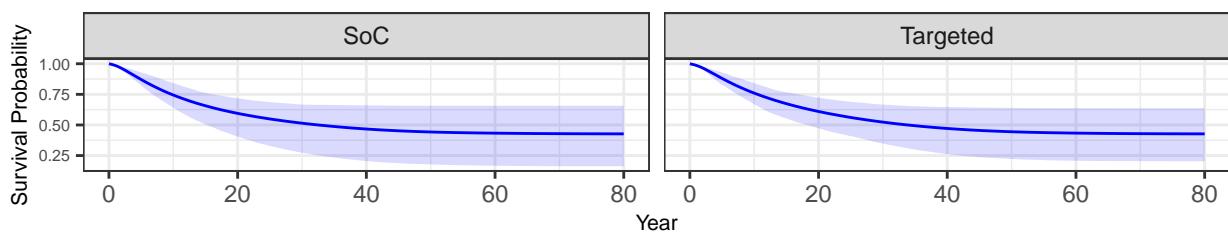
Cumulative Incidence of Background Late Effects Across Cycles



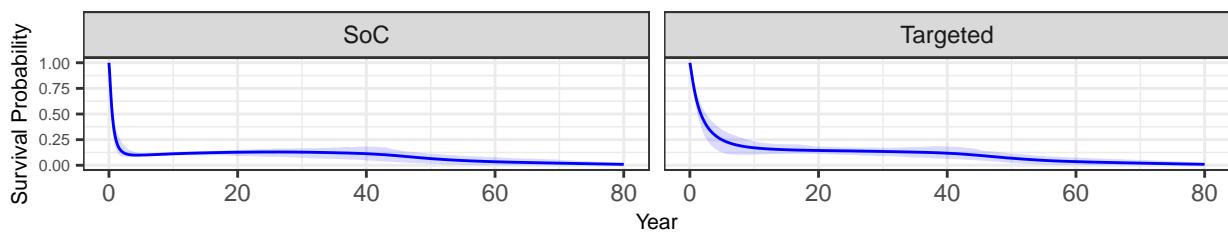
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



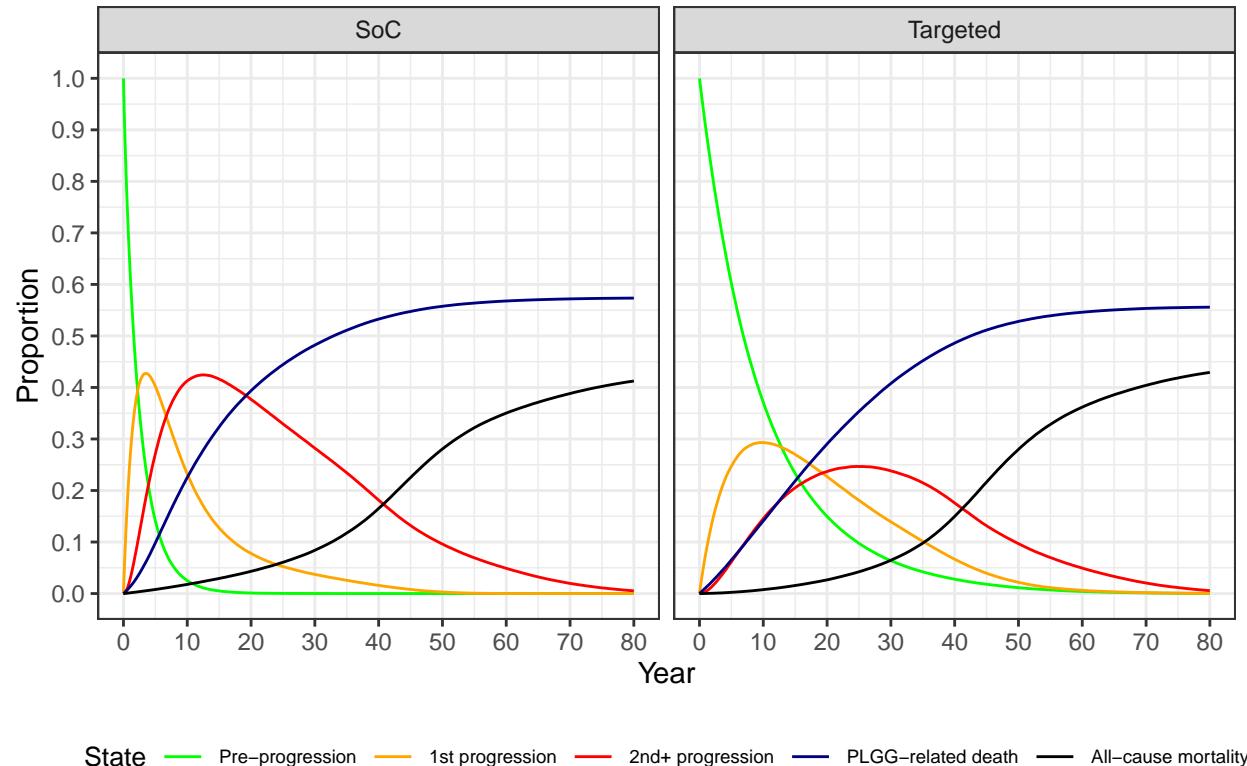
Scenario #1e

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 20% radiation at progression
- 100% combo price
- Discount rate: 1.5
- **Data source for controls: n=34 SickKids controls**
- **Data source for exposed: Investigator assessment - Bouffet et al., NEJM 2023.**
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

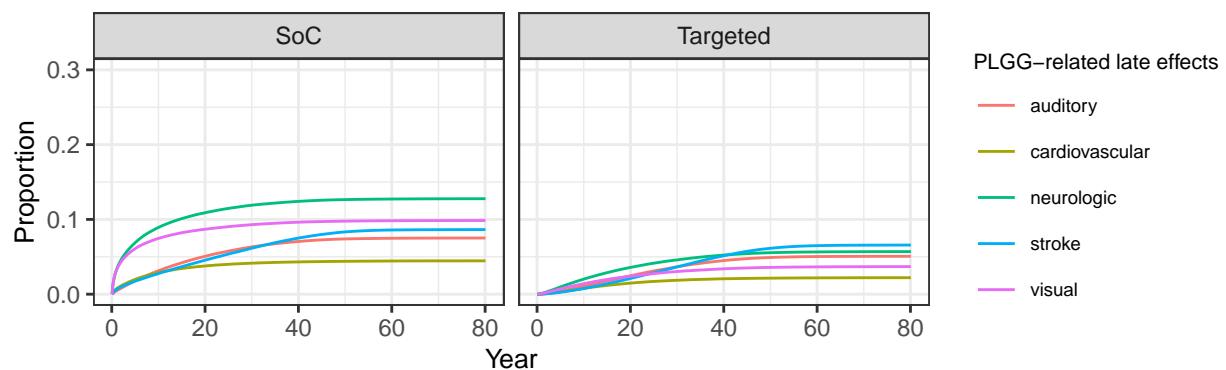
Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	32.48 (25.96;39.25)	28.34 (19.7;35.06)	4.15 (0;11.93)
QALY	14.83 (11.84;18.04)	11.95 (8.45;14.64)	2.88 (1;6.55)
Total Cost	\$2,403,280 (\$1,879,717;\$3,012,999)	\$400,826 (\$376,720;\$421,040)	\$2,002,454 (\$1,499,949;\$2,606,272)
Non-Targeted PLGG related costs	\$166,697 (\$112,032;\$211,304)	\$248,842 (\$200,358;\$300,312)	-\$82,145 (\$-122,905;\$-55,496)
Late effect costs	\$98,249 (\$64,144;\$143,861)	\$123,085 (\$61,914;\$183,553)	-\$24,836 (\$-41,397;\$2,941)
General population costs	\$45,481 (\$28,493;\$64,999)	\$27,552 (\$13,834;\$41,932)	\$17,929 (\$8,792;\$36,308)
Targeted costs	\$2,091,605 (\$1,576,380;\$2,713,489)	\$0 (\$0;\$0)	\$2,091,605 (\$1,576,380;\$2,713,489)
Radiation costs	\$1,247 (\$1,029;\$1,363)	\$1,347 (\$1,293;\$1,390)	-\$100 (\$-343;\$29)

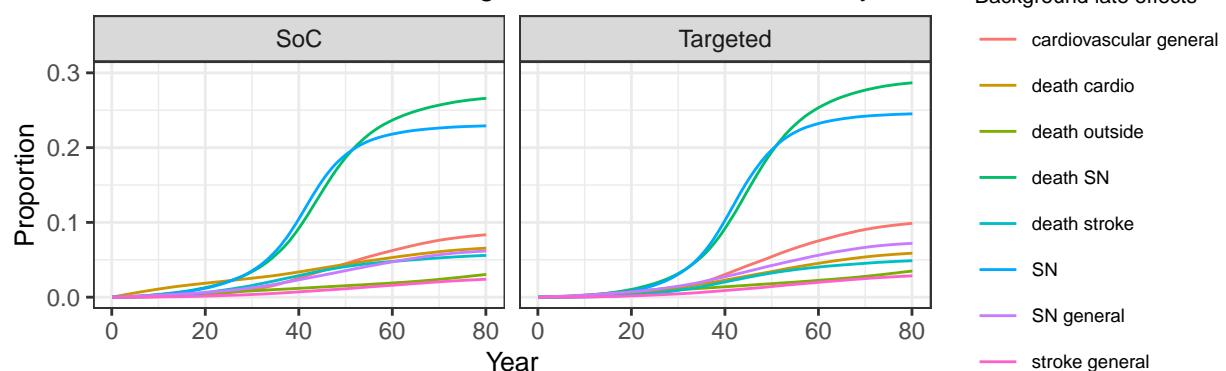
Trace Plot of PLGG States Across Cycles



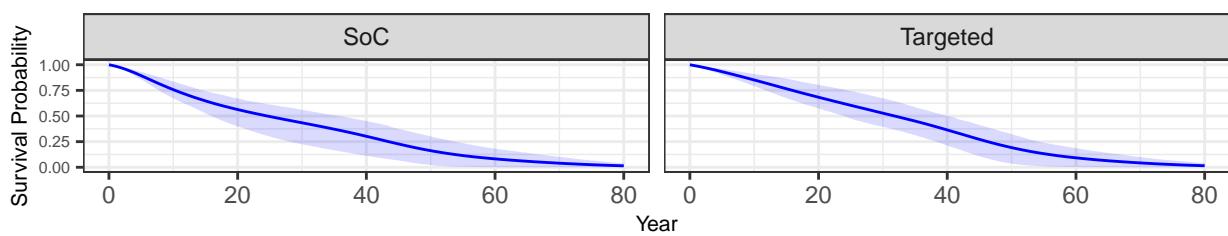
Cumulative Incidence of PLGG-related Late Effects Across Cycles



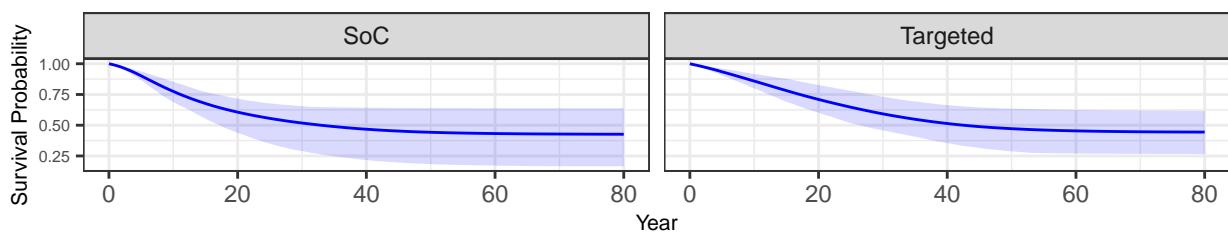
Cumulative Incidence of Background Late Effects Across Cycles



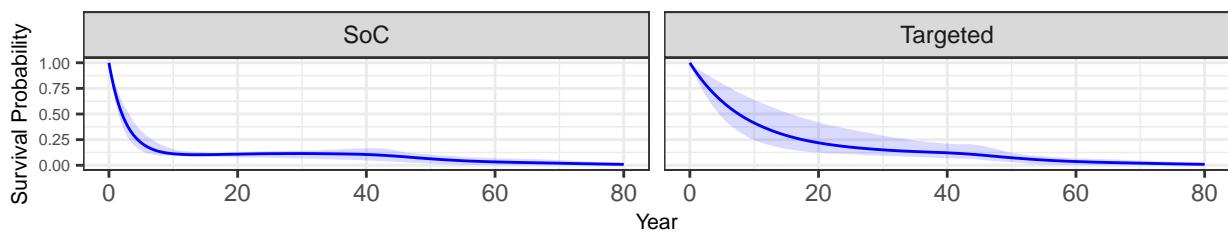
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



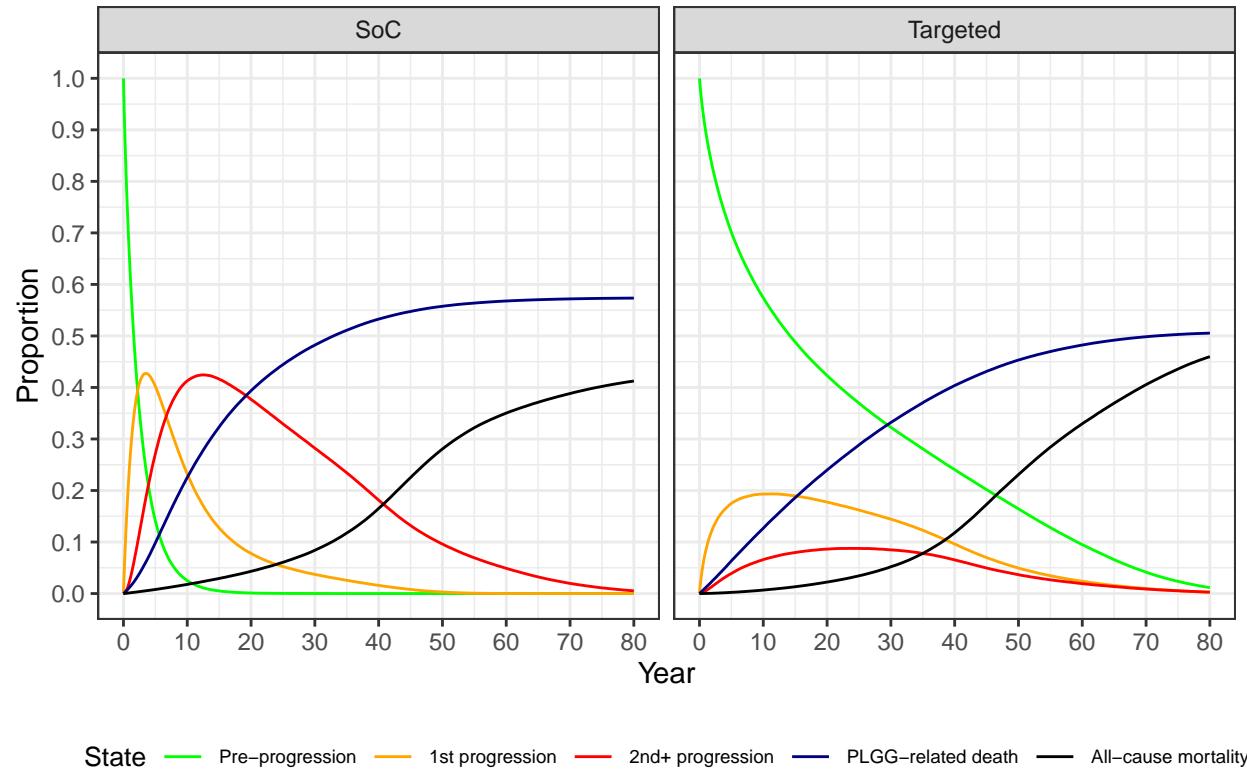
Progression–Free Survival with 95% CI



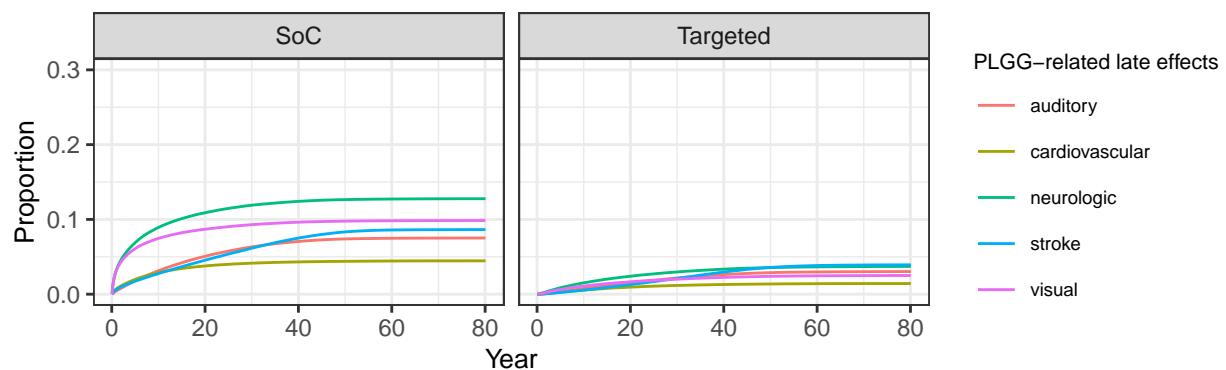
Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	38.06 (31.16;45.41)	28.34 (19.7;35.06)	9.72 (2.42;22.02)
QALY	17.64 (14.54;21.11)	11.95 (8.45;14.64)	5.69 (2.46;10.99)
Total Cost	\$3,045,842 (\$2,446,468;\$3,738,489)	\$400,826 (\$376,720;\$421,040)	\$2,645,017 (\$2,047,347;\$3,332,937)
Non-Targeted PLGG related costs	\$140,866 (\$104,855;\$179,269)	\$248,842 (\$200,358;\$300,312)	\$-107,977 (\$-170,018;\$-60,943)
Late effect costs	\$89,726 (\$66,048;\$126,864)	\$123,085 (\$61,914;\$183,553)	\$-33,359 (\$-71,190;\$8,480)
General population costs	\$65,694 (\$45,261;\$91,539)	\$27,552 (\$13,834;\$41,932)	\$38,142 (\$20,229;\$62,469)
Targeted costs	\$2,748,871 (\$2,145,824;\$3,452,211)	\$0 (\$0;\$0)	\$2,748,871 (\$2,145,824;\$3,452,211)
Radiation costs	\$686 (\$315;\$1,036)	\$1,347 (\$1,293;\$1,390)	\$-661 (\$-1,041;\$-326)

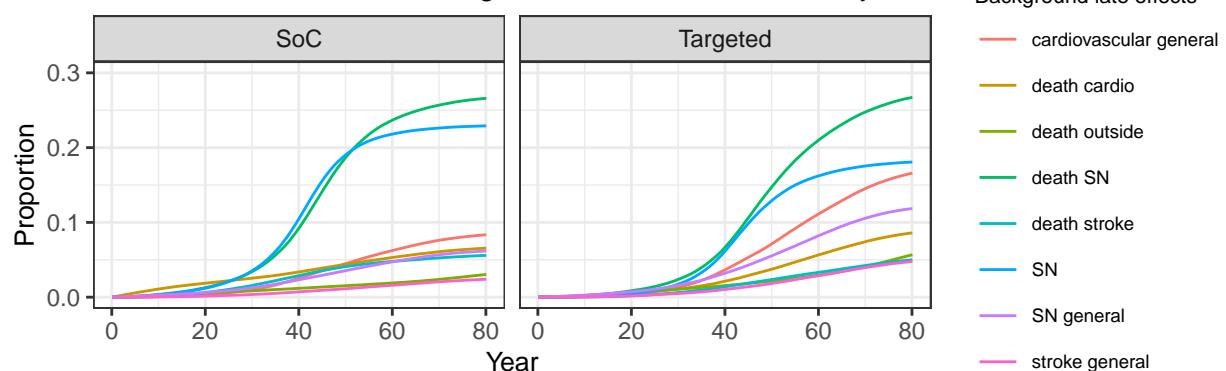
Trace Plot of PLGG States Across Cycles



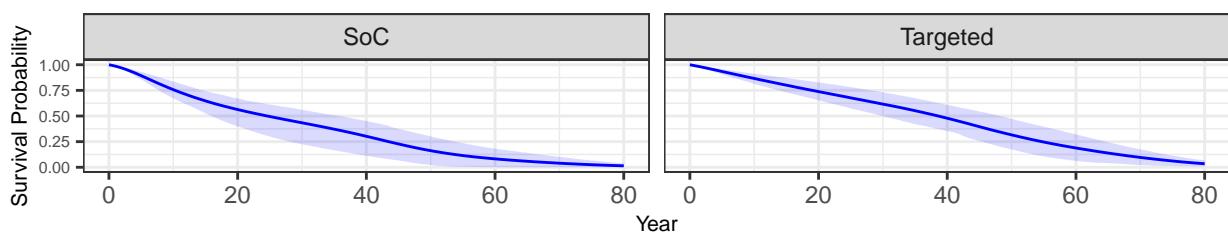
Cumulative Incidence of PLGG-related Late Effects Across Cycles



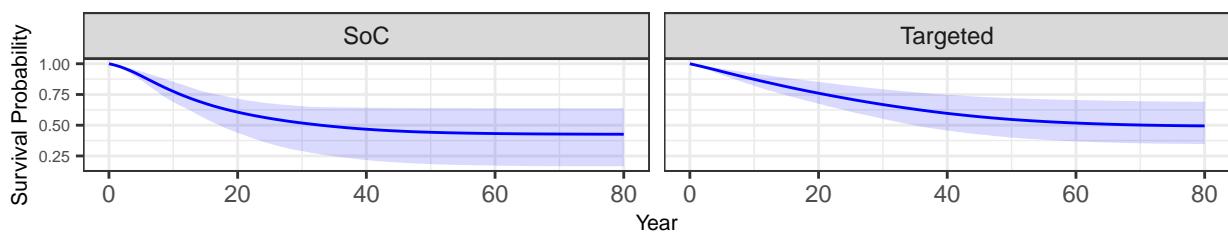
Cumulative Incidence of Background Late Effects Across Cycles



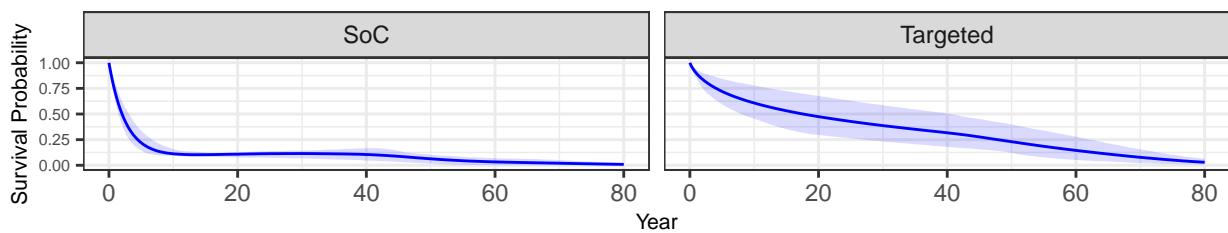
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI



2-year treatment duration - Basecase

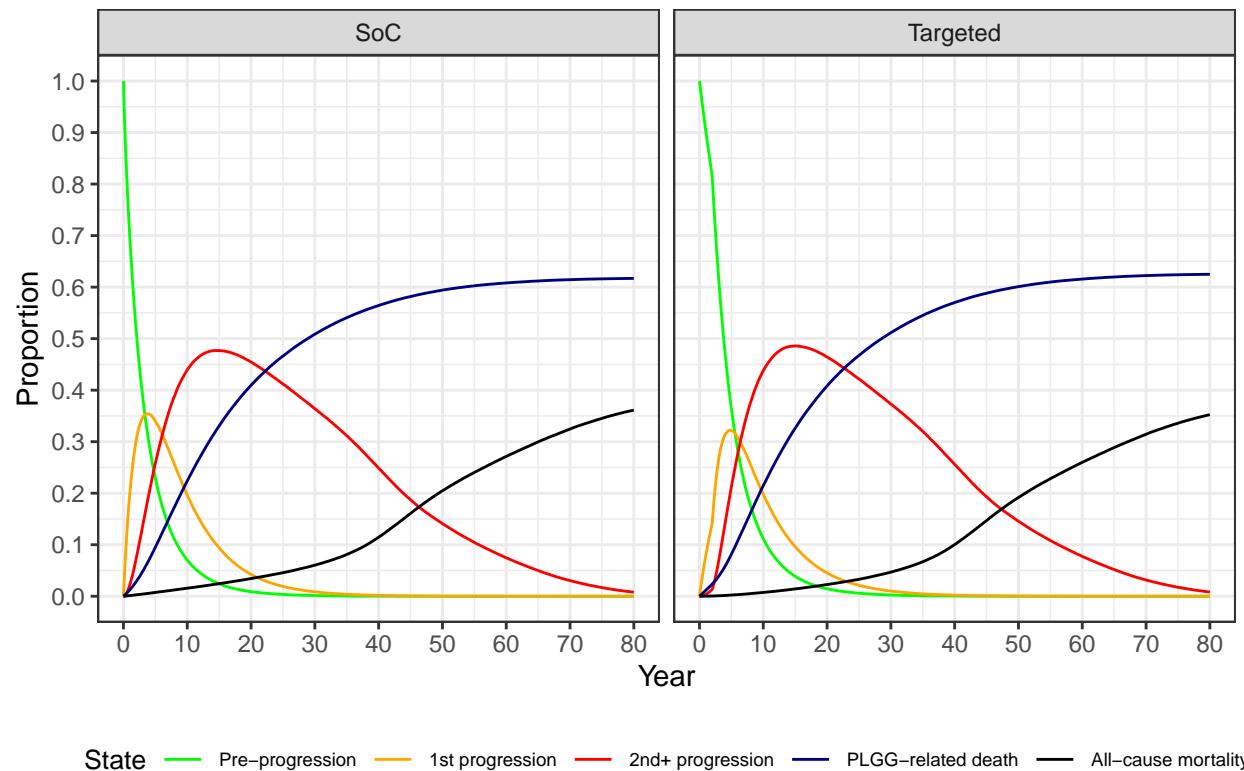
Scenario #1a

- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

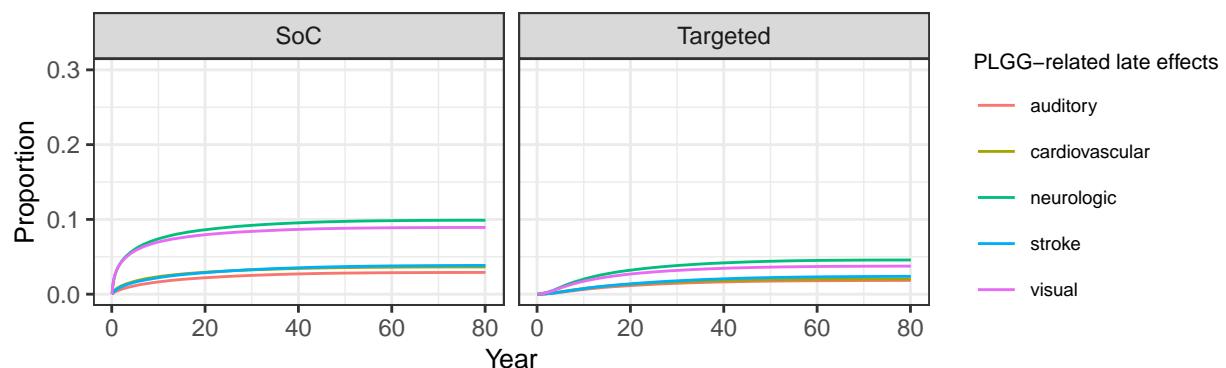
Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	30.18 (20.46;38.59)	29.5 (20.11;37.73)	0.67 (-1.28;1.83)
QALY	13.82 (9.58;17.43)	12.76 (8.92;16.08)	1.06 (0.03;1.72)
Total Cost	\$480,268 (\$449,754;\$504,584)	\$389,911 (\$360,422;\$415,954)	\$90,357 (\$79,169;\$99,631)
Non-Targeted PLGG related costs	\$208,254 (\$155,480;\$266,294)	\$255,203 (\$201,070;\$310,562)	\$-46,949 (\$-55,462;\$-33,519)
Late effect costs	\$78,182 (\$25,009;\$152,498)	\$100,978 (\$40,220;\$177,609)	\$-22,796 (\$-29,660;\$-14,673)
General population costs	\$43,593 (\$21,102;\$67,506)	\$33,730 (\$15,256;\$54,700)	\$9,863 (\$5,261;\$13,887)
Targeted costs	\$150,239 (\$149,341;\$151,057)	\$0 (\$0;\$0)	\$150,239 (\$149,341;\$151,057)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

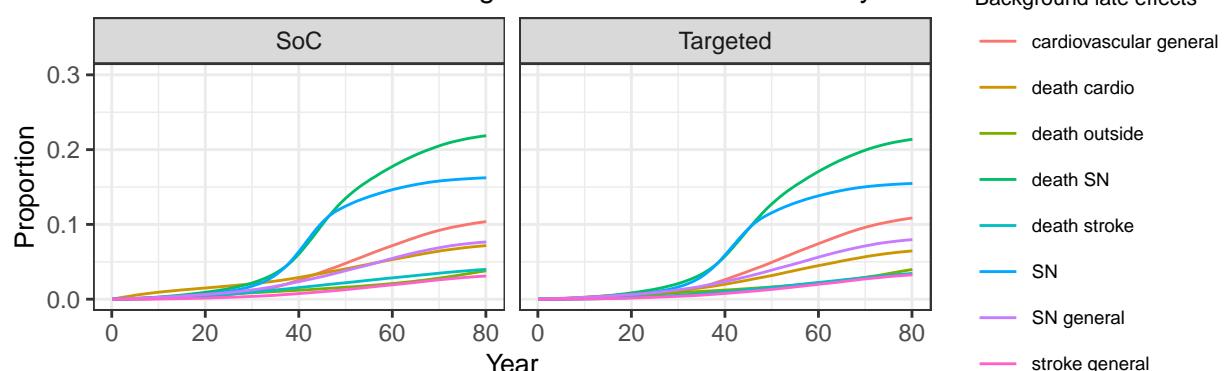
Trace Plot of PLGG States Across Cycles



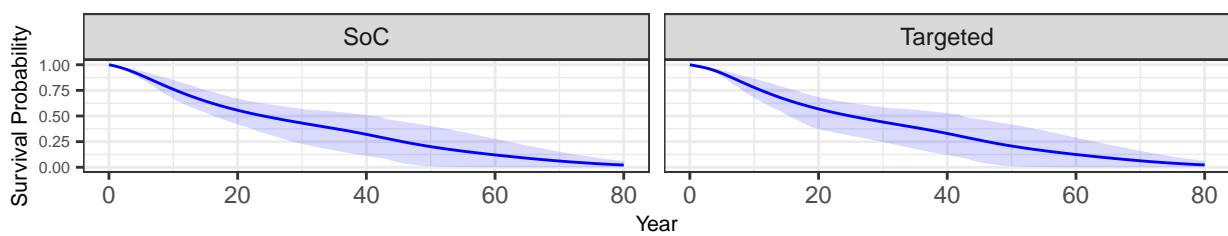
Cumulative Incidence of PLGG-related Late Effects Across Cycles



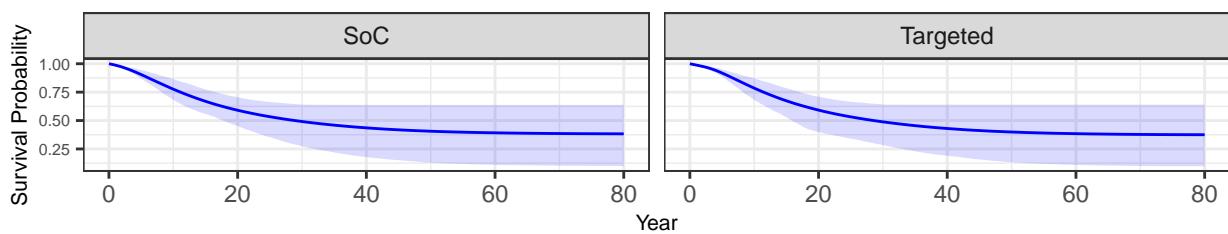
Cumulative Incidence of Background Late Effects Across Cycles



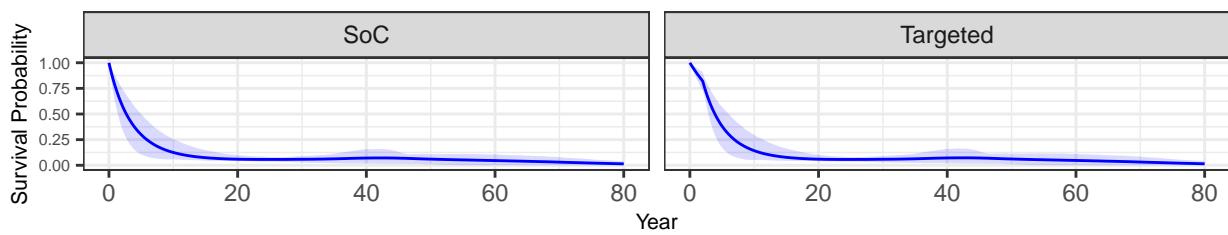
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



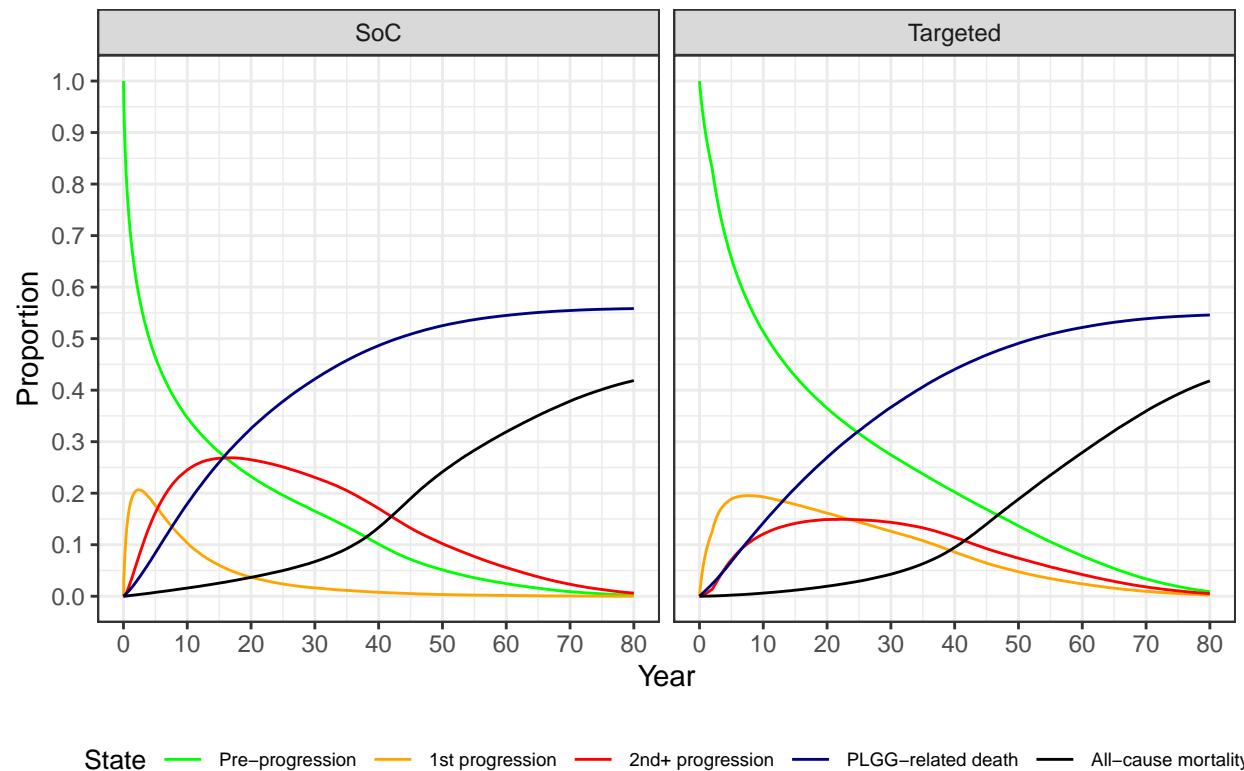
Progression-Free Survival with 95% CI



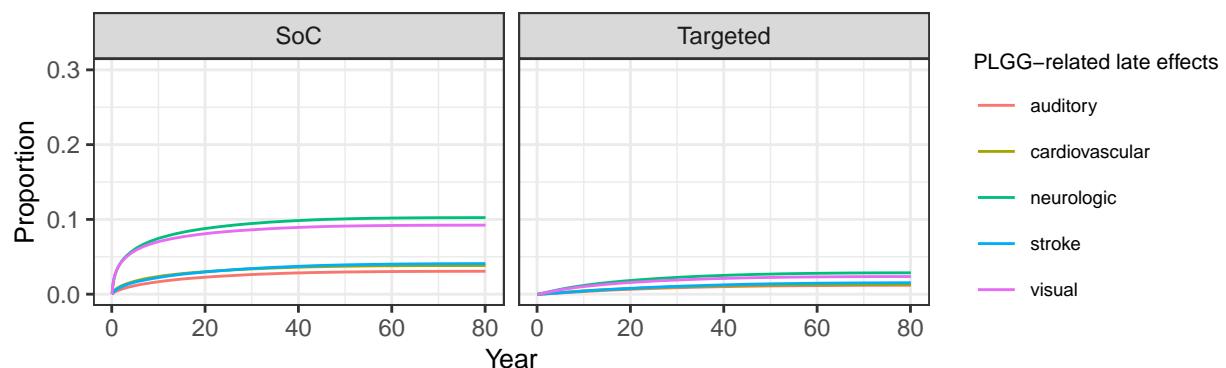
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	37.48 (29.63;44.55)	32.68 (26.31;39.54)	4.8 (1.34;11.06)
QALY	17.44 (13.88;20.81)	14.07 (11.27;16.86)	3.37 (1.78;6.37)
Total Cost	\$448,953 (\$431,943;\$466,386)	\$371,619 (\$354,092;\$392,255)	\$77,334 (\$64,066;\$88,373)
Non-Targeted PLGG related costs	\$154,729 (\$109,574;\$195,629)	\$218,112 (\$161,312;\$259,601)	\$-63,383 (\$-83,657;\$-44,395)
Late effect costs	\$78,482 (\$44,534;\$126,610)	\$115,226 (\$75,174;\$185,091)	\$-36,744 (\$-73,541;\$-15,135)
General population costs	\$65,521 (\$39,700;\$88,641)	\$38,281 (\$20,916;\$59,355)	\$27,240 (\$16,821;\$46,866)
Targeted costs	\$150,221 (\$149,321;\$150,984)	\$0 (\$0;\$0)	\$150,221 (\$149,321;\$150,984)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

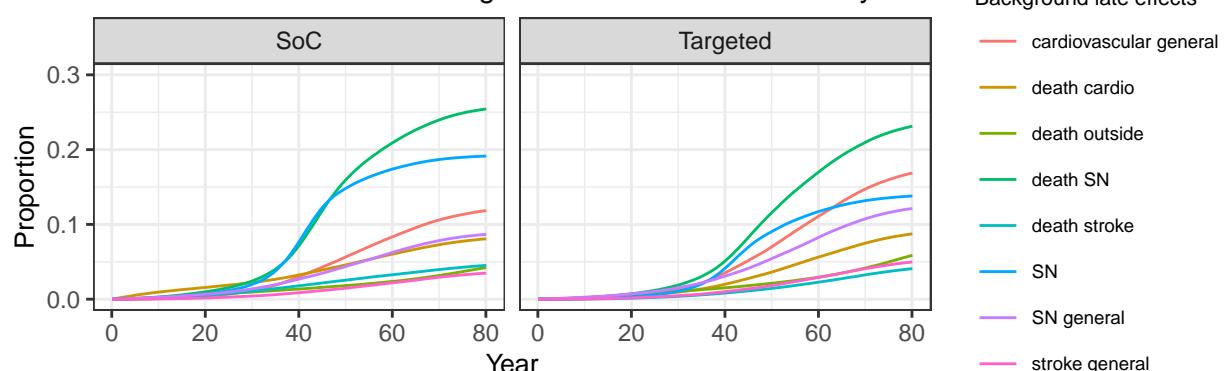
Trace Plot of PLGG States Across Cycles



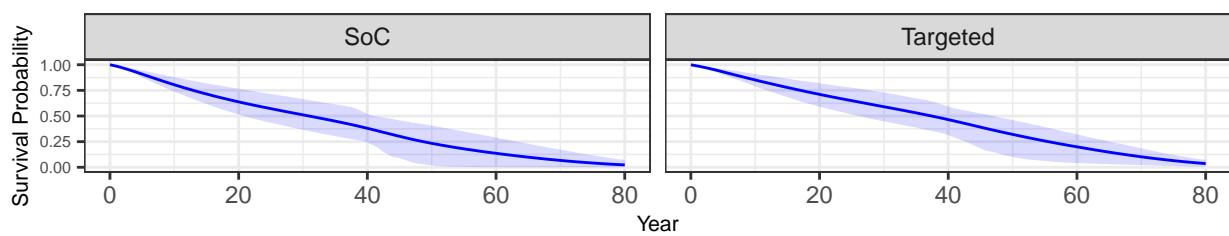
Cumulative Incidence of PLGG-related Late Effects Across Cycles



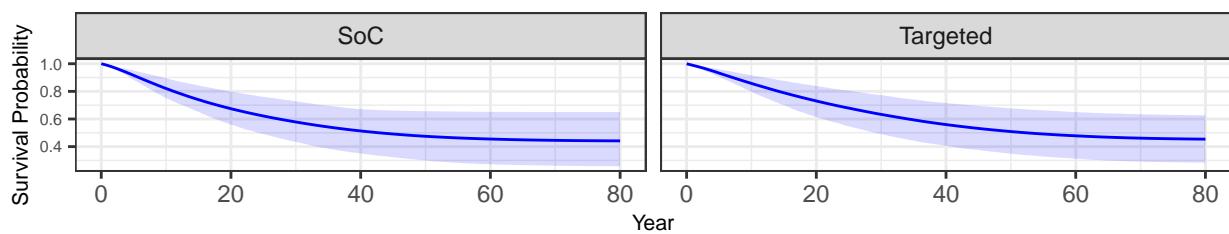
Cumulative Incidence of Background Late Effects Across Cycles



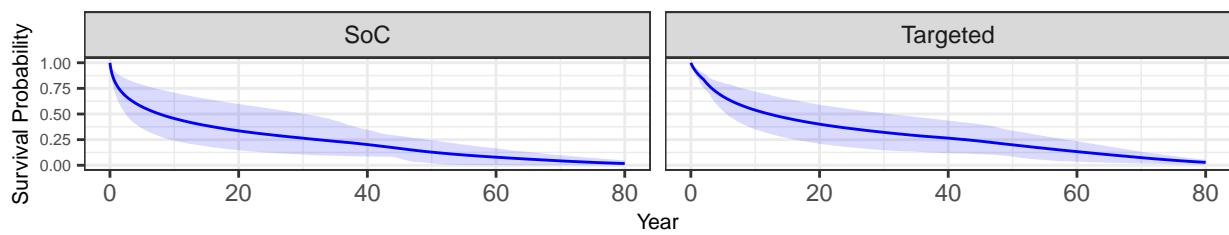
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



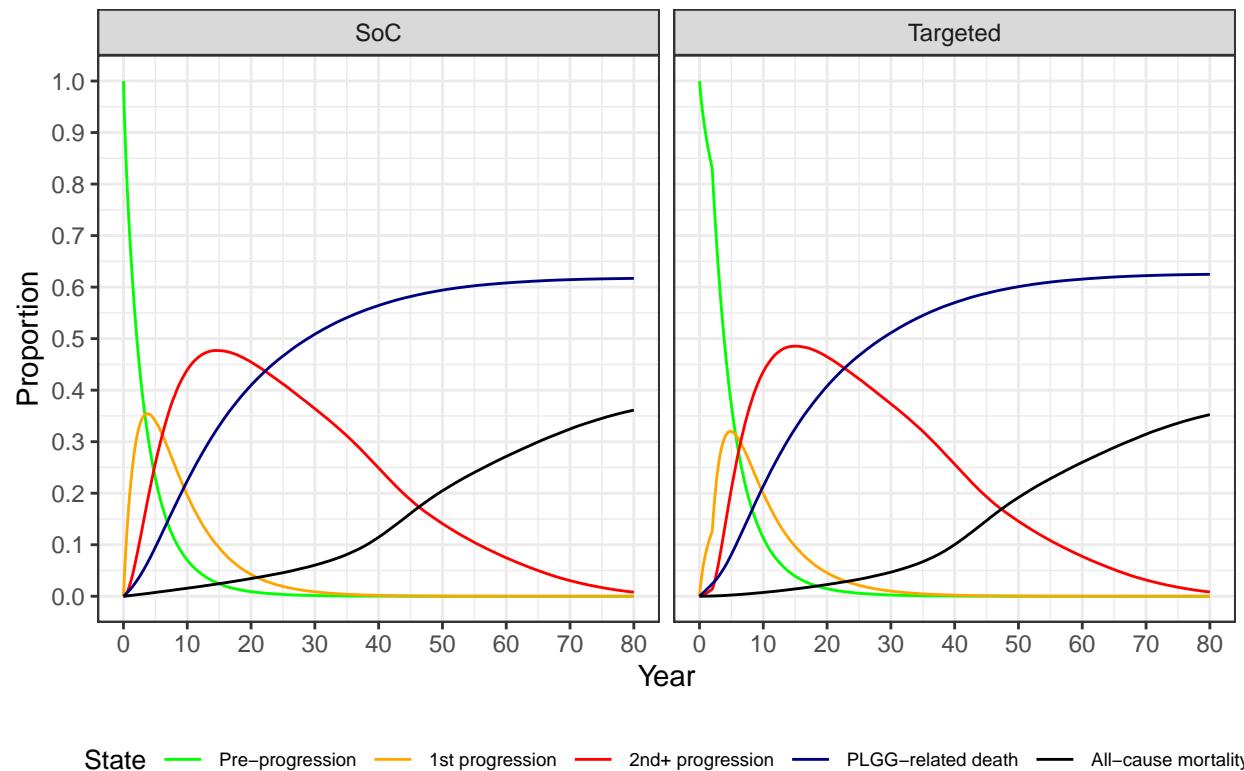
Progression-Free Survival with 95% CI



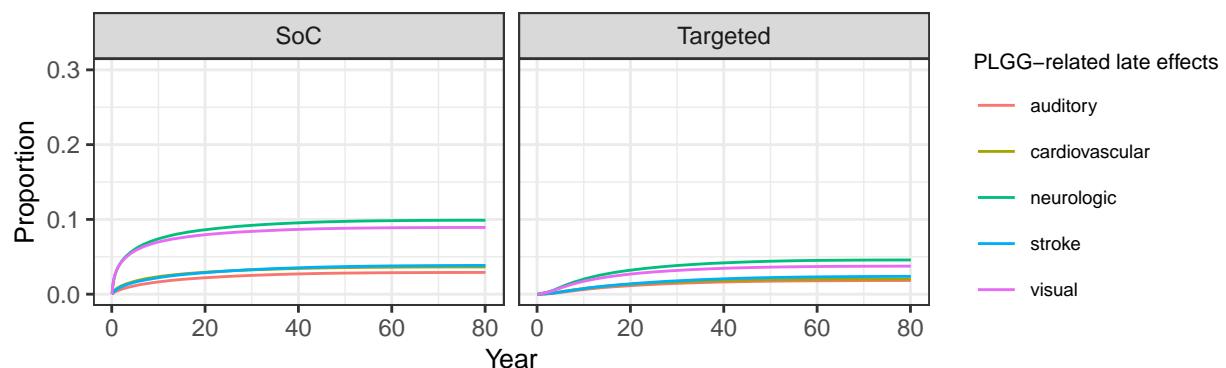
Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

Variable	intervention	control	Delta
Life-years	30.2 (20.51;38.61)	29.5 (20.11;37.73)	0.69 (-1.27;1.96)
QALY	13.83 (9.62;17.45)	12.76 (8.92;16.08)	1.07 (0.04;1.67)
Total Cost	\$479,907 (\$450,131;\$503,977)	\$389,911 (\$360,422;\$415,954)	\$89,996 (\$80,373;\$98,414)
Non-Targeted PLGG related costs	\$207,776 (\$154,575;\$262,736)	\$255,203 (\$201,070;\$310,562)	\$-47,426 (\$-54,076;\$-35,609)
Late effect costs	\$78,278 (\$25,065;\$152,544)	\$100,978 (\$40,220;\$177,609)	\$-22,700 (\$-28,526;\$-14,925)
General population costs	\$43,632 (\$21,293;\$67,688)	\$33,730 (\$15,256;\$54,700)	\$9,902 (\$5,588;\$13,430)
Targeted costs	\$150,221 (\$149,321;\$150,984)	\$0 (\$0;\$0)	\$150,221 (\$149,321;\$150,984)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

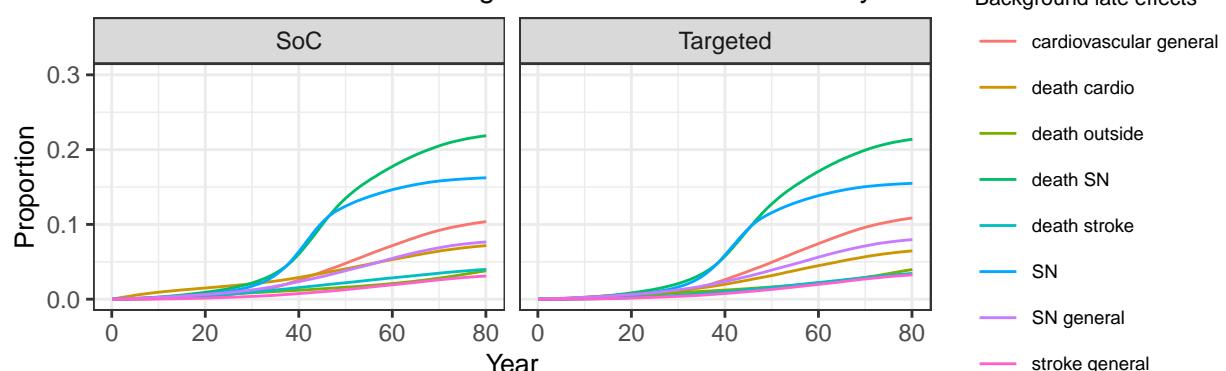
Trace Plot of PLGG States Across Cycles



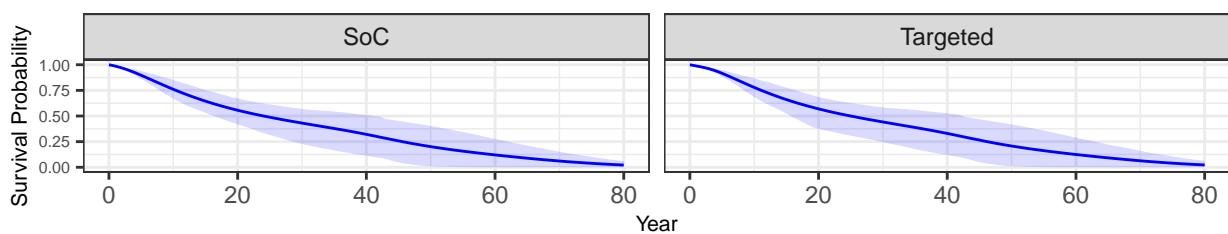
Cumulative Incidence of PLGG-related Late Effects Across Cycles



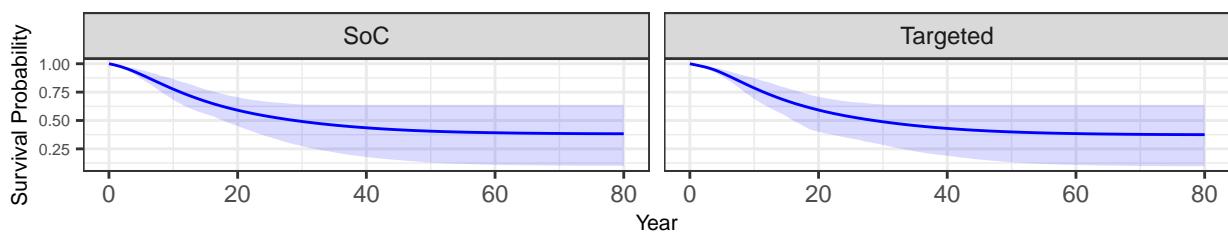
Cumulative Incidence of Background Late Effects Across Cycles



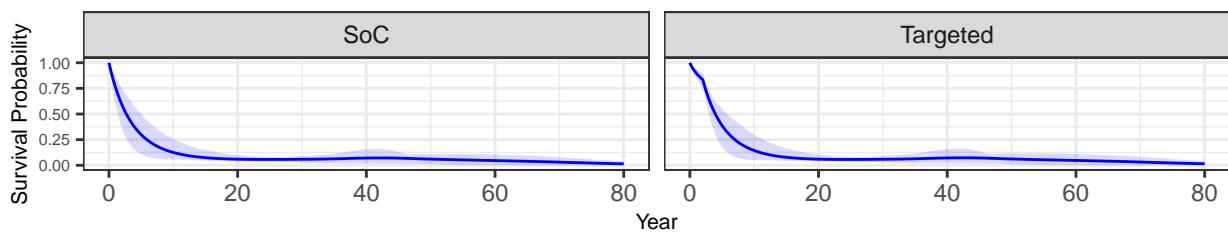
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



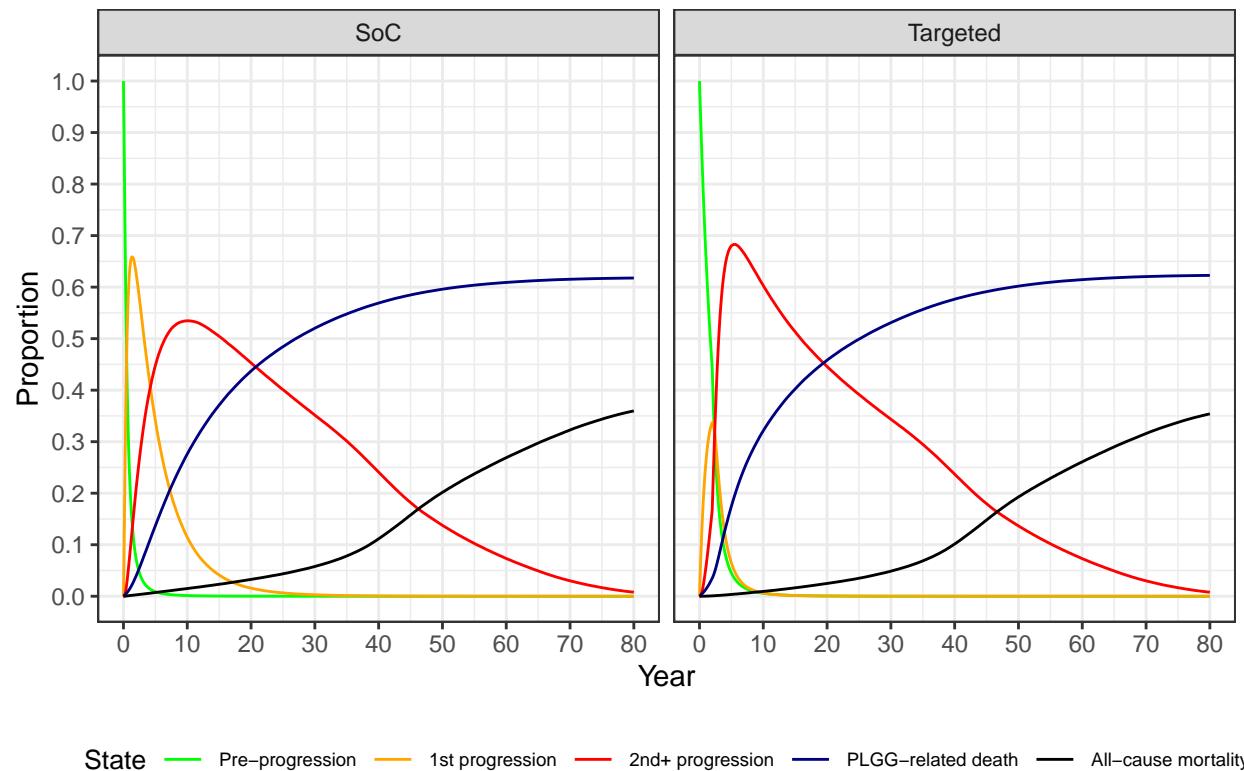
Progression-Free Survival with 95% CI



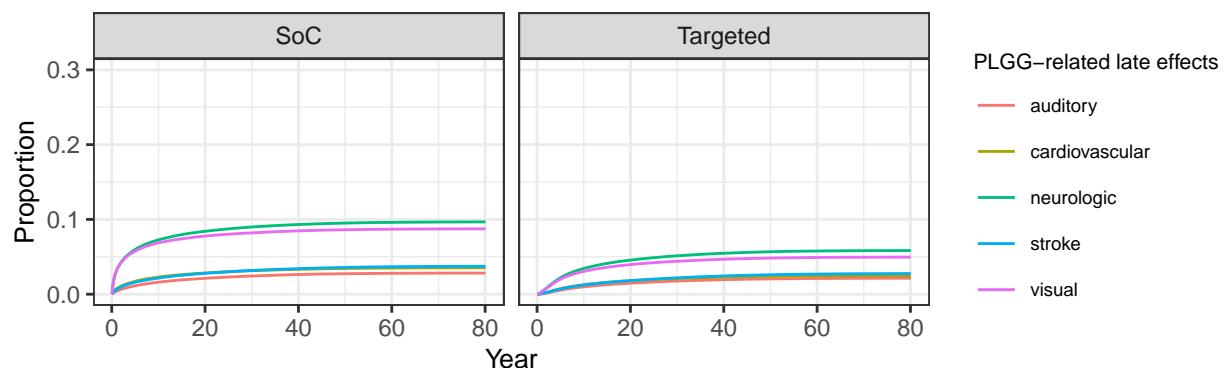
Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.14 (15.36;38.93)	28.6 (17.23;38.19)	-0.46 (-2.27;0.71)
QALY	12.64 (7.07;17.29)	12.36 (7.65;16.39)	0.28 (-0.7;0.93)
Total Cost	\$509,038 (\$479,067;\$539,816)	\$395,495 (\$365,854;\$423,395)	\$113,542 (\$104,974;\$120,647)
Non-Targeted PLGG related costs	\$237,303 (\$170,775;\$295,376)	\$262,516 (\$200,713;\$317,931)	\$-25,213 (\$-33,698;\$-14,796)
Late effect costs	\$84,153 (\$21,643;\$172,520)	\$99,863 (\$34,492;\$182,812)	\$-15,710 (\$-22,310;\$-9,497)
General population costs	\$37,865 (\$14,372;\$64,471)	\$33,116 (\$13,362;\$56,145)	\$4,749 (\$577;\$8,574)
Targeted costs	\$149,716 (\$148,601;\$150,728)	\$0 (\$0;\$0)	\$149,716 (\$148,601;\$150,728)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

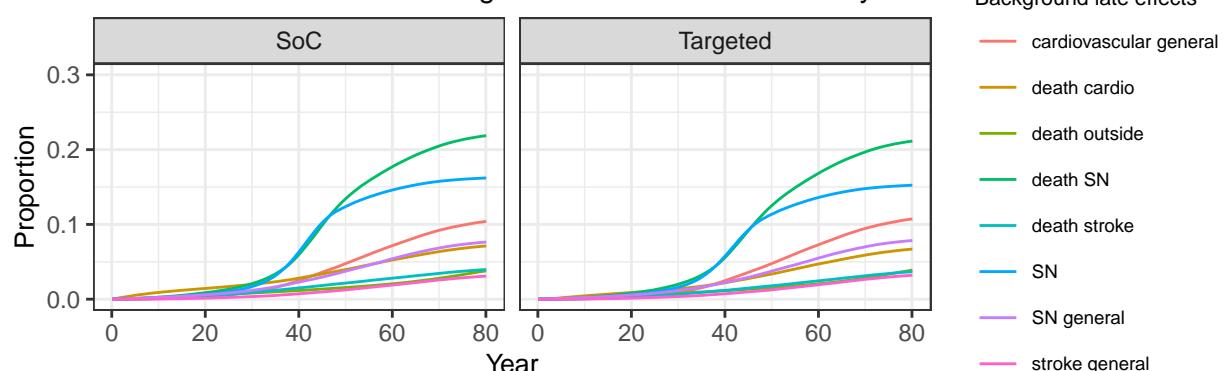
Trace Plot of PLGG States Across Cycles



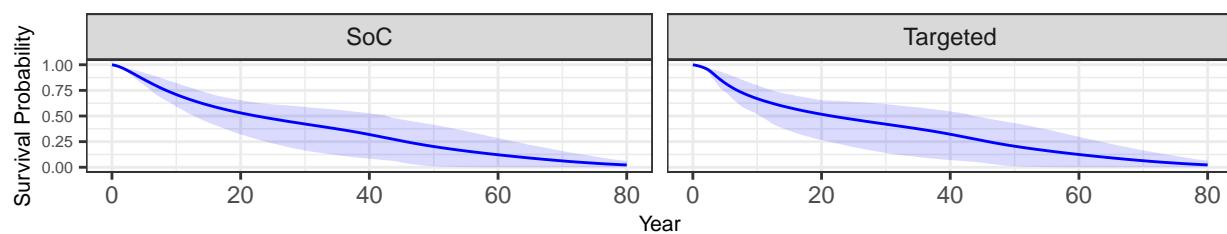
Cumulative Incidence of PLGG-related Late Effects Across Cycles



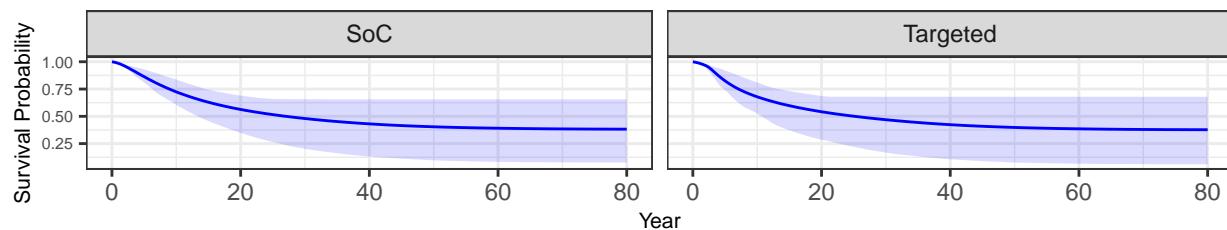
Cumulative Incidence of Background Late Effects Across Cycles



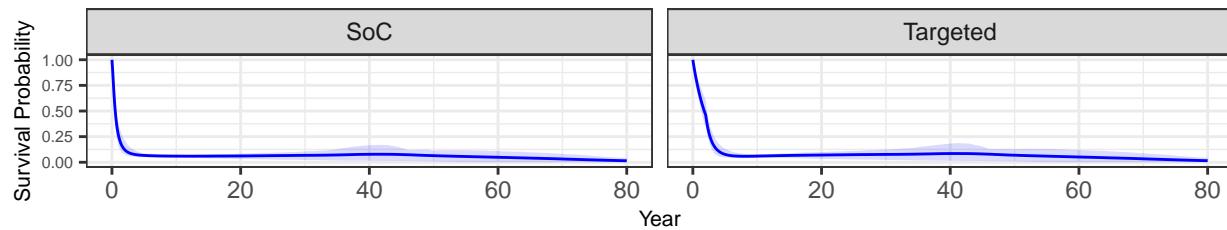
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



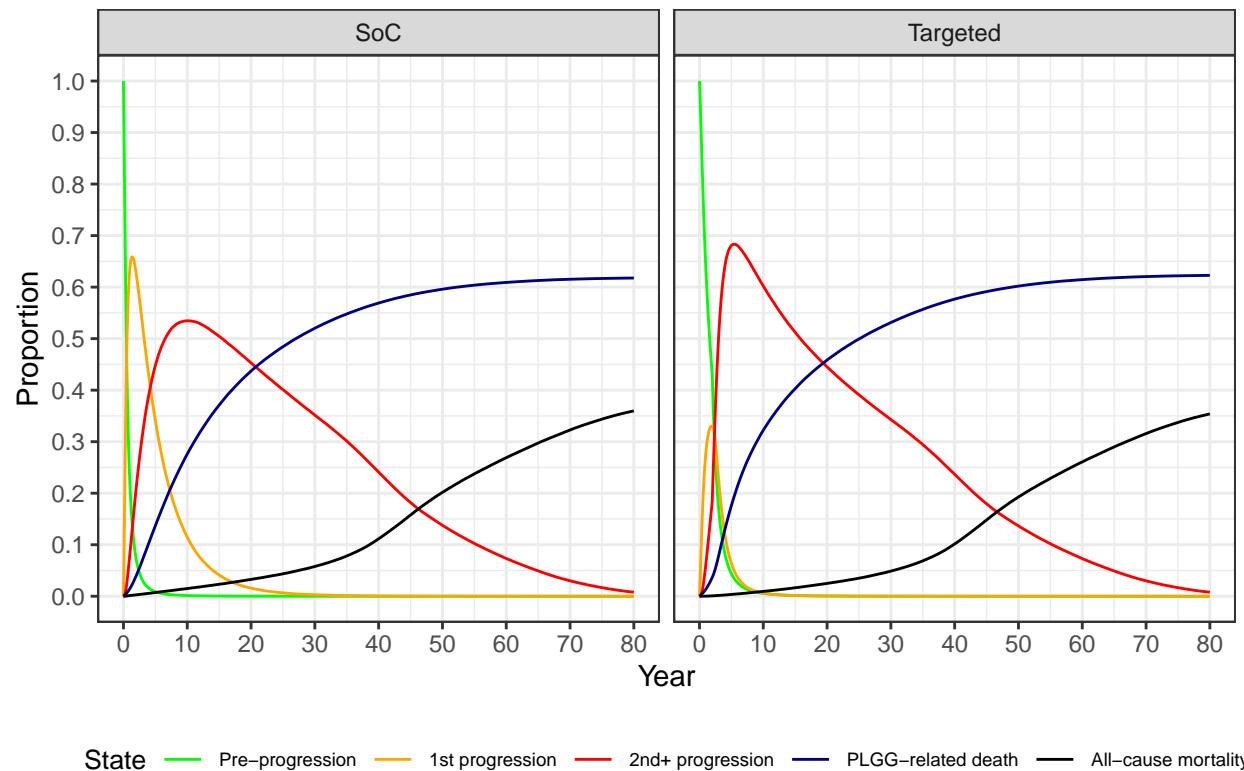
Progression-Free Survival with 95% CI



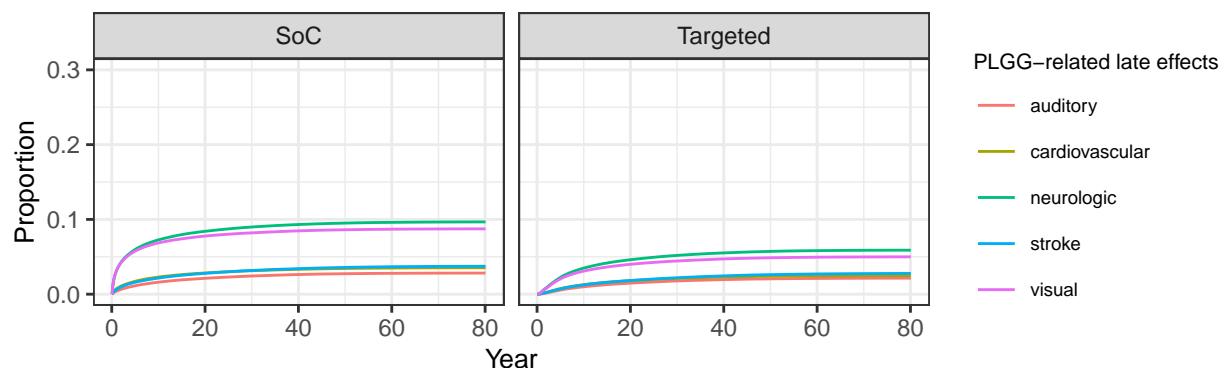
Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

Variable	intervention	control	Delta
Life-years	28.12 (15.31;38.96)	28.6 (17.23;38.19)	-0.48 (-2.28;0.78)
QALY	12.62 (7.04;17.32)	12.36 (7.65;16.39)	0.26 (-0.72;0.99)
Total Cost	\$509,641 (\$477,263;\$539,777)	\$395,495 (\$365,854;\$423,395)	\$114,146 (\$105,812;\$119,828)
Non-Targeted PLGG related costs	\$237,855 (\$170,300;\$294,751)	\$262,516 (\$200,713;\$317,931)	\$-24,661 (\$-32,175;\$-15,045)
Late effect costs	\$84,388 (\$21,302;\$173,462)	\$99,863 (\$34,492;\$182,812)	\$-15,476 (\$-21,764;\$-8,988)
General population costs	\$37,747 (\$14,294;\$64,792)	\$33,116 (\$13,362;\$56,145)	\$4,631 (\$1,413;\$8,737)
Targeted costs	\$149,652 (\$148,841;\$150,410)	\$0 (\$0;\$0)	\$149,652 (\$148,841;\$150,410)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)

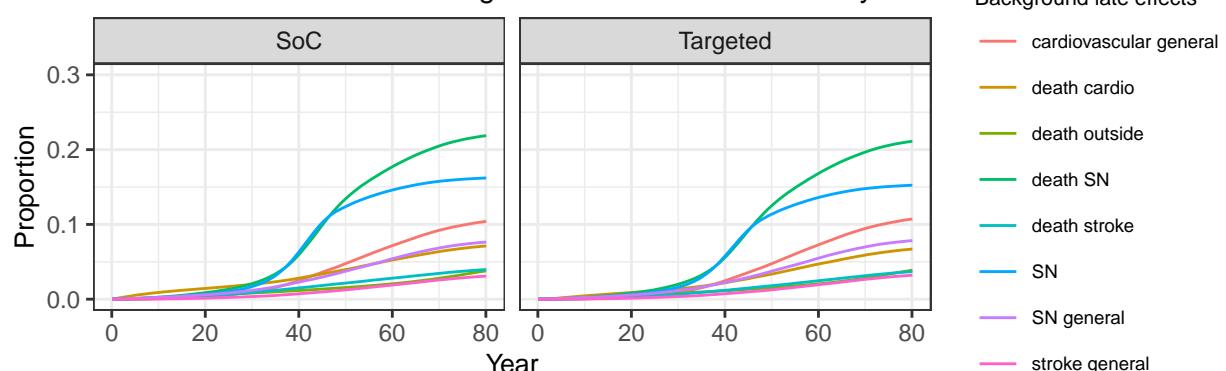
Trace Plot of PLGG States Across Cycles



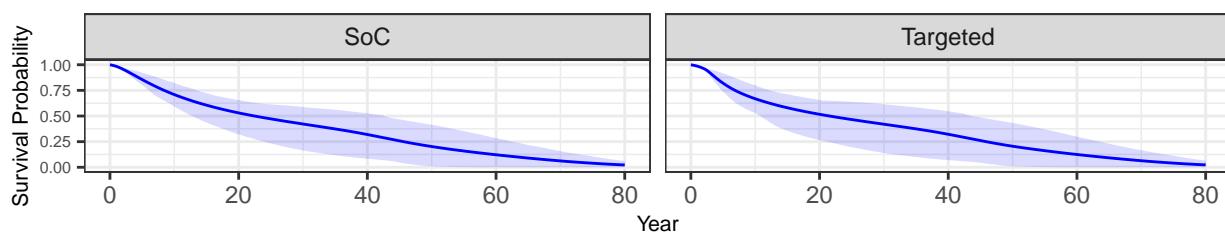
Cumulative Incidence of PLGG-related Late Effects Across Cycles



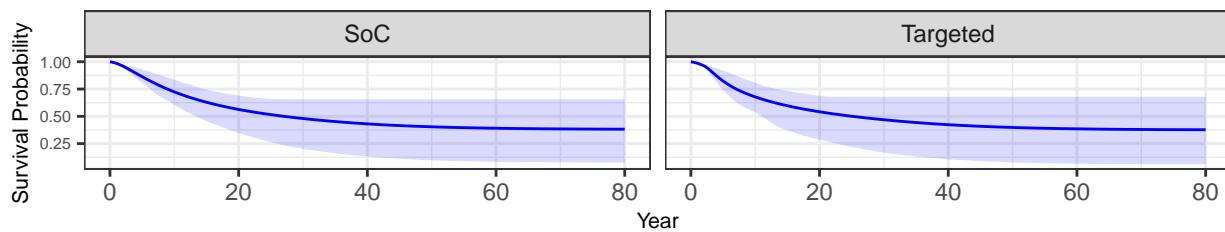
Cumulative Incidence of Background Late Effects Across Cycles



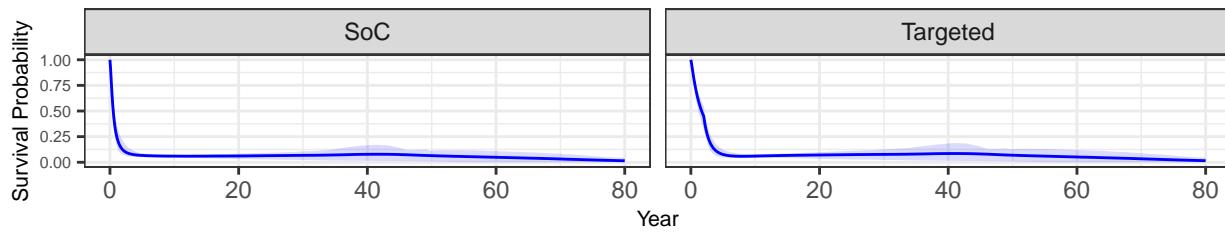
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI



Progression–Free Survival with 95% CI

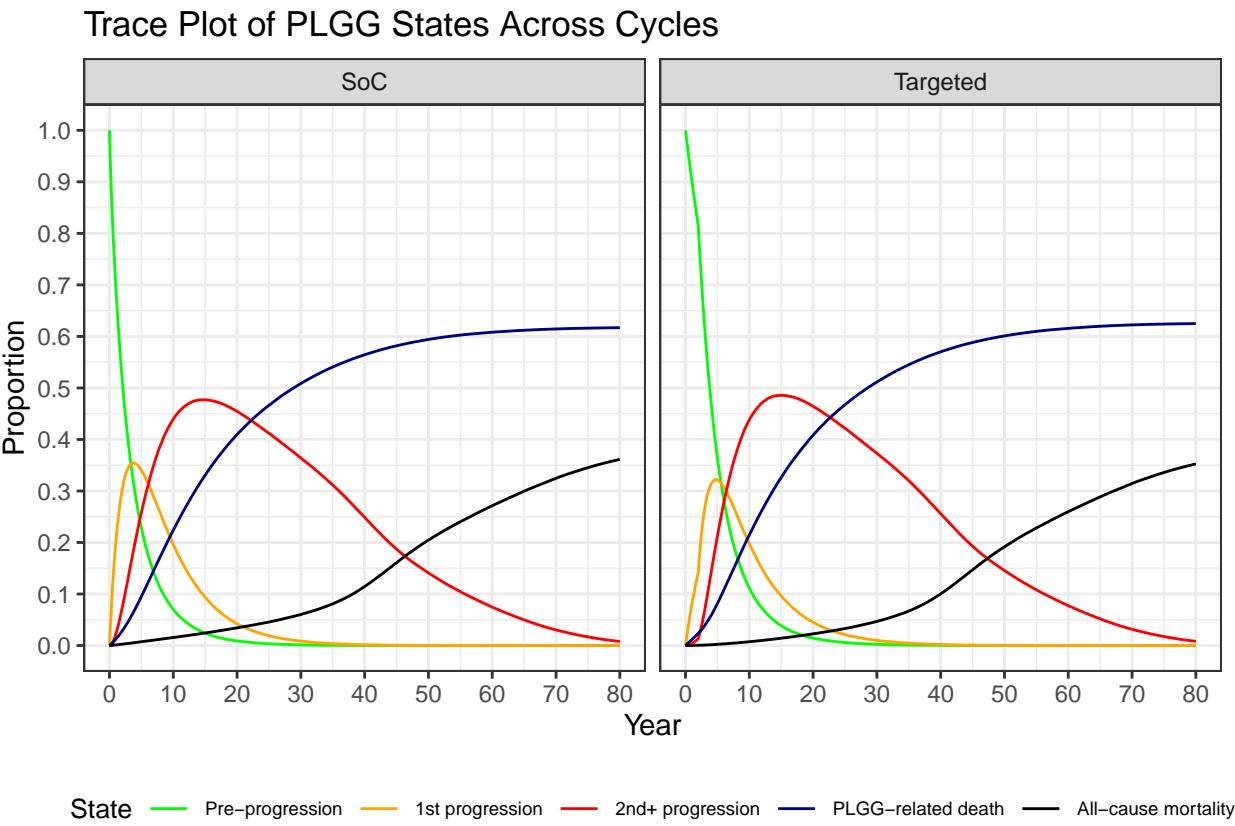


Scenario #1c

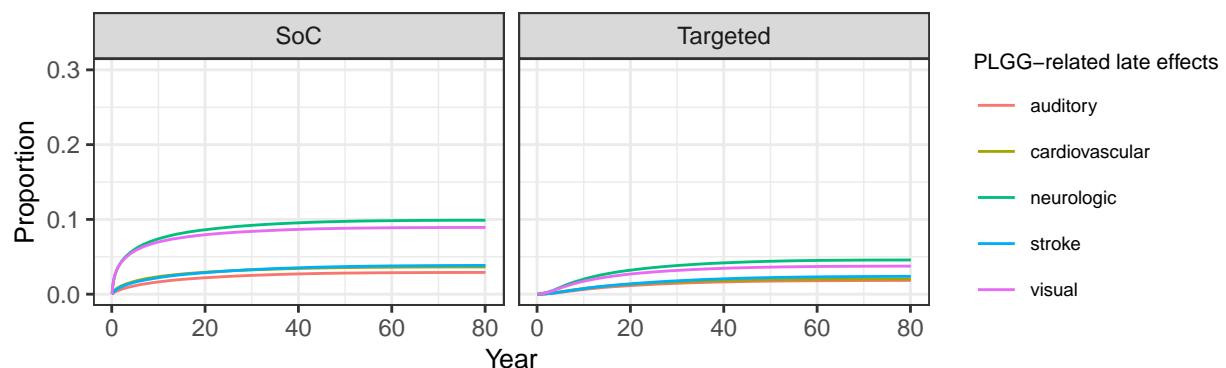
- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **50% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

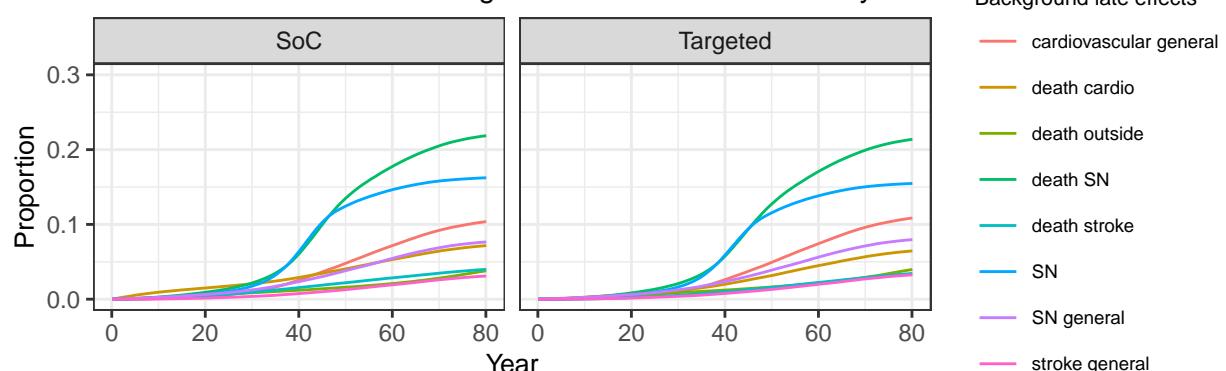
Variable	intervention	control	Delta
Life-years	30.18 (20.46;38.59)	29.5 (20.11;37.73)	0.67 (-1.28;1.83)
QALY	13.82 (9.58;17.43)	12.76 (8.92;16.08)	1.06 (0.03;1.72)
Total Cost	\$405,148 (\$374,878;\$429,550)	\$389,911 (\$360,422;\$415,954)	\$15,238 (\$3,706;\$24,517)
Non-Targeted PLGG related costs	\$208,254 (\$155,480;\$266,294)	\$255,203 (\$201,070;\$310,562)	\$-46,949 (\$-55,462;\$-33,519)
Late effect costs	\$78,182 (\$25,009;\$152,498)	\$100,978 (\$40,220;\$177,609)	\$-22,796 (\$-29,660;\$-14,673)
General population costs	\$43,593 (\$21,102;\$67,506)	\$33,730 (\$15,256;\$54,700)	\$9,863 (\$5,261;\$13,887)
Targeted costs	\$75,120 (\$74,671;\$75,528)	\$0 (\$0;\$0)	\$75,120 (\$74,671;\$75,528)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



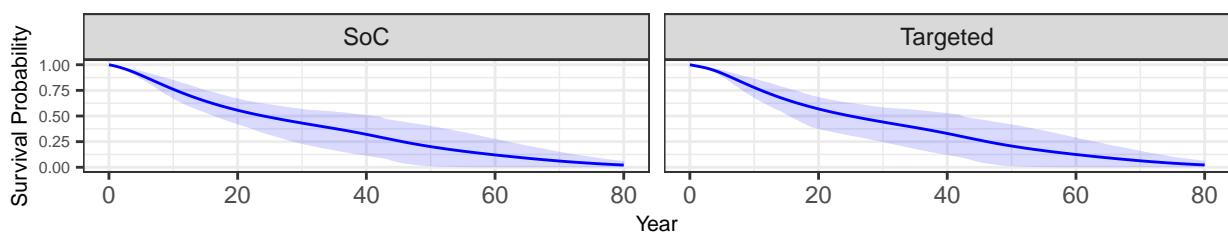
Cumulative Incidence of PLGG-related Late Effects Across Cycles



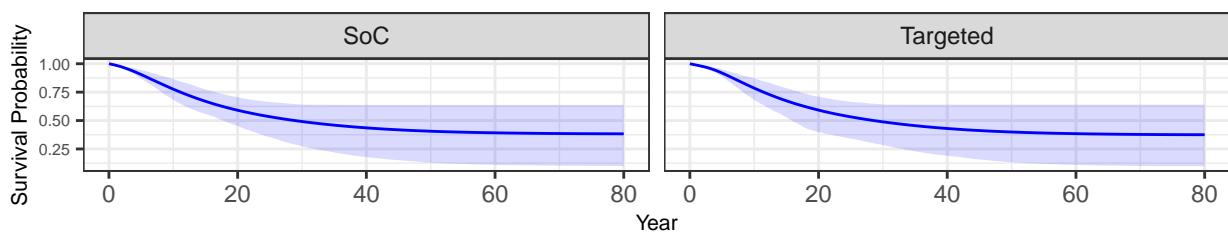
Cumulative Incidence of Background Late Effects Across Cycles



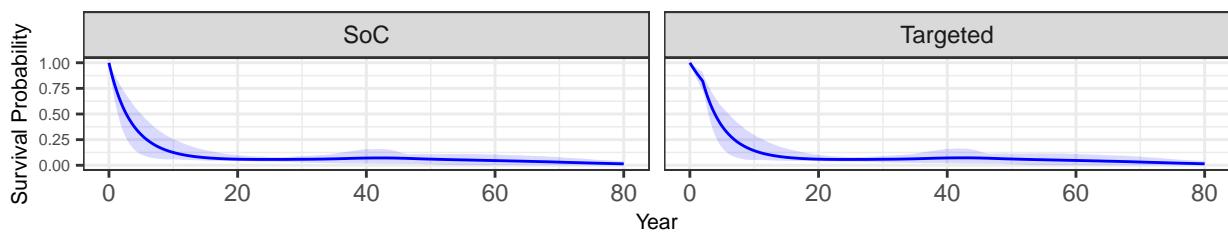
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI

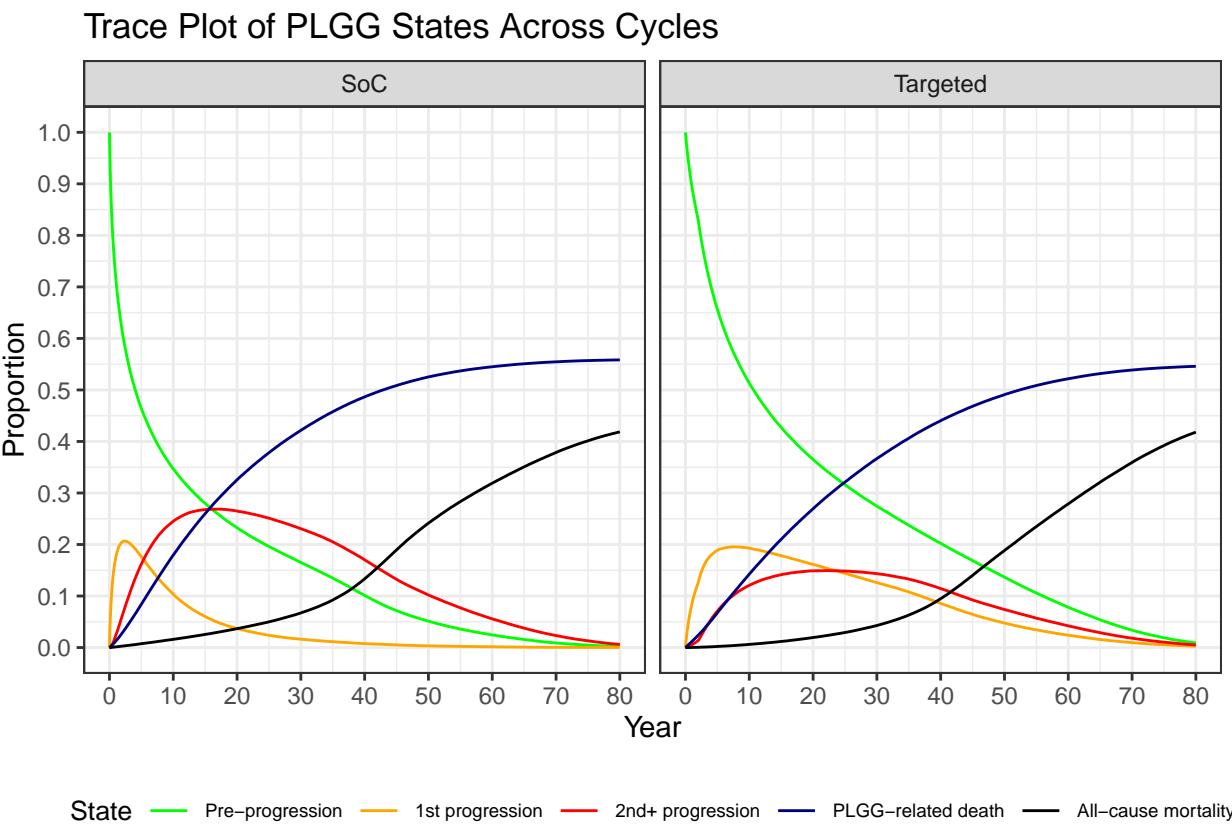


Progression-Free Survival with 95% CI

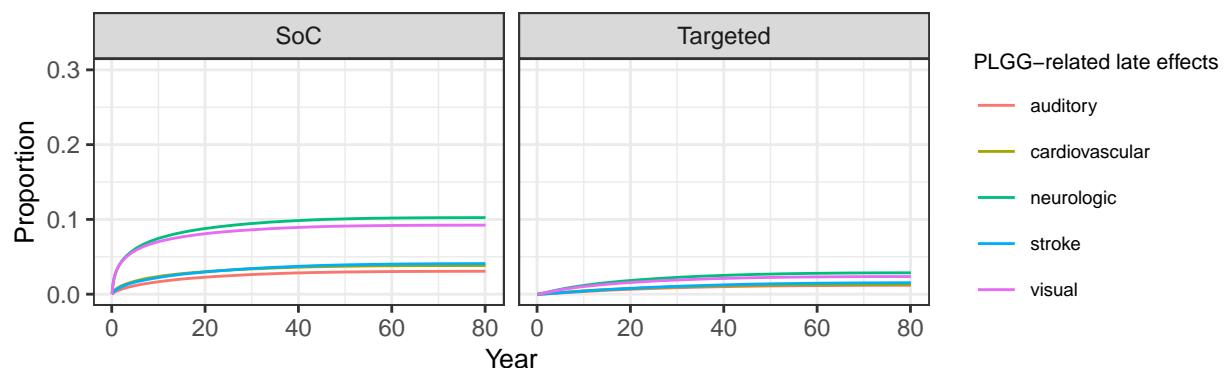


Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

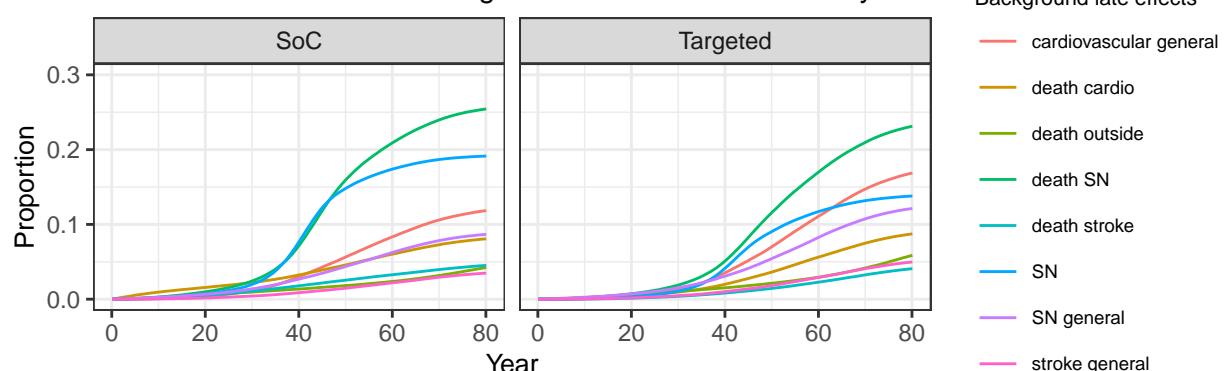
Variable	intervention	control	Delta
Life-years	37.48 (29.63;44.55)	32.68 (26.31;39.54)	4.8 (1.34;11.06)
QALY	17.44 (13.88;20.81)	14.07 (11.27;16.86)	3.37 (1.78;6.37)
Total Cost	\$373,843 (\$357,197;\$391,203)	\$371,619 (\$354,092;\$392,255)	\$2,224 (\$-11,125;\$13,128)
Non-Targeted PLGG related costs	\$154,729 (\$109,574;\$195,629)	\$218,112 (\$161,312;\$259,601)	\$-63,383 (\$-83,657;\$-44,395)
Late effect costs	\$78,482 (\$44,534;\$126,610)	\$115,226 (\$75,174;\$185,091)	\$-36,744 (\$-73,541;\$-15,135)
General population costs	\$65,521 (\$39,700;\$88,641)	\$38,281 (\$20,916;\$59,355)	\$27,240 (\$16,821;\$46,866)
Targeted costs	\$75,110 (\$74,660;\$75,492)	\$0 (\$0;\$0)	\$75,110 (\$74,660;\$75,492)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



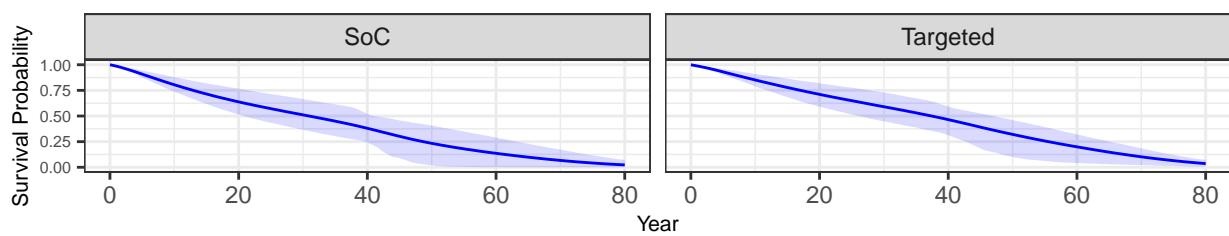
Cumulative Incidence of PLGG-related Late Effects Across Cycles



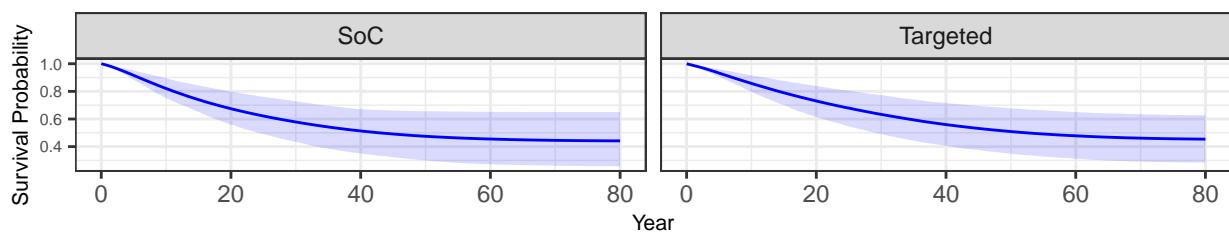
Cumulative Incidence of Background Late Effects Across Cycles



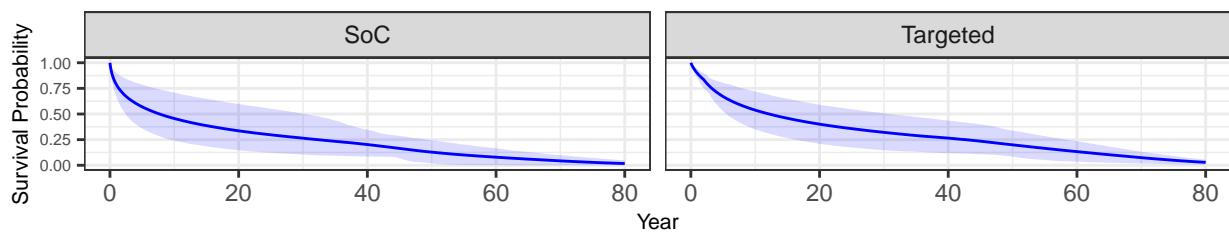
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

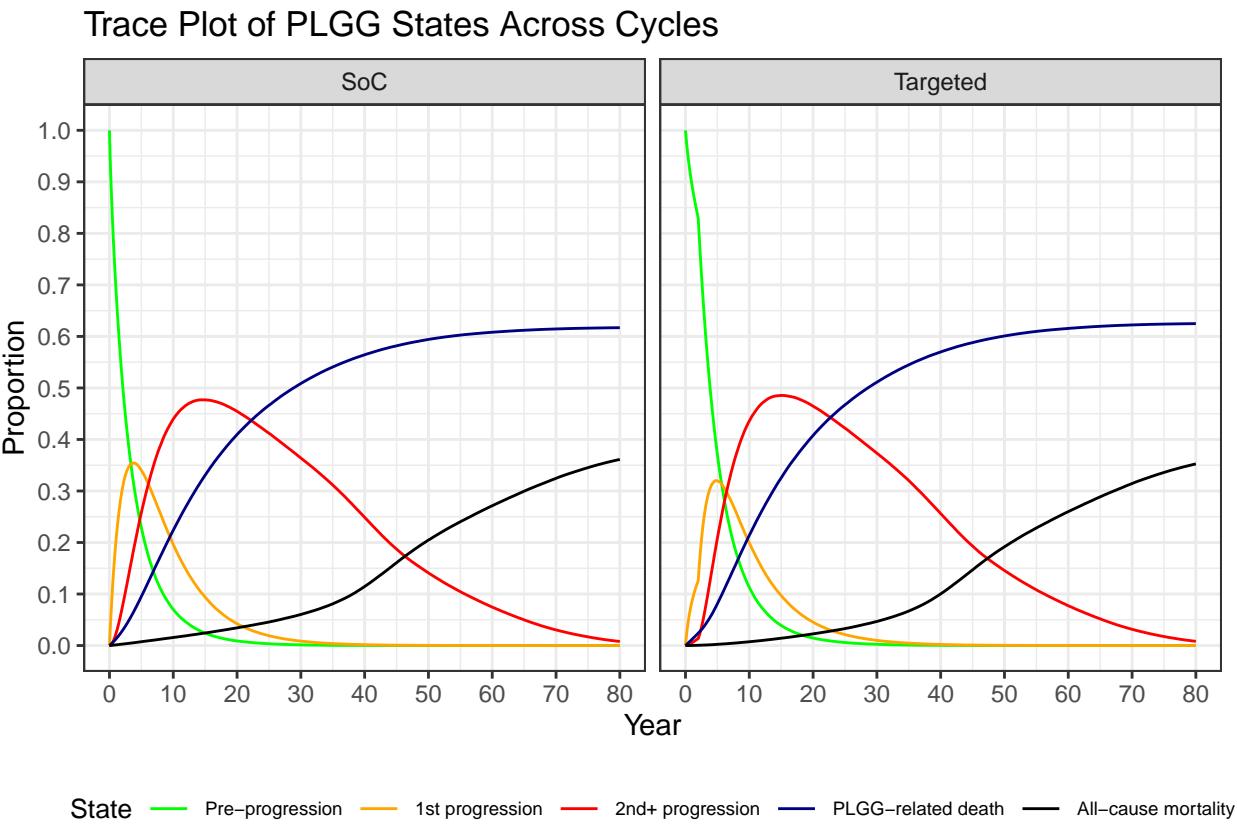


Progression-Free Survival with 95% CI

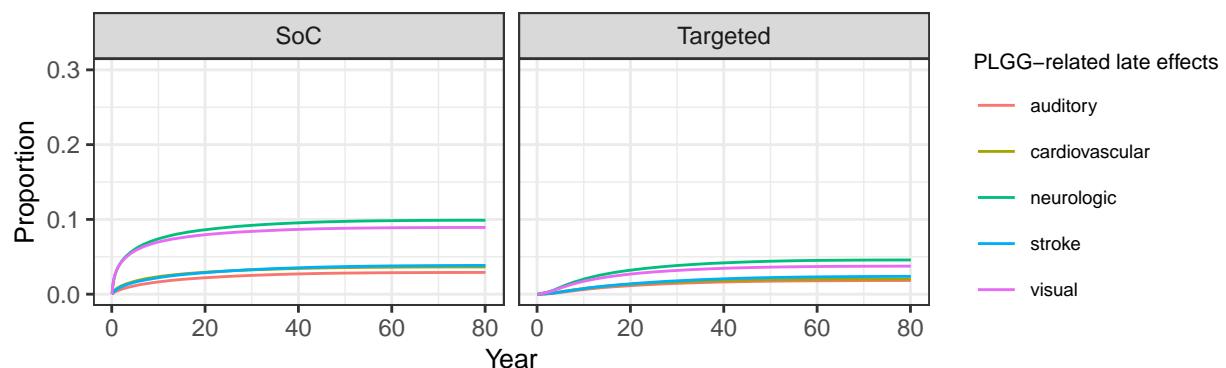


Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

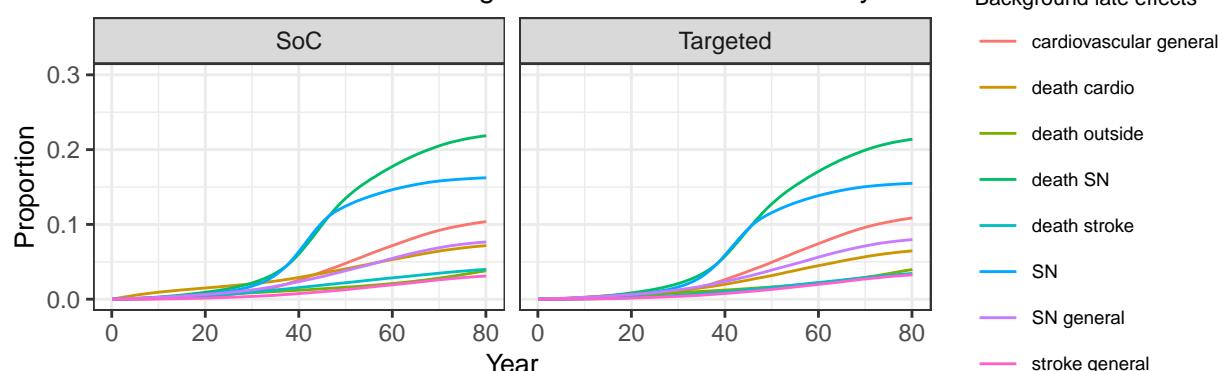
Variable	intervention	control	Delta
Life-years	30.2 (20.51;38.61)	29.5 (20.11;37.73)	0.69 (-1.27;1.96)
QALY	13.83 (9.62;17.45)	12.76 (8.92;16.08)	1.07 (0.04;1.67)
Total Cost	\$404,796 (\$375,286;\$428,703)	\$389,911 (\$360,422;\$415,954)	\$14,886 (\$5,505;\$23,299)
Non-Targeted PLGG related costs	\$207,776 (\$154,575;\$262,736)	\$255,203 (\$201,070;\$310,562)	\$-47,426 (\$-54,076;\$-35,609)
Late effect costs	\$78,278 (\$25,065;\$152,544)	\$100,978 (\$40,220;\$177,609)	\$-22,700 (\$-28,526;\$-14,925)
General population costs	\$43,632 (\$21,293;\$67,688)	\$33,730 (\$15,256;\$54,700)	\$9,902 (\$5,588;\$13,430)
Targeted costs	\$75,110 (\$74,660;\$75,492)	\$0 (\$0;\$0)	\$75,110 (\$74,660;\$75,492)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



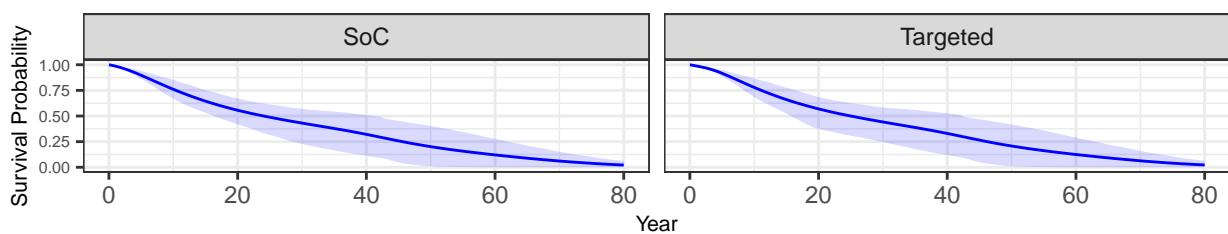
Cumulative Incidence of PLGG-related Late Effects Across Cycles



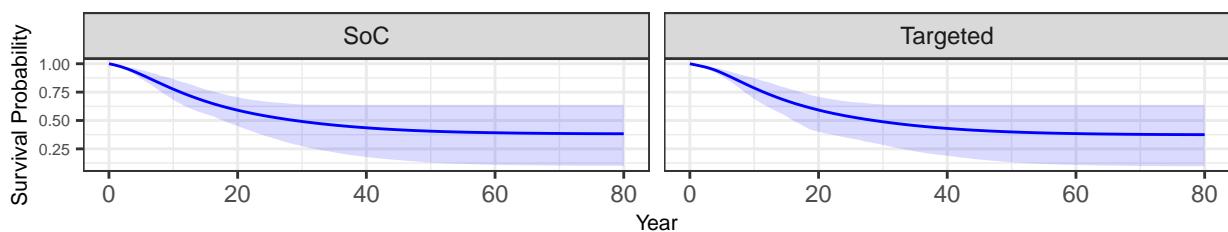
Cumulative Incidence of Background Late Effects Across Cycles



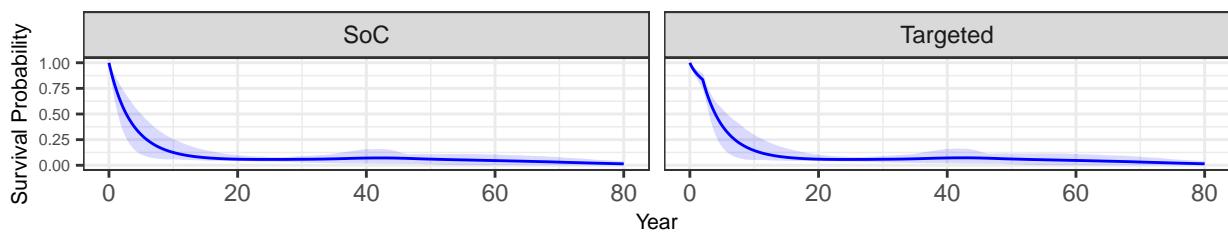
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

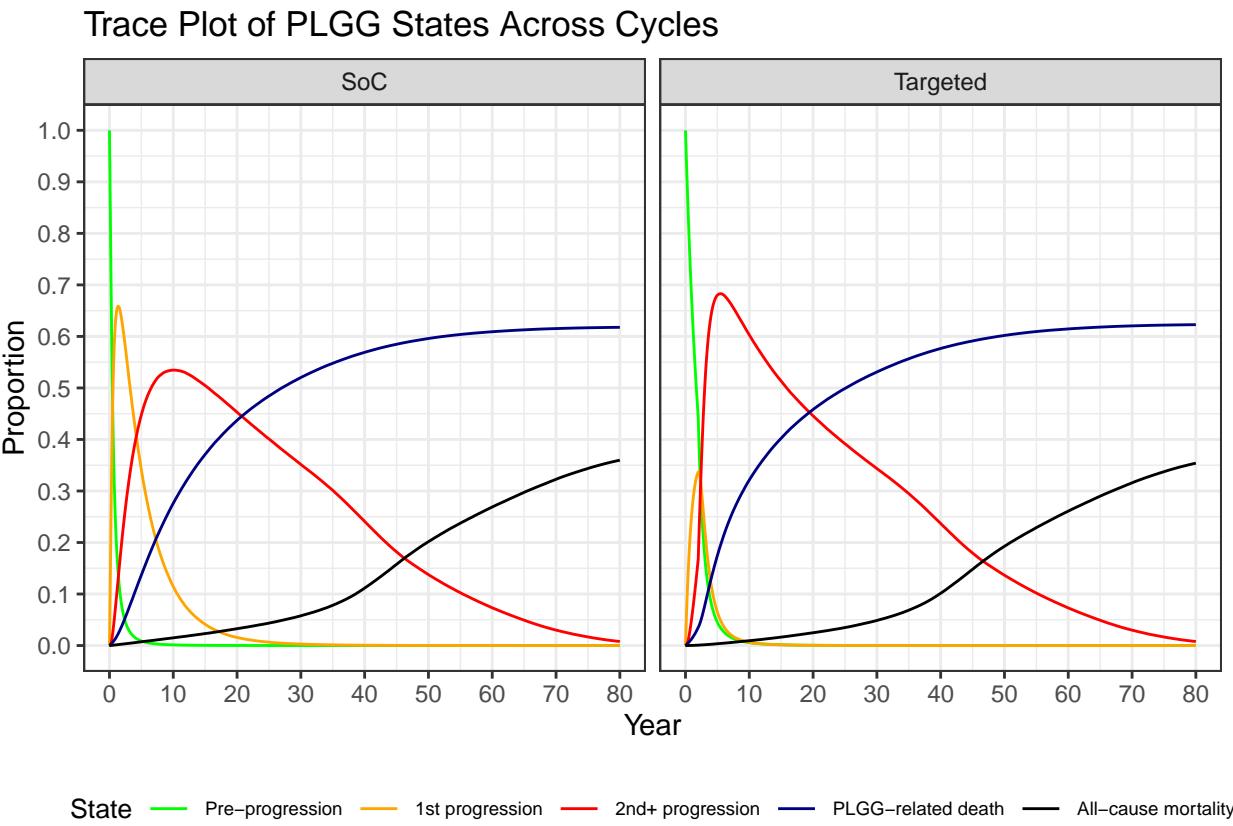


Progression-Free Survival with 95% CI

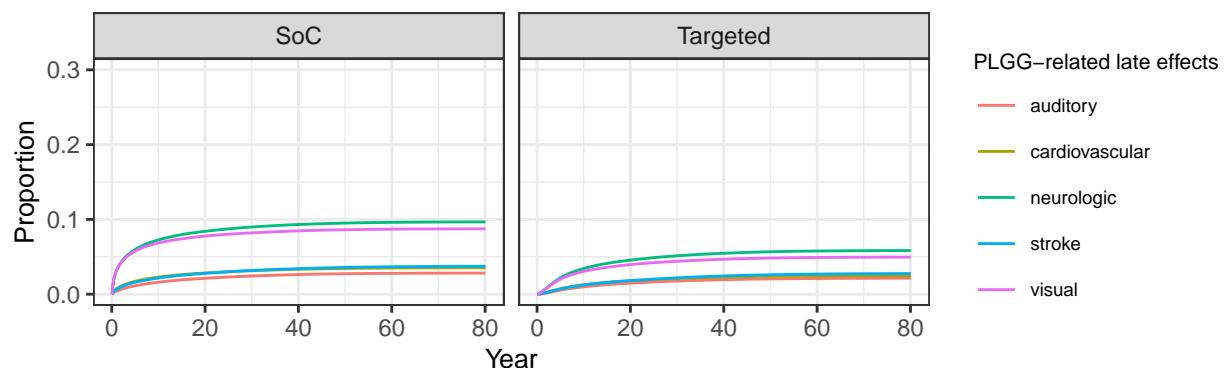


Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

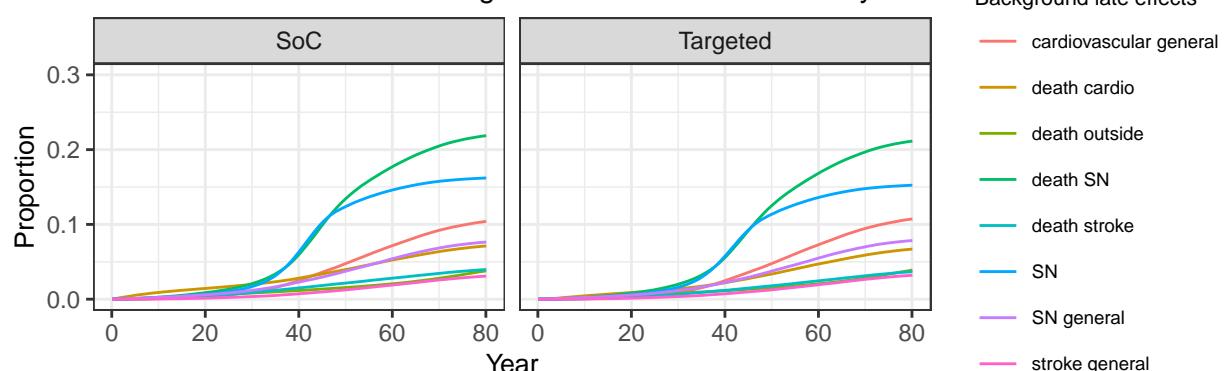
Variable	intervention	control	Delta
Life-years	28.14 (15.36;38.93)	28.6 (17.23;38.19)	-0.46 (-2.27;0.71)
QALY	12.64 (7.07;17.29)	12.36 (7.65;16.39)	0.28 (-0.7;0.93)
Total Cost	\$434,179 (\$404,205;\$465,286)	\$395,495 (\$365,854;\$423,395)	\$38,684 (\$29,643;\$45,973)
Non-Targeted PLGG related costs	\$237,303 (\$170,775;\$295,376)	\$262,516 (\$200,713;\$317,931)	\$-25,213 (\$-33,698;\$-14,796)
Late effect costs	\$84,153 (\$21,643;\$172,520)	\$99,863 (\$34,492;\$182,812)	\$-15,710 (\$-22,310;\$-9,497)
General population costs	\$37,865 (\$14,372;\$64,471)	\$33,116 (\$13,362;\$56,145)	\$4,749 (\$577;\$8,574)
Targeted costs	\$74,858 (\$74,301;\$75,364)	\$0 (\$0;\$0)	\$74,858 (\$74,301;\$75,364)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



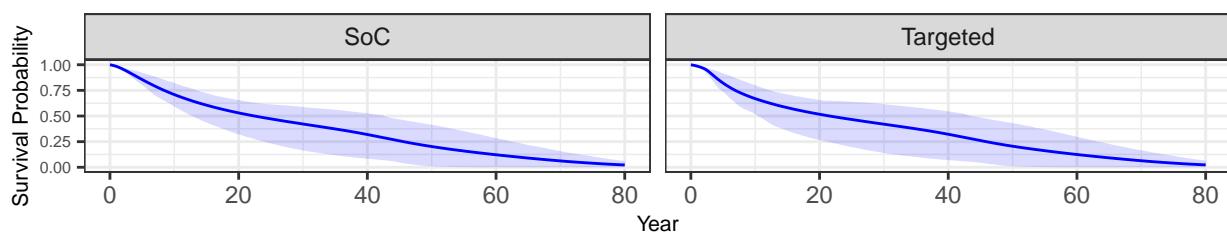
Cumulative Incidence of PLGG-related Late Effects Across Cycles



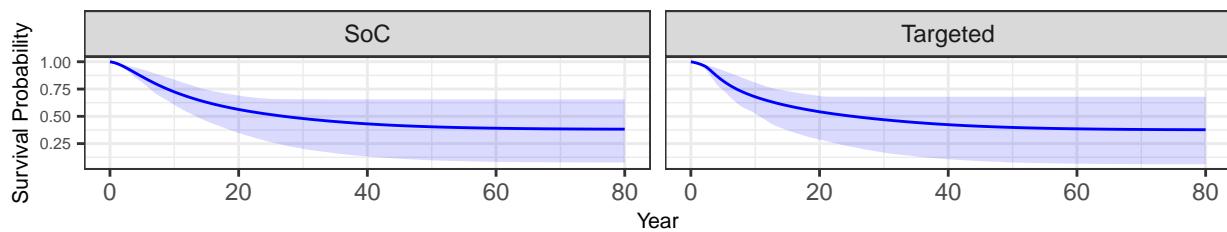
Cumulative Incidence of Background Late Effects Across Cycles



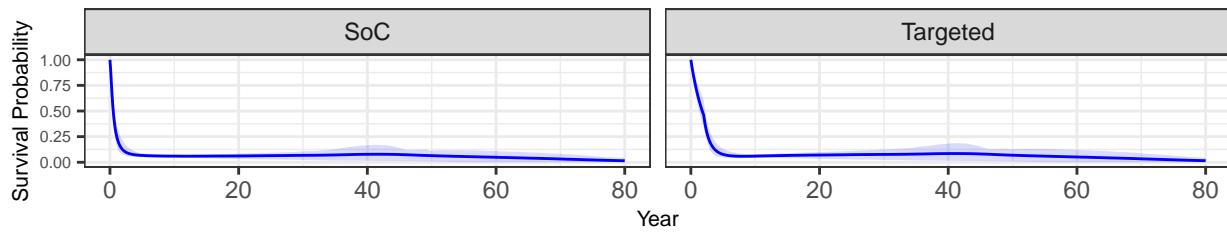
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI

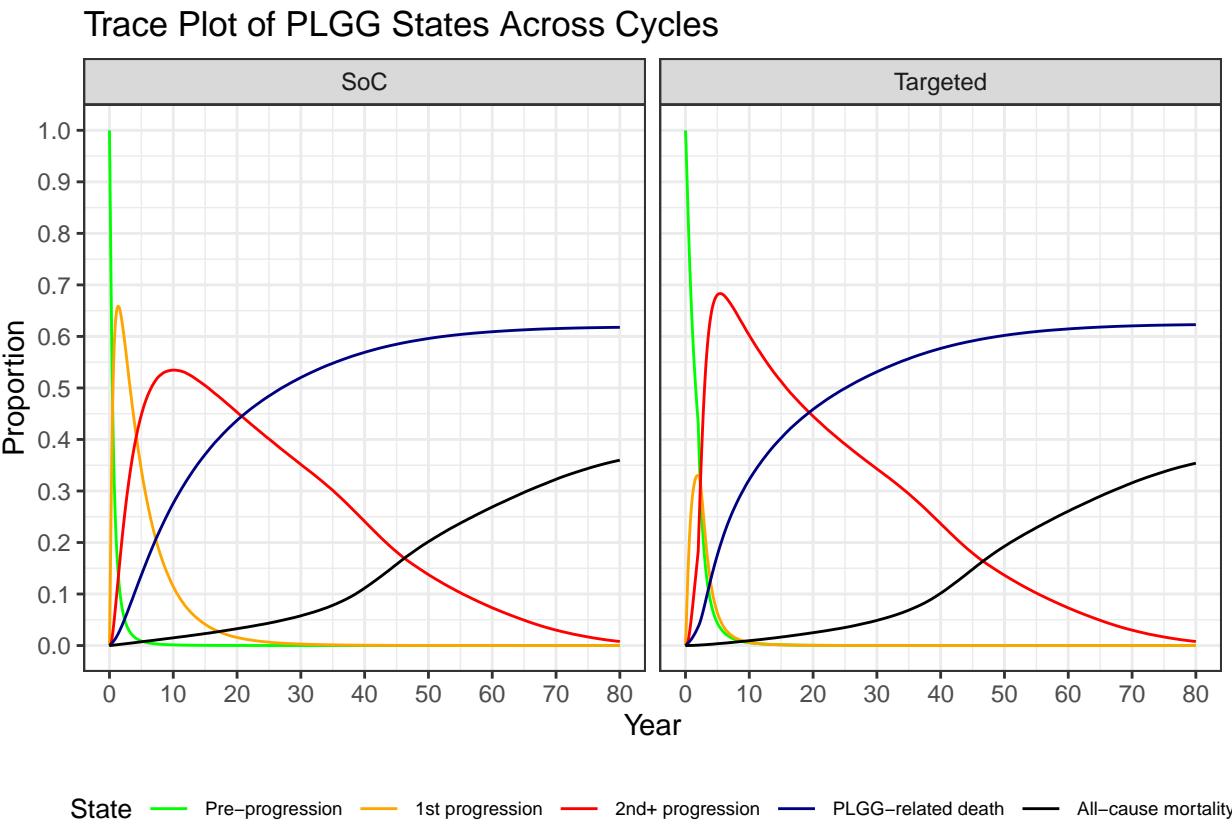


Progression-Free Survival with 95% CI

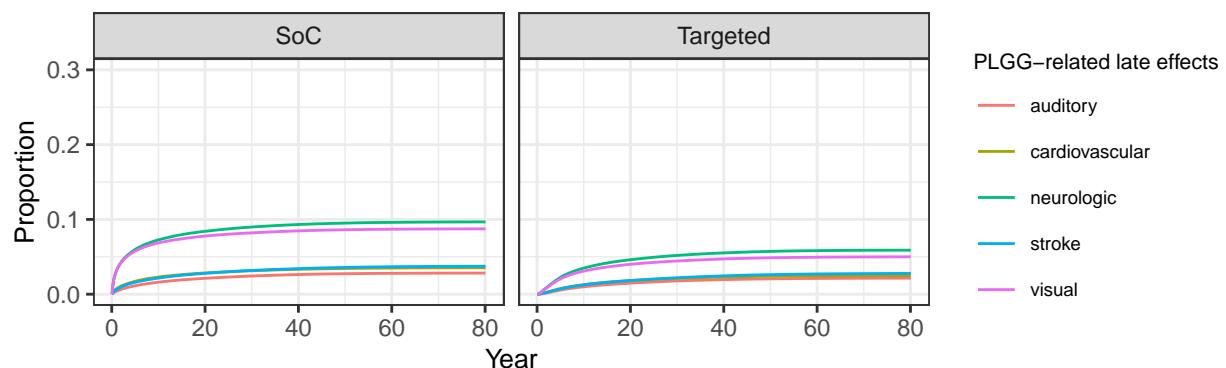


Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

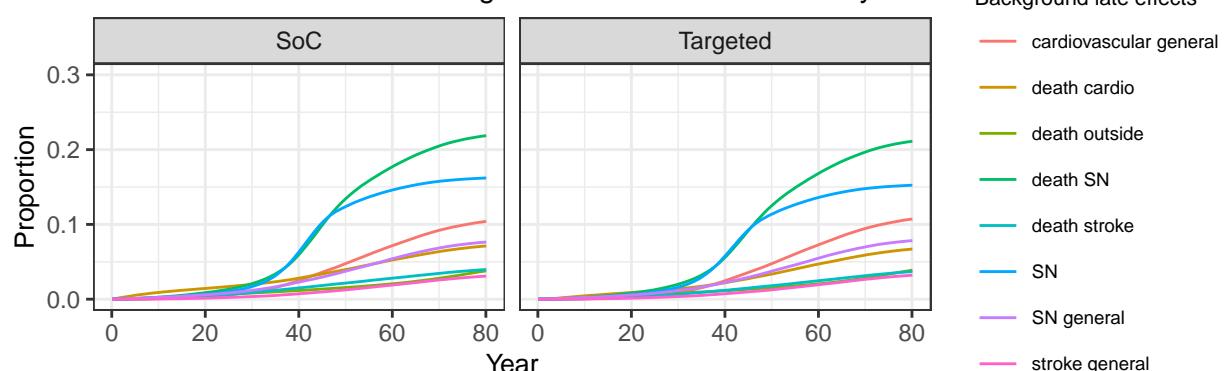
Variable	intervention	control	Delta
Life-years	28.12 (15.31;38.96)	28.6 (17.23;38.19)	-0.48 (-2.28;0.78)
QALY	12.62 (7.04;17.32)	12.36 (7.65;16.39)	0.26 (-0.72;0.99)
Total Cost	\$434,815 (\$402,285;\$465,313)	\$395,495 (\$365,854;\$423,395)	\$39,320 (\$30,996;\$45,099)
Non-Targeted PLGG related costs	\$237,855 (\$170,300;\$294,751)	\$262,516 (\$200,713;\$317,931)	\$-24,661 (\$-32,175;\$-15,045)
Late effect costs	\$84,388 (\$21,302;\$173,462)	\$99,863 (\$34,492;\$182,812)	\$-15,476 (\$-21,764;\$-8,988)
General population costs	\$37,747 (\$14,294;\$64,792)	\$33,116 (\$13,362;\$56,145)	\$4,631 (\$1,413;\$8,737)
Targeted costs	\$74,826 (\$74,421;\$75,205)	\$0 (\$0;\$0)	\$74,826 (\$74,421;\$75,205)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



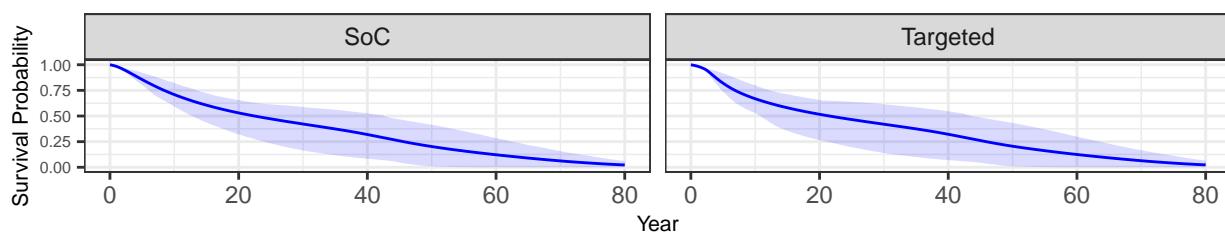
Cumulative Incidence of PLGG-related Late Effects Across Cycles



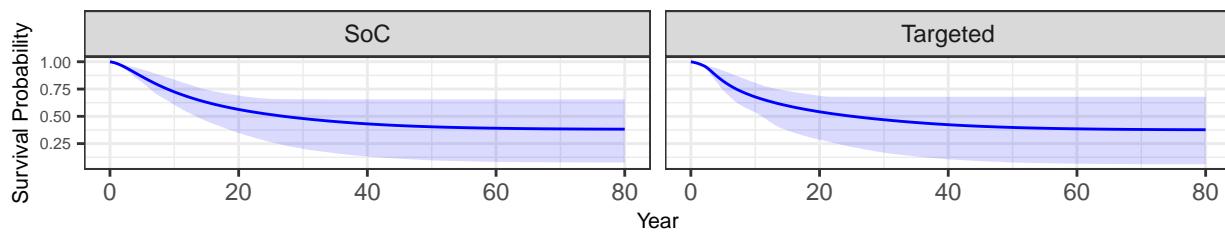
Cumulative Incidence of Background Late Effects Across Cycles



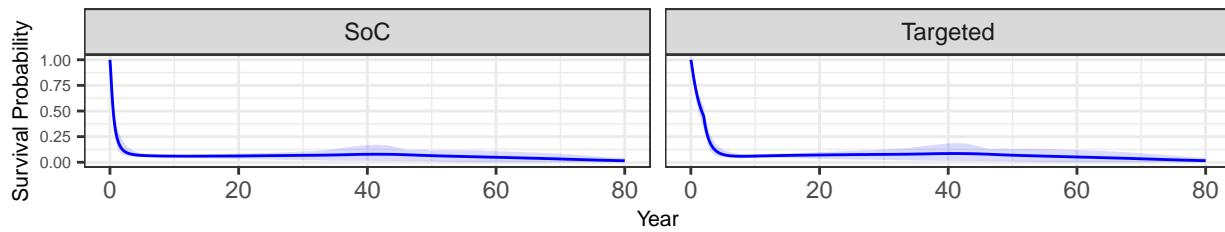
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI

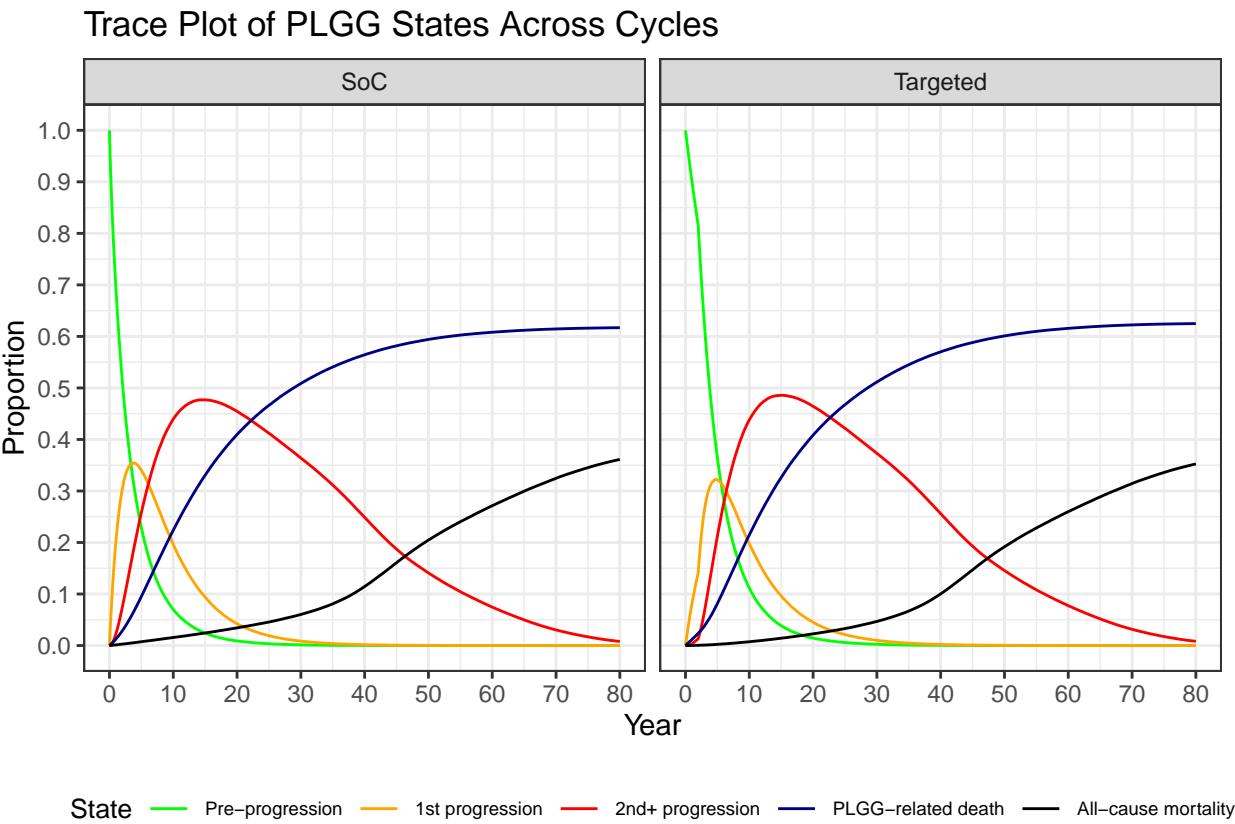


Scenario #1d

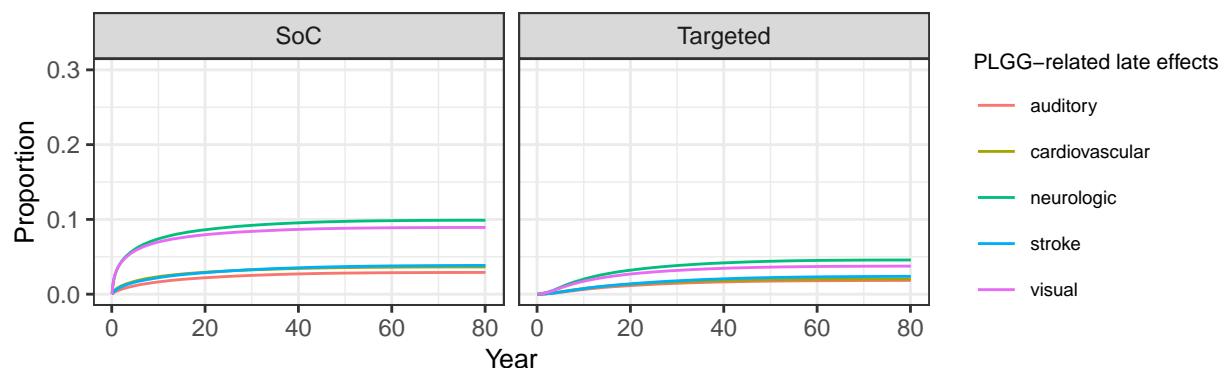
- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- **75% combo price reduction**
- Discount rate: 1.5
- Data source for controls & exposed: Investigator assessment - Bouffet et al., NEJM 2023.
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Investigator assessment, Targeted curve – Exponential, SoC curve – Exponential

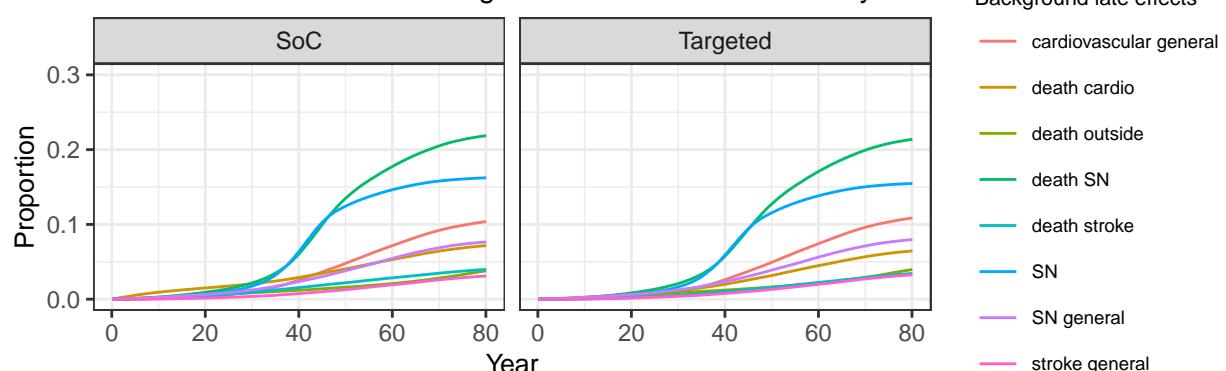
Variable	intervention	control	Delta
Life-years	30.18 (20.46;38.59)	29.5 (20.11;37.73)	0.67 (-1.28;1.83)
QALY	13.82 (9.58;17.43)	12.76 (8.92;16.08)	1.06 (0.03;1.72)
Total Cost	\$367,589 (\$337,441;\$392,033)	\$389,911 (\$360,422;\$415,954)	\$-22,322 (\$-33,920;\$-13,040)
Non-Targeted PLGG related costs	\$208,254 (\$155,480;\$266,294)	\$255,203 (\$201,070;\$310,562)	\$-46,949 (\$-55,462;\$-33,519)
Late effect costs	\$78,182 (\$25,009;\$152,498)	\$100,978 (\$40,220;\$177,609)	\$-22,796 (\$-29,660;\$-14,673)
General population costs	\$43,593 (\$21,102;\$67,506)	\$33,730 (\$15,256;\$54,700)	\$9,863 (\$5,261;\$13,887)
Targeted costs	\$37,560 (\$37,335;\$37,764)	\$0 (\$0;\$0)	\$37,560 (\$37,335;\$37,764)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



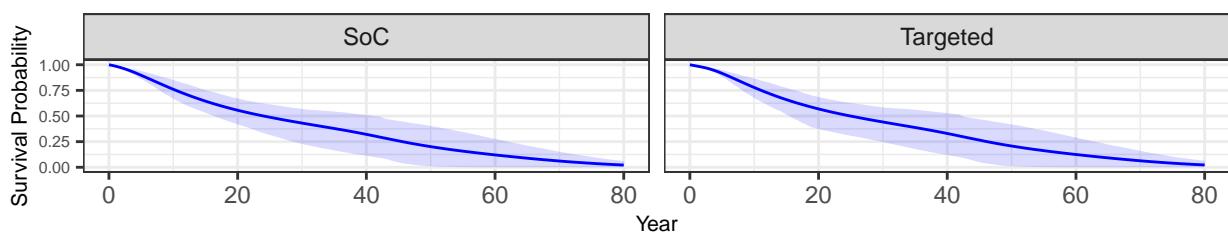
Cumulative Incidence of PLGG-related Late Effects Across Cycles



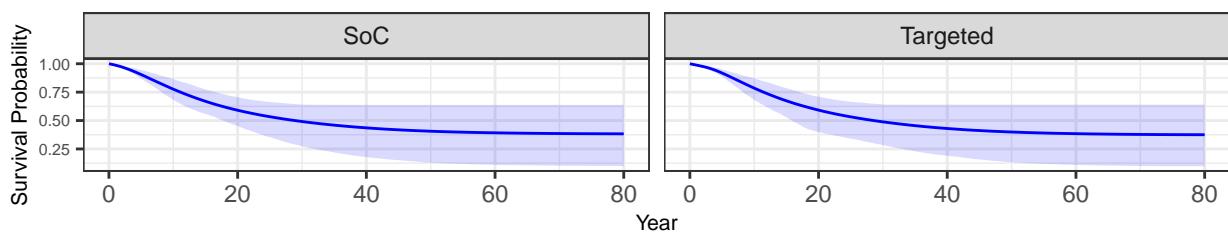
Cumulative Incidence of Background Late Effects Across Cycles



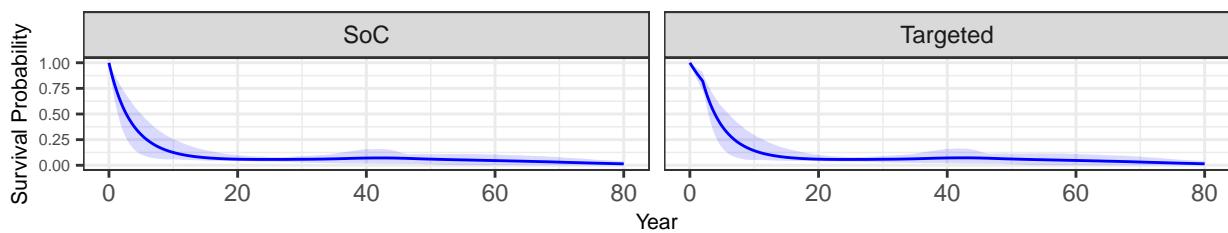
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

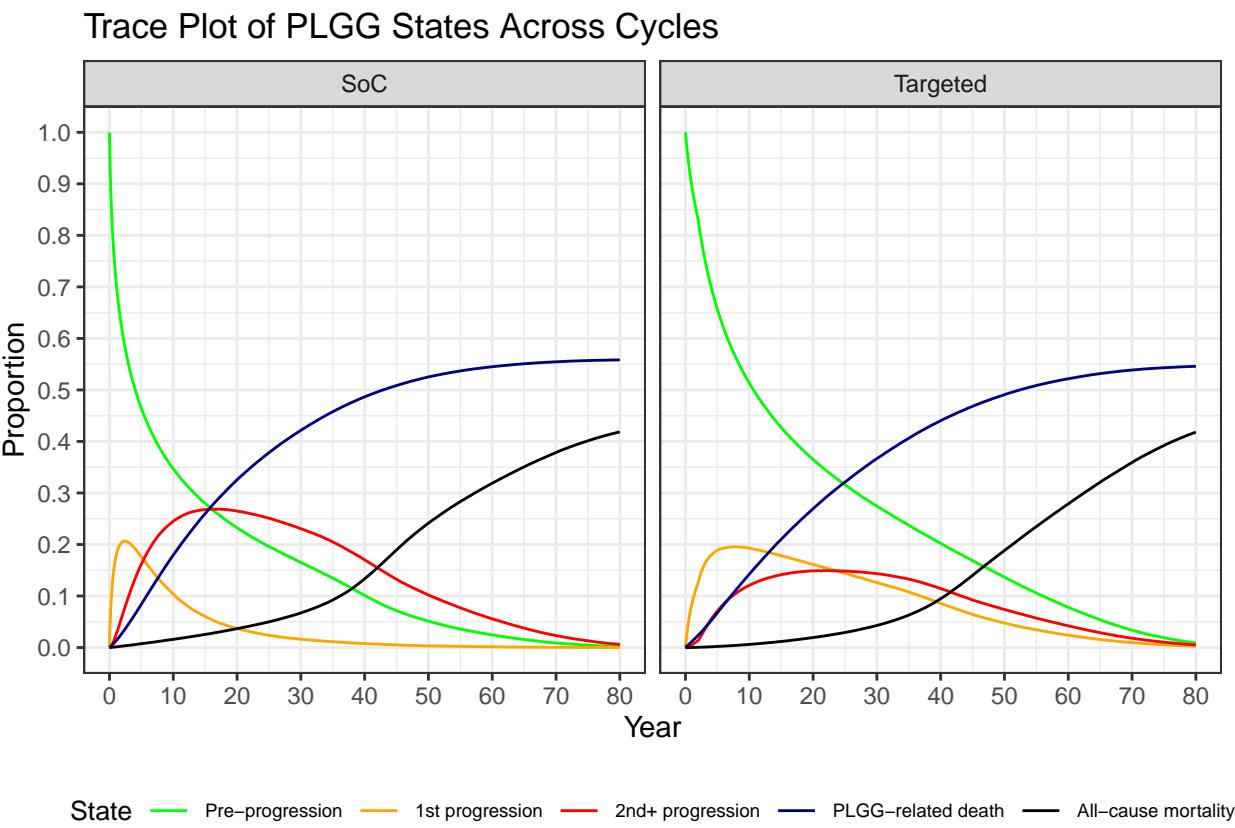


Progression-Free Survival with 95% CI

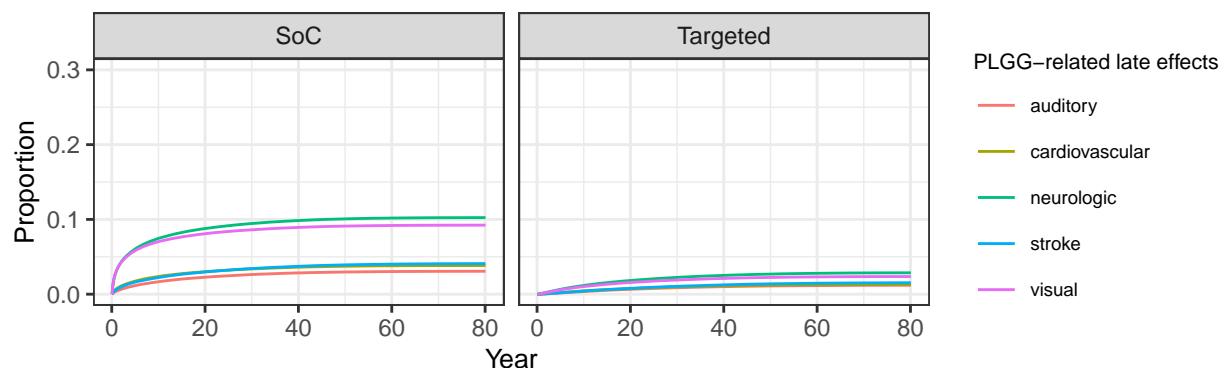


Investigator assessment, Targeted curve – Log-Normal, SoC curve – Log-Normal

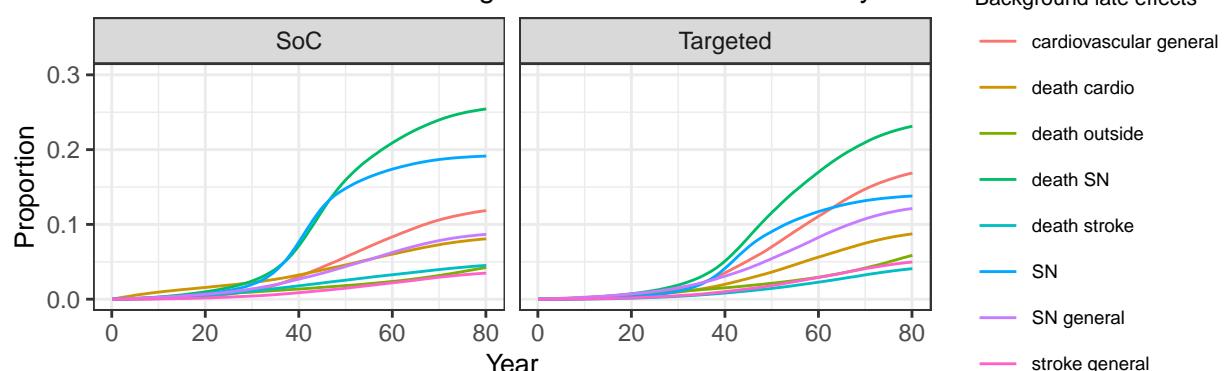
Variable	intervention	control	Delta
Life-years	37.48 (29.63;44.55)	32.68 (26.31;39.54)	4.8 (1.34;11.06)
QALY	17.44 (13.88;20.81)	14.07 (11.27;16.86)	3.37 (1.78;6.37)
Total Cost	\$336,287 (\$319,824;\$353,611)	\$371,619 (\$354,092;\$392,255)	\$-35,331 (\$-48,720;\$-24,495)
Non-Targeted PLGG related costs	\$154,729 (\$109,574;\$195,629)	\$218,112 (\$161,312;\$259,601)	\$-63,383 (\$-83,657;\$-44,395)
Late effect costs	\$78,482 (\$44,534;\$126,610)	\$115,226 (\$75,174;\$185,091)	\$-36,744 (\$-73,541;\$-15,135)
General population costs	\$65,521 (\$39,700;\$88,641)	\$38,281 (\$20,916;\$59,355)	\$27,240 (\$16,821;\$46,866)
Targeted costs	\$37,555 (\$37,330;\$37,746)	\$0 (\$0;\$0)	\$37,555 (\$37,330;\$37,746)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



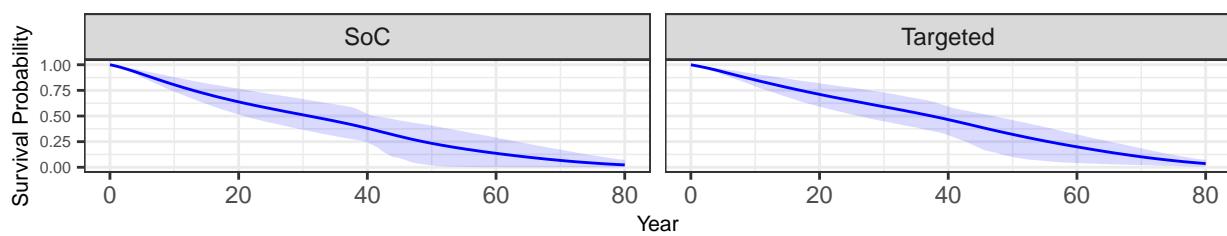
Cumulative Incidence of PLGG-related Late Effects Across Cycles



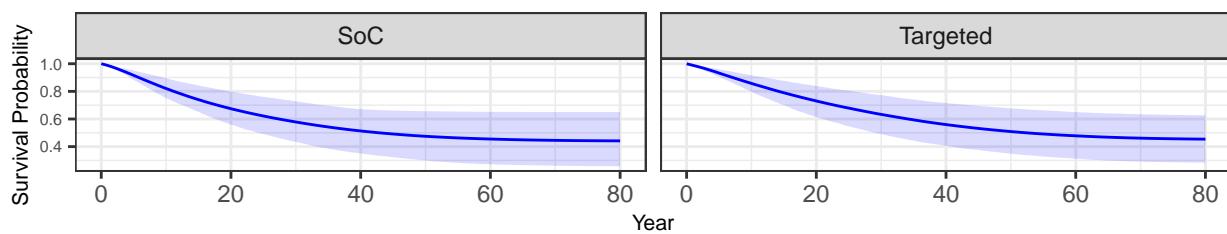
Cumulative Incidence of Background Late Effects Across Cycles



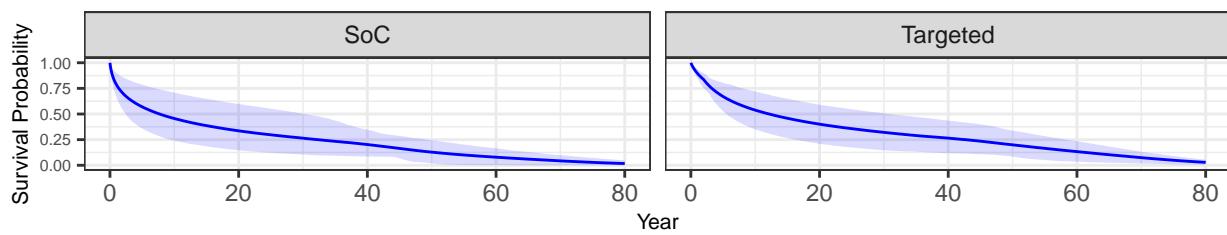
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

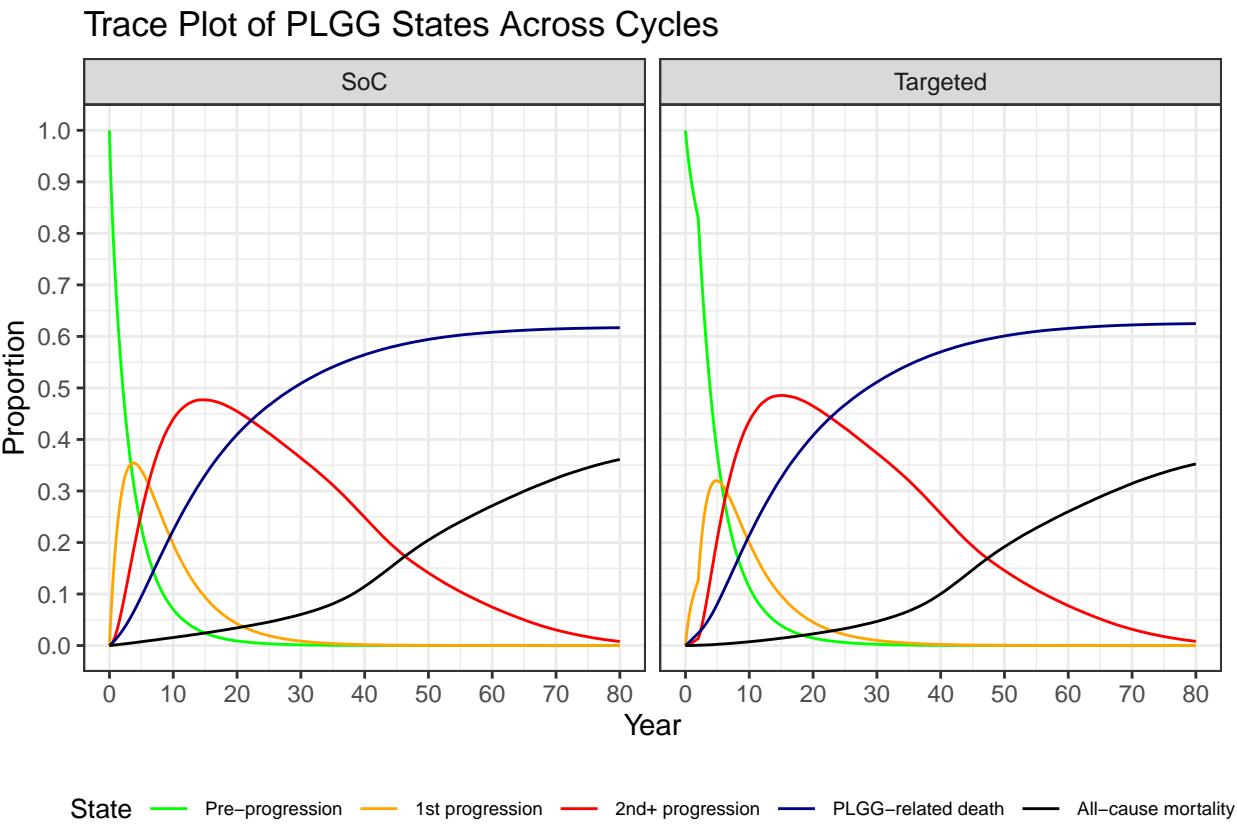


Progression-Free Survival with 95% CI

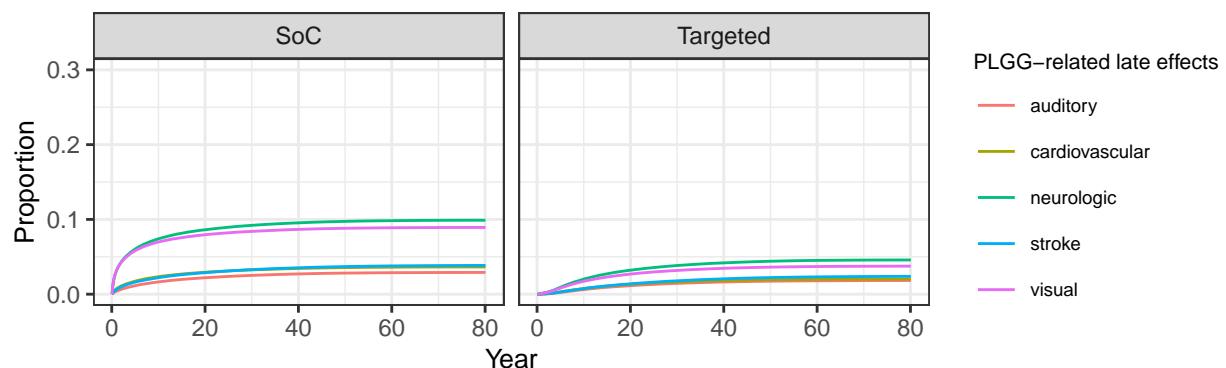


Investigator assessment, Targeted curve – Log-Normal, SoC curve – Exponential

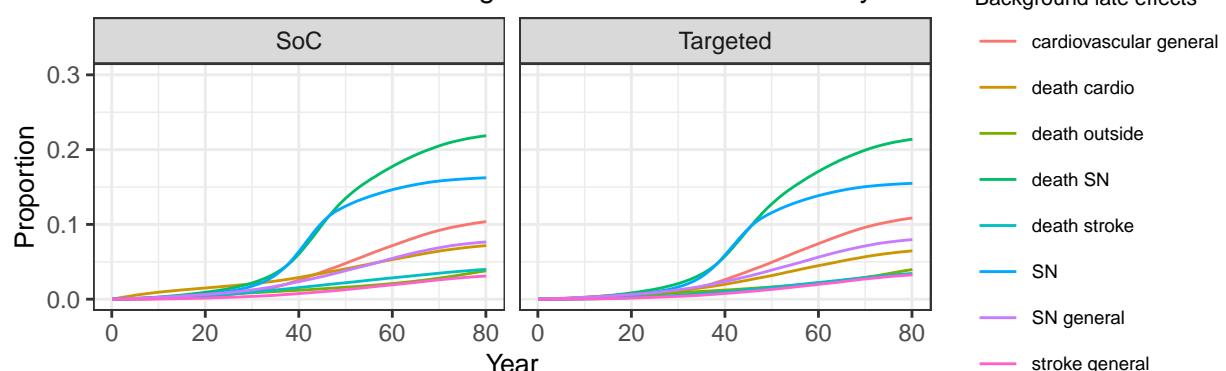
Variable	intervention	control	Delta
Life-years	30.2 (20.51;38.61)	29.5 (20.11;37.73)	0.69 (-1.27;1.96)
QALY	13.83 (9.62;17.45)	12.76 (8.92;16.08)	1.07 (0.04;1.67)
Total Cost	\$367,241 (\$337,863;\$391,066)	\$389,911 (\$360,422;\$415,954)	\$-22,670 (\$-31,929;\$-14,259)
Non-Targeted PLGG related costs	\$207,776 (\$154,575;\$262,736)	\$255,203 (\$201,070;\$310,562)	\$-47,426 (\$-54,076;\$-35,609)
Late effect costs	\$78,278 (\$25,065;\$152,544)	\$100,978 (\$40,220;\$177,609)	\$-22,700 (\$-28,526;\$-14,925)
General population costs	\$43,632 (\$21,293;\$67,688)	\$33,730 (\$15,256;\$54,700)	\$9,902 (\$5,588;\$13,430)
Targeted costs	\$37,555 (\$37,330;\$37,746)	\$0 (\$0;\$0)	\$37,555 (\$37,330;\$37,746)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



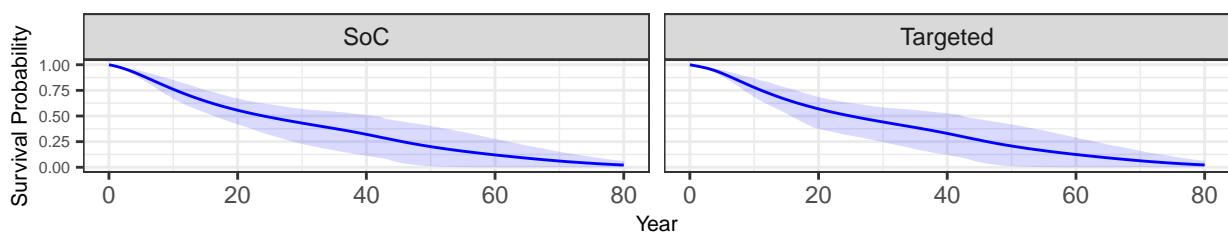
Cumulative Incidence of PLGG-related Late Effects Across Cycles



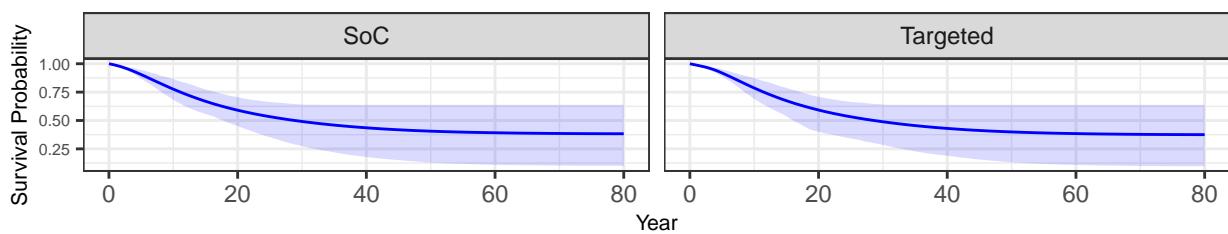
Cumulative Incidence of Background Late Effects Across Cycles



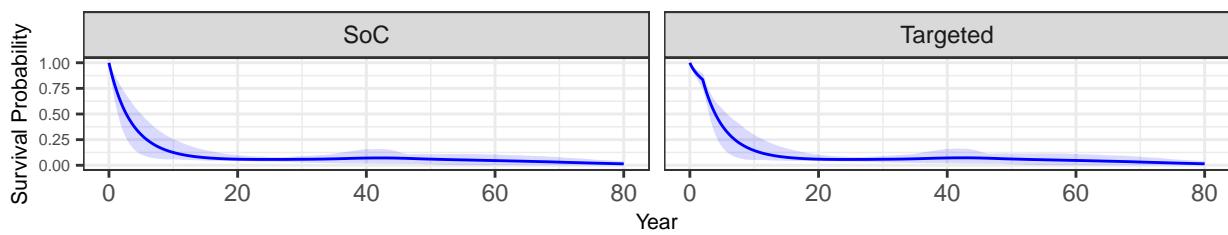
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

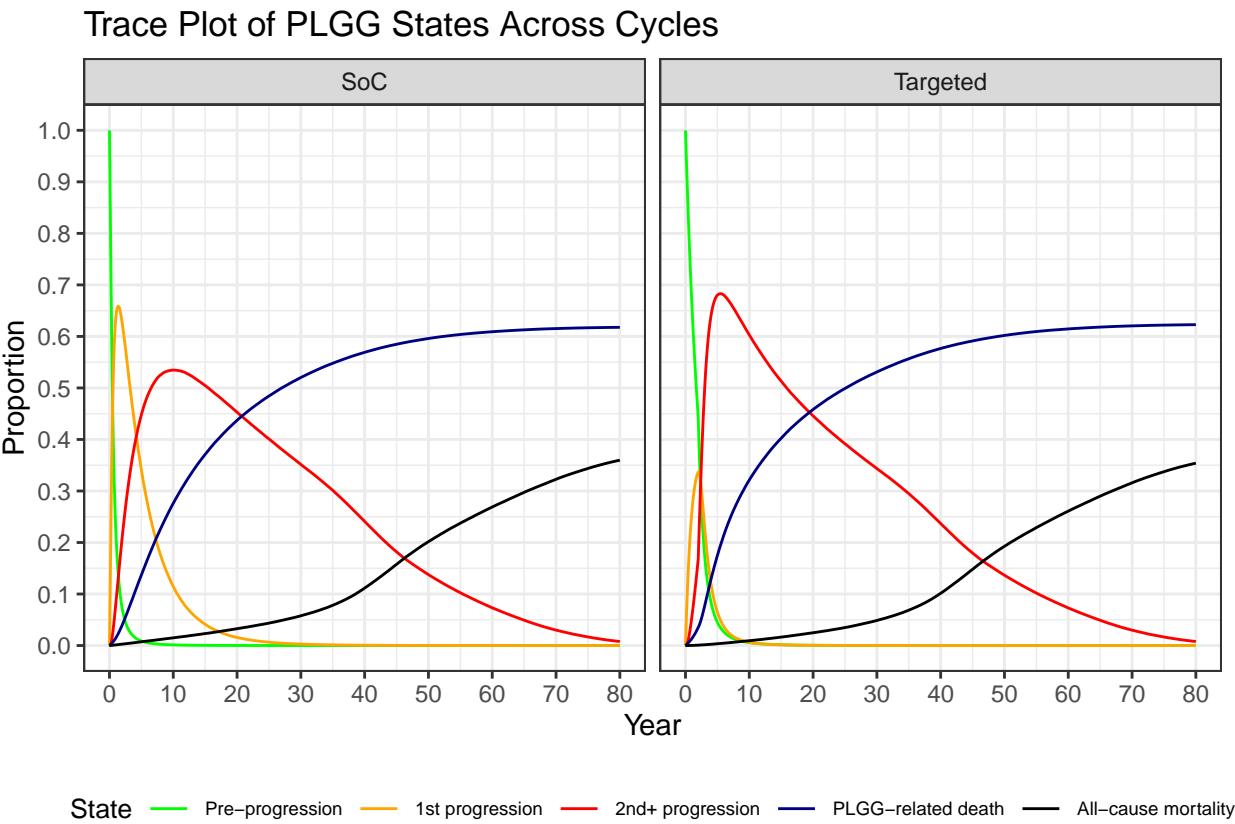


Progression-Free Survival with 95% CI

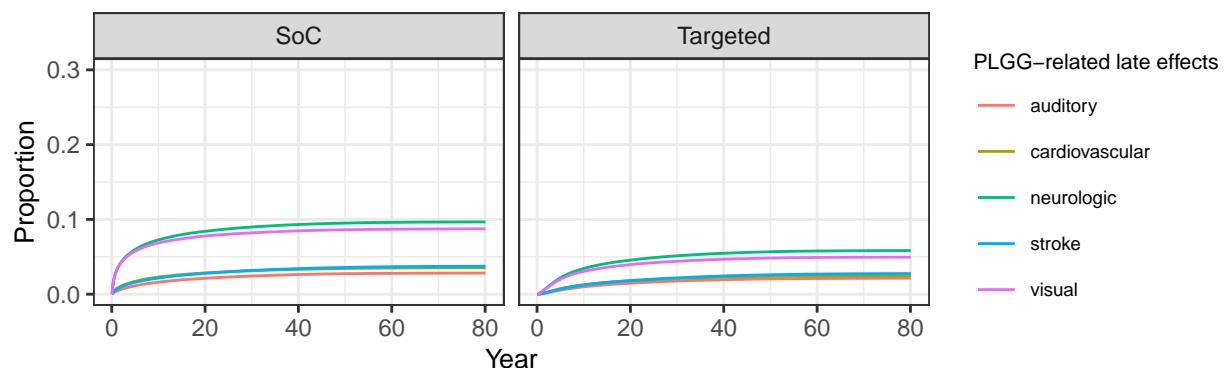


Independent reviewer, Targeted curve – Exponential, SoC curve – Log-Normal

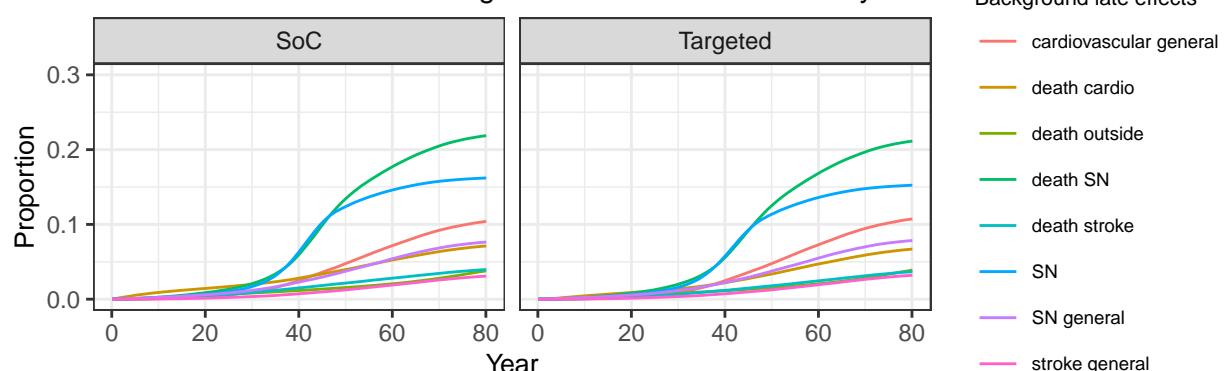
Variable	intervention	control	Delta
Life-years	28.14 (15.36;38.93)	28.6 (17.23;38.19)	-0.46 (-2.27;0.71)
QALY	12.64 (7.07;17.29)	12.36 (7.65;16.39)	0.28 (-0.7;0.93)
Total Cost	\$396,750 (\$366,773;\$428,021)	\$395,495 (\$365,854;\$423,395)	\$1,255 (\$-8,025;\$8,636)
Non-Targeted PLGG related costs	\$237,303 (\$170,775;\$295,376)	\$262,516 (\$200,713;\$317,931)	\$-25,213 (\$-33,698;\$-14,796)
Late effect costs	\$84,153 (\$21,643;\$172,520)	\$99,863 (\$34,492;\$182,812)	\$-15,710 (\$-22,310;\$-9,497)
General population costs	\$37,865 (\$14,372;\$64,471)	\$33,116 (\$13,362;\$56,145)	\$4,749 (\$577;\$8,574)
Targeted costs	\$37,429 (\$37,150;\$37,682)	\$0 (\$0;\$0)	\$37,429 (\$37,150;\$37,682)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



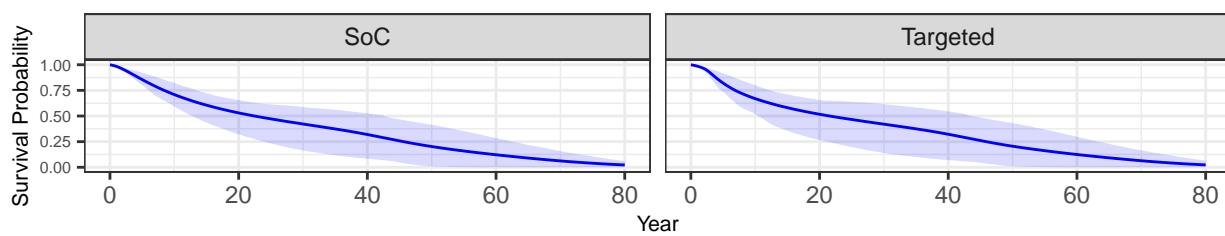
Cumulative Incidence of PLGG-related Late Effects Across Cycles



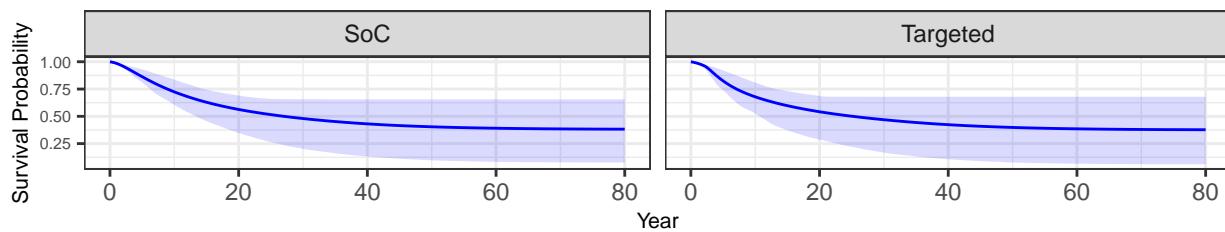
Cumulative Incidence of Background Late Effects Across Cycles



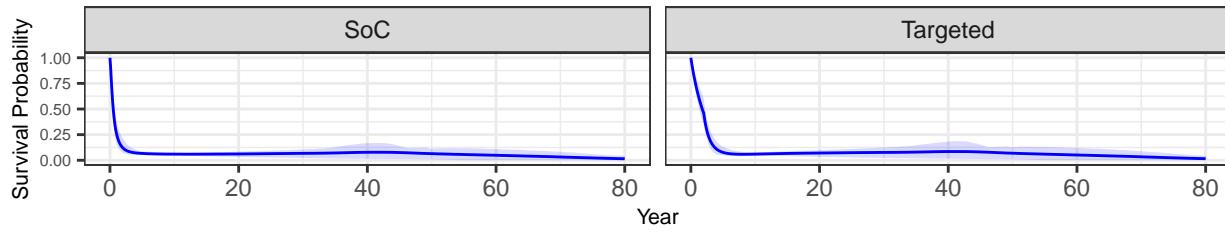
Overall Survival with 95% CI



PLGG–death–related Survival with 95% CI

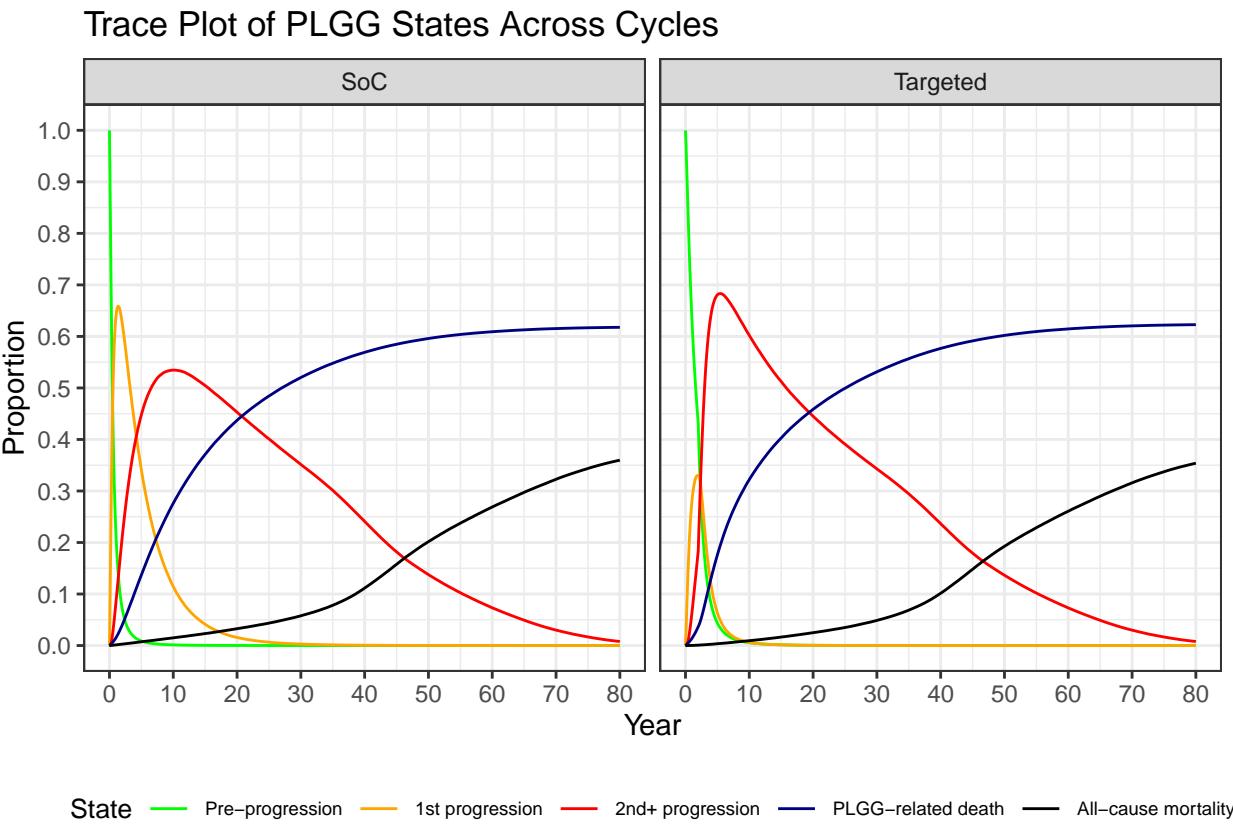


Progression–Free Survival with 95% CI

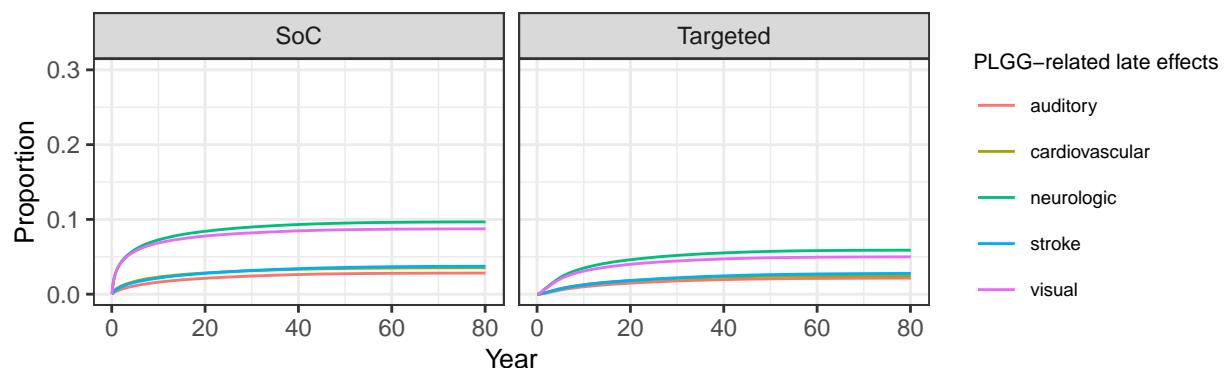


Independent reviewer, Targeted curve – Log-Normal, SoC curve – Log-Normal

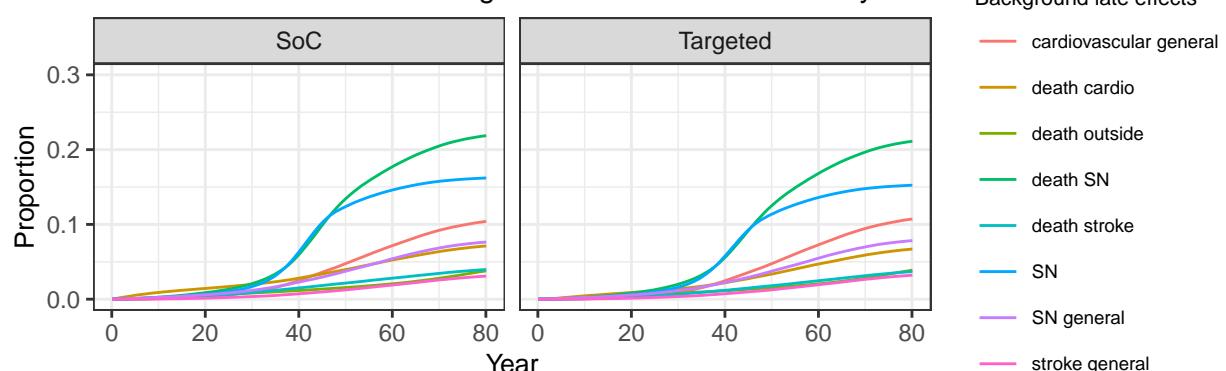
Variable	intervention	control	Delta
Life-years	28.12 (15.31;38.96)	28.6 (17.23;38.19)	-0.48 (-2.28;0.78)
QALY	12.62 (7.04;17.32)	12.36 (7.65;16.39)	0.26 (-0.72;0.99)
Total Cost	\$397,402 (\$364,795;\$428,081)	\$395,495 (\$365,854;\$423,395)	\$1,907 (\$-6,412;\$7,793)
Non-Targeted PLGG related costs	\$237,855 (\$170,300;\$294,751)	\$262,516 (\$200,713;\$317,931)	\$-24,661 (\$-32,175;\$-15,045)
Late effect costs	\$84,388 (\$21,302;\$173,462)	\$99,863 (\$34,492;\$182,812)	\$-15,476 (\$-21,764;\$-8,988)
General population costs	\$37,747 (\$14,294;\$64,792)	\$33,116 (\$13,362;\$56,145)	\$4,631 (\$1,413;\$8,737)
Targeted costs	\$37,413 (\$37,210;\$37,602)	\$0 (\$0;\$0)	\$37,413 (\$37,210;\$37,602)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



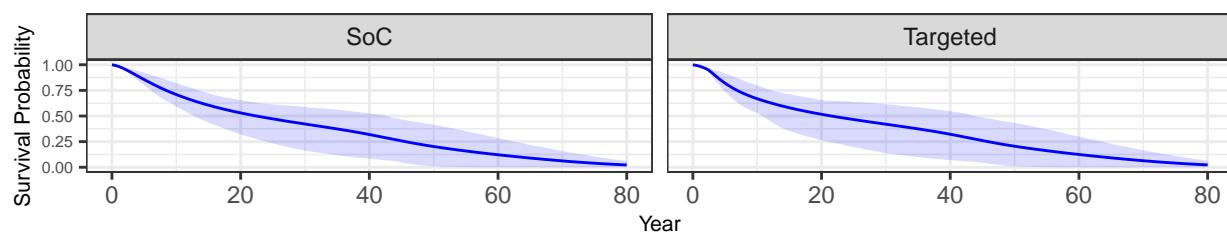
Cumulative Incidence of PLGG-related Late Effects Across Cycles



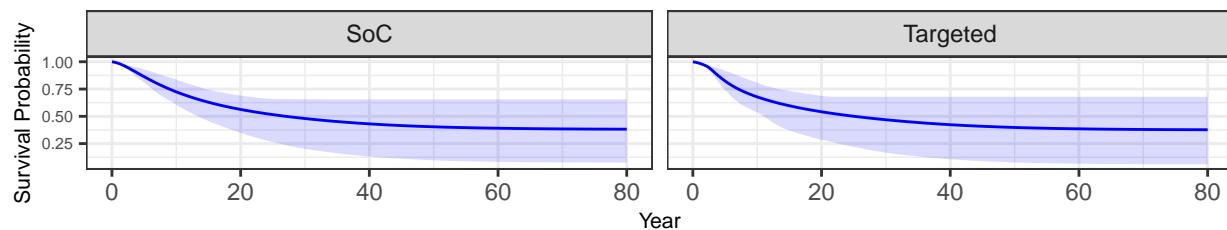
Cumulative Incidence of Background Late Effects Across Cycles



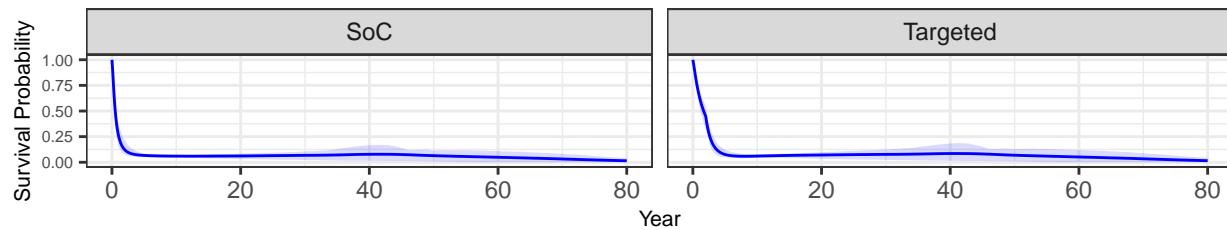
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI

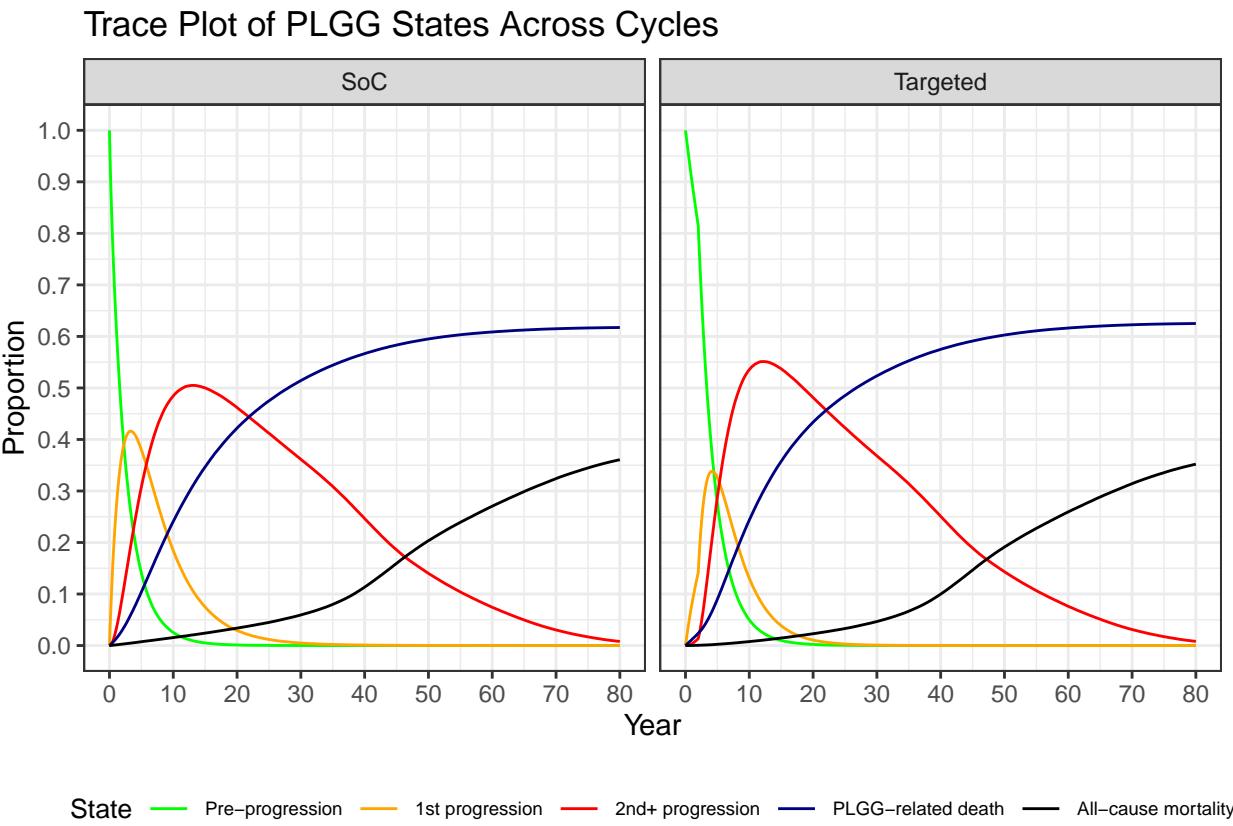


Scenario #1e

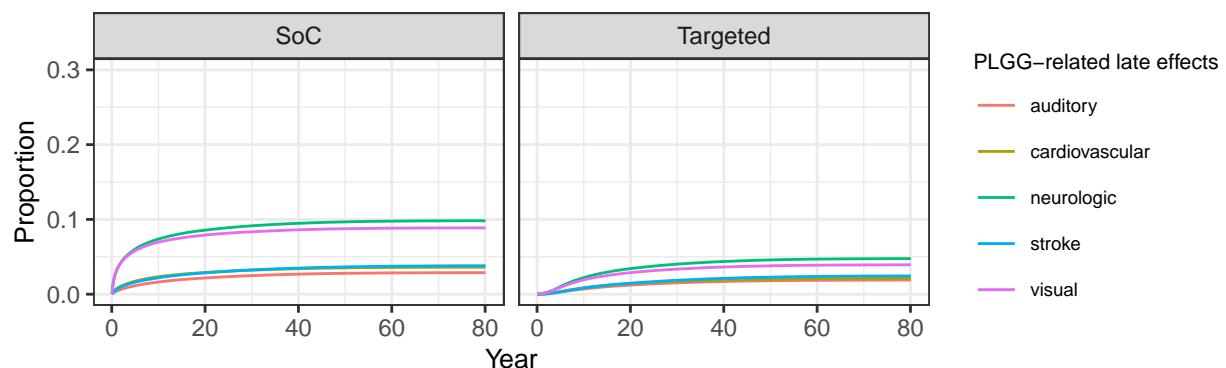
- Combo vs. chemo as first-line treatment
- Lifetime duration of combo therapy
- 0% radiation at progression (Post-2014 SickKids data indicates that no patients who received chemo and progressed were radiated)
- 100% combo price
- Discount rate: 1.5
- **Data source for controls: n=34 SickKids controls**
- **Data source for exposed: Investigator assessment - Bouffet et al., NEJM 2023.**
- **Post-progression risk for subsequent progression = pre-progression risk for first progression in combo arm
- 10,000 individuals
- 50 simulation runs

Targeted curve – Exponential, SoC curve – Exponential

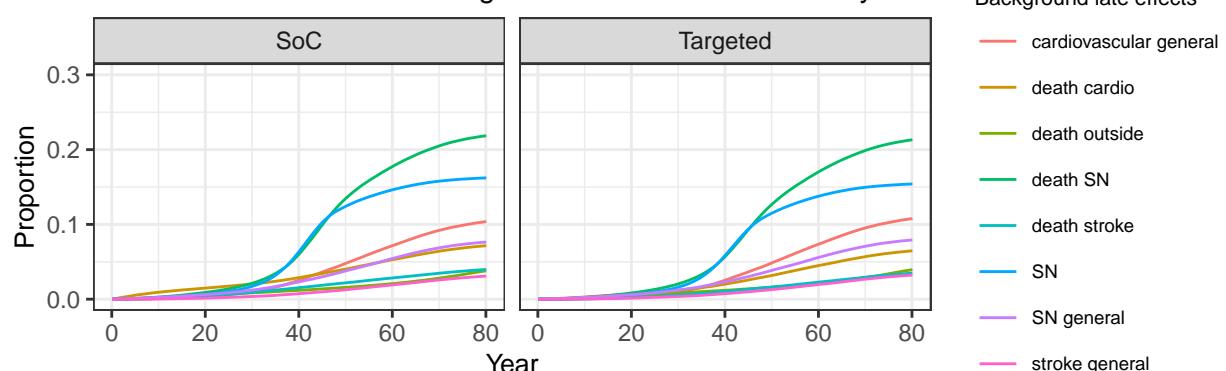
Variable	intervention	control	Delta
Life-years	29.48 (18.48;38.74)	29.17 (18.71;37.96)	0.31 (-1.03;1.12)
QALY	13.46 (8.62;17.43)	12.61 (8.3;16.24)	0.85 (0.19;1.38)
Total Cost	\$412,514 (\$389,843;\$434,779)	\$394,517 (\$368,238;\$419,239)	\$17,996 (\$9,829;\$25,287)
Non-Targeted PLGG related costs	\$216,361 (\$157,673;\$274,586)	\$260,478 (\$202,621;\$318,205)	\$-44,117 (\$-51,284;\$-32,813)
Late effect costs	\$79,020 (\$22,233;\$158,045)	\$100,564 (\$36,947;\$180,699)	\$-21,544 (\$-27,718;\$-13,689)
General population costs	\$42,012 (\$19,786;\$67,144)	\$33,475 (\$14,717;\$54,983)	\$8,538 (\$5,016;\$12,397)
Targeted costs	\$75,120 (\$74,671;\$75,528)	\$0 (\$0;\$0)	\$75,120 (\$74,671;\$75,528)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



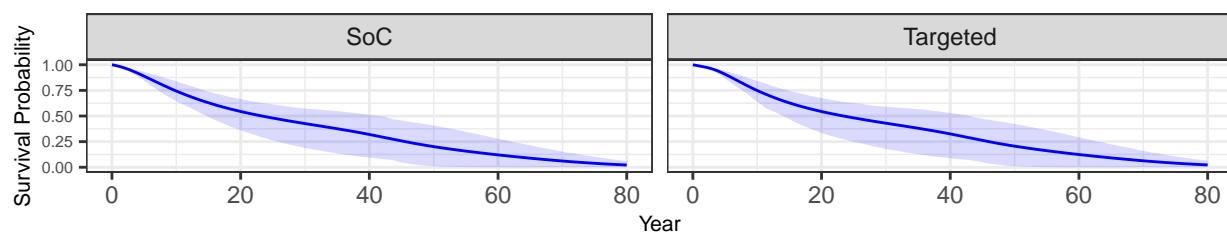
Cumulative Incidence of PLGG-related Late Effects Across Cycles



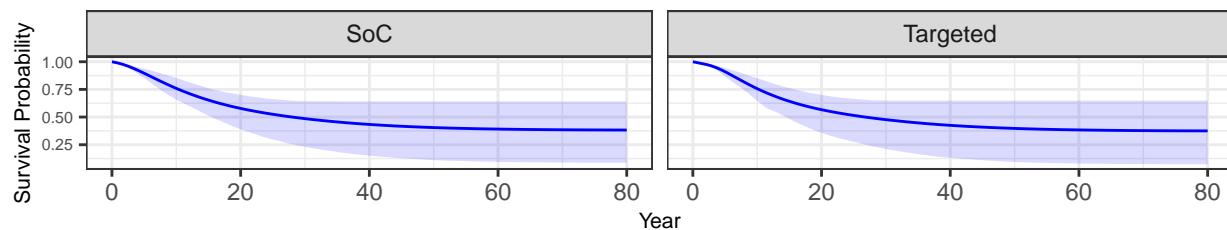
Cumulative Incidence of Background Late Effects Across Cycles



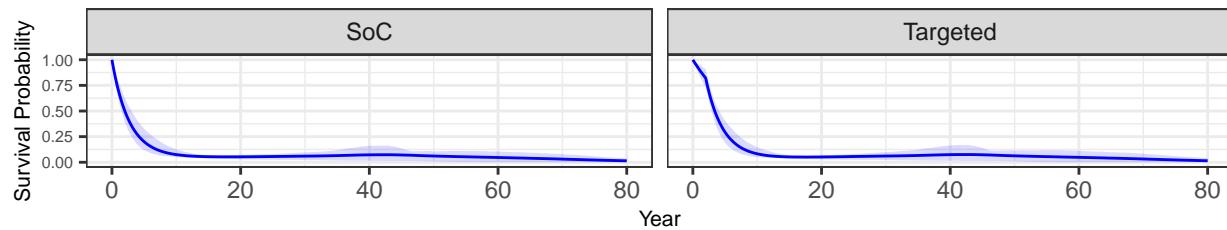
Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI

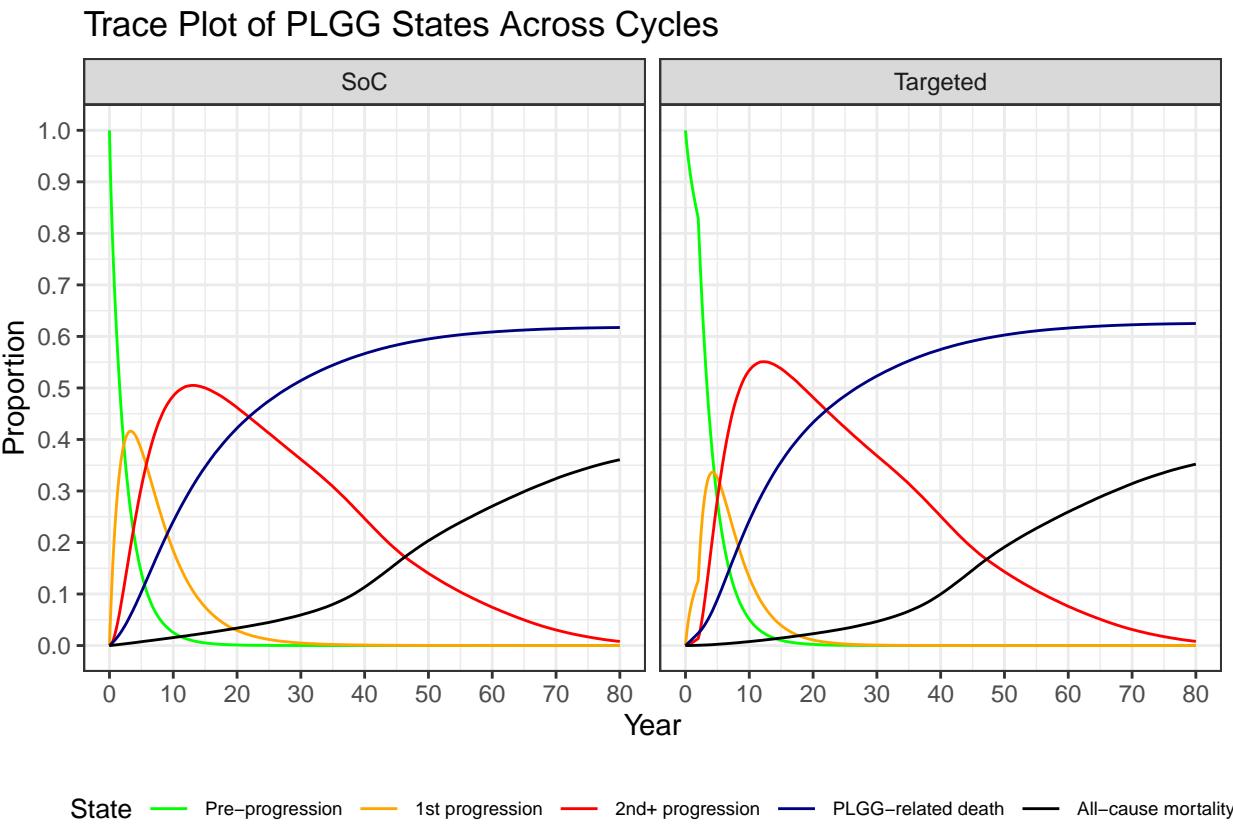


Progression-Free Survival with 95% CI

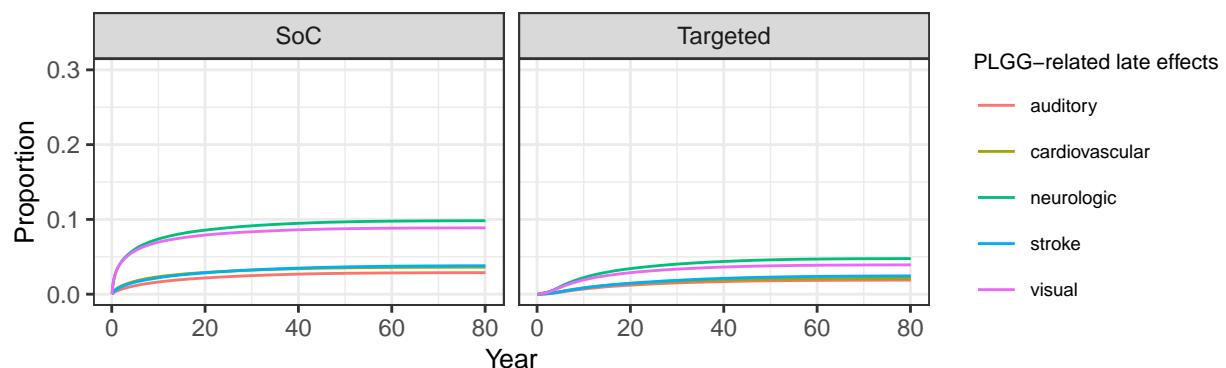


Targeted curve – Log-Normal, SoC curve – Exponential

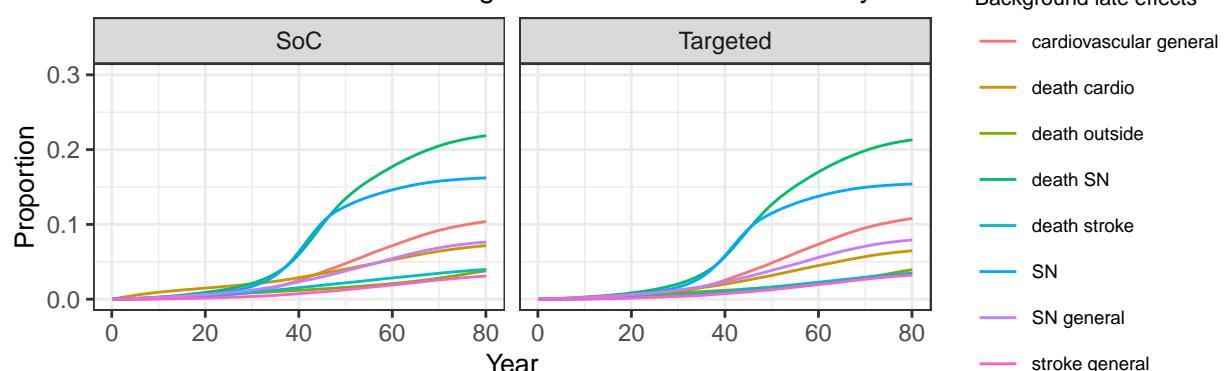
Variable	intervention	control	Delta
Life-years	29.5 (18.38;38.71)	29.17 (18.71;37.96)	0.33 (-0.95;1.1)
QALY	13.47 (8.57;17.41)	12.61 (8.3;16.24)	0.86 (0.16;1.34)
Total Cost	\$412,219 (\$389,683;\$434,901)	\$394,517 (\$368,238;\$419,239)	\$17,702 (\$11,230;\$24,024)
Non-Targeted PLGG related costs	\$215,945 (\$156,721;\$275,331)	\$260,478 (\$202,621;\$318,205)	\$-44,534 (\$-51,162;\$-35,526)
Late effect costs	\$79,107 (\$22,053;\$157,561)	\$100,564 (\$36,947;\$180,699)	\$-21,457 (\$-27,213;\$-13,529)
General population costs	\$42,057 (\$19,526;\$67,302)	\$33,475 (\$14,717;\$54,983)	\$8,582 (\$5,460;\$12,337)
Targeted costs	\$75,110 (\$74,660;\$75,492)	\$0 (\$0;\$0)	\$75,110 (\$74,660;\$75,492)
Radiation costs	\$0 (\$0;\$0)	\$0 (\$0;\$0)	\$0 (\$0;\$0)



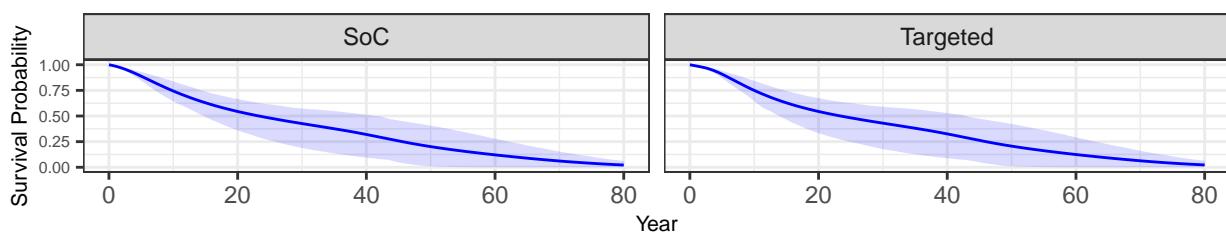
Cumulative Incidence of PLGG-related Late Effects Across Cycles



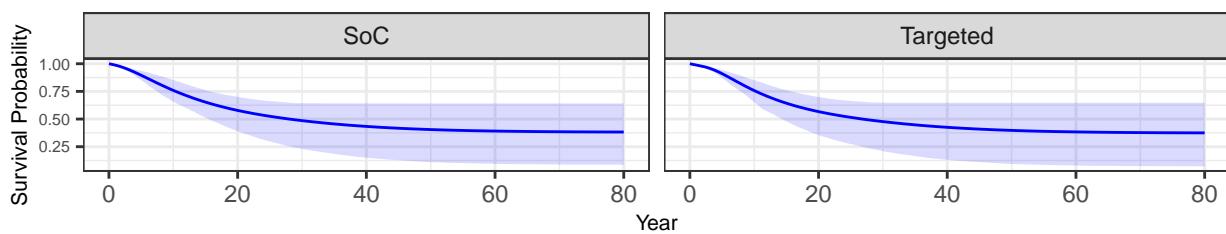
Cumulative Incidence of Background Late Effects Across Cycles



Overall Survival with 95% CI



PLGG-death-related Survival with 95% CI



Progression-Free Survival with 95% CI

